A SYSTEM OF MEDICINE

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TORONTO

A SYSTEM OF MEDICINE

BY MANY WRITERS

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VOLUME V

DISEASES OF THE RESPIRATORY SYSTEM
DISORDERS OF THE BLOOD

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PREFACE

THIS volume, though dealing with the same subjects, differs very considerably from the corresponding volume in the original edition. The first article—that on Physical Signs of the Lungs and Heart—was originally in Vol. IV., and the account of Aero-therapeutics has been transferred from the original Vol. I., so as to be in closer relation to the diseases of the lungs, to which it almost exclusively refers. The article on Acute Lobular Pneumonia and Broncho-pneumonia has been rewritten by Dr. Beddard and Dr. Eyre; and the articles on Lobar Pneumonia and on Chronic Interstitial Pneumonia have been extensively revised by Dr. Beddard and Dr. Eyre and by Dr. Fawcett respectively. Sir Thomas Oliver has rewritten the article on Pneumoconiosis; and extensive additions have been made to the article on Pulmonary Tuberculosis by Dr. Bulloch, who has given a very full account of the present state of knowledge of the Paths of Infection of Tuberculosis, and of the specific treatment. Dr. Perkins has written new articles on New Growths of the Bronchi and on Abscess and Gangrene of the Lung, and has collaborated with Dr. Frederick Roberts in the descriptions of New Growths of the Lung and of the Pleura, which are now, together with mediastinal new growths, separated from the inclusive article Intrathoracic New Growths formerly in Vol. VI. The article on Pleurisy has been revised by Dr. Horder, and Dr. Bosanquet has dealt with the Diseases of the Thymus Gland.

The remainder of the Volume contains what may perhaps most conveniently be described as the Disorders of the Blood. Among these articles, that on Pernicious Anaemia by Dr. French, that on Splenic Anaemias by Dr. Hutchison and Dr. Ledingham, and that on Haemophilia by Sir Almroth Wright, have been entirely rewritten. Completely fresh articles on Polycythaemia and Erythraemia, and on Cyanosis have been contributed by Dr. Parkes Weber and by Dr. Garrod.

The editors are indebted to Dr. John Tatham of the General Register Office for generous help in connexion with statistical questions, to Dr. W. Bulloch for assistance in various ways, and to Dr. A. J. Jex-Blake for a number of corrections.

CLIFFORD ALLBUTT.
H. D. ROLLESTON.

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In order to avoid frequent interruption of the text, the numbers indicative of items in the lists of "References" are only inserted in cases of emphasis, where two or more references to the same author are in the list, where an author is quoted from a work published under another name, or where an authoritative statement is made without mention of the author's name. In ordinary cases an author's name is sufficient indication of the corresponding item in the list.

DISEASES OF THE LUNGS

PHYSICAL SIGNS OF THE LUNGS AND HEART

By Hector Mackenzie, M.D., F.R.C.P.

Inspection.—In the routine examination of the chest the first method to be employed is inspection, and important information may be obtained as to the condition of the internal organs by observing the shape and movements of the chest walls. In order that inspection of the chest may be made to the greatest advantage, a good light must be thrown on its surface. The examination should be made, if possible, with the patient sitting up and standing, as well as recumbent, and the patient should be looked at, not only from the front, but also from behind, from side to side, and from above downwards. The shape and movements of the two sides should be carefully compared. Although the shape of the chest varies considerably among healthy persons, it is convenient to bear in mind the characteristics of a typical well-formed adult chest. The thorax should be symmetrical and evenly expanded. The anterior and lateral walls should be slightly arched from above downwards. In transverse section the thorax is oval, with the long diameter from side to side. The thorax of the adult male has its widest diameter about the level of the seventh or eighth rib, and thus may be compared to a truncated cone. In the female there is a drawing in of the lower part, so that in shape the thorax more nearly resembles a truncated barrel than a truncated cone. The subcostal angle in the male is nearly a right angle, but in the female it is somewhat more acute. In infancy the thorax is relatively small, the transverse section is more nearly circular than oval, and the ribs are more horizontal than in later life. In old age, on the other hand, the ribs lie more obliquely, the curve of the spine is accentuated and the movements are diminished. There are certain deviations from the normal which have been specially described, and have received separate names. First, in the *phthinoid* or *alar* chest, which is long and narrow, the upper ribs are straight, their interspaces are widened, and the lower ribs lie more obliquely than usual, and below are close together or in actual contact. The subcostal angle is acute, and the lower margin of the ribs may reach or even overlap the iliac crests. The manubrium sterni is depressed, and the angle it makes with the gladiolus (*angulus Ludovici*) is more pointed. There is droop-

ing of the shoulders and tilting outwards of the lower angles of the scapulae, their vertebral borders standing out like wings, whence the term alar. A subvariety of the phthinoid chest is the *flat chest*, in which the thorax is flattened from before backwards, with diminished antero-posterior diameter. The costal cartilages are flat or concave instead of convex forwards. The phthinoid and the flat chest are generally associated with badly developed lungs and poor physique, and not infrequently the lungs are the seat of pulmonary tuberculosis.

Another variety of thorax is known as *pigeon-breast* or *pectus carinatum*. In this the sternum is unusually prominent, so that it projects like a keel, whilst the sides of the chest are flattened. Thus the anterior half of the transverse section is more triangular than oval. This deformity is usually the result of obstructed respiration during the early years of life when the ribs are soft. In the *rickety* chest the sides are drawn in, the anterior part of the thorax is more prominent than normal, and there is a furrow on each side of the sternum in the situation of the junctions of the ribs and cartilages.

In some cases, instead of the sternum being unduly prominent, there is a deep hollow in the situation of its lower half. This deformity has been called *cobbler's chest*, as it is met with in shoemakers and other artisans whose work entails pressure on the lower end of the sternum. It, however, occurs without the operation of this cause, and then usually dates from early childhood.

In some cases there is a transverse furrow called *Harrison's sulcus*, which passes outwards and downwards from the lower end of the sternum as far as the mid-axillary line. This furrow results from sinking in of the lower part of the thorax with inspiration, counteracted to a certain extent by the resistance of the liver and other abdominal viscera. It is not uncommonly present to a slight degree in normal cases; but when the sulcus is well marked, it points to the existence of past impediment to the free entry of air into the lungs.

In women there may be deformity of the chest as the result of *tight lacing*. Corsets produce the greatest constriction about the level of the distal end of the 9th rib. The pressure tends to raise the arch of the diaphragm, to impede the movement of the lower ribs, and to diminish the thoracic capacity, especially below. The diameter of the thorax deformed by tight lacing is greatest at the level of the 4th rib, below which it diminishes gradually as far as the 6th rib, then more abruptly to the 9th rib.

The thorax may be much deformed as the result of *spinal curvature*. Kyphosis in which there is an exaggeration of the normal dorsal curve is associated with a type of thorax resembling the so-called barrel-shaped chest of emphysema. Asymmetry of the thorax may be due to skoliosis or lateral curvature; but sometimes the latter is the consequence of unilateral contraction of the thorax as the result of disease.

Enlargement of the thorax may be general, unilateral, or local. General enlargement of the chest may be observed when the lungs are

hypertrophied or emphysematous. In the hypertrophous form of emphysema the thorax is enlarged chiefly in its antero-posterior diameter, so that in transverse section it approaches a circle. The sternum is prominent and arched instead of being straight, the ribs are more horizontal than usual, the costal angle is obtuse, the shoulders are raised, and the back is rounded. Unilateral or local enlargement may be caused by pleural effusion or pneumothorax, or by tumour, hydatid, or aneurysm. General contraction of the thorax is usually a senile change, the result of the atrophic form of emphysema. The thorax is rounded, not from increase of the antero-posterior diameter, but from contraction of the lateral diameter, the ribs are more oblique and the sternum more convex than normal. Local contraction of the thorax is usually the result of collapse, excavation, or fibrotic contraction of the lung. The region of the precordia should receive careful scrutiny. Local bulging over the precordia may be observed in cases of cardiac hypertrophy, and points to the origination of the latter in childhood, while the chest wall was still yielding.

Measurement of the thorax or *mensuration* is a useful supplement to inspection. Measurements are made by means of a tape for the circumference, and by means of calipers for the diameters. The circumference of the thorax at the nipple level averages in adult men $32\frac{1}{4}$ inches at the end of expiration, and 35 inches on deep inspiration. The transverse diameter is found to average in men from 10 to $10\frac{1}{2}$ inches, and in women from $9\frac{1}{2}$ to $9\frac{3}{4}$ inches at the nipple level. The antero-posterior diameter averages $7\frac{1}{2}$ inches at the same level. When the thorax is misshapen, more exact information may be obtained by means of the cyrtometer, which is an instrument composed of two pieces of flexible lead-piping, hinged together by a piece of rubber tubing. The lead piping when closely applied to the chest wall takes its outline, and it may be removed without disturbing its form so that a tracing may be taken on a sheet of paper, which may be preserved for future reference and comparison.

Observation of the *movements of the chest wall* is a useful aid to diagnosis. In men the abdominal respiratory movements are more pronounced than in women and children, in whom the intercostals play the more prominent part and the upper part of the chest expands to a greater extent than the lower. The extent of the movement of the chest wall at the level of the nipple in the adult male amounts to from $2\frac{1}{2}$ to $3\frac{1}{2}$ inches. When the lungs have lost their elasticity, as in emphysema, the respiratory movements are much diminished, and measurement with the tape will shew that the expansion of the chest during deep inspiration does not nearly reach the normal limits, the movements of the chest being principally elevatory from action of the accessory muscles. Obstruction to the free entrance of air into the lungs leads to retraction of the lower costal margin and the lower end of the sternum during inspiration, especially in children in whom the parts are yielding. Diminution or absence of respiratory movement on one side, or over

part of one side, points to some abnormal condition interfering with the entrance of air to the corresponding lung or part of lung. Movements when painful, as in pleurisy, are usually diminished, and when there is air or fluid in the pleural cavity, there is little or no excursion of the affected part. Pulmonary excavation, consolidation, or collapse results in diminished movements. The movements of the chest wall due to the cardiac systole and diastole should be carefully noted. The position and extent of these movements is a guide to the position and size of the heart. Displacement or hypertrophy of the heart may frequently be recognised by the eye alone. Pulsation of the chest wall may be observed in cases of aneurysm and dilatation of the aorta, and when the great vessels are uncovered in consequence of retraction of the lungs.

PALPATION.—This is usually the second step in the systematic examination of the chest; it may be employed to assist the eye in estimating the extent of the thoracic movements, and by placing the hands on corresponding positions the movements of the two sides may be compared. The extent and position of the cardiac pulsations may be similarly estimated by palpation with the hands. Pulsation in abnormal positions, due to aneurysm, or uncovering of the great vessels, may likewise be detected by palpation. Pulsation in exceptional cases may be felt over a pleural effusion, but this has been observed almost exclusively in the case of purulent effusions on the left side (pulsating empyema), and is usually limited to the intercostal spaces near the sternum, and to the left of the apex of the heart.

Palpation may be employed to elicit the presence and situation of local tenderness, and for this purpose firm pressure should be made with the ends of the fingers. By means of palpation the amount of the resistance offered by the various portions of the thoracic surface may be estimated, and the presence of fluctuation in subcutaneous swellings, such as abscesses or pointing empyemas, determined. A fluid thrill or sense of fluctuation may occasionally be felt in the case of large pleural effusions, especially in children, by placing one hand in front of the thorax and at the same time tapping with the other behind, or vice versa.

Palpation has, however, a special application in the examination of the thorax, as by its means we are able to appreciate the vibration of the chest wall produced by the spoken voice or by sounds evolved in the chest itself through the presence of abnormal secretions or through roughening of the serous membranes. The vibration of the chest wall produced by the spoken voice is called the *vocal fremitus*. It is generally to be felt most plainly when the hand is placed flat on the chest wall, and the patient repeats in a loud voice "ninety-nine," or some such words. The due appreciation of vocal fremitus is to a considerable extent a matter of education, and I have found that students are sometimes very slow to recognise differences in its degree. Corresponding parts on the two sides should be carefully examined for vocal fremitus, and its intensity noted and recorded. Deep sonorous tones set up more

vibration than sounds of higher register, and the voice of the adult male produces more fremitus than that of a child or a woman. In healthy subjects the vocal fremitus is to be felt wherever the lungs are in contact with the chest wall. It is nearly equal on the two sides, but is stronger over the front of the chest than posteriorly at the base, and it is affected by the thickness of the tissues covering the thoracic wall. The vocal fremitus is damped by pleural effusion or thickening, or by excess of fat or oedema in the subcutaneous tissues. The vocal fremitus is increased when the sound-conducting powers of the subjacent structure is heightened, as in the case of consolidated lung or pulmonary cavities. Fremitus may be perceived when the patient coughs (*tussive fremitus*) or cries, a point sometimes useful when examining children. The vibrations which reach the ear as sonorous rhonchi may be felt by the hand (*bronchial fremitus*); and the rubbing of one rough surface on another, which gives rise to the sounds known as pleural or pericardial friction, may sometimes produce vibrations capable of being felt by the hand (*pleural* or *pericardial fremitus*). The vibrations which result in rough or purring cardiac or vascular murmurs can often be detected by means of palpation, and are spoken of as *thrills*, presystolic, systolic, or diastolic, according to the time at which they occur. The sudden, sharp first sound of mitral stenosis is similarly felt as a short, sharp impulse.

Percussion and Auscultation.—The methods of physical examination next to be employed in the study of the chest have specially to do with the vibrations of sound, and the impressions they make on the organs of hearing. These two methods are known as percussion and auscultation. In percussion, we strike or tap on the surface of the body in a special way, and note the kind of sound thus produced. In auscultation, we listen to the sounds which are produced within the body.

In order clearly to understand the meaning of the physical signs connected with sound so as to interpret them properly, it is essential to bear in mind certain elementary acoustical principles which govern (I.) the production, and (II.) the conduction of sound

I. **The Production of Sound.**—All sound depends upon the production of vibrations, which may occur primarily in solids, liquids, or gases; and they may be conducted from one medium to another before ultimately reaching the ear.

Sounds in general may be divided into musical sounds and non-musical sounds or noises, according as the vibrations which produce them are regular, continuous, and periodic, or the reverse. Musical sounds are more or less agreeable to the ear, whereas noises are irregular, confused, and interrupted, and as a rule seem harsh or jarring. In practice, however, it is difficult to draw a sharp distinction between a musical sound and a noise. Few musical sounds are entirely free from noise, and many noises have some suggestion of music. The distinguishing feature of a musical sound is that it possesses what is known as

pitch, which is determined by the frequency of the predominant vibrations per second, being high or low according as these are more or less numerous. Very slight differences in pitch can be accurately distinguished by the trained ear. No sound which has pitch can be wholly unmusical. We refer to pitch when we say a sound is acute or grave, shrill or low, high or deep, sharp or flat. Musical, like other sounds, may be loud or feeble, short or long; but in addition to pitch there is one important property they possess which must be specially mentioned, namely, character, quality, or *timbre*. It is this property which distinguishes notes of the same pitch as produced by different instruments, so that we speak of their quality in different cases as being rich, sweet, mellow, or full, on the one hand, or poor, harsh, nasal, or thin, on the other.

Some confusion has been introduced into medical literature by the use of the word *tone* in a sense different from what it has in acoustics. It has been stated, for instance, that musical sounds possess loudness, duration, pitch, and tone, and that what distinguishes one percussion-sound from another is the possession of tone, thus using the term "tone" in the sense of "timbre." Now a tone in acoustics is a sound of a definite pitch, and is incapable of analysis into simpler sounds. All musical sounds are either tones or harmonious combinations of tones. Where the periods of vibration are as 1, 2, 3, 4, etc., the corresponding sounds combine more or less agreeably. No pure tone can be said to have timbre. *Timbre* depends on the mode in which higher tones, called harmonics, whose frequencies are multiples of that of the lowest or fundamental tone, are combined together in a musical sound. A trained ear can recognise the individual tones which go to make up a note, as sounded by such instruments as the piano or violin.

The subject of musical tones is closely connected with the theory of what is known as *resonance*, another term which in medicine and in acoustics has been used with different significations. The acoustical theory of resonance has an important connexion with some of the sounds to be heard on percussion and auscultation, and it is therefore necessary briefly to refer to it.

Sounds may be produced by setting into vibration circumscribed portions of a gas as well as of a liquid or a solid. An enclosed column or other mass of air which can vibrate with a definite period and produce a sound of definite pitch, will also possess the property of giving out such a sound when a sound of similar pitch reaches it from without. The term *resonance* is used to denote the reinforcement of sound by a sounding body called a *resonator*, when there is synchronism between its vibrating period and that of one of the tones which compose the sound. The disturbance of the air produced by a mere noise in the neighbourhood of a resonator may throw it into vibration, and cause it to give out its own note.

The *resonators* devised by Helmholtz are hollow globes possessed of an ear-piece fitting into the external meatus at one pole, whilst at the opposite

pole is a larger opening communicating with the external air. When the note which corresponds to this resonator is sounded it becomes intensified by the resonator. With a series of such resonators an ordinary musical sound can be analysed into its component parts, and the presence of a variety of simple tones may be revealed in what might itself be regarded as a simple sound.

When a body, able and free to vibrate, is struck it will emit a sound; and conversely if a body emit a sound when struck it is able and free to vibrate. Every body which is capable of vibrating is in some degree elastic. The sounds emitted by different bodies vary widely, depending, as they do, on the nature of the substances, on their size, shape, elasticity, and so forth, as well as on the conditions under which they are placed.

Bodies with slight elasticity can vibrate little, and at the best can produce but feeble sound, and that of a dull damped character without much of the musical element. Thus fleshy organs, like the liver, spleen, kidneys, heart, or consolidated or collapsed lung, produce only a dull dead sound when percussed.

More highly elastic bodies, on the other hand, will in favourable circumstances vibrate freely; they may be made to produce a considerable volume of sound, and this with a good deal of the musical character. The air-containing lung when distended will vibrate freely when struck, producing a full rotund sound.

In the case of membranes and strings a certain degree of tension is required before vibration, in such a way as to produce a musical sound, is possible. The membrane of the stomach or intestines, when distended by the gases in its interior, can vibrate freely, and on percussion gives out a drum-like sound. When the pleural cavity is filled with air the thoracic wall, which is elastic, can vibrate freely, and a full-toned sound is produced. When, on the other hand, the pleural cavity is filled with fluid, vibrations of the thoracic wall are damped, and a dull dead sound is the result.

PERCUSSION.—Long use has rendered classical the terms *resonance* and *dulness* as applied to the sounds elicited on the one hand by percussion of a part of the body which can vibrate freely, as the chest wall over the lungs or a pneumothorax, and on the other by percussion of a part incapable of vibration, as the chest wall over a pleuritic effusion or solid tissue, such as the heart, liver, growth, or consolidated lung.

The acoustical theory of resonance has been appealed to by some writers as giving an explanation for the resonance just mentioned, and they have accounted for the kind of note obtained by percussion over the lungs, by supposing it to be due to the occurrence of resonance in the larger bronchial tubes. This explanation, however, is not the correct one, for the lungs remain resonant when the larger bronchial tubes are filled with gelatin; and when the alveoli are filled with coagulum, although the bronchi still contain air, the resonance is completely lost. The resonance of the lungs, indeed, as Flint has maintained, is very similar to that of a loaf of bread, and depends on the physical properties of

the tissue and on the character of the vibrations set up in it by percussion.

When percussion was first practised, the part of the body to be examined was struck directly by the fingers, or by a small hammer called a plessor. This method, "immediate percussion," was soon superseded by that now in vogue, known as "mediate percussion," in which the stroke is made by the finger or fingers of one hand upon a plate of bone or other material called a pleximeter, or more commonly upon one of the fingers of the other hand applied to the part of the body under examination. There is a decided advantage in using the fingers instead of a plessor and pleximeter, inasmuch as by doing so we can appreciate by the sense of touch the degree of resistance at the particular spot percussed.

In the analysis of the percussion-sound as usually produced, then, there are three elements which have to be taken into consideration: (α) the sound produced by the impact of the percussing finger on the one percussed; (β) the sound produced by the vibration of the chest wall; (γ) the sound produced by the vibration of the lung, or of the air in a pulmonary cavity or a pneumothorax.

The first sound can be recognised, if one finger be percussed in the free air, as a noise of feeble intensity and indefinite pitch. If now, instead of percussing the finger in free air, we do so holding it over an open-mouthed jar it will be evident that the sound, though of no greater intensity, is altered so that it has a definite pitch. It will be found that the pitch varies with the size and shape of the jar; or that if water be poured into a jar, the pitch of the note produced by percussion of the finger over its mouth will gradually rise with the level of the water. When the jar is filled the percussion note is as dead as it is in free air. Again, percussion over the slightly opened mouth will produce a note of a definite pitch, which can be altered by altering the shape and size of the buccal cavity.

The character which the percussion-note acquires when thus elicited over the entrance to a cavity, is due to acoustical resonance. The percussion of the finger sets the air vibrating in a certain mode fixed by the form of the cavity, and the result is a note of definite pitch. The sound produced arises primarily from the vibration of the air in the cavity, and not from that of the walls of the cavity; although the latter by their vibration are capable of increasing and modifying the sound. When the air-containing but undistended stomach or loop of intestine is percussed, a definite note is produced which similarly arises from the vibration of the contained air. The membrane, indeed, being slack, is not in the physical condition to produce a musical sound. In the case of a superficially situated cavity in the lung a similar result will be obtained, a note of definite pitch being produced. If the lung be percussed outside the body a sound is produced which closely resembles that of the ordinary thoracic sound, the character of the note depending, as already said, on the spongy and elastic physical condition of the lung-tissue.

The percussion-sound when the pleural cavity is filled with air has a resemblance to the sound of a drum. The sound is modified, and becomes somewhat muffled, when, instead of air, the thoracic cavity contains the fully expanded lung.

The alteration which takes place when the pleural cavity is partly filled with fluid is a very interesting one, and helps to shew the part taken by the vibration of the lung in modifying the percussion-note. In such a case the note which would be elicited on percussion would be of higher pitch if air filled the upper part of the cavity only than if it filled the whole. Where the upper level is occupied by lung, the same is true; the lung is slack, there is no tension of the lung-tissue, and the air it contains vibrates almost as freely as if no lung-tissue were present. The note consequently is high-pitched, although less pure and less distinctly musical than it would be in the case of a cavity of corresponding size. This peculiarity in the percussion-note above a pleuritic effusion was pointed out by Skoda, whence it has been called *Skodaic*.

Another variety of the percussion-note is the *tympanitic*. This should properly denote a low-pitched, full note, such as is obtained on percussion of the abdomen when the intestines are distended. The term, however, has been by some transferred to the rather high-pitched note elicited over the undistended stomach or intestine. This latter note closely resembles the Skodaic note, or that obtained by percussion over a moderate-sized superficial pulmonary cavity.

Over a cavity in the lung which is in a free communication with a bronchus, the percussion-sound not infrequently has a peculiar quality called *pot fêlé* or "cracked pot." This is generally noticeable only when the percussion stroke is sudden and forcible, and the patient holds his mouth open. The cause of this modification of note is the sudden forcing of air out of the cavity into the bronchus, giving rise to a hissing or chinking sound. It may be produced without there being a cavity when the thoracic walls are yielding, as in the case of children, air being suddenly displaced forcibly from part of the lung by a sharp stroke.

The special value of the percussion-note as a physical sign depends on the definite information which, as a rule, it gives about the structures underlying the spot percussed. We know that the only structures of the body capable of producing a resonant note are such as contain air. In the normal chest the lungs and the air-passages alone can give rise to a resonant note. Under abnormal conditions, air in the pleura or in a cavity will produce altered resonant notes. When the percussion-note is dull we know there is little or no air present beneath the part percussed. In this way by percussion we are able to map out the superficial boundaries of tumours, of fluid effusions, or of solid organs surrounded by air-containing viscera. When there is a cavity, the peculiar quality already described which the percussion-note assumes, helps in the recognition of its existence.

In the practical employment of percussion it must be borne in mind that there is no standard of resonance which can be applied to all cases.

The percussion-note on one side of the chest must be carefully compared with that on the other, and also the percussion-notes at various points of the same side must be contrasted.

A reference may be made to what has been called *superficial* and *deep dulness*. Where the lungs overlap a solid organ the ordinary dull area does not represent the size of the organ, but only that portion uncovered by the lungs. This is the area of superficial dulness, and it is obtained by light percussion. When strong or heavy percussion is employed it is sometimes possible to recognise a difference in the resonance where the solid organ underlies the lungs. The comparative dulness so obtained is what is called the deep dulness. The results, however, so obtained are not very trustworthy.

A knowledge of the normal limits of thoracic dulness and resonance is most essential. In front there is resonance on the right side from the apex to the sixth rib, where the liver dulness begins, and on the left side from the apex to the fourth costal cartilage, where the cardiac dulness commences. The limits of cardiac dulness are the mid-sternal line on the right, and on the left a line slightly concave outwards, extending from the sternal end of the fourth costal cartilage to the apex of the heart. To the left of the cardiac dulness the pulmonary resonance is continued downwards until it reaches the area of the stomach resonance. The thoracic portion of the latter, called *Traube's space*, may be recognised by its different note and characters. Traube's space is semilunar in shape, is about $3\frac{1}{4}$ inches wide, and extends along the anterior border of the costal margin as far to the left as the eighth or ninth rib. This space is diminished or obliterated when the lung is enlarged, as in hypertrophous emphysema, or when there is effusion into the left pleura, and it is enlarged when the lung is atrophied as in the atrophous or senile form of emphysema. Behind, the pulmonary resonance extends from the apex to the tenth or eleventh rib on both sides. In the right axillary region it extends as far as the eighth rib, and in the left as far as the ninth. The percussion-note is less resonant posteriorly, especially in the supra- and infra-spinous regions than in front. The thoracic percussion-note has more resonance when the parietes are thin, and there is little subcutaneous fat and poor muscular development, also when the lungs are over-expanded as in emphysema.

Grocco has pointed out that in cases of pleural effusion there may be recognised a triangular area of dulness on percussion of the non-affected side when the patient is examined in the standing or sitting position. The apex of this triangle, which is close to the spine, is at the upper level of the effusion, and its base, which is seldom more than 2 or 3 inches, is below. The area disappears when the patient is examined lying on the affected side. *Grocco's triangle* is not constant, but its presence may sometimes help in the recognition of fluid effusions.

In the case of large cavities, which contain both air and fluid, the percussion-note is altered by a change in the patient's position. When the thorax is erect the area of resonance is less than when the patient is

supine, due to the gravitation of the fluid to the lowest part; the pitch of the note is also altered. When the long diameter of the cavity is directed from above downwards the note is of higher pitch when the thorax is erect, of lower when the thorax is supine. The reverse is the case when the long diameter of the cavity is from before backward. This change in the note is known as *Gerhardt's sign.*

In pyo-pneumothorax a change of note similarly follows a change of the patient's position, on account of the fluid gravitating to the lowest part. When the thorax is erect there is dulness in the lower part, which disappears when the patient is supine. The pitch of the note of the resonant portion is also altered with position, being usually higher when the thorax is erect, and becoming lower when the patient is supine.

Percussion Resistance.—The sense of resistance experienced on percussion by means of the fingers only, and especially when immediate percussion is employed, is observed to be greater when there is unusual thickness of the bony framework, close proximity of the ribs, brawny muscles, or much subcutaneous fat. It is also increased in the following conditions: consolidated lung in proportion to its extent, pleural effusions and thickened pleura, but most of all in the case of solid growths of lung, pleura, or mediastinum. Diminished resistance is less common as well as less important, and is observed when the bones are attenuated, the ribs widely apart, the chest poorly covered, the lungs over-expanded, or the pleura filled with air.

We may now recapitulate the different kinds of percussion-sounds which have been referred to:—(1) *Increased resonance*, such as the note obtained over an emphysematous lung. (2) *Normal resonance*, that over a normal lung. (3) *Cavernous or amphoric resonance*, a sound possessed of definite pitch, depending on the size of the cavity. The pitch of the note is lowered by opening the mouth, raised by closing it (*Wintrich's sign*), and may be altered by change in position as already described (*Gerhardt's sign*). (4) *Tympanitic resonance*, a term sometimes applied to cavernous resonance, but more properly to a full-toned sound, such as is obtained over a tympanitic abdomen. (5) *Skodaic resonance*, a high-pitched sound obtained by percussing the upper part of the lung when the lower part is compressed by pleural effusion. (6) *Diminished resonance*, in various degrees up to absolute dulness. (7) *Cracked-pot sound*, or *bruit de pot fêlé*, a sound often obtained on forcible percussion over a cavity, but also in other conditions.

AUSCULTATION.—Thus far we have been concerned with the sounds which are produced by percussion. We must now discuss those which are to be heard on auscultation.

Most of these sounds arise from the movements of fluids through tubes and cavities. Among these are the bruits which have their origin in diseased conditions, either of the valves of the heart or of the large vessels, the respiratory sounds audible in health and disease, and the adventitious sounds, crepitations or rhonchi, due to the presence of secretions in the tubes.

For the proper understanding of the nature of these sounds it is advisable first to consider their mode of production. To Chauveau we are indebted for an elaborate experimental study of the conditions under which sounds are produced by fluid moving through tubes and tubular spaces, which it completely fills. His conclusions may be summarised as follows:—(*a*) No sound is produced by a fluid flowing through a tube as it passes along a uniform portion or from a wider to a narrower part, whatever be the velocity of flow or whatever be the condition of the wall of the tube as regards smoothness or roughness. (*b*) A sound may be produced when a fluid flows from a narrower to a wider space, and this sound will depend upon the velocity of flow and the relative size of the tubes. The cause of the sound produced by a flow from a comparatively narrow to a wider part of a tube is the formation of what is called a *fluid vein*, that is, a small portion of the fluid is thrown into vibration by the physical conditions under which it is placed. These results are the outcome of observation and experiment. The statement that no sound is produced in passing from a wider to a narrower part of a tube has been shewn by Bergeon to be too general. If the narrower part of the tube have a lip projecting into the wider part it is capable, under certain conditions as to rate of flow, of producing a bruit. With this exception the laws of Chauveau may be accepted as true and capable of general application.

If now we apply these laws to the flow of blood in the vascular system, we can state in what circumstances bruits will arise. The flow of blood through the arteries will ordinarily be unattended with sound. If, however, pressure be exerted on the wall of an artery, so as to flatten it, a murmur can be produced by the flow of the blood through the artificially narrowed portion to the wider part beyond. In aneurysmal dilatation, a bruit may be produced by the passage of the blood through the dilated portion. Similarly in the case of the veins no sound will ordinarily accompany the flow of the blood. Pressure on one of the larger veins diminishing the lumen without stopping the flow, or the existence of a communication between a vein and an artery will produce the physical condition requisite for the production of a murmur.

As regards the heart and its valves, the relation between the orifices, the cavities, and the great vessels is such that under normal conditions no bruit is produced by the motion of the blood itself. When the aortic valve is narrowed, or the aorta dilated just beyond the valve, then the passage of blood through the valve may be accompanied by a murmur, and the same is true in the case of narrowing of the mitral or tricuspid valves. When a chink is left in a valve, through imperfect closing, so that a stream of blood trickles back in the contrary direction to the general flow, the physical condition for the production of a murmur is again satisfied. Communications between the auricles or between the ventricles will also obviously admit of the generation of murmurs.

Next let us consider how and where bruits can be produced by the movements of air in the respiratory passages.

(i.) In inspiration a bruit may be produced at the external nares or naso-pharyngeal openings; at the mouth; at the glottis, and, as some maintain, also at the termination of the bronchiole in the alveolus. It is only with regard to the question of the production of sound by the influx of air into the alveolus that any difference of opinion exists. Some hold that no sound can be produced in this way, and in support of their opinion point out the small, almost microscopic, size of the alveolus and of the bronchiole leading to it, the slightness of the current of air and the small velocity with which it can enter the alveolus. But the experiments of Chauveau and others seem to have proved that experimental obliteration of the glottic sounds does not annul the inspiratory sound heard by auscultation over the lungs. It appears to be a logical conclusion that an alveolar inspiratory sound is produced by the formation of innumerable small fluid veins at the terminations of the bronchioles.

(ii.) In expiration a bruit can be produced in the same situations as in inspiration, except at the last-mentioned—the alveoli.

Further consideration of these bruits must be reserved until we come to deal with the subject of the conduction of sound.

We may next discuss what effects pathological conditions, such as consolidation of a portion of lung, can have in modifying the respiratory sounds.

In the case of consolidation, where the alveoli of a portion of the lung are completely filled with exudation, it is obvious no air can enter or leave the affected part, and that portion of the inspiratory bruit due to entrance of the air into the alveoli will be abolished. Whatever sounds, then, are audible over such a consolidated area must be conducted from other parts.

The resonating property of a cavity will materially modify not only the sounds produced in the cavity but also those reaching it, and this depends on the laws of acoustical resonance, which have already been considered in part when dealing with percussion. Air may be drawn into the cavity during inspiration by the expansion of its walls, and expelled from it during expiration by their retraction; or the walls may be perfectly rigid and incapable of movement. The entrance of air into the cavity will be attended with the formation of a fluid vein and the production of a murmur, but its issue will not. When air is forcibly expelled from a cavity, as sometimes happens during coughing, the succeeding inspiration may be accompanied by a distinct suction-sound produced by the sudden rush of air into the cavity. Further discussion of the character of the sounds conducted to, or produced in, a cavity will be more appropriate in connexion with the laws of conduction.

We must next consider what sounds depend on the presence of secretions in the respiratory tubes.

If a mass of mucus or thick secretion partially blocks one of the larger tubes the air-currents may produce a murmur both with

inspiration and expiration. If the mass of secretion be viscid, it may form a projecting tongue capable of moving backwards and forwards and of giving rise to a snoring sound. It is obviously in the larger tubes only that such sounds can be produced; they are generally described as *sonorous rhonchi*, and are often distinctly musical. Similar sounds but with more of a whistling character, *sibilant rhonchi*, may be produced by the presence of viscid secretion in the medium-sized tubes.

When the tubes contain thin secretion through which the air can bubble, quite different sounds may be produced. From their mode of production such sounds will generally be of a bubbling or crackling character, in which case they are called *crepitations*. The different kinds of crepitations depend principally on resonance, and also on the nature of the tissues through which the sounds are conducted.

When both air and liquid are present in the pleura, a splashing sound may be produced by shaking the patient. This *succussion-sound*, the origin of which is sufficiently obvious, is specially interesting as having been observed by Hippocrates.

What is appropriately called a friction-sound is produced by the rubbing together of two roughened surfaces, such as the two layers of pleura or pericardium when inflamed and covered by fibrinous exudations.

In the case of the smaller bronchi or alveoli crepitation-sounds may be produced by the separation of surfaces previously in contact.

II. **The Conduction of Sound.**—The following may be stated as the chief laws which govern the conduction of sound.

(*a*) Sound emanating from a single source in a uniform medium diminishes in intensity according to the inverse square of the distance. The same amount of energy acts on surfaces whose areas increase as the square of the distance. This law has but little bearing on the sounds with which we are concerned in auscultation and percussion as the media are far from uniform.

(*b*) The medium in which sound travels or is produced may be gaseous, liquid, or solid. The velocity with which sound travels varies with the medium in which it is propagated. Sound travels faster in a solid medium than in a liquid, and in a liquid than in a gas. The velocity of sound in a solid is 5 to 16 times as great as it is in air.

(*c*) When sound travelling in one medium meets the boundary of another medium it is partly reflected and partly transmitted. Sound propagated in one medium such as air is badly transmitted to another of a different character, such as a liquid or a solid.

(*d*) Sounds due to the movements of fluids through orifices are best conducted in the direction of these movements.

(*e*) Sounds may be conducted to a considerable distance by tubes, rods, or wires, by means of which dissipation of energy is prevented. The sectional area remaining practically the same, the law of the inverse square does not come into operation. In the case of the tube, the sound

is almost entirely conducted by the air in its interior, and only to a negligible degree by its walls. The walls of the tube must be of sufficient thickness to prevent energy leaving it transversely. In the case of the rod and wire the sound is conveyed directly along the wood or metal of which they are composed. A tube is specially adapted for the conduction of sounds of feeble intensity, such as the whispered voice, breath-sounds, and vascular murmurs. As is well known, the speaking-tube will conduct the whispered voice a long distance. Stethoscopes are either solid rods or tubes, with end-pieces for application to the surface of the body, and ear-pieces for apposition to the ear. The tubular form is nearly always used at the present time. The tube may be made of some rigid material such as wood or metal, or of some soft material such as india-rubber. The ear-piece may be single, adapted for one ear only; or double, so that both ears may be employed simultaneously, the sound being conducted by a tube to each ear.

We may now consider how sounds produced in the interior of the body are conducted to the surface.

First, let us take the breath-sounds which are to be heard on auscultating over the trachea. In ordinary circumstances the glottic breath-sounds, modified by resonance in the tracheal cavity, only will be audible. By resonance the intensity of the glottic breath-sounds is increased, and they acquire a character peculiar to the resonating cavity through which they are conducted. Expiration and inspiration are about equally loud, and have a harsh blowing character. To the glottic breath-sounds, as audible over the trachea or one of the larger tubes, the name of "*tubular*" or "*bronchial breathing*" has been given.

Next let us take the sounds to be heard by listening over the region of the lungs on the surface of the body. These sounds are of such feeble intensity that they are inaudible unless the ear be applied close to the chest wall, or diffusion be prevented by the interposition of a stethoscope between the latter and the ear. We shall take it for granted that the sounds ordinarily heard on auscultation over the lungs are the sounds produced at the glottis modified by conduction, and supplemented by the sounds produced at inspiration by the entrance of air into the alveoli. The smaller tubes, thin-walled themselves and surrounded on every side by thin-walled air-cells with which they freely communicate, do not prevent the diffusion of sound. If we take the main bronchus as a centre, and describe a series of spheres round it, we shall have a series of surfaces over which the glottic sounds will diminish in intensity. The glottic sounds should be better audible when the chest walls are thin, when the pleura is not thickened, and the nearer the point of auscultation to the main bronchi. The sounds produced by the entrance of air into the alveoli should everywhere be of about the same intensity. The result of these two sources of sound is to make the inspiratory sound considerably longer and louder than is the expiratory.

Consolidation of the lung acts in two ways—(i.) As no air enters the alveoli of the affected area the alveolar part of the respiratory murmur

will be suppressed. (ii.) The alveoli being filled with exudation, the glottic sounds will be more perfectly conducted along the tubes, the dissipation of sound arising from the free communication of the tubes with the air-spaces being prevented. The result is that the glottic sounds are better conducted to the surface, and are unmingled with breath-sounds of local origin. This explanation assumes the patency of the tubes, the alveoli alone being blocked. If the tubes also are blocked, the consolidated lung will not conduct quite as well as normal lung, as has been shewn experimentally. In this case the breath-sounds will be diminished in intensity, faintly tubular, or entirely absent.

When the lung is collapsed, the tubes are flattened and partially obstructed. Collapse will, however, bring about a result which consolidation does not; and that is the approximation of the larger bronchi and the surface, as the result of which tubular breathing may be more or less clearly audible. In some cases the breath-sounds may be entirely suppressed.

Emphysema is a condition in which, through dilatation of the alveoli and impairment of their elasticity, a lessened amount of air enters and leaves the lungs. The alveolar part of the respiratory sound is therefore diminished, while there is increased dissipation of the glottic part.

When a large bronchus is completely blocked by a foreign body, or is completely obstructed by external pressure, the only sounds which can reach the ear must come from the tubes on the tracheal side of the obstruction. These, from the nature of the case, will be badly conducted, and will be almost, if not quite, inaudible.

The presence of a cavity in the lung, communicating freely with a bronchus, will make an important modification in the sounds. (α) Suppose air neither enters nor leaves the cavity during respiration. The dense walls of the cavity will prevent the diffusion of the sounds conducted from the bronchus; they can therefore reach the ear with increased distinctness. (β) Practically in most cases air will enter and leave the cavity during respiration. We have already (p. 15) considered what effect this will have on the production of sounds.

Sometimes the amount of air entering will be so small that the sound so produced may be neglected. The glottic inspiratory sound may thus be augmented by the whiff, if any, produced by the entrance of air into the cavity, while no alteration will take place in the expiratory sound, which will be purely conducted glottic.

Frequently it will be impossible to say from the character of the breath-sounds alone, whether we are dealing with consolidated lung, permeated by patent or dilated bronchi, or with a cavity. The breath-sounds audible over a cavity may, however, have a certain distinctive character, like that of the sound produced by blowing over a bottle or jar, and they are then spoken of as *cavernous* or *amphoric*. The cause of this peculiar quality is probably resonance or reflection of the sounds at the walls of the cavity.

In discussing the percussion-note it has been pointed out that in the case of a cavity the air contained by it is capable of vibrating so as to produce a note with a definite musical pitch. Any sounds conducted to, or produced in, the cavity will, when it is of sufficient size and of definite shape, similarly acquire that peculiar resonance quality which gives pitch and timbre to them, and makes them cavernous or amphoric. In the same way this property of resonating will give the definite cavity-quality to sounds otherwise essentially unmusical, such as crepitations. In the case of a large cavity, such as a pneumothorax or one involving the greater part of a lung, the corresponding sounds will be proportionally loud and will have definite musical pitch. In this way crepitations frequently acquire a metallic character.

Of the same nature is the *bell sound* or *bruit d'airain*. This is observed when percussion is practised over a large cavity, or a pneumothorax, by means of two coins, one of which is used as plessor the other as pleximeter. The sound so produced excites resonance in the cavity, and a peculiar metallic clink may be heard on auscultation with the stethoscope.

What is the effect of liquid in the pleura on the conduction of the breath-sounds? (1) Fluid in the pleura is necessarily attended with collapse of the part of the lung subjected to the pressure of the fluid, and consequently the only sounds which can be audible will be conducted from the glottis or from other parts of the lung. (2) The interposition of a layer of liquid between the lung and the surface will cut off a considerable portion, if not the whole of the sounds produced in other parts. Thus, at the upper margin of the liquid the breath-sounds will probably be faintly tubular; at the lowest part they will be almost, if not quite, annulled.

In the case of air in the pleura, the problem will differ according as there is or is not a fairly free communication with a bronchus. In the absence of adhesions the lung becomes collapsed. Whatever sounds are heard will be conducted from the glottis and air-tubes. If the communication of the bronchi with the pleural cavity be free, then tubular breath-sounds, augmented by resonance and probably thereby invested with metallic quality, will be audible. If, on the other hand, there be no communication with the bronchi, then such breath-sounds as may be audible will be very feeble.

We may now briefly consider the laws governing the conduction of the spoken and whispered voice-sounds to the surface of the chest. The spoken voice-sounds are produced at the larynx, and are modified and augmented by resonance in the cavities of the mouth and nose. The whispered sounds are produced by the lips, tongue, etc., and not at the larynx. As already mentioned, whispered sounds are well conducted by means of tubes. It therefore happens that whatsoever promotes the conduction of the breath-sounds will similarly assist the conduction of the whispered sound. Ordinarily the whisper is scarcely audible over the chest wall. It will be well conducted, however, wherever there is under-

lying consolidation with patent bronchial tubes or a cavity opening into a bronchus: in the latter case it may acquire the cavernous quality. It may be audible over the upper part of an effusion, but will be absent at the lower part.

The spoken voice-sounds will be conducted well or badly under similar circumstances. As they are of considerable intensity they have the power of throwing into vibration the tissue through which they are well conducted. Thus over consolidated lung-tissue with patent bronchi there will be increased vibration, which can be distinctly felt on the surface on application of the hand. The opposite is the case where there is effusion of fluid. The voice-sounds are then badly transmitted, and the vocal fremitus to be felt by the hand is greatly diminished, or may be absent altogether.

Sometimes a peculiar modification of the voice-sounds may be observed in cases of pleural effusion. About the upper level of the fluid the spoken voice-sounds have a peculiar bleating quality; a modification usually spoken of as *aegophony*. No completely satisfactory explanation of this phenomenon has yet been given, but that most generally received we owe to Stone, who found that when a pure tone was produced by the patient by means of a pitch-pipe there was no aegophony. The ordinary spoken voice is a compound sound, composed of fundamental tones and their harmonics. Low tones are known to travel from air to liquid with greater difficulty than higher tones. A sound composed of a fundamental tone and harmonics will be altered on passing through the fluid by the deadening of the fundamental, the higher harmonics in consequence becoming relatively louder.

On the conduction of the adventitious sounds, such as *rhonchus* and *crepitation*, only a few words are necessary. Rhonchi, being produced in the larger tubes, usually in the trachea, will be audible all over the chest wall. Crepitations, on the other hand, arising in the smaller tubes will, as a rule, be audible only over the limited portion which is supplied by these tubes. As crepitations usually arise under conditions which are associated with consolidation, the former are generally conducted clearly to the surface, for the same reason that the breath- and voice-sounds are so distinctly conducted. When a cavity exists, crepitations are modified by resonance, and then frequently acquire a metallic character.

In the case of the heart-sounds, normal and abnormal, the question of conduction is not of so much importance. The normal sounds are best heard over the situation of their place of production. Murmurs produced by the formation of fluid veins are conducted in the direction of the current. Hence the murmur due to mitral incompetence is conducted towards the left auricle, and is therefore generally audible towards the axilla and behind at the angle of the left scapula, as well as at the apex of the heart. The murmur due to mitral stenosis is conducted from the mitral valve to the apex, and is therefore often only audible at and near the apex. The murmur due to aortic stenosis will be audible not only at the base of the heart but also in the direction of the great vessels.

The murmur due to aortic incompetence will be conducted down the left ventricle, and can often be well heard along the left border of the sternum.

When a pulmonary cavity or consolidated lung lies near the heart or great vessels, the heart-sounds will often be distinctly audible on listening over them, in the case of the cavity being augmented by resonance.

Friction-sounds, such as those of pleurisy and pericarditis, are already superficial, are best heard at and near the place of production, and are not conducted to any great distance from it.

We may now give a short account of the various sounds to be heard on auscultation of the chest. The character and origin of the normal breath-sounds have been fully discussed. *Vesicular breath-sounds* can generally be heard over the whole thoracic area wherever there is resonance, but they are most distinct where the chest is most thinly covered. They are weak where there is only a thin subjacent layer of lung, as along the anterior borders. Wherever normal vesicular breath-sounds are to be heard it means that the lung-tissue beneath is permeable to air. We speak of the breath-sounds as *exaggerated* when the inspiratory sound is louder and harsher than normal. Exaggerated breath-sounds may be heard over one lung when for any reason the other is not acting well. In children the breath-sounds are usually exaggerated (*puerile breathing*), the probable cause being the thinness of the chest wall and the greater elasticity of the lungs. The terms *diminished* and *suppressed* breath-sounds need no explanation. Normally the expiratory sound succeeds the inspiratory so closely as to be almost a continuation; but under certain conditions, as advanced emphysema, a distinct pause divides them (*divided respiration*), and the same thing occurs in "bronchial breathing." Sometimes the inspiratory sound is not continuous, but is broken up into a number of short sounds. The breath-sounds are then called wavy, jerky, or interrupted, or in very pronounced cases cog-wheel. In some cases this is a nervous phenomenon, inspiration being slow and shallow, so that air does not enter different parts of the lungs simultaneously, and when due to this cause it disappears when a full, deep inspiration is taken. It occurs also when there is tuberculous infiltration interfering with the even and regular entrance of air into the different parts of the lung, and in this case it only temporarily disappears as the result of deep inspiration or coughing. *Prolonged or harsh expiration* is usually due to some obstacle to the free escape of inspired air, as in bronchial catarrh, asthma, and emphysema.

Bronchial or tubular breath-sounds are similar to those audible over the trachea. The inspiratory and expiratory sounds are about equal in length and intensity, have a distinctly blowing or whiffing character, and are separated by a short interval. The expiratory sound is usually the louder and harsher. Sometimes a distinction is drawn between bronchial and tubular breath-sounds, the latter being of higher pitch and more whiffy than the former, but it is easier to describe the distinction than to act on it in practice. The pitch and intensity of bronchial or tubular

breath-sounds differ widely in individual cases. The practical importance of these sounds is due to their occurring only in abnormal conditions, such as consolidation, collapse, or excavation of lung. *Cavernous or amphoric breath-sounds* have been already discussed (p. 18). They possess a distinctive character, like the sounds heard when blowing over a bottle or jar. The term "amphoric" is used when the peculiar character is most pronounced. The sounds sometimes have a metallic quality. A cavity must be of considerable size and superficial in order that the amphoric quality may be pronounced. *Broncho-vesicular or indeterminate breath-sounds* are sounds intermediate between vesicular and bronchial. They may normally be heard over the manubrium sterni and in the space between the spines of the scapulae on account of the mingling of the tracheal and bronchial sounds with the pulmonary. In disease they may be heard over parts of the lung where air is not entering properly into the vesicles.

Post-tussive suction-sound is the sound sometimes heard over a pulmonary cavity when the patient takes a deep inspiration after a cough, on account of air being suddenly sucked into the cavity with a hissing sound.

Stridor is a peculiar harsh vibrating sound occurring with inspiration, which is generally audible at some distance from the patient. It proceeds from laryngeal or tracheal stenosis.

Pectoriloquy.—This word is employed when the whispered voice is conducted to the chest wall so as to be audible through the stethoscope. It is present in those conditions which give rise to tubular breath-sounds. *Vocal resonance* is the term applied to the sound heard through the stethoscope when the patient speaks. Ordinarily we hear the noise of the voice only, not the articulate utterance. The vocal resonance depends on the same causes which produce the vocal fremitus, and whatever increases or diminishes the one will affect in the same way the other. Increased vocal resonance is called *bronchophony. Cavernous voice-sounds* are the voice-sounds audible over a cavity, and they have a hollow or metallic quality. *Aegophony* is the modification of the voice-sounds observed in cases of pleural effusion, whereby they acquire a bleating character. Sometimes aegophony is audible over consolidated lung although no fluid is present.

The adventitious sounds which arise in the respiratory tract may be classified as follows:—*Rhonchi* are snoring or whistling sounds produced in the trachea or bronchi. When the lumen of one of the larger or medium-sized tubes is partially blocked by a mass of mucus or thick secretion, or by irregular swelling of the mucous membrane, the breath-sounds are accompanied by rhonchi. These sounds arise chiefly in bronchitis. They are generally audible over a wide area of the chest wall. The low-pitched and snoring or sonorous rhonchus is produced in the larger tubes and may sometimes be made to disappear by dislodging the secretion. The whistling and high-pitched or *sibilant* rhonchus, sometimes called *sibilus*, is due to the presence of secretion or irregular

swelling of the mucous membrane of the medium-sized tubes, and generally is not altered by coughing.

Rales.—The term rale is applied to those sounds which are produced by the passage of air through the smaller tubes when they contain thin secretion, or when their surfaces are sticky from the presence of viscid secretion and alternately separate and adhere. The classification of rales presents some difficulty on account of the want of uniformity in the names which have been given to the various sounds. It is convenient to divide them into the moist or bubbling and the dry or crackling rales. These again may be divided, according to their quality or loudness, into fine, medium, or coarse rales. The moist or bubbling rales are due to the passage of bubbles of air through fluid secretion; the dry or crackling rales are probably produced by the separation of surfaces rendered sticky by the presence of viscid secretion. Rales may be audible during both inspiration and expiration, or during one or other only. They may be few or numerous, according as there is little or much secretion and as there is impeded or free entry of air into the affected part. Their intensity depends on the size of the tubes, the depth of the breathing, and the situation of the affected part in relation to the surface. When rales of nearly equal intensity are to be heard over a wide area and the lung is not consolidated, a large number of tubes must be affected. Rales are transmitted from one side to another with difficulty, so that the presence of rales on both sides generally means that both sides are affected.

When the pulmonary tissue is consolidated, if rales be audible they have a clear or bright quality, which was attributed by Skoda to resonance, or, as he termed it, "consonance" in the bronchial tubes, whence the term *consonating* rales. *Crepitant rale* or *crepitation* is a sound which has been aptly compared to the sound audible when the hair is rubbed between the fingers close to the ear. It is due to the entrance of air into alveoli which contain sticky secretion, and they are audible mainly at the end of inspiration. *Metallic rales* may be heard when a cavity is present, rales from resonance in the cavity acquiring a metallic or tinkling quality. It is only, however, when the cavity is large and superficial that characteristic metallic rales are to be heard. *Tinkling sounds* are heard in greatest perfection over a pneumothorax, and then may be likened to the sound produced by letting a pin fall into a hollow metal jar. They are produced by the bursting of a bubble, or by the fall of a drop of secretion in the cavity.

In the examination of the lungs it is always useful to auscultate while the patient coughs. The cough sound is better conducted over consolidated tissue, and over a cavity it has a hollow or possibly metallic quality. Coughing by dislodging secretion may alter the character of the breath-sounds and bring out rales previously unheard. After coughing, the breath-sounds may be tubular where previously they were weak. Coughing may shake up the secretions in the tubes or in a cavity and give rise to gurgling, bubbling, or crackling sounds. The patient should be told to take a deep breath after coughing, and the following

deep inspiration may be accompanied by rales. After coughing, the situation of rales may be altered, as the result of the altered situation of the secretion. The *post-tussive suction-sound* has already been referred to (p. 22).

Auscultatory Percussion.—A combination of auscultation and percussion is sometimes of use in determining the limits of cavities. The stethoscope is placed over a cavity, the position of which has been diagnosed, and during auscultation light percussion is made in the neighbourhood. The character of the sound alters as soon as the limits of the cavity are reached, the position where the sound alters being noted, both when the chest wall is percussed from the centre outwards and from a distance inwards. By this means the size and shape of the cavity may be approximately determined. This method, however, has a limited application only, and the results obtained are not always trustworthy. Auscultatory percussion has similarly been applied to map out solid organs. A different method of employing auscultatory percussion is to percuss the thorax and listen with the stethoscope over the patient's open mouth; in this way the cracked-pot sound or the cavernous percussion sound can sometimes be more readily recognised. The sound is conducted from the chest along the bronchi and trachea to the mouth.

Bruit d'airain, otherwise known as *bell-sound* or *coin-sound*, which has already been described (*vide* p. 19), is a familiar example of auscultatory percussion.

Succussion-sound.—In hydro- or pyo-pneumothorax, in which both air and liquid are present in the pleural cavity, a splashing sound may be heard when the patient is suddenly shaken. It may be heard not only with the stethoscope, but frequently also without applying the ear or stethoscope to the chest, and it is often plainly audible to the patient himself.

Friction-sounds, produced by the rubbing together of the roughened surfaces of the serous membranes, pleura or pericardium, are of varying intensity, and are referred to as rubbing, grating, creaking, and so forth. Pleural friction may be heard throughout both inspiration and expiration or only at the height of inspiration and the beginning of expiration. Usually a friction-sound is not conducted to any great distance from its place of origin. Sometimes it is intensified by pressure from the stethoscope, which acts by bringing the surfaces closer together. It is sometimes difficult to say whether a sound is of pleural or pulmonary origin, but in the case of the latter it is usually altered by coughing, and is not affected by pressure with the stethoscope. The friction-sound is increased by taking a deep breath. Creaking sounds of pleural origin, but closely resembling rales, are sometimes due to the presence of partial adhesions, or local irregularities, or thickening of the pleura.

Pericardial friction-sounds are usually to and fro with the systole and diastole, but they occur more irregularly than bruits of endocardial origin. They sound as if they had a superficial origin. They are

seldom audible except over the precordia. Change of position of the patient will sometimes alter the position and character of the friction-sound, while the endocardial murmur will be unaffected. Friction in the pleura overlying the heart (pleuro-pericardial friction) may closely resemble true pericardial friction. The former, however, in some cases temporarily disappears when the patient holds his breath after a deep inspiration or at the end of expiration.

Endocardial Murmurs.—The mode of production and the laws of conduction of these murmurs have already been discussed (*vide* p. 14). In time endocardial murmurs correspond to the auricular or ventricular systole or to the diastole, and there is usually no difficulty in determining their time by observing their relation to the cardiac impulse. In different cases the character of endocardial murmurs varies, so that they may be described as soft and blowing, or rough and rustling, sawing, grating, or musical with a humming, whistling, or singing quality. The murmurs due to obstruction or narrowing are usually noisier and harsher than those due to incompetence and regurgitation. Diastolic murmurs due to aortic incompetence are often very soft and difficult to hear and may require long and careful examination for their detection. The loudness of a murmur is no criterion as to the seriousness of the lesion producing it. The diastolic murmur diminishes in intensity from the second sound; the presystolic murmur increases in intensity towards the first sound. The character of the heart-sounds should always be carefully noted, as well as that of the murmurs. In mitral stenosis the first sound of the heart becomes short, sharp, and snapping in character, so that the beginner is apt to mistake it for an accentuated second sound, and then to mistake the presystolic murmur for a systolic.

Haemic murmurs, which are often to be heard in anaemic subjects without there being any valvular lesion, are usually loudest over the situation of the pulmonary valve, and are always systolic in time. They also differ in character, but are commonly soft and blowing.

Cardio-pulmonary Murmurs.—Murmurs of cardiac origin are occasionally present in cases of pulmonary disease without there being any cardiac lesion. A blowing systolic murmur may sometimes be heard over or near the situation of a pulmonary cavity. This is caused by the sudden expulsion of air from the cavity by the cardiac impulse, and accordingly resembles in its origin the *bruit de pot fêlé*. The air returns during diastole, but without sufficient force to cause a murmur. A systolic murmur with greatest intensity in the second left interspace is sometimes audible; this is caused by pressure on the pulmonary artery, by contraction of adhesions or fibrous bands. Similarly there may be a systolic murmur in the subclavian region from pressure on the subclavian artery in cases of apical induration. Displacement of the heart from contraction of the lung, deformity of the chest, or other cause may lead to the production of a systolic murmur which has been attributed to the expulsion of air from the larger bronchi with each impact of the heart.

Conduction of the Heart-Sounds in Pulmonary Disease.—The heart-sounds are normally badly conducted by the healthy lung. When the lung is consolidated it conducts the heart-sounds better; accordingly the heart-sounds are heard with increased intensity over a portion of a solid lung which lies near the heart. The heart-sounds are similarly heard more loudly over a pulmonary cavity in close relation with the heart, and may as the result of resonance in the cavity acquire a cavernous or metallic quality. In the case of pneumothorax this phenomenon is seldom noticed, because the heart is generally overlapped by collapsed lung, which prevents it from coming in direct contact with the cavity of the pneumothorax. The heart-sounds are conducted with diminished intensity by emphysematous lung or a pleural effusion.

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ARTIFICIAL AERO-THERAPEUTICS

By C. Theodore Williams, M.V.O., M.D., F.R.C.P.

By artificial aero-therapeutics we mean the treatment of disease by atmospheres artificially prepared, and differing from the normal either in composition, pressure, or temperature. This will serve as a rough definition of our subject, but it must not be considered as exhaustive, for Nature herself supplies exceptions to the normal standard in the varieties of atmosphere caused by the emission of gases in volcanic districts, in the density of air in mines, and in its rarefaction on mountains.

The subject may naturally be divided into two portions—

A. Artificial atmospheres produced by variations in the relative proportions of the gaseous components of air, or those produced by admixture with gases or elements other than those of the atmosphere.

B. Artificial atmospheres produced by variation in the barometric pressure.

Of **artificial atmospheres** we have a familiar example in the air of great cities which contains impurities, varying with the materials used for heating, lighting, and manufactures. In foggy states of the air, such as occasionally prevail in London and other towns, sulphuretted hydrogen and various hydrocarbons have been detected in the atmosphere; the former arises from sewer gas, and can easily be demonstrated by the blackening of white-lead paint on the exterior of buildings; various hydrocarbons, the result of the escape of coal gas, may be detected by the odour, unless they have passed through some thickness of earth. In addition to excess of carbonic dioxide and aqueous vapour, carbonic monoxide, sulphurous acid and ammonia, and organic matter are present; and if there be factories, unless the Smoke Abatement Act be rigidly observed, their products mingle with the atmosphere, making it deviate still more from the normal. Forty years ago the air of Manchester contained so much sulphurous acid that the late Dr. Angus Smith was in the habit of saying that when it rained in Manchester it did not rain water, but dilute sulphuric acid from the condensation of the sulphurous acid fumes in water.

We must, however, confine ourselves to those modifications of atmosphere which can be applied to the treatment of disease, and we must likewise extend our observations to the application of gases of different kinds to therapeutic uses.

A. **Medicated Atmospheres.**—*Inhalation* is the most common form of applying medicated atmospheres to the human body, the lungs being the medium of communication. The best instances of inhalation are certain gases, such as oxygen, nitrous oxide and carbonic acid, which have been used for therapeutic purposes; and again the vapour of certain medicines

volatile at low temperatures, such as ether, chloroform, nitrite of amyl, tetrachloride of carbon, iodide of ethyl and the like.

There is no method of artificial aero-therapeutics so successful as this; in most cases the full physiological effects of the drug are produced very speedily, as is seen in chloroform inhalation, in which a few seconds or minutes suffice to render the patient unconscious: as the gaseous nature of the agent renders it easy of absorption by the lungs, it passes speedily by the circulation to the brain and spinal cord, producing characteristic effects.

The methods of inhalation principally in use are as follows:—

I. Inhalation of gases, such as oxygen and nitrous oxide. II. Inhalation of vapours of certain medicines volatile at low temperatures, such as ether and chloroform. III. Vapours of substances requiring heat for volatilisation, such as mercury and sulphur. IV. Moist warm inhalations. V. Cold medicated sprays.

I. Of the first class the inhalation of *oxygen* is extensively used to relieve dyspnoea and cyanosis in pneumonia, capillary bronchitis, and like states. It would appear that oxygen combines with the haemoglobin of the red corpuscles of the blood, and that the quantity absorbed depends upon its pressure in the atmosphere and the amount of haemoglobin present in the blood. Paul Bert took blood which, under the ordinary atmospheric pressure, absorbed 14 per cent by volume of oxygen, and shook it up with oxygen under increased atmospheric pressure; he found that under 6 atmospheres it contained 19·2 per cent by volume of oxygen, under 12 atmospheres 26 per cent, and under 18 atmospheres 31·1 per cent, thus absorbing the element in accordance with Dalton's law of the partial pressure of gases. The highest limit of absorption reached in animals inhaling an atmosphere containing oxygen of increased density was 28 to 30 per cent by volume of oxygen in arterial blood. Pure oxygen under a pressure of 3·5 atmospheres was fatal to animals, inducing first slight trembling of the extremities, followed by stronger convulsions repeated at regular intervals, but becoming weaker and weaker till death supervened. For therapeutic purposes oxygen is supplied under high pressure in iron cylinders; the gas is admitted into an intermediate india-rubber bag whence it flows through a mouthpiece or tube into the mouth. Patients often complain of the coldness of the oxygen, due to its expansion in passing from high pressure to low, and it may be warmed by passage through a Woulfe's bottle or by immersing the supply-pipe in a reservoir of warm water. The most convenient mouthpiece in my experience is a glass funnel, which diffuses the oxygen over both nose and mouth, and prevents choking or irritation from too rapid delivery of the oxygen.

This means has been tried in apparently desperate cases of pneumonia and of capillary bronchitis, in which cyanosis and unconsciousness have been the striking features. In almost all these patients improvement has followed; the colour has brightened, consciousness has returned, and the respiration- and pulse-rates have fallen; but in many of

them the improvement was only temporary, though the rally might be repeated more than once before death, which was usually sudden. Such is my general experience; but in one case it certainly bridged over the crisis, and permanently relieved the dyspnoea and cyanosis. In all the successful cases of oxygen administration in pneumonia the improvement and ultimate recovery seem to have depended on the continuous use of the remedy; it is therefore better to administer oxygen in smaller quantity for hours, possibly for days, than in a large quantity for a short time. It is possible that the sudden deaths recorded may be due to over-stimulation and exhaustion of the respiratory or cardiac centre by the oxygen. This inhalation has been used in the cyanosis of advanced emphysema and in asthma, but only with temporary benefit in either. During their balloon ascents the French aeronauts Croce-Spinelli and Sivel succeeded in alleviating and even dispelling the symptoms of giddiness, nausea, faintness, and the increased respiration- and pulse-rates by inhaling a mixture of oxygen and nitrogen containing from 40 to 70 per cent of the latter; this they began to use at an elevation of 5000 metres.

The great use of oxygen inhalation is to restore oxidation, and it is found to increase the formation of red corpuscles and haematoblasts in the blood. It was noted that after breathing pure oxygen, the patient may remain a long time without breathing, doubtless on account of the hyper-oxygenation of the blood. Oxygen inhalation does not appear to increase the combustion of sugar in the system in diabetes. In most cases of cyanosis, whether cardiac or pulmonary, it is advisable to use pure oxygen, as the symptoms urgently demand relief, but in less pressing cases an admixture of one part of oxygen and two parts of pure air is often advisable.

Cole of New York, and other American surgeons, as early as 1895 used oxygen inhalation in surgical operations to avert or mitigate the unpleasant sequels of anaesthesia by chloroform or ether, and this practice is adopted largely in England.

Nitrous oxide, or laughing gas, on account of its harmlessness, is largely used as an anaesthetic, especially by dentists. It is also employed during surgical operations, but seldom alone, as its effect is not sufficiently lasting.

Carbonic acid in small quantities has been inhaled for phthisis and other lung affections, and is reported to have a sedative effect on the cough. It is far too dangerous a gas to use as a therapeutic agent,[1] though we often witness its influence on man in atmospheres rendered impure by human exhalations: here, however, the percentage of carbonic

[1] Carbonic acid, mixed with sulphuretted hydrogen, has been used by Bergeon of Lyons, as a gaseous injection per rectum. Claude Bernard shewed that certain gases, toxic when inhaled, might be absorbed by the colon in large quantities without any bad effects, and thence passing into the portal system, and reaching the heart and pulmonary circulation, be eliminated from the system through the lungs. Bergeon professed to cure lung tuberculosis in this way, but the treatment failed after a fair trial at the hands of myself and others.

acid is still small, and possibly some of the evil effects may be due to other impurities, such as the organic matters mingled with it. The symptoms of excess of carbonic acid in the air are headache, drowsiness, vertigo, and, in time, increasing feebleness of the heart's action with slowness of pulse, the respirations being quickened even to gasping. I have often thought that the relief which suddenly comes to asthmatics at the height of a paroxysm, when lividity and feebleness of pulse proclaim the accumulation of the products of respiration in the blood, may be due to the lowering of the sensibility of the nerve centres by the carbonic acid. I remember a female asthmatic in whom, during a severe spasm, there was complete cyanosis, the nails and lips turning quite blue. The respirations became fearfully laboured, the pulse slow and irregular, and at last apparently stopped altogether. She fell back in the bed, and my assistant thought she was dead; but at the next moment the colour returned to her lips and face, the pulse beat again, she heaved a deep sigh, and her breathing once more became easy. I could not account for these phenomena in any other way than that the accumulation of the gases of respiration, and principally the carbonic acid, acted as an anaesthetic to the medulla and the pulmonary and cardiac plexuses.

Chlorine was largely used by the late Dr. A. T. Thomson, who considered it "the best topical expectorant and the most salutary excitant to the mucous membrane that had yet been inhaled"; other authorities, such as Laennec and Stokes, found chlorine too irritating for inhalation. It was at one time largely used for disinfecting purposes, and is very effective, but its strong, pungent smell is offensive. A useful and less pungent form of inhalation is chloride of ammonium vapour: this is made by mixing the vapours of liquid ammonia and fuming hydrochloric acid; the chloride of ammonium fumes are then purified from any excess of hydrochloric acid by passing them through water. Thence they are drawn through a tube into the pharynx, larynx, and nasal passages, and prove beneficial in pharyngeal and nasal catarrh.

Iodine was employed for inhalation by Laennec, Berton, Murray, and Scudamore in the treatment of phthisis; the patients either inhaling the vapour itself for a short period, or being surrounded by an atmosphere strongly impregnated with iodine. All these authors speak very favourably of the results obtained. My personal experience of the iodine vapour is favourable, but I have never seen it arrest tuberculosis. Iodine is a strong antiseptic, and probably exercises a bactericidal action on surfaces immediately exposed to its influence, but that it has any effect on the progress of tuberculous disease in the lung itself I much doubt. Iodine vapour has been administered with advantage in laryngeal diseases.

II. In the second method certain liquids are used which are volatile at low temperatures, such as ether, chloroform, bichloride of methylene, tetrachloride of carbon and the like. These are almost entirely employed as anaesthetic inhalations, either in a pure condition or occasionally, as in the case of chloroform, mixed with a certain percentage of air; their uses as anaesthetics, however, will not be considered here.

III. The chief substances requiring heat for volatilisation which are used in aero-therapeutics are *mercury* and *sulphur*. In the so-called mercurial and sulphur baths the patient, covered up with a sheet, sits on a chair, with a spirit-lamp or gas-jet underneath by which the drug is heated to vaporisation; the vapour envelops the patient, and is absorbed to a large extent by the skin. If the evaporation of steam accompany this process the skin is better prepared for the reception of the drug. From time immemorial, mercurial vapour has been used in India and Arabia for exciting salivation in certain diseases, and it was employed later in the South of Europe. In England the practice was resuscitated by Jackson, and more completely by Henry Lee, who introduced mercurial baths largely into the treatment of syphilis. Lee used calomel, and, in order to get rid of the possible excess of hydrochloric acid, baked the calomel before each bath: in this method the powder is laid on a circular plate, surrounded by a trough containing water which the flame soon converts into steam; at the same time the calomel is vaporised. The patient is enveloped in a cloak which, fastened round the neck, prevents the calomel vapour from escaping; this is occasionally unfastened during the fumigation to allow of a short period of inhalation also. Another method of mercurial fumigation is by Trousseau's cigarettes, which consist of blotting-paper soaked in a solution of nitrate of mercury and nitric acid. These were recommended by Trousseau for chronic laryngitis, as well as for syphilitic pharyngitis and laryngitis. The sulphur baths are prepared and conducted in the same way as the mercurial, and have been employed for scabies and other parasitic affections of the skin.

IV. For moist, warm inhalations, where steam or warm water vapour is the medium for applying medicinal agents to the lungs, the apparatus vary greatly. The simplest form is a wide-mouthed jug or gallipot filled with boiling water into which a drug is thrown; the patient, taking deep respirations, draws the vapour into his mouth and nostrils through a napkin arranged in the form of a tube. More complicated are the steam-spray apparatus of Siegel, Oertel, Robert Lee, Codman and Shurtleff, and others. In some hospitals, as in the Brompton, steam and sprays are fitted up in separate rooms, so that the patients can inhale without admission of the moist air into the ward. This class of inhalations beneficially affects the bronchial tubes, especially in inflammatory or catarrhal conditions, by promoting secretion; but it is doubtful whether they penetrate deeply, or go beyond the primary and secondary bronchi. *Steam sprays* saturate the atmosphere with moisture, which is not always desirable in lung diseases; moreover, they cause excessive skin perspiration. The spray, whether it be a steam or handball apparatus, is produced by a strong transverse current passing over a perpendicular tube; as the air in the upper part of that tube is thus rarefied, any liquid in which the tube may be immersed ascends, and, as it meets the current, is broken into spray. Boyle's well-known ventilating extractors act in the same manner. The apparatus introduced by Sales-Giron, Matthieu, and Bergson consisted of two pointed tubes at right

angles, placed with their extremities together, and so joined that the extremity of the perpendicular tube should stand in front of the axis of the horizontal tube. As the stream of air or steam passes along the horizontal tube the medicated fluid rises in the vertical tube, and, on meeting the air current, is broken into fine spray.

The method is the same, whether air be used, as in the well-known handball spray apparatus, or steam, as in Siegel's or Oertel's "steam nebulisers."

The *handball sprays* are used at ordinary temperatures, and as a rule

FIG. 1.—Oertel's steam nebuliser.

are not so grateful to the patient as warm vapours. They are very useful for the medication of the mouth, the pharynx, and even the larynx; and solutions of quinine, chlorine, or carbolic acid can be well applied through them. They seldom penetrate beyond the larynx and larger bronchi, and generally condense into liquid on the fauces and pharynx. The sprays of mineral water in use at Aix-les-Bains, Pierrefonds, Mont Dore, Cauterets, etc., belong to this category, and are of use in laryngeal and bronchial affections, but seldom in lung diseases. The free application of antiseptic sprays for purifying the atmosphere of sick chambers and of hospital wards is excellent—carbolic acid (1 in 50), thymol, eucalyptol, or chlorine being adapted to the purpose.

Artificial atmospheres for invalids may be made by *respirators* which

cover the mouth, or, still better, the nose and mouth. These generally consist of metal or celluloid, with two layers of wire gauze or perforated iron plates containing between them cotton wool, tow, or sponge on which are sprinkled a few drops of carbolic acid, creosote, terebene, eucalyptol, or other disinfectant. Thus with each respiration the patient breathes an impregnated air, and may do so for any length of time desired. The advantages of these respirators are—1st, that they admit of the use of certain drugs for long periods; 2nd, that in cases of foul breath, as in bronchiectasis and abscess of the lung, the wearing of an antiseptic respirator purifies the patient's exhalations, to the advantage of his friends and attendants. The patterns are very numerous, such as Roberts's, Coghill's, Curschmann's, Hunter Mackenzie's, Wordsworth's, and Yeo's. The most comfortable is Curschmann's: it consists of half a globe of metal, enclosing the mouth, nose, and a portion of the face, from which a short tube passes for the admission of air. This contains the antiseptic sprinkled on wool or tow between two folds of wire gauze; a strap behind holds the instrument on, and any uncomfortable pressure of the metal against the face is prevented by a layer of air cushion next the skin. The great objection to all respirators is that they interfere with free respiratory movement.

On the efficacy of inhalations as a method of artificial aero-therapeutics, some experiments made by myself in 1888 throw great doubt; these shew that inhalations of iodine, supplied by steam or handball sprays, even when given for a considerable period, produce no trace of iodine in the urine; whereas iodine can be detected in the urine after a few doses by the mouth. Turpentine inhalations, on the other hand, produced the characteristic odour in the urine, but not to so marked a degree as when the medicine was administered by the mouth. Hassall came to the conclusion that the greater part of the substances inhaled remained in the inhaler; and that, in the case of the ordinary ori-nasal respirators, four-fifths of the carbolic acid, creosote, and other drugs were recoverable from them after the inhalations.

B. **Artificial atmospheres varying in barometric pressure** must now be considered as therapeutic agents—atmospheres, that is, denser or more rarefied than at sea-level.

The average barometric pressure at sea-level is 29 to 30 inches; at Davos (5200 feet) it is 25 inches; on the summit of Pike's Peak, Colorado (14,147 feet), it is 17·54 inches; and during the famous balloon ascent of Glaisher and Coxwell, at a height of 29,000 feet, a pressure of $9\frac{3}{4}$ inches was registered; indeed so low a pressure as 7 inches was seen afterwards by Coxwell, though he could not record it. On the other hand, the air is far denser in the deepest mines than at sea level; and it has been calculated that if a shaft could be sunk forty-five miles into the earth, the air at the bottom of it would be as dense as quicksilver.

The effects on the human frame of air at increased pressures has been demonstrated in the case of divers and workers in caissons used for the

construction of bridges, docks, and submarine tunnels. In these caissons workmen have to labour for several hours at a time, at 7 atmospheres pressure and upwards. Nevertheless this is well borne, provided, as the experience of many observers, including Dr. Leonard Hill and Mr. Greenwood, jun., has shewn, that decompression be effected gradually, and the capillary circulation be aided by repeated contractions of muscles, joint-movements, and changes of posture. The changes in the percentage of carbon dioxide in the alveolar air are regulated solely by physical variations and not by any increase or diminution in the respiratory metabolism.

Junod was one of the first to apply air at *diminished barometric pressure* to the human body: in 1835 he contrived a hollow copper ball, $1\frac{1}{3}$ metre in diameter, capable of containing an adult man, and by an exhausting apparatus he reduced the barometric pressure one-third, producing distension of the membrana tympani; dyspnoea, chiefly in the form of short, quick respirations; turgescence of the superficial vessels of the body, as seen in the eyelids and lips; and diminution of the salivary, renal, and other glandular secretions. Junod did not continue his experiments on the general influence of rarefied air on the human body, but turned his attention to the local effects, which were also being studied by Neil Arnott, Murray, and Clanny, and invented the Junod boot and the cupping-glasses which are still in use. The Junod boot and Sir James Murray's instrument are apparatus for enclosing a limb, or a part of a limb, in an air-tight vessel, and exhausting the atmosphere by an air-pump; the atmospheric pressure being thus removed from the surface of the limb, blood is drawn to the part, the vessels become gorged, and blood is diverted from the internal organs. The action of cupping-glasses is, of course, the same in principle.

Dry cupping is useful in congestion of certain internal organs, such as the lungs, kidneys, or brain. From the ease and readiness of its application it is of value in cases in which blood is to be drawn rapidly from an organ, and especially in haemoptysis. I have witnessed some of the most profuse haemorrhages from the lung suddenly brought to a termination by the use of dry cupping to the chest wall; and I have often observed that so long as the cupping-glasses are kept on, the haemorrhage has been controlled, and that on their removal it may return. Hence the great advantage of cupping-glasses with exhausters attached by which a partial vacuum can be maintained. This treatment, if carefully applied, leaves no mark, and it is to be preferred to blistering or strong poulticing in cases of gouty disposition or where the patient has a very irritable skin.

The artificial application of air at varying pressures to the lungs is carried out by various apparatus, most of which are constructed both for rarefaction and for condensation.

It is possible to apply air to the lungs in four different ways:— 1. Inspiration of rarefied air. 2. Expiration into rarefied air. 3. Inspiration of compressed air. 4. Expiration into compressed air.

Of these varieties the only ones found generally useful are the second and third; though in the pneumatic cabinet, to be presently described, the other changes can also be carried out.

The earliest instrument for condensing and rarefying the air was constructed by Hauke, of which Waldenburg's well-known apparatus is a modification (Fig. 2). This last consists of a hollow metal cylinder or bell, containing a certain volume of air, which is plunged into a second and inverted cylinder containing water. By means of pulleys and weights an equilibrium is established, and a pipe is passed from the air cylinder through a drying box to a mask fitting the patient's mouth; through this he respires the air, which can be rarefied or condensed by raising or lowering the cylinder in the water. This is done in the first instance by drawing off water, in the second by placing weights on the cylinder.

Some apparatus, like Cube's and Schitzler's second form, are double, and consist of two cylinders, one for condensing and the other for rarefying the air; thus, by changing the tube connexions, expiration into a rarefied atmosphere can be followed by the inspiration of condensed air. Others, as Biedert's and Fraenkel's, contain a kind of leathern bellows to compress or rarefy the air as required. Fraenkel's ingenious instrument resembles a concertina with a tube and mouth-

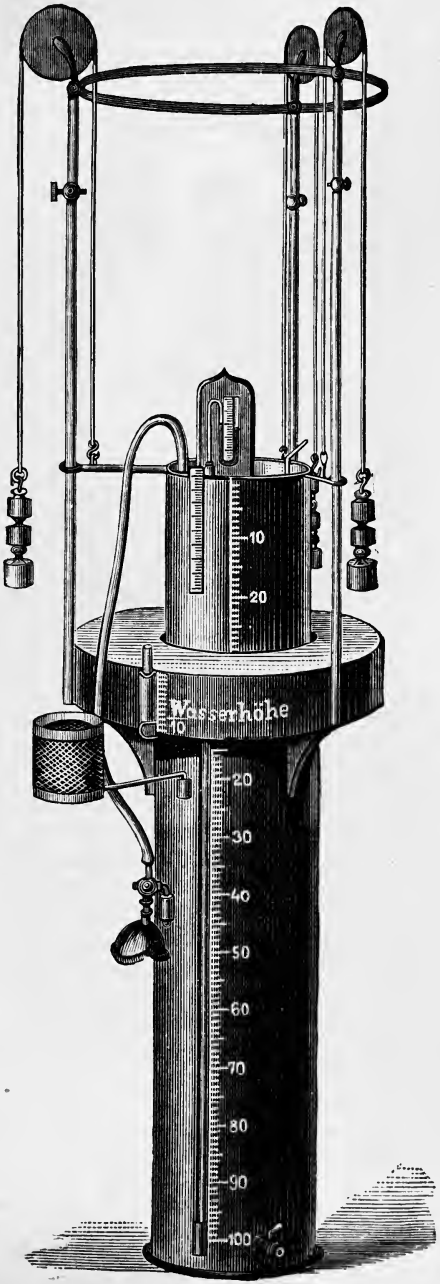

FIG. 2.—Waldenburg's apparatus.

piece; it is simple and cheap, and can be worked by the patient himself. The obvious objections to it are the contracted attitude of the patient, and the impossibility of regulating the pressure.

Lastly, the principle of the centrifugal pump is adopted in Geigel and Mayer's machine, which seems the most complete apparatus of all; in it air, compressed or rarefied by the action of water, is stored up in a central reservoir.

Fig. 3.—Fraenkel's apparatus.

"By the simultaneous use of two apparatuses placed in communication with the mouth of the patient by means of two flexible tubes and a double respiratory valve, and by maintaining the constancy and continuity, a simultaneous rarefaction and condensation of the air can be established, which enables the patient to *inspire* compressed air and to *expire* into rarefied by one and the same respiratory act." For further particulars of this apparatus the reader is referred to Oertel's article on "Respiratory Therapeutics," in the 3rd vol. of *Ziemssen's Handbook of General Therapeutics.*

One of the most ingenious portable instruments for using air at various pressures is the *pneumatic cabinet* of Mr. Ketchum of the United States. A rhomboidal cupboard on wheels, large enough to hold a man in a sitting position, is constructed of steel with a plate-glass window in front; at the back is an air-tight door, which forms the whole side. Above this cabinet is a bellows, worked by a lever, with one set of valves opening into the cabinet, and a second set communicating with the external air: these valves can be reversed, so that by the bellows the air of the cabinet may be condensed or rarefied at will. An artificial wooden glottis regulates the air-stream into the patient's lungs, passes through an aperture in the glass plate, and is connected by india-rubber tubing with the patient's mouth. The pressure within the cabinet is increased by working the lever, or decreased by turning a tap communicating with the external air. In this machine a pressure of two inches of mercury can be obtained.

Fig. 4.—The pneumatic cabinet.

Various modifications of the respiratory act are possible with this

machine. When the artificial glottis is closed, the bellows worked or rarefaction, and the patient makes deep expirations, (1) *residual air-expansion* results. If he put a nose clip on and adjust his mouth to the glottis tube, which is opened gradually, air from the outside is admitted, (2) *forced inspiration* results, and a larger volume than usual enters the lungs. The alternation of these two movements, viz. residual air-expansion and forced inspiration, constitutes (3) *respiratory differentiation*, an exercise for the purpose of expanding the lungs; (4) *forced expiration* takes place when the air of the cabinet is condensed, and the patient, having taken a deep breath, expires through the artificial glottis.

The pneumatic cabinet is used for lung gymnastics of different kinds. A committee of the Brompton Hospital, appointed to investigate its capabilities, found that its use caused (*a*) increase of chest circumference, (*b*) increase of spirometric capacity, and (*c*), in many cases of consolidation, diminution in the area of dulness. The cabinet was found less successful as a vehicle for medicinal agents, and the remedial effect of medicated sprays in this machine was not greater than at normal pressures. Great caution is necessary in the selection of appropriate cases, and the cabinet must not be used in cases of vascular weakness or of pyrexia—haemoptysis has followed its use in the former and increased temperature in the latter class of patients.

Many of the described methods of aero-therapeutics depend for success on the exact adjustment of mouthpieces or masks, which are often exceedingly irksome and induce headache and faintness. Another difficulty in many of the instruments is that of supplying sufficient fresh air at the proper pressure; the consequence is that patients have to inhale rebreathed air. To meet this objection the compressed air bath was invented, in which patients are surrounded with an atmosphere in which they can respire air at any desired degree of pressure for hours at a time, and in some cases, as in the St. Petersburg establishment, for days together. Different forms of the bath have been devised, and the size varies according to the number of occupants. The essential elements appear to be (*a*) an air-tight oval chamber of sufficient strength to resist the variations of atmospheric pressure, and (*b*) an efficient compressing apparatus. The chamber may be constructed of masonry or of iron, but more generally it is of wrought iron $\frac{1}{16}$ inch thick, in a circular or ovoid form, and, if possible, with a domed roof to resist pressure, the whole being strengthened by girders and ribs of iron. The compressing apparatus generally consists of a steam-engine, but in some places, as in M. Fontaine's establishment at Paris, hydraulic power is used which has the advantage of compressing the air, without materially increasing its temperature, and any smell arising from contact with boilers is also avoided. The advantage of steam is the rapidity with which pressure can be increased and steadily maintained.

The annexed woodcut of the compressed air bath in use at the Brompton Hospital will give some notion of the details of the apparatus.

The drawing is supplied by Mr. Blake, the manager of Messrs. Haden and Sons of Trowbridge, the constructors of the bath.

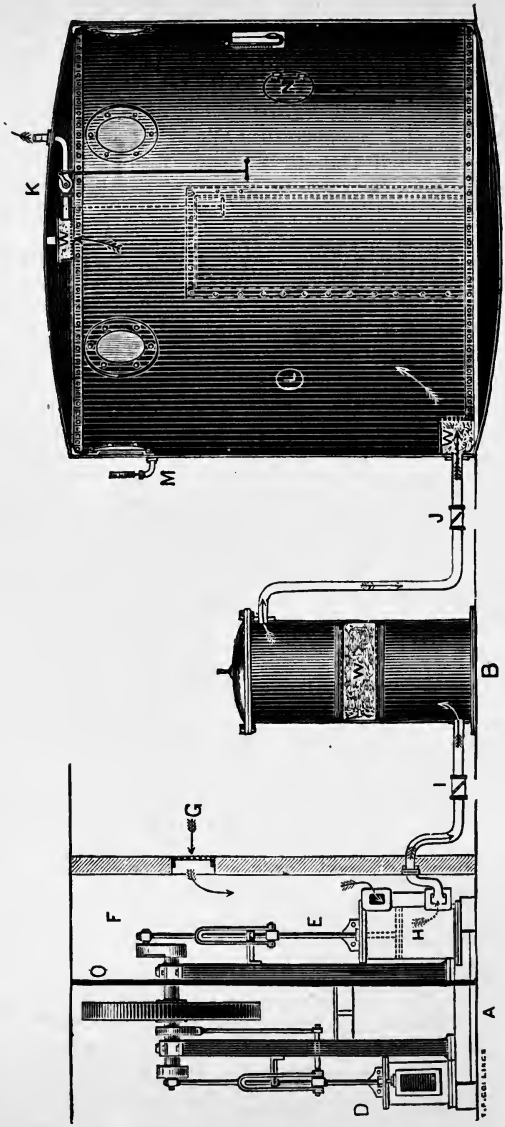

FIG. 5.—Compressed air bath.

The bath consists of three parts: the engine (A), the receiver (B), and the air-chamber (C). A includes a steam-engine D, which, by means of a flywheel and crank, works a second engine E in another and sepa-

rate compartment F. E is the air-compressing engine, with a cylinder containing an inlet hole and an outlet hole, and in this cylinder works the piston H, the plate of which is perforated by diaphragm valves, not here shewn, which close during the descent of the piston and open during its ascent. The air from outside enters the compartment F through the inlet G, and follows the course indicated by the arrows. Entering the air-cylinder it is driven forward by the piston through the pipe I into the receiver B, containing layers of cotton wool W, into the air-chamber. Both I and J contain valves to prevent a return current. The air leaves the bath by an outlet pipe in the roof, which is always open, the strength of the current through it depending on the rate at which the engine works. M is a safety-valve which opens wide and blows a whistle when the full pressure of 10 lbs. is reached. L is a glass spy-hole through which the inmates can be watched. N is an air-tight cupboard, fitted with double bolts to adjust the pressure, by which food and messages, and, if necessary, medicines, may be passed in. Apparatus to regulate the escape of air (K), which can be worked both from within or outside the bath, complete the chamber, which is lit from without by stout plate-glass windows, and fitted with a strong iron door. The air can be changed about five times in two hours, and must be supplied from a pure source, such as a garden or open space, away from machinery and drainage; and in cities it must be filtered through cotton wool in the receiver B. The air rises in temperature during compression, and in summer it is often necessary, for cooling purposes, to pass it over ice before it enters the bath. The extra pressure used for medical purposes varies from $\frac{1}{2}$ to $1\frac{1}{2}$ atmospheres, pressures very different from those which produce the well-known caisson disease and amount to more than four atmospheres. For most diseases, and certainly for lung affections, the added pressure does not exceed 10 lbs. ($\frac{2}{3}$ of an atmosphere); and 9 lbs. above the mean atmospheric pressure is usually sufficient for aero-therapeutic purposes.

The bath or sitting lasts two hours; half an hour is spent in increasing pressure, which is maintained for one hour at the maximum, and half an hour in reducing pressure to the normal. In some obstinate cases of asthma it might be well to maintain the pressure for long periods, and thus enable the patient to live in a compressed air atmosphere for days together. This would be quite possible by means of the air-tight cupboard, through which supplies could be passed. The rate of increase or decrease of pressure should be about 1 lb. in three minutes.

As during compression there is increase of temperature, so during reduction there is a slight fall, accompanied by deposition of moisture in the interior of the chamber. In the management of the bath the chief points to be borne in mind are four:—(1) To increase and reduce the pressure as gradually as possible. (2) To keep the temperature below 65° F. (3) While increasing or maintaining the pressure, to provide for the escape of the used-up or contaminated air. The air should be pumped *through* the chamber, not merely into it; and, as the stream is

always flowing, accumulation should only be the result of the outlets being somewhat smaller than the inlets. (4) In case of bad symptoms arising from increase or decrease of pressure, to reverse the process at once.

A healthy person taking a compressed air bath first experiences, as the pressure increases, an unpleasant sensation in the throat, referred to the pharynx immediately behind the tonsil; this is relieved by swallowing saliva or drinking water. Pain is also felt in the membrana tympani, which is due to the different calibres of the external auditory meatus and the Eustachian tube. The latter being much smaller than the former, the column of air, during increase of pressure, penetrates with difficulty to the internal surface of the membrana tympani, and changes of pressure are slowly communicated; whereas through the meatus air passes freely, and causes in these circumstances a convexity inwards of the auditory membrane. The opposite change takes place when pressure is diminished. Hence the pain and discomfort in the membrane are at the beginning and end of the bath. The voice becomes shriller, and I have known singers gain a note or two above their average while in the bath. The arch of the abdominal wall is flattened, which has been ascribed by Panum to compression of the intestinal gas.

Experiments made by myself and others on healthy individuals shew the following results from compressed air :—

Respiration.—The patient breathes slower, deeper, and with greater ease. The respiration rate falls from 16 or 15 to 14 or 12 a minute. Von Vivenot records its falling to 5 or even 4 a minute. Inspiration becomes easy, but expiration less so, and the relation between the two becomes changed; whereas at normal pressure the ratio between them is as 4 to 3, it becomes in compressed air as 4 to 6 or 4 to 8. Von Vivenot tells of one case in which it was as 4 to 11.

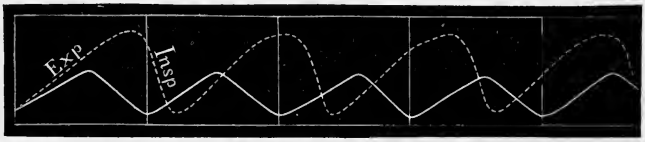

Fig. 6.

The annexed diagram from von Vivenot shews this as well as the depth of the respiration in compressed air (dotted line) compared with that of ordinary breath (unbroken line).

Spirometric observations shew a marked augmentation of lung capacity and chest measurements, a slow but considerable increase in circumference. It would appear that breathing compressed air increases lung capacity, probably by opening up alveoli not previously in use; and the amplitude of each respiration makes up for the smaller number.

Circulation.—The influence of compressed air on the circulation is

that the pulse becomes slower and reduced in volume; but the arterial pressure is raised, the superficial capillaries are smaller, and the veins less full of blood. Von Vivenot's white rabbit, when placed in the compressed air bath, admirably exhibited the effect on the circulation. Under normal pressure, the rabbit being quiet and at liberty, the ears were full of blood, the conjunctival vessels injected, and the iris tinted deep red; when pressure was increased, the conjunctival vessels became finer and paler, and in one experiment they visibly filled and emptied.

When pressure was maintained at the maximum, the iris and pupil became discoloured, and the ears, seen by transmitted light, shewed empty vessels; even the larger vessels were scarcely visible.

In man the pulse rate diminishes four to twenty beats a minute; but this depends very much on the temperature of the bath; for, though a

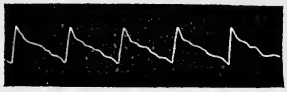

FIG. 7.—Before bath, ordinary pressure.

FIG. 8.—Pressure, 3 lbs.

FIG. 9.—Pressure, 6 lbs.

FIG. 10.—Pressure, 9 lbs.

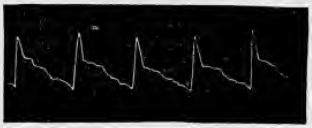

FIG. 11.—After bath, ordinary pressure.

prolonged sitting generally causes a fall in the pulse rate, a hot atmosphere will make the pulse rise at first. Sphygmographic tracings shew a lowering in the height of the tidal and dicrotic waves, but this change is only maintained during the bath; after it the pulse tracing returns to its former standard. To the finger the pulse appears small and hard. All observations indicate that compressed air exerts an intropulsive influence, affecting naturally the surfaces most exposed to it, such as the skin and lungs, and drives the blood into the organs protected from air pressure, such as the brain, heart, liver, spleen, and kidneys. The pressure is exerted more on the capillaries, and superficial veins and arteries; and its tendency must be to reduce pressure on the right side of the heart and to increase it on the left. A proof of the fulness of the arterial system is to be found (1) in the sphygmographic tracings, and (2) in the fact that when haemorrhage occurs in the bath the blood is invariably bright red (arterial). The slower pulse rate,

according to the late Sir John Burdon-Sanderson, is the effect of the diminished pressure in the venous system, which retards the filling of the ventricles during the period of relaxation, and consequently lengthens the diastolic period; thus the pulse frequency is diminished.

Again, the introduction of a larger amount of oxygen causes greater absorption of this gas by the lungs, and increased oxidation and tissue change; this is proved by the increase in the amount of carbonic acid exhaled from the lungs, and in that of urea from the kidneys. Appetite is improved and weight is generally gained. Muscular power is stated by Lange to be increased; he found that men could carry weights better after the bath than before it.

The internal temperature of the body is slightly raised, sometimes half a degree in the mouth, that in the axilla being diminished; the rectal temperature (Stembo) rises, as might be expected, from the intropulsive action of the bath on the circulation.

From the preceding observations it will be understood that, on account of this intropulsive action on the circulation, the use of the compressed air bath is contra-indicated in congestion, or inflammation, or haemorrhage of any of the organs which are wholly or partially protected from air pressure in bony cavities, such as the brain, spinal cord, heart, liver, spleen, kidneys, uterus and ovaries. Again fever, in which there is congestion of internal organs, is increased by it.

The intropulsive action is sometimes serviceable, as, for example, in long-standing *amenorrhoea*; for by its effect on the ovaries the bath will often restore the menstrual flow. *Anaemia*, too, is greatly relieved by compressed air baths, probably on account of the large amount of oxygen supplied. Certain it is that under their use pallor gives way to the blush of health, anaemic murmurs disappear, and the number of red corpuscles, as noted by the haemocytometer, largely increases. This has been my experience in all the cases of anaemia I have treated in this way.

The diseases in which compressed air baths have been found to do most good are bronchial asthma, chronic bronchitis, and emphysema.

Emphysema. — In the tense or large-lunged form, which accompanies bronchitis and asthma, and has been so well described by Dr. C. J. B. Williams and Sir William Jenner, a course of these baths effects a wonderful change. The patient finds he can breathe more freely, and can ascend steps and hills with greater ease. His cough and expectoration are reduced. His respirations are slower and deeper, and the pulse is slower and firmer. Physical examination shews the thoracic distension to be diminished. The line of hepatic dulness, long absent, reappears and rises to the old level, the area of cardiac dulness can again be detected, and the impulse is felt, not in the epigastrium, but in the normal position between the fifth and sixth ribs, slightly to the right of the nipple. Hyper-resonance of the thorax gives place to something more like the normal note; and although there may be prolonged expiration with occasional wheezing sounds, the air is heard to penetrate into blocked

portions of the lung in which breath sounds were previously absent. Cyrtometric measurements shew a reduction in the chest circumference at different levels of from ½ to 1½ inches; and the spirometric observations yield evidence of "increased vital capacity."

These changes appear to be due to the removal of some of the causes of the emphysema, such as bronchial catarrh and bronchial spasm, thus allowing the escape of some of the distending air from portions of the lung in which the emphysema was perhaps temporary. Theoretically expiration into rarefied air ought to give most relief to emphysematous patients, but, as a matter of fact, inspiring condensed air (pressure, 8 to 10 lbs.) is far preferable, for the reasons above given.

Bronchial Catarrh and Bronchitis.—The effect on this class of diseases is excellent; cough is diminished, expectoration first becomes easier and then lessened in amount, breathing is freer, and any accompanying emphysema is reduced considerably. I have used the compressed air bath in a large number of cases of bronchitis and emphysema, and in every case there has been relief, though it has not always proved permanent. Oertel considers the improvement to be due to the increased pressure in the larger tubes, causing diminution of the blood in the bronchial system, and consequently less exudation of serum into the coats of the bronchi, and less pressure on the lymphatic system.

Bronchial Asthma.—The principal effect of the treatment on asthma seems to be sedative to the pulmonary plexuses and to the pneumogastric nerves. The attacks are rendered less severe, and after a course of twenty or thirty baths the intervals between the attacks become much longer and the spasms finally cease. I have several times placed a patient in the bath during an asthmatic attack, and always with relief to the spasms. In addition to the soothing influence on the nerve-storm, the baths reduce the accompanying emphysema, and more so than in the emphysema of bronchitis, probably because the bronchial obstructions are of a more transitory character. The patient is able to breathe more freely and to take deeper inspirations, the chest distension, as shewn by the measurements, diminishes, and the spirometric records increase in amount. Thus an improvement in the general condition ensues. Exercise can be more freely taken, digestion and assimilation are carried on with greater ease and comfort, and strength and colour are gained. During the last twenty years I have treated some hundreds of asthmatics in the compressed air bath, and I know no means of relief equal to it. In many cases the reduction of all spasm and attacks for months has resulted in freedom from the complaint for years, and in some instances in complete cure. Sandahl reported improvement or recovery in 75·3 per cent of his patients, and Bertin in 95 per cent.

Pulmonary Tuberculosis.—I have tried the treatment in a large number of cases, generally those of limited lung tuberculosis; and except that cough and expectoration slightly diminish, and that some portions of the lung become more expanded, I could see no good result. In several of the cases haemoptysis came on either in the bath or after

the treatment, and this constitutes a fresh danger. In some of the patients there was improvement of appetite and gain of weight, but it cannot be said that any lasting benefit resulted.

I tried the treatment in cases of chronic pneumonia and chronic lung infiltration, and also in commencing pleuritic effusion—in the latter case with the view of inflating the lungs and thus opposing the increasing fluid pressure; but in none of these instances did the bath do any good, and the progress of the disease was unchecked. Tissier found that in a case of chronic pleurisy, in which progress was at a standstill, two sittings in a compressed air bath brought about a considerable amount of absorption of the exudation.

The number of compressed air baths sufficient to produce a therapeutic effect varies greatly, but in asthma or bronchitis about thirty are necessary; in chronic emphysema a larger number, sixty to seventy, are often required.

It is remarkable that, whilst there are numerous establishments for compressed air baths on the Continent and elsewhere, in England there are scarcely any: those best known are the one at Ben Rhydding in Yorkshire, and the admirable one of the Brompton Hospital, which is largely used, and is now made available for private patients.

Respiratory Gymnastics.—Marcet insisted on the advantage of training the respiration, not only for physiological exercise, but as an important aid in the treatment of such diseases as asthma. He shewed that after forced breathing more than double the weight could be lifted than after ordinary breathing; and he instanced the well-known fact of the asthmatic spasm being sometimes momentarily suspended by a forced inspiration, as a proof that a deficient supply of oxygen to the respiratory centres bears a definite relation to the causation of asthma.

Marcet advocated, as a method of therapeutics for asthma, the practice of the respiratory movements required to carry the air through the lungs in order to oxidise the blood and exhaust the carbonic acid; this practice, at the same time, brings the circulation into better co-operation with the respiratory function. A good form of exercise, according to this author, is "cycling, which increases the depth of breathing and this without fatigue, the respiratory movements being automatic; at the same time, it accustoms the rider instinctively to take in at each respiration the volume of air required to aerate the blood, and to eliminate a certain proportion of carbonic acid, leaving in the circulation that amount which is compatible with health."

The Swedish system of gymnastics, and Sandow's exercises, if properly applied, may act usefully as respiratory gymnastics.

C. THEODORE WILLIAMS.

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ASTHMA AND HAY-FEVER

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ASTHMA is a paroxysmal dyspnoea which often manifests itself quite suddenly, and may subside again with like rapidity. It may be due to one or more of a great number of causes. The respiration in the intervals may or may not be normal.

Asthma is usually divided into (i.) primary, idiopathic, or true spasmodic asthma, and (ii.) asthma arising as a complication of pre-existing bronchitis. In the management of the disease this distinction needs full consideration, but it is essentially with true spasmodic asthma that this article deals.

Hay-fever is often a spasmodic asthma in its purest form, so that the two maladies will be considered in common.

Etiology.—As to *sex*, it is usually stated that asthma occurs twice as often in men as in women. In Salter's series there were 102 men to 51 women; in Dr. Francis's, 282 to 120; and 94 to 65 in the cases observed by us. It might have been anticipated that the less stable centres of the woman would be the more likely to shew a predominance, but it may well be that the instability of womanhood works off in other ways.

Age.—Asthma is not confined to any one time of life, though more cases take origin in the first ten years than in any subsequent decade. Of 149 of our cases in which the point is noted, 55 began in children of ten years and under—32 in males, 23 in females: it is

interesting to note that one of the youngest cases was in a little boy 3½ years old, whose father suffered from hay-fever and asthma and was said to have been cured by local treatment of his nose by the cautery. In 34 cases the disease began between ten and twenty, 19 being males and 15 females. In the period from twenty to thirty 17 cases only are reported, 6 males and 11 females. In 43 cases, 29 men and 14 women, the disease arose after the age of thirty. These figures indicate, too, that the excessive incidence of the disease upon males is all along the line, with the exception of the decade from twenty to thirty, in which perhaps the numbers are not sufficient to allow of any conclusion. Thus, in 89 cases out of 149 asthma began in subjects under full age. Hyde Salter's table of the age at which people have become asthmatic is as under :—

During first year . .	11 cases	31·6	per cent.
From 1 to 10 . . .	60 ,,		
,, 10 ,, 20 . . .	30 ,,	13·3	,,
,, 20 ,, 30 . . .	39 ,,	17·3	,,
,, 30 ,, 40 . . .	44 ,,	19·6	,,
,, 40 ,, 50 . . .	24 ,,	10·7	,,
,, 50 ,, 60 . . .	12 ,,	5·3	,,
,, 60 ,, 70 . . .	4 ,,	1·8	,,
,, 70 ,, 80 . . .	1 ,,	0·4	,,
	225		

Heredity.—In a certain proportion of cases asthma appears to be inherited. Thus, Berkart in some carefully selected cases found that in 16 per cent one or other parent suffered from the disease. Out of 136 cases observed by us, there was direct transmission of asthma or hay-fever in 28, or 21 per cent. Still more commonly is the patient related to sufferers from other neuropathic diseases, such as migraine, epilepsy, neuralgia, or angina, rheumatic fever, and diabetes. Thus, 55 of the 136 cases shewed a well-marked neurotic inheritance of one form or another. In all this group of diseases—in asthma, hay-fever, and paroxysmal sneezing—the number of the nervous phenomena that are to be found in the different members of the family is conspicuous.

Of other remoter causes one must certainly mention an idiosyncrasy on the part of the subject—"individual constitution," as Wilson Fox called it. What this is we know no more than why certain foods, which for the majority of mankind are perfectly harmless, for a small minority are active poisons. We are inclined to doubt whether this constitution is ever wanting in the case of asthma, even though diseased conditions be actually present that seem so immediately provocative of an attack as naturally to be regarded as sufficient causes.

Morbid Conditions of the Nose and Naso-pharynx.—In 1872 Voltolini reported 11 cases of asthma relieved by the removal of nasal polypi. Since then much has been written about the relation between nasal disease and asthma. Some asthmatics are the subjects of polypi, nasal spurs or ridges, septal irregularities, or hypersensitive areas over the

upper part of the septum. In others hypertrophy of the erectile tissue over the turbinals is present. Others have acquired the habit of breathing through the mouth, as the result of adenoid vegetations present in early life, with the consequence that the nose and naso-pharynx are not properly developed and are liable to morbid changes. In 500 cases of asthma reported by Lublinski, some morbid condition was found in the nose in 29 per cent; in 402 cases reported by Dr. A. Francis, in 14 per cent. Such nasal abnormalities exist in a large number of people, without giving rise to asthma (28, 67). The percentage of asthmatics among the sufferers from nasal polypus is variously given by Baecker, Hering, and Schmiegelow (57, 67) as 3·9, 2·5, and 22 per cent; of 514 patients with chronic rhinitis, Schmiegelow found asthma in 8 per cent. By adding together the figures of these observers, it is found that, of 1163 cases of nasal disease, 87, or 7·5 per cent, were the subjects of asthma. Too much stress must not be laid on such figures as these, for there is room for divergence of opinion as to when a slight nasal deformity is to be regarded as definitely morbid; on the other hand, it is probable that some forms of dyspnoea are included which are not true spasmodic asthma, or, conversely, that the slighter degrees of asthma have been overlooked by observers who have not paid special attention to this disease. That the connexion between nasal disease and asthma may be a close one is shewn by the beneficial results which have been found to follow local treatment, and the observations on the reflex production of bronchial spasm by experimental stimulation of the nasal mucous membrane, which will be dealt with more in detail on p. 52, support this conclusion. Cases have also been recorded, though but rarely, in which asthma has followed nasal operations (40, 57). The following case may be quoted to illustrate these points: a man, aged twenty-eight years, who came of healthy, non-asthmatic stock, fell off a bicycle and smashed his nose. Ever since that time he has required for his daily use six or seven pocket-handkerchiefs, and now he has become asthmatic. His asthmatic attacks come on every month or six weeks, and last from half an hour to a day and a half. He has had his nose treated with decided benefit to his asthma, but he derives most benefit from smoking medicated cigarettes. In another case slight asthma of four months' standing, following influenza, passed into a very severe form after removal of some nasal polypi.

Immediate Causes.—Given a certain morbid sensitiveness of the nervous centres, anything seems capable of producing an attack. It may be a nervous shock, anger or other emotion, over-fatigue of mind or body, too monotonous a habit of living, too little exercise, too much food, indiscretions in the nature of the diet, constipation, uterine disorders, changes of temperature, changes of climate, a thunder-storm—changes in the weather seem to be particularly prone to induce asthma,—microscopic organisms in the atmosphere, such as the pollen of hay, or dust and fluff, or emanations of various kinds from animals (cat or horse asthma), and so on. W. E. Steavenson, in describing his own case,

wrote: "I never brush my own coat, unless I feel particularly well, without paying a severe penalty; and the dust from blankets is particularly objectionable to me." And later, referring to the connexion of asthma with certain conditions of the mind: "I have never been prevented by an attack of asthma from going in for and completing any examination; but, when completed and the strain on my mind relieved, it has always been followed the succeeding night and day by a severe attack."

Of some of these one would not wonder that dust, fog, or pungent fumes of various kinds should now and again be responsible for the production of the disease. But the peculiarity of asthma would seem to be that it is evoked by irritants that in ordinary circumstances are no irritants at all (Salter). "One asthmatic is obliged to expatriate himself in the hay season and take a sea-voyage; another cannot stay in a room in which a bottle of ipecacuan is opened; a third cannot stroke or nurse a cat; another cannot go near a rabbit hutch; another is immediately rendered asthmatic by the neighbourhood of a privet hedge; another cannot sleep upon a pillow stuffed with feathers; another cannot use mustard in any shape, or bear it near her, so that she dare not even apply a mustard plaster; and one young lady I know who dare not pass a poulterer's shop."

One of us has knowledge of two cases of cat asthma. In one of these the existence of cats is the bane of life, for before accepting an invitation she is obliged first to ask, "Is there a cat?" An attack of urticaria and coryza followed by asthma has been noticed to come on within ten minutes of having stroked a cat. At other times sitting in a room in which there was a cat, without any actual contact with it, was sufficient to produce a bad attack, beginning within ten minutes of entering the room. Sir Clifford Allbutt knew a little boy in whom horses work similar effects. He cannot, therefore, ride in carriages or cabs; and it has been necessary to let him run home and get wet through, rather than incur the greater evil of asthma, likely to be provoked by a ride in a cab with his mother. Such statements as these, Salter truly says, one would hardly believe, were not their reality placed beyond doubt; there is neither invention, nor imagination, nor exaggeration about them. Surgeon-Major Lethbridge Swaine has found that in Aurangabad asthma is quite common in association with malaria; and that asthma often ushers in an attack of malarial fever, and has done so in his own case several times. Potain alludes also to the frequency with which amongst the infections paludism plays the part of an exciting cause. The same thing has been noticed with regard to influenza. A case will be mentioned later in which influenza ushered itself in by provoking a severe attack of asthma. But far oftener asthma comes on as a result of the post-influenzal exhaustion of the nervous centres. We have notes of seven cases of the kind. Under diseased or ill-regulated conditions other illnesses become an active source of worry and excitement. Such are pneumonia, pleurisy, bronchial catarrh,

whooping-cough, and measles. Twenty-one cases out of 159 are attributed to such a cause.

Of nervous shock, or strong emotion, we will only add that, as such impressions are well known to bring on attacks, so they may also remove attacks instantaneously and completely.

In all these cases examine the patient in an interval of freedom, and there may be no evidence whatever of any disease. But of a large class of asthmatics this cannot be said, for in 80 per cent of all cases, according to Dr. Theodore Williams, there is evidence of permanent catarrh of the bronchial tubes. Others there are in whom gout or a high blood-pressure seems to provoke attacks. The alterations of the ribs in old age lead to pulmonary obstruction and emphysema, and so favour an asthmatic paroxysm. The pulmonary congestions of chronic heart disease and renal disease bring about the same end.

In one group of cases, however, asthma appears for the first time in middle life in a patient, in whom there are no obvious tendencies to neurotic ailments, and no evidence of existing disease that might act as proximate cause. It is possible that a percentage of these may belong to the group already mentioned, in which gout in the system or excessively high arterial blood-pressure has been the cause; but we are not satisfied that these things explain all the cases of later appearance. To judge from our experience, they are prone to be very severe, and to be but little amenable to treatment; and we have come to the conclusion that in certain cases there may be some rapid onset of emphysema, some process of degeneration in the tissue of the lung, such as was described by Greenhow.

Simple spasmodic asthma is very seldom seen in the wards of a general hospital. It is of course found often enough in the degenerate, in association with emphysema, chronic bronchitis, gout, and renal disease. But in the primary pure form it occurs seldom indeed. There are many reasons for this. Chief of them, perhaps, is that this disease comes and goes; and for maladies of that kind the working-man cannot afford to lie up. Indeed, this applies to all classes of society. As Berkart truly says, "Asthmatics are not disposed to consider themselves as patients. Their suffering is forgotten as soon as it is over." But we cannot help thinking that the affection is one that belongs more peculiarly to the upper ranks of society. It may be, perhaps, that the angular condition of the nervous centres, to which the disease may be attributed, becomes rubbed down, so to speak, by the harder life of the labouring classes; just as such persons are less sensitive to noise, less sensitive altogether to what one may call the smaller ills of life.

The morbid anatomy of asthma, saving perhaps one particular detail, is comparatively small in amount and simple in kind. It is obvious that all diseases, as they fall under the denomination of "functional," must proportionately be wanting more or less in those coarser changes in structure which we look for in the study of morbid anatomy; and so

it is here. The leading departures are most of them certainly conditioned by, and secondary to asthma of long standing: they are the results, not the cause, of the repeated asthmatic paroxysm. These are more or less chronic inflammation of the bronchial tubes, shewn by injection and thickening of the mucous membrane, thickening of the muscular coat of the bronchial tubes, dilatation of the tubes, emphysema of the vesicular structure, more or less thickening and atheroma of the branches of the pulmonary artery in the lung, and hypertrophy and dilatation of the right side of the heart. The changes in the skeleton that go with these are those of emphysema, the curved dorsal spine, the barrel-shaped chest, the stiffened ribs, the generally wasted frame.

But we have still to consider in more detail the state of the bronchial tubes, and the products that are shed from their mucous surface. The most regular condition to be found in the asthmatic is more or less mucus or mucopus in the smaller tubes. The presence of pus should be regarded as evidence of secondary bronchitis, but from a very early time Lefèvre, himself an asthmatic, as recorded by Berkart, had described the expectoration of a peculiar kind of sputum; at a later date Curschmann reobserved and redescribed peculiar elongated plugs or spiral bodies in the expectoration of the asthmatic, to which he was inclined to attribute considerable importance. The small round gelatinous masses, brought up with such difficulty in an attack, are found, when unfolded, to be mucinous casts of the fine bronchial tubes. In their simplest form, they are thin fibres of mucin. The spirals contain eosinophil cells (Adolf Schmidt) held together by mucin, and wound around a central clear fibre. Epithelial cells, some pigmented and some ciliated, and Charcot-Leyden crystals are often wrapped in the spirals. This arrangement is attributed to a rotatory action of the cilia of the bronchial epithelium. Gerlach, however, considers that the spirals arise in the larger tubes by the rolling round of mucinous fibres in the sputum. According to Stschastnyi, eosinophil cells are found in any region in which haemolysis may occur, and their presence in the bronchial tubes is the result of vascular disturbance with hyperaemia. Spirals have been found in some other affections, but those containing eosinophil leucocytes are stated to be characteristic of asthma (Predtetschensky). The Charcot-Leyden crystals are small colourless crystals found in the centre of the pellet of sputum, and present the appearance of two very sharp pyramids with the bases together. They were formerly said to be composed of the phosphate of an organic base, spermine, and to belong to the octahedral system, but, according to Cohn, they are hexagonal on cross-section and cannot, therefore, be composed of spermine. The crystals are found where eosinophil cells are abundant, and have been observed in the sputum of plastic bronchitis and of pneumonia, in the blood of leukaemia, in semen, and in the faeces of amoebic dysentery and of enteric fever. The sputum is crowded with micro-organisms; Kanthack found streptococci, staphylococci, an encapsuled diplococcus, a black mould, and a bacillus similar to, but not identical with, the diphtheria bacillus.

Pathogeny.—A disease that is, or may be, so sudden as to be well-nigh instantaneous in its onset—one produced under the influence of strong emotion, one which, in such and other circumstances, may subside as quickly as it came—is most likely to be some functional aberration of normal structures. The changes that seem most competent to explain the phenomena of asthma are: (i.) A muscular spasm of the smaller bronchi; (ii.) Some rapid tumefaction of the mucous membrane of the bronchi. Each of these can be defended by more or less cogent arguments. The one most generally accepted of recent years, it need hardly be said, is that the production of asthma is due to spasm of the muscular coat of the smaller bronchi. Hyde Salter, who was the chief and most able expositor of this view, makes use of the following arguments in its favour:—"In the first place, the sudden induction and remission of the asthmatic paroxysm is consistent with this supposition; in the second place, there is abundant proof that the air in the lungs is locked up, and can neither be got in nor out; there is evidently plenty of air in the chest, percussion is even over-resonant, yet the patient is as unable to drive air out as to draw it in; he can neither inspire nor expire; he cannot discharge breath enough to whistle, to blow out a candle, or to blow his nose. The muscles of respiration tug and labour to fill and empty the chest, but the chest walls remain almost immovable; the inspiratory muscles cannot raise them, the expiratory cannot depress them. On listening to the chest we find corroborative evidence of the stagnation of the air. The respiratory murmur is in a great degree lost. This absence of respiratory sound, accompanied by violent respiratory effort, is one of the most striking and suggestive of the facts of asthma. How can we explain it except by supposing that there is some bar to the ingress and egress of air; and what can this bar be, unless it be spasm of the bronchial tubes? It cannot be inflammatory thickening of the mucous membrane lining them; for the sudden, almost instantaneous establishment and remission of the dyspnoea is incompatible with this. It cannot be mucus plugging the tubes, for the attack will often come and go without any expectoration whatever. But we have still more positive and precise evidence of the circumscribed narrowing of the air-tubes in the musical sounds that are present in asthmatic breathing. This symptom has all the certainty and precision that characterise physical phenomena; and it shews that the air-tubes are the seat of constrictions which throw the air passing through them into vibrations, and convert them into musical instruments: since these musical sounds are multitudinous, the points of constriction must be many; since they are constantly varying in locality and character, the constrictions of the tubes must be undergoing similar change."

This view, originally stated by Reisseissen, receives strong confirmation from experimental evidence. Involuntary muscle fibres surround the bronchi, and can constrict them (C. J. B. Williams, 1840). They are supplied, as the researches of Longet (1842), MacGillavry, Roy and Brown, Einthoven, and Beer have shewn, by the vagus nerve. Stimula-

tion of the nerve causes constriction of the tubes. The thorough investigation of the innervation and contraction of the bronchial muscle, by Profs. Brodie and Dixon, published in 1903, has added much to our knowledge of the whole question of bronchial constriction and its relation to asthma. These observers shewed that the vagus supplies dilator as well as constrictor fibres to the bronchial muscle, and studied the changes in the ventilation of the lungs brought about by direct and reflex stimulation of this nerve, and by drugs. Their method was to observe the volume of air entering and leaving the lung at each respiration in a decerebrate or anaesthetised animal kept under artificial respiration, the force and duration of the inflation being kept constant. It was demonstrated that the constriction of the bronchi, produced by vagal stimulation, leads to distension of the lungs with air. This is because the deflating force, which is mainly the elastic recoil of the thoracic and abdominal walls, is weaker than the inflating force, though it makes up for its weakness by acting for a longer period. Bronchial constriction of moderate degree can therefore be compensated by increasing the length of time allowed for deflation. In asthma the same conditions prevail. The powerful inspiratory movements are able to overcome the resistance of the narrowed tubes to a considerable degree. In expiration, however, the forces which can be employed are less efficient, and, in spite of the prolongation of this phase, air accumulates in the alveoli, and the chest becomes fixed in the position of extreme distension. Of special interest was an experiment in an animal, one of whose lungs was adherent to the chest wall from old pleurisy, and in which there was some emphysema. Profs. Brodie and Dixon found that distension was very easily produced in a lobe of this lung, whereas it is not easy to over-distend a healthy lung with normal inflating pressures unless the bronchi are constricted. The distensibility of the emphysematous lobe was therefore increased, whilst its elasticity was very imperfect, and "the time required by the lobe to empty itself was much greater than in the case of a normal one." As regards reflex bronchial constriction, they found that the most definite results were obtained from stimulation of the nasal mucosa, either by thermal, chemical, mechanical, or electrical means, and especially of the upper and posterior part of the septum. A gradual and very persistent contraction was called forth, which could be terminated by section of the vagi. François Franck and Lazarus had previously described a certain relationship between the nasal mucous membrane and the bronchial muscles; by the application of weak electrical currents to the nasal mucous membrane, Lazarus was able to register a slight increase in the intrabronchial pressure; his results were, however, much less definite than those of Brodie and Dixon. Riegel and Edinger, Sandmann, and Einthoven demonstrated a similar effect with irritating gases. These experiments are of great importance in view of the connexion between asthma and pathological conditions of the naso-pharynx.

Equally interesting observations were made by Profs. Brodie and Dixon upon the pharmacology of the subject. Chloroform, ether,

atropine, and lobelia paralyse the nerve-endings of the vagus in the bronchial muscle. Muscarine stimulates them, and will, in an animal, produce a characteristic attack of asthma, with the sudden onset, the dyspnoea and extended thorax, the increase of secretion, and the development of sibilant rales in the chest. With a smaller dose an attack of milder degree may be brought about, without the signs of engorgement. These attacks can be cured by paralysing the stimulated nerve-endings with atropine. An accumulation of carbon dioxide in the lungs also causes constriction of the tubes, and this will naturally aggravate the asthmatic paroxysm when once it is set up (Zagari, Brodie and Dixon).

No one who has seen the forced action of the ordinary and extraordinary muscles of respiration in the exceeding labour of inspiratory effort during an attack of asthma can have any difficulty in believing that the air is really sucked past the obstruction, so that the lung becomes over-distended. Nor is it unimportant in this regard to insist that the obstruction may flit about from one part of the lung to another, and from one side to the other.

It must be admitted that the hypothesis of muscular spasm is at any rate fairly complete. It is a reasonable and satisfactory explanation of the facts, and it does not appear that there is much that is convincing to be said against it. Nevertheless, the hypothesis placed second in order, which assumes some rapid turgidity or erection of the bronchial mucous membrane, must be discussed, as it is held by many physicians, especially on the Continent, and among recent writers by A. Strumpell, Pieniazek, and A. Schmidt. We all know how near a common cold may come to an attack of asthma; there is the initial irritation of the nostrils, then the sneezing, then sore or dry throat, then some little tracheal worry, and finally a definite, albeit slight, bronchial stuffiness and wheezing. Now in these cases the initial change is certainly turgescence of the upper air-passages; and so also is it in the cases of paroxysmal sneezing, and in certain cases of local disease of the nasal mucous membrane, of deflected septum, or of polypus.

It has, therefore, been thought that what can be proved to exist in the upper air-passages, namely, a definite erection or turgidity of the nasal mucous membrane, may also take place lower down in the bronchial mucous surface; and, so doing, accomplish much of what we call spasmodic asthma. Thus, Blackley contends that the asthma of hay-fever is the turgescence in the nose extending to the general bronchial mucous membrane. But such a hypothesis does not take into account the essential difference in structure between the nasal and the bronchial mucous membranes. The former contains much vascular erectile tissue, and is prone to turgescence, whereas the latter is thin and has a relatively insignificant blood-supply; as Profs. Brodie and Dixon point out, the inhalation of ether produces much hyperaemia and increase of secretion from the respiratory tract, and should therefore, on this hypothesis, aggravate an attack, whereas it relieves it. A further striking experi-

ment was performed by clamping the pulmonary artery. The consequent engorgement of the lung did not produce any effect upon the respiratory inflation and deflation comparable to the effect of bronchial constriction. Traube considered asthma to be a very acute hyperaemic catarrh. And Sir Andrew Clark explained the phenomena of an attack by a vasomotor neurosis, by which changes analogous to those of urticaria upon the skin are produced. This has little to support it, and even the existence of vasomotor nerves in the lungs is problematical.

Berkart, however, will not allow that the history of the asthmatic attack, as regards its sudden onset and sudden subsidence, is anything but vague and untrustworthy, and concludes that what is commonly described as bronchial asthma is an acute and progressive, nay almost erysipelatous, form of inflammation, which extends from the pharynx upwards and downwards, and is accompanied by a croupous exudation. This is similar to the "bronchiolitis exudativa" of Curschmann. But such a view may well be thought to land its advocate in even greater difficulties, seeing that the disease is seldom associated with fever, seldom with any pneumonia, and, as an attack, is never a cause of death.

We believe, on the contrary, that the explosive character of asthma is absolutely certain. Let two cases suffice:—A gentleman was seized with influenza, which was ushered in by an attack of asthma. This condition was supposed to have gone on to bronchopneumonia, and this proved intractable. At great inconvenience to himself, therefore, he obeyed the order to take a long holiday; and it was the good fortune of one of us to see him as he passed through London, within two or three hours of his leaving home. A particular focus of disease had been found at an indicated spot. The man related, as so many asthmatics do, that he felt his breath relieved after he had been twenty minutes in the train; and when examined an hour or two later, no one could say that he was other than absolutely healthy. In the second case Sir Clifford Allbutt was examining by auscultation the backs of the lungs of a gentleman of neurotic habit, who was overworked and suffering from pains which were suspected to be of the nature of angina pectoris. The patient was sitting up in bed, and his face was under the observation of his own medical attendant. After a few inspirations of a normal character the inspiratory murmur began to diminish on the left side, and in a few moments ceased. Perplexed by this strange event Sir Clifford Allbutt quickly percussed the left side of the chest, but with negative results. During this time the family attendant saw the patient striving for breath; and attention being drawn to his state, it became manifest that he was in his first attack of asthma: respiration quickly became almost inaudible over both lungs, and then, after a definite interval, sibilus supervened. The attack followed the usual course, and the asthma thereafter frequently recurred.

Lastly, we must consider how the muscular constriction is likely to be excited. Such a neuro-muscular activity might be aroused either

peripherally, reflexly, or directly from the central nervous system. It can hardly be doubted that, given a certain predisposition, asthmatic attacks are brought about in all these ways. The asthma which follows bronchitis may be regarded as excited locally in the bronchial tubes; that form associated with nasal disease and with the inhalation of dust and pollen as reflexly called forth from the mucous membrane of the nose; and attacks following anger and other emotions, from the cerebrum. The Charcot-Leyden crystals were formerly looked upon as possible irritants of the bronchial mucous membrane, and credited with the power of exciting attacks, but Mr. S. G. Shattock has shewn that neither local application nor injection of a saline extract of asthmatic sputum will produce bronchial constriction.

Symptoms.—*The asthmatic paroxysm* may come on at any time. A susceptible or morbidly paroxysmal subject—to be paroxysmal more or less is a universal attribute of organic action—comes into contact with, say, some animal or vegetable exhalation; eats some indigestible article of diet, or something that, whilst innocuous to the majority of mankind, is known to be in some way prejudicial to particular individuals; or in some other of many ways taxes his range of accommodation beyond the margin of its power, and within a few minutes an attack may begin. Commonly there are premonitory symptoms, such as yawning, itching, sneezing, flatulence, the passage of a large quantity of urine, or "abnormal buoyancy of spirits" (Steavenson). The beginning is said to be most frequent during the night, when the patient has had his first sleep; for instance, at two or three in the morning he suddenly awakes with a stuffy feeling in his chest, and within a short time he is in the throes of an attack of asthma. Thereupon he is compelled to sit up in bed, perhaps to get out; the head is fixed, the shoulders raised, the hands are often planted well down upon anything firm on each side to give purchase to the respiratory muscles, and so the sufferer sits labouring at his breath. Sometimes he bends forward, sometimes stands leaning upon some support; but the object in all cases is the same, to give the respiratory muscles better or more fixed support from which to act. The pulse is usually but little affected, and the temperature is normal.

In bad cases the face is of an ashy pallor, or it is grey and leaden, or dusky from want of oxygenation of the blood; the skin is covered with perspiration, the eyes may look prominent, the nostrils may be dilated. Few diseases produce appearances so distressing and so grave, and yet it can fortunately be said that an attack of spasmodic asthma never kills. Probably it supplies its own corrective in this, that after a certain time of intense distress and anxiety to the patient, the irritated centres become exhausted, the spasm is gradually relaxed, and the patient sinks to sleep. In some cases the relief appears to be absolute; in the majority, however, it is only comparative, and a degree of oppression is experienced for a few days or longer; or the malady may abide with the patient more or less continuously. The abdominal muscles are painful

and tender for a day or two after the attack from the strain which has been put upon them in aiding the forced expiration.

During an attack, although the patient is making violent efforts with all the respiratory muscles, the actual movements of the chest wall are little indeed. The chest may plunge, but there can be no further expansion of the thoracic cavity. As the chest walls are pulled outwards all the more yielding parts are depressed and thus the intercostal spaces may become troughs. The epigastrium may be hollow or full; the suprasternal and supraclavicular spaces are greatly exaggerated.

The actual condition of the chest during a paroxysm has been the subject of some discussion. According to the generally accepted description, it is in a state of over-distension, the diaphragm being depressed and the upper part of the abdomen being full (Hyde Salter and Biermer). The movement is much restricted, and thus there is a very short, abortive, suddenly pulled-up inspiration, and an expiration perhaps four or five times as long as it should be. The percussion of such a chest gives a hyper-resonant note. But there is, as stated by Riegel and others, another form of chest, in which the lower parts, if not retracted as some contend, are not unduly distended, and where diminished rather than increased resonance is detected. And it has been supposed that in these cases the obstruction in the smaller bronchi is so extreme as to lead to a state of collapse. Wilson Fox offered this explanation, and the whole subject will be found discussed in his posthumously published work, *A Treatise on Diseases of the Lungs and Pleura*.

The attack is, however, by no means always sudden in its onset, perhaps not generally so. More or less wheeziness and constriction of the chest may exist for a day or two beforehand; there may be a short, rather hollow cough, and, if the dyspnoea be at all pronounced, much weariness on exertion. Thus, a mild or threatening attack may be recognised by the onlooker in the disinclination to all movement generally shewn by persons thus affected.

If the chest of the asthmatic be auscultated during the paroxysm the chief feature is an almost complete absence of respiratory murmur. The chest plunges, but there is no corresponding inspiratory wave; there are sibilant rhonchi and muscular rumbles, and a number of odd noises, but no real ingress of air; and with the expiration there may be, perhaps, a long, distant, soft sibilus, the sole evidence of the respiratory ebb. The disease is often unequally distributed: one side, or this or that portion of one lung is affected more than the other; the asthmatic storm flits about the lung, now here, now there, and when the disease is thus unilateral or partial it is liable to repeat itself thus; so that we surmise that there is some local disease in the form of bronchitis, emphysema, adherent pleura, and so on, which exercises a permanently determining effect.

It is said that when an attack is over the patient is free from liability to a recurrence for some time. But this depends upon the past

duration of the asthmatic habit. Asthma, like gout, although in its earlier years markedly periodic in recurrence, tends, as the patient grows older, to become erratic in its manifestations, both as regards the time of its appearance and the form in which it comes. So that whereas in its earliest appearances it comes and goes, maybe with some special regularity, later in life it comes but it does not go, and the patient thenceforward is subject to a more or less chronic impediment to the free play of the lungs. And in all old cases, in which the chest is damaged by the repetition of the paroxysms, emphysema is produced with its attendant chronic bronchitis.

As the attack ends, expectoration usually begins. In the earlier stages of the paroxysm the bronchial tubes—to judge from the character of the signs—are dry ; the prevailing sounds in the chest being wheezing sibilus and rhonchus. Under the intense oppression the patient longs to expectorate, but is not able to do so. But when subsidence approaches, small grey pellets of mucus, of characteristic appearance, "like tapioca" (Salter), "often filamentous in shape like boiled macaroni" (37), begin to appear and gradually increase. In association with the appearance of crepitation in the chest the sputum becomes more and more copious, thin and frothy, till it may reach some considerable quantity. Blood is occasionally seen, especially in severe attacks, and, if so, generally in streaks.

The clinical history of spasmodic asthma is, however, by no means completed by this description of a characteristic attack. There are several other irregular states that are no less parts of the disease. First of all there is hay-fever, in which brow ague, coryza, a general disagreeable stuffiness of the respiratory tract, rendering nasal breathing a difficulty and producing a more or less chronic wheeziness and distress, last throughout the summer months. At times there is some slight febrile reaction, but it is not often great in degree ; there is rather the subjective feeling of lassitude and heat than the objective evidence of actual pyrexia ; and perhaps, on the whole, these rather indefinite symptoms are the more usual mode of its attack, although a definite attack of spasmodic asthma is by no means uncommon.

Paroxysmal sneezing is another way in which the asthmatic respiratory tract explodes. If we study asthma or the history of the asthmatic in any comprehensive way, we cannot but be sure that, either as a substitute or as part and parcel of the asthmatic attack, this sneezing must be taken into account. It is often found in asthmatic subjects and in asthmatic families, in which one member may have asthma and another exhausting paroxysms of sneezing ; moreover, it often goes with asthma, the sneezing gives the impetus of origin to the asthma, the irritation in the upper air-passages gradually affects the bronchial tubes, and asthma more or less severe results. In the history of asthma, cases of this sort are to be found in numbers ; but they need not be more particularly described, for they are fully dealt with elsewhere ("Nasal Neuroses," Vol. IV. Part II. p. 65). We may say this, however, that

most of the cases of sneezing we have met with have been in women, which is against the rule that prevails in asthma, in which case men are in the proportion of two to one. Such cases may sometimes be due to local disease in the nose, and they may certainly sometimes be much relieved, as also the asthma that accompanies them, by local treatment of the nasal mucous membrane.

There is at least one other affection that we would include in the clinical history of asthma, namely, the paroxysmal bronchitis of infants and young children. It has always seemed to us that one of the most interesting features in the study of medicine is the modification that disease appears to undergo in the successive periods of life. It is not certain, perhaps, that disease is so modified, but there is plenty of evidence in that direction. For instance, when a man who in earlier years had acute rheumatism is attacked in middle age with well-marked gout, we may suppose that a common factor has been modified, so that what did produce acute rheumatism at a later date produces gout. Now, as regards asthma, we believe that something of this kind takes place. Asthma has been shewn to be largely a disease of childhood, but it is not clearly present in the earliest years. Hyde Salter saw two cases in infants of fourteen and twenty-eight days, but such instances are very rare. It frequently begins to appear at six, seven, or eight years of age, and there are a fair number of possible cases at earlier periods than this. In infancy, if asthma exist, as we believe it does, it shews itself as a bronchitis, so far as the physical signs go; but, if so, it is a strange and interesting bronchitis, apart from the physical signs. It comes on with remarkable suddenness; it is mostly associated with fever; it is generally attributed to chill by the relatives: but there are reasons for thinking that it owns a much greater variety of causes, such as over-excitement, errors in diet, dentition, and so on. It clears up with remarkable celerity and certainty; it often leaves the child no worse than it was before the attack. Such attacks as these occur in a particular class of children—children that give conspicuous evidence either of coming of a nervous stock, or of nervousness and excitability in themselves. The whole history of these cases is explosive and nervous; and it may well be that, in the early history of the child's life, the ribs and other parts of the respiratory apparatus are not sufficiently developed to produce asthma, as we expect to see it; so that the mode of the disease is atelectatic or bronchitic. Asthma, in its ordinary manifestations, requires certain conditions of respiratory power, which, in all probability, the thoracic walls do not readily supply at that early period. Moreover, there can be no doubt that in the seven stages of our existence—and this answers to some extent the question we have already mooted—our various viscera change places in their relative importance, not only in their several bearings upon the well-being of the organism, but also in the absolute degrees of their activities; now one, now another, becoming a centre of excitement and explosion, and thus of break-down in ill-balanced organisations. In infant life the stomach tends to play the part of the

spoilt darling, and the lungs often have to pay the penalty for its caprices. However well it may be, it would appear that often it is not equal to the occasion; the household's teeth are set on edge, and pulmonary catarrh or oedema or collapse is set up. These storms, which so expend themselves on the lungs, or in the achievement of pyrexia, have much similarity to spasmodic asthma in their sudden mode of outburst; they involve a similar area, and may therefore not inappropriately be considered in the youngest children as the representative of asthma. Having thus diverged from the immediate subject to introduce that of the correlatives, substitutes, or derivatives of asthma, several other diseases may be briefly indicated that may in this respect be considered with the gastro-pulmonary fever that we have just mentioned. Some persons, for instance, have laid stress upon psoriasis in this connexion. One of us has known a case in which asthma and psoriasis seemed to alternate, and we have also come across this suggestive alternation as regards eczema. The mother of a family is the subject of spasmodic asthma. She has had four children. In the first and third pregnancies she had no asthma, and in each child bad eczema appeared, and death resulted in one from convulsions. In the second and fourth pregnancies the mother had bad asthma, and the children hitherto have been healthy. In a collation of the notes of our cases no less than eight out of 159 cases of asthma were associated with severe eczema, and in two or three of these as the eczema went the asthma came. Carl v. Noorden has drawn attention to the frequency with which asthma is associated with eczema, but the connexion has long been noted.

Of other affections that surely belong to the same category is that form of looseness of bowels which is so common in nervous subjects, and in excitable children, where the mere ingestion of food seems sufficient to provoke a stomach-ache and a profuse liquid evacuation from the bowels. This is perhaps the very commonest of the kind. Another is urticaria, and it is not uninteresting to note that it is sometimes associated with or takes the place of asthma, as a case of asthma produced by contact with cats will shew. One of us (J. F. G.) has records of three such cases.

Results of Asthma.—When a man has been the subject of asthma for a long time, it is likely that he will present characteristic appearances in his general physique and gait. He is usually very thin; his back is rounded, his shoulders are high, and he walks lethargically, with a well-marked forward stoop. He sits, may it be said, turtle-like, with his neck dropped into his chest. In long-standing cases the face is a little dusky, the eye watery and perhaps congested; and there is often a cough of peculiar timbre, moist and hollow, not easy to describe, but evidently the product of feeble expiratory power. The asthmatic speaks, too, as he coughs; and for the same reason, that the tidal wave of the chronic asthmatic is exceedingly shallow: for the spine is rounded, the ribs stiffened and fixed, the chest elongated and depressed.

Apart from the above-mentioned consequences of repeated attacks, *complications* are uncommon. Oedema of the lung, followed by pneu-

monia, has been recorded (30); pneumonia in asthmatics is usually mild (Dünges). Subcutaneous emphysema has twice been noted (14, 68), coming on in an attack and implicating the neck, doubtless from a rupture at the root of the lung. In Dr. Whitby's case it extended over the thorax and back. Both patients recovered. Asthma is rarely followed by tuberculosis of the lung (twice in 70 cases, Dünges), but, if it is, becomes less severe. A patient with pulmonary tuberculosis may become asthmatic, especially if of a neurotic disposition.

Diagnosis.—It is not necessary to linger over this section of the subject. It is true that many affections are called asthma that are not so regarded in this article. The short breath and the dyspnoea of chronic bronchitis and emphysema, and the dyspnoea and orthopnoea of heart disease, are often thus designated; in both of these the dyspnoea is rather a subdued distress than the acute disturbance of spasmodic asthma; so with the air-hunger of some cases of renal disease, and of dilatation of the heart. The inspiration is free in such cases, but panting; it is not a dyspnoea. And yet it must be added that sometimes, in the early history of a granular kidney, the complaint of the patient may be chiefly of asthma of a mild kind; and without a general investigation of the case, without the hard pulse, the thick first sound, and perhaps the retinal changes, the real nature of the case might be overlooked. Plastic bronchitis is rare, but may give rise to confusion in the case of a first attack. The cough is much more forcible than that of asthma, and the nature of the expectoration soon places the diagnosis beyond doubt (*vide* p. 101). Among other conditions more likely, perhaps, to give rise to mistake, hysteria may be mentioned, for there may certainly be occasionally a difficulty between the one and the other, more particularly when it has been necessary to depend upon the history of the attack as submitted for an opinion, some time, it may be, after all the symptoms have passed away.

There is also a restless disturbed sleep, experienced by some persons, that is really a mild asthma, although not recognised as such by them; and that curious faucial or laryngeal suffocative spasm, often in gouty people, that awakens the subject of it in the middle of the night in terror lest he should choke.

Mediastinal tumours and aneurysm of the aorta, by leading to paroxysmal dyspnoea of a sort, are sometimes liable to be overlooked in a hasty diagnosis of the more familiar disease. And there are various obstructive maladies in the upper air-passages that may, in like manner, cause difficulty at times. The safeguard against mistake lies in the unfortunate fact that asthma is common, and therefore in its usual features is very generally known; and in respect of other maladies, even should they be entirely paroxysmal, which is uncommon, each one has usually some peculiar feature of its own that is sufficient to arrest the attention. Any one of these things may, of course, exist in association with the special nervous proclivities of asthma, and it might then become a matter of the greatest difficulty to distinguish between the morbid

occasions of the spasm. Nevertheless, it may be doubted whether in practice this difficulty often arises.

Prognosis.—Asthma may be treated with a large measure of success if it be taken in hand at the proper time, that is in childhood; and if it be possible to put the patient under suitable conditions—these conditions being, in brief, such as will allow of the patient being turned into a good healthy animal. It is in childhood, if at any time, that the opportunity offers of educating the patient out of a faulty habit into a better regulated state of his nervous centres. In the case of the adult one cannot be so hopeful. One could not be so hopeful of successfully combating convulsive attacks occurring late in life as in those occurring in infancy; and it is possible that the asthma that begins in adult age is indicative of some deep ingrained nervous fault, which is not easy to control. Moreover, adults fall in less readily with counsels of perfection, such as the radical cure of faulty habits; they are in distress, they insist upon a dose to set them right, and if one man will not give it them, or does not hit upon the right thing, they quickly resort to some one else, who manages things, as they think, better. Still, even the adult asthmatic is sometimes a sensible person, and many agree to desist from inhalations; to take a drug, such as arsenic, patiently; or iodide, when an attack threatens; or such other drug as may seem best suited to the particular case: to act thus is in most cases to procure considerable relief. In such cases as originate clearly in some local disease of the nose, it may also be legitimate to speak sanguinely of the future if proper treatment be adopted; but even then caution is necessary, for in some of the most rebellious cases of asthma polypi have been removed from the nose time after time without much permanent relief.

With regard to that other group, when spasmodic asthma occurs in middle age, and after; when, as causes or provocatives, certain changes in the tissues and organs, gouty and other, come into prominence; and when age with its paling vigour of function and its conscious or unconscious indiscretions of living and other habits leads to the overcharging of the blood with waste products, and to excess of arterial blood-pressure, and thus to a true spasmodic asthma analogous to the gouty vertigo and gouty convulsion occasionally seen in adult life; then no doubt great relief, and even cure, may result from such drugs as blue pill, iodide of potassium, and others, given with the purpose of reducing the arterial pressure, or of eliminating waste products. More difficult to speak of hopefully are the cases associated with and perhaps produced by a pre-existing bronchial catarrh. As Hyde Salter remarks, we send such patients to the Riviera to relieve the bronchitis, and the asthma is aggravated; and thereby we see in a measure how essentially independent the two conditions are; and when, after travelling about, they come to the land of promise so far as their asthma is concerned, then perchance the climatic conditions are not suited to the bronchitic affections. But even in such persons there is no doubt that, by dealing with the bronchitis and by endeavouring to ameliorate it by means of a suitable climate, the

bronchial tubes will become more healthy, and there may yet be scope for carrying out those principles of reinvigoration of the nervous tone upon which we have dwelt; and thus some of the stress of the asthma may be relieved.

Nevertheless, when the best has been done, one cannot but regard the disease as serious, and in too many cases baffling; for even in cases in which much good seems to have been effected, the disease reappears again, perhaps after many years. In looking over notes of a number of cases, it comes out clearly that in several in which the disease existed from, say, the age of three to ten years, it reappeared at forty or fifty. We have already alluded to the many points of similarity between asthma and epilepsy; and this is another feature of resemblance. We meet, too, with many people who have lost the tendency, and who are still free; but many of these, although they say they have lost the asthma, are still a little wheezy, and undoubtedly have some slight amount of bronchial catarrh. So that on the whole there is a degree of uncertainty about the fate of those who are asthmatic in early life. As regards the actual duration of life, perhaps all that can be said is that spasmodic asthma is compatible even with a long life. Of those who become asthmatic in later years, excepting the group of cases due to high arterial pressure already mentioned, which may be a fairly large one, most are likely to suffer severely; and their disease is but too likely to become more or less permanent.

Treatment.—We will first consider the principles and afterwards the details, lest in the multiplicity of the latter, and in the urgency and intractability of the disease, we fail to subordinate the one to the other. As we have already said, it seems impossible to doubt that asthma is one of those nervous actions of which we see so many examples in our economy, and which have been well called paroxysmal neuroses (Edward Liveing).

Epilepsy is one of these; some forms of insanity are others; migraine is another; asthma is another, and so on. Now all these more or less obey this law, that the more they come the more they may. Nervous actions, which in their essence and initiation are not abnormal, by excess of energy, or of frequency, or of both, become abnormal; and ultimately a bad habit becomes fixed. Surely, both in epilepsy and asthma there is much of habit in the intractability of the disease; and if control is to be gained over either, it must be by catching it in the earlier days of its appearance, and by arresting it before it becomes confirmed. We think that we can sometimes gain some control over the convulsions of infancy; we can perhaps keep them at bay sometimes, and so stop the child from becoming epileptic. But what case is more hopeless than that of the confirmed epileptic, even though he be persistently stupefied with bromides?

The case of asthma is a parallel one. It has been contended that it is a disease rather of childhood than of adult age; and that to pay attention to this fact, and to the suggestions that flow therefrom, offers

the best possible chance of stopping the attack, and of preventing the fixation of the habit and the establishment of chronic asthma. The chronic asthmatic is almost as hard to cope with as the chronic epileptic.

There are two methods of dealing with the asthmatic. On the one hand, we may attempt to make the environment conform to the conditions required by the patient; or, on the other hand, to harden the individual, to widen his range of accommodation, and so to make him less susceptible. And in the matter of drugs somewhat similar alternatives present themselves; we may either give sedatives to the over-sensitive nerve structures concerned, or give drugs, if such there be, to raise the level of nervous action to that higher platform that shall enable the perceptive centres to take less heed of their unnatural worries.

But the asthmatic paroxysm is so distressing that, almost always, the treatment of it usurps the first place; and too often this urgency of the situation upsets the perspective. If we have to deal with the stress of a paroxysm of asthma, clearly, on all accounts, it must be arrested as quickly as may be; there is no time to be very careful and consistent about ways and means. And the quickest way to relieve a paroxysm of asthma is to make the patient inhale some fume or other, as of nitre, nitrite of amyl, or chloroform; or to give him an injection of morphine or a dose of chloral; indeed, as we all know very well, doctors see paroxysms of this kind less often, because various patent powders for creating fumes hold the field so largely that most people do without us, and stick to their patent remedy.

Thus the treatment of asthma too often becomes a repeated sacrifice to the paroxysm; and the patient drags along, thankful for the small mercy of temporary freedom from his troubles, and easy in mind if he can carry in his pocket protection from those that are to come. But this plan of campaign is ultimately a most disastrous one. It unquestionably produces temporary ease; but what happens afterwards is this: the vapour, on reaching the mucous membrane, arrests the spasm for a time; but by stimulating the mucous membrane and provoking the flow of mucus, makes the local condition rather worse than it was before. The more sedative kinds of inhalations do but appease by offering bribes to vicious nervous influences. By and by the nervous centres wake up again to find matters no better, rather the contrary; and then on comes the spasm again, and the whole process is repeated; and, with each repetition of the cycle, the nervous centres, as their nature is, become more exhausted or more irritable, their sleep is shorter, their spasm is more and more quickly repeated, and the poor patient ultimately lands himself, with perhaps some lessening of the severity of each paroxysm, in a more prolonged or persistent stuffiness hardly less distressing to bear: all day long he appeals to his powder or spray, and becomes, in fact, the slave of an appetite that he has whetted and that he cannot now control. Thus ends the chronic asthmatic who betakes

himself to vapours. But this is not all, for by common consent a repeated application to some of these drugs tends to dilatation of the heart, and is equivalent to a good many nails in the coffin of the asthmatic. Moreover, this dread of the paroxysm itself is carried into the preventive treatment of the disease, and the patient is submitted to what may be called the glass-case treatment; that is to say, the temperament of the patient is ignored, or not considered as of importance, and the disease is supposed to be brought on by chill. If he be wealthy and adventurous, he fights his environment by running away; and thus he may, perhaps, get along pretty well. If the patient be a child, it is probably kept indoors, except in the finest of summer weather; yet, nevertheless, the history too often is that "it has caught another chill," but no one can say how. At first, perhaps, the child had the whole house to roam about in, but, as the "colds" recur, it is confined to one room with a south aspect; and yet things do not mend. So the doors of the room are carefully screened, the windows perhaps pasted up, and still the success being not all that can be desired, extra clothing may be piled on. And ultimately the doctor finds somewhere hidden under this heap of precautions a pale, moist, flabby, steamy thing, with big eyes, thin cheeks, protruding ribs, and a more or less general bronchitis; a case of "successful" management, because no attack has occurred for some weeks! But is this to be called success? This is to nurse the powers into imbecility; and the inevitable result is, that the first time the patient puts his head outside the door a fresh cold is "caught," and a fresh term of imprisonment is ordered. We venture to say that if asthma is to be prevented at all, it will never be kept at bay by hot-house treatment such as this.

The first requirement for the asthmatic is to put him into a climate in which he can be much out in the air. But there is the difficulty: we know so little about climate; and asthma is so individual a disease. No one can foresee in a particular case whether this place or that will be suitable, and for this reason very long journeys should not be advised at first. But for most asthmatic persons there is generally for each his own place or places where he is better or well. Thither he should be sent, at any rate, for a time. This place may be at the sea; or it may be inland; sometimes it is a dry place, sometimes a humid; often even it is a large town: "In the great majority of cases an urban air is the air that cures; and of a city air, that seems to be the best which is the most urban—the densest and smokiest" (Salter); but wherever it be, the patient should be out and about with very little restriction; and an attempt should be made by this means to render the morbid circuit less prone to discharge. Of games and sports, all should be encouraged that are outdoor and healthful and invigorating. In cases in which a persistent bronchial catarrh is at the bottom of the trouble, a dry and bracing air promises best. A man thus circumstanced found himself almost renewing his youth as he climbed the Malvern Hills. Others again find more relief in such places as Hastings, Ventnor, Bournemouth;

some even in Torquay. Some further remarks on climate in the treatment of asthma will be found in the first volume of this work (p. 335).

Any source of peripheral irritation should be dealt with. The most important are *morbid conditions in the naso-pharynx* and *errors of diet*. If polypi, spurs or ridges, hypertrophy of the turbinal mucosa, or hypersensitive areas upon the septum be present, they should receive attention from the surgeon. A large number of cases in which the asthma has disappeared for some years at least after such treatment is now on record, though the published cases are most of them so recent that it is not yet possible to speak of permanent results. In many other cases great relief is obtained, though in some no result follows (8, 13, 15, 18, 27, 40, 43, 48, and 63). The figures of Bosworth (23) added to those of Heymann, Schmiegelow, and Lublinski (67), together give 335 cases of asthma with nasal lesions: suitable local treatment is reported to have resulted in the cure of 130 of these, 39 per cent, and relief in a further 21 per cent. Dr. A. Francis has reported a series of cases treated by cauterisation of the nasal mucous membrane, irrespective of whether a recognisable lesion is present there or not, and states that the best results are obtained with the patients in whom there is none. Of 402 cases, including 56 with nasal lesions, complete relief is reported in 194; 14 were not relieved, and 17 lost sight of. All the rest received relief of greater or less duration. These results are of great interest, since, as has been mentioned above, it has been shewn experimentally that it is possible to excite reflex contraction of the bronchial muscle from the nasal mucous membrane. (*Vide* also art. "Nasal Neuroses," Vol. IV. Part II. p. 66.)

All must agree that if there be any actual disease of the mucous membrane, whether due to the existence of polypus, of a deflected septum, or what not, it must be advisable to get the mucous surface into as healthy a state as possible so as to remove one obvious source of possible irritation. But for cases of asthma in which there is no definite nasal worry, the question must at any rate be considered an open one. If the neurotic origin of the disease be accepted, no one can rest content with the treatment of a peripheral symptom. Still, if it can be shewn that a large measure of relief is thus obtained, such an experience must of course be utilised upon the principle that half a loaf is better than no bread. The difficulty of arriving at any sound conclusion as to the value of such treatment lies in this, that the specialist and the physician see the cases at different times: the one in the first flush of that post-operative quiescence that we all so well recognise as a characteristic of nervous ailments; the other, when that quiescence has passed off, and the old habit has resumed its sway. We have known some patients to be apparently benefited, but others have not received any adequate reward, and, as already mentioned, removal of a nasal obstruction intensified the asthma in one case.

In *diet* it is necessary to be careful, but not too much so. It is very

easy to give a number of restrictions about food, and thus to make matters worse; yet asthma certainly often does seem to start from a meal that has not been digested—one which may have been too large, of an improper character, or taken at some irregular hour: the points to aim at are good, plain, light food in moderate quantity and slowly ingested. Asthmatics, particularly children, are often deprived of potatoes, of puddings, jam and sugar, and goodness knows what else, and on the other hand are put on various meat-juices and other good things in the wrong place, so as to remove all rocks of offence from the path of their pneumogastrics. But "if they do these things in the green tree, what shall be done in the dry?" What chance has such a child of reaching old age? Any food that is plain and wholesome and not known to disagree may be allowed. It may be necessary to exercise careful control over the use of starchy foods, suet puddings, and jam. It is advisable to have the chief meals early in the day, when digestion is vigorous; therefore breakfast and lunch—an early dinner—should be the main meals; anything taken later must be small in quantity and of the most digestible kind. Milk is regarded as harmful in any excess, especially in the gouty (Mitchell Bruce). All meals should be small; the stomach should never be distended. The bowels should be kept carefully regulated and sufficiently open by some saline aperient, or other simple laxative. Every effort should be made to keep the patient in as healthy and physically fit a condition as possible. A tepid or cold bath should be taken in the early morning, and the living room well ventilated. Thin patients are benefited by cod-liver oil.

These must be the general principles upon which to deal with the asthmatic; and the more unhesitatingly so the younger the patient, and the earlier in the course of the disease that he comes under treatment.

In considering the treatment by drugs, two divisions of the subject naturally suggest themselves; namely, those medicines that are useful in preventing asthma, and those that are so when the actual attack is threatening or in progress. Again, a distinction must be made between the cases which seem to be pure nervous asthma, those which have any degree of persistent bronchial catarrh, and those already mentioned, which come on in later life, and may not irrationally be attributed, on the one hand, to blood conditions that as a group may for convenience be called gouty, and, on the other, to degenerative changes in the tissues.

As a preventive remedy in the pure form of asthma, no drug is in our opinion equal or nearly equal to arsenic. It should be taken for three or four weeks in doses of five minims of the liquor three times a day, or more if well borne; then omitted, and then resumed after an interval of equal length; and so on for three or four courses: and the drug should from time to time be resorted to in periods when from any cause the nervous centres begin to shew signs of lowered tone. We have not made much use of phosphorus, but it has been spoken well of, and

it might also upon occasion be of value; and likewise such remedies as bromides or hydrobromic acid.

Good results are claimed in the cases associated with bronchitis for the sprays and waters of the sulphurous springs of Mont Dore, of the Pyrenees, of Harrogate, and of the arsenical waters of La Bourboule. The two chief drugs from which much benefit is often derived are strychnine in three- to five-drop doses given steadily for some days, and the iodides which often prove of great value. Perhaps the one acts as a stimulant to the respiratory centre, the other as an expectorant. Many writers speak highly of potassium iodide for all cases, and give it in doses of fifteen to thirty grains daily for some months, omitting every tenth day (W. A. Wells, W. T. Gairdner). For the asthma that occurs in later life an eliminant treatment is on the whole the best. It is in such cases that blue pill and colocynth in moderate doses once or twice a week are useful, or saline laxatives with careful attention to and restriction of diet. The inhalation of creosote several times a day, with a dose of phenazone at night, is recommended in bronchitics.

It is said by some that the asthmatic state is much benefited by brine baths and systematic exercises, such as have been elaborated at Nauheim, for the treatment of certain forms of disease of the heart; one can well understand that means of this kind, by stimulating the circulation and facilitating the flow of blood through the lungs, may sometimes prove of service. Saenger recommends regular respiratory exercises. The patient breathes easily and deeply and counts five and its multiples between each inspiration, increasing the intervals daily.

To relieve an attack, or the semi-asthma that forebodes or lingers after an attack, other means must be used. In the threatening of an attack, or in the dyspnoea that persists when the more acute symptoms have subsided, many drugs have been tried, and at one time or another succeeded. Of these we should put first a combination of iodide of potassium with the ethereal tincture of lobelia; five, ten, or even fifteen grains of the one, and ten or fifteen minims of the other, seem to bring relief when other things may have failed. Some prefer stramonium to lobelia. Hyde Salter thought very highly of the *Datura stramonium* and the *D. tatula*; their best effects are observed when smoked like tobacco; but they may also be given in a pill, extract, or tincture. Sometimes a combination of iodide of potassium and chloral hydrate has been effectual. Macgregor speaks well of paraldehyde in half-dram doses at night after the patient is in bed, increased in adults, if necessary, to a dram. The taste may be modified by giving it with cinnamon and orange-peel water. The *Euphorbia pilulifera* and *Grindelia robusta* are also used; the former may be given in a decoction, a wineglassful twice a day; or in tincture, ten to thirty minims, twice or three times a day, or as often as may be requisite. The grindelia is in the form of a liquid extract, and is given in doses of ten to twenty minims. This drug is also recommended at the onset of an attack, in half-hourly doses, until relief has been attained. It may produce decided relief,

but, upon the whole, neither this drug nor euphorbia is very successful. Phenazone is also used, as are nitroglycerin and the nitrites. In the thick of an attack the remedies most in use are inhalations of various vapours; and of these, perhaps the commonest, and one of the most harmless, is blotting-paper soaked in nitrate of potassium, which will often relieve and sometimes very conspicuously. There are many other powders made for the production of fumes; some are stimulating, and seem to act by provoking cough and the free secretion of mucus; others, and the less harmful, are of a sedative nature. Some of them are made into cigarettes for smoking, and most of them contain stramonium in some form.

Of inhalations available for more strictly medical uses, three may be mentioned: nitrite of amyl, iodic ether (spoken well of by Dr. Thorowgood), and of course chloroform. In severe cases the last-named may be of the greatest possible value, although its effect is apt to be but transitory, and the attack may resume its severity as the stupor of the drug wears off. W. A. Wells has found pyridine efficient, ten to fifteen drops being inhaled from a handkerchief. Of all the other drugs that have been recommended for the relief of the paroxysm, morphine probably stands first; a hypodermic injection of a sixth of a grain will often procure almost immediate diminution of the violence of the dyspnoea, which gradually ends in complete cessation of the spasm. Pilocarpine is also a valuable drug; a tenth to a quarter of a grain may be given hypodermically; a free secretion from the mouth and fauces is the result, and the spasm is relieved. Profs. Brodie and Dixon find that in small doses this drug does not cause bronchial constriction; in larger doses it does, and is likely to do more harm than good. We have heard it said of pilocarpine that the remedy is worse than the disease; and, considering the distressing nature of the malady, this is a serious attack upon the benefit derived from it. If this be true as regards pilocarpine, it must be still more apt for tobacco, which produces a dreadful malaise, and is a difficult drug to control in those who are unaccustomed to its use, in whom alone it appears to have the effect wished for. The subcutaneous injection of $\frac{1}{75}$ of a grain of atropine is an old remedy which is strongly supported by the experimental work already referred to. Adrenalin solution (1 in 1000) in a dose of 10 to 25 ♏ is spoken well of by Kaplan, and should be injected into a muscle. Large injections of adrenalin are known to produce arterial degeneration in animals, and in this connexion it may be noted that Brooks and Kaplan have lately recorded the case of a woman, aged 35, who had received 2000 injections of from 10 to 120 ♏ of a 1 in 1000 solution of adrenalin for asthma in the course of three years, and whose arteries were found to be the seat of nodular subendothelial thickenings and focal necroses, similar to those produced in experimental adrenalin poisoning. There was no glycosuria. Such an extreme instance has not necessarily any bearing upon the moderate use of the drug.

Atropine may be used in the form of a spray, with cocaine, prepared

by Messrs. Oppenheimer. Tucker's spray is reported to contain cocaine, atropine, and a nitrate or nitrite (4, 9). Dr. Francis remarks that he has found the slaves of these sprays specially resistant to treatment. A combination of bromide of potassium and chloral is also a good sedative to give at the onset of a paroxysm. Belladonna, hyoscyamus, and conium, though not of so much value, are all of use in their way. Occasionally the patient is sick; this is by no means undesirable, for an emetic is one of the means advocated for arresting an attack, and sometimes with marked success.

Of stimulants, coffee and alcohol may be mentioned. Strong coffee is indeed a popular remedy that has often given relief, as also has citrate of caffeine. As regards alcohol, we have no personal knowledge of any special virtue; but Hyde Salter says of it, that whilst in many cases it does not do much good, in some it has a most powerful effect, particularly when all other remedies have failed. The compressed-air treatment of asthma is described on p. 43.

Hay-fever, or hay-asthma, is in the opinion of many a pure form of asthma, and in this opinion we concur; it is accordingly more or less amenable, as are other forms of asthma, to treatment by drugs of the same character, more particularly to arsenic, and this even for nasal cases: it relieves the itching and smarting of the eyes, the aching of the frontal sinuses, the itching of the nasal mucous membrane and of the nose itself, the sneezing, the watery discharge, the occlusion of the nostrils, the dryness and irritation of the lips and throat. But Karl Binz and others have maintained that local remedies, used upon germicide principles, give great relief in many of these cases; and those who have worked in the special department of diseases of the nose and throat declare that, by paying due attention to the morbid erectility of the mucous membrane over the spongy bones of the nose, this disease may be much reduced. Binz advocated the irrigation of the nostrils with a solution of quinine; Sir Andrew Clark suggested some carbolic preparation; and of late many have tried the application of solutions of cocaine, more upon alleviative than upon curative principles perhaps, unless alleviation be an earnest of cure. No one can doubt that these various measures are all useful in their proper place, nor can any one doubt that they have their dangers. For instance, a lady who for the discomfort arising from the frequently recurring turgidity of the nostrils, which is characteristic of hay-fever, had betaken herself by medical advice or without it to the use of cocaine locally. Accordingly, more or less, both by day and night, she would pack her nostrils with a solution of cocaine, of which one grain at each time was put into each nostril; and thereafter, by means of hawking and spitting, and other contortions of her pharyngeal muscles, the solution was spread all over the affected area, and temporary ease was obtained. At least six grains a day were thus disposed of, and sometimes more. Pollantin, "a serum-antitoxin obtained by injecting the toxic substances isolated from the pollen of certain grasses into animals," has given relief (*vide* art. "Nasal Neuroses,"

Vol. IV. Part. II. p. 68). The position to take with regard to local treatment is this, as it seems to us: the local symptoms are not the disease, and therefore, however necessary it may be at times to relieve by means of this kind conditions that cause great distress, harm may be done by inducing other morbid changes in the part, and conditions that were but temporary may thus be rendered permanent. For instance, a paroxysmal sneezing will stop immediately under the influence of some diverting train of thought, just as asthma will stop under any sudden and powerful mental stimulus.

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BRONCHITIS

By William Ewart, M.D., F.R.C.P.

The affections of the bronchial system had not any separate history before the beginning of the nineteenth century, when Badham (1810) introduced the name bronchitis, and Laennec gave his masterly description of the disease. Previously bronchitis was not clearly differentiated from phthisis or pneumonia, though it was distinguished from catarrhal pneumonia which was called "peripneumonia notha," a term which has now lost its significance. A permanent addition has since then been made to our nomenclature in "peribronchitis," which expresses a definite pathological lesion.

The clinical type of the disease is apt to vary with its distribution in the chest, with the degree of its severity, with its course and duration, and with its kind; and additional subvarieties arise from its manifold associations with other diseases and from the multiplicity of its causes. The size and calibre of the bronchi concerned are also important factors. The patency of the smaller, and especially of the non-cartilaginous, tubes largely depends on a free transmission of the mechanical forces of respiration; that is, on the even and symmetrical play of the surrounding pulmonary tissue. Tubes of minute diameter, whilst easily blocked by tenacious secretion, have little expulsive force for its removal; their inflammation is thus fraught with special consequences. The pathological results of bronchitis are not, however, limited to an interference with the air-conducting function, nor to changes in the mucous membrane; collateral changes may be set up. Bronchitis and bronchiectasis cannot, therefore, be satisfactorily studied in their various aspects without a brief preliminary reference to the anatomy and relations of the bronchial system.

The Normal Structure and Relations of the Bronchial Tubes.—The distribution of the air-tubes in relation to the pulmonary substance is such that the lobules, which may be regarded as the pulmonary periphery, occupy not only the surface but also the centre of the organ.

The perfect and even respiratory movements of the lung, associated with a minimum of pleural friction, are essentially dependent upon a uniform patency of the air-tubes. If the central lobules should fail to expand, compensating stress will fall upon the outer periphery—a result clearly seen in emphysema. The bronchi distributed to the more central parts of the lung being shorter and narrower than those proceeding to the surface may, perhaps, be more easily obstructed; and in any portion of the lung structural conditions may place some of the tubes at a possible disadvantage. The part which these easily obstructed bronchioles may play in the genesis of bronchiectasis will be explained under that heading. Their temporary obstruction in bronchitis would tend to increase any pre-existing over-distension of collateral lobules.

The relation of the bronchi to the pulmonary parenchyma is not merely one of direct continuity; close vascular connexions establish a functional relationship between the respiratory surface of the air-cells and that of the intralobular bronchioles. With the pulmonary stroma the connexion is also intimate. In each lobule the peribronchial tissue (as well as the periarterial) is continuous with the perilobular tissue, and therefore also with the interlobular connective-tissue which binds together all the lobules. Lastly, with the visceral pleura the bronchi present a definite, though more distant, relation. The deep layer of the visceral pleura is fused with the perilobular investment of the superficial lobules; and the interlobular septa throughout the lung may be regarded as a continuous prolongation of this subpleural layer. The structure of the bronchi is as follows:—The epithelial lining, consisting of three layers of cells, (*a*) columnar ciliated, (*b*) pyriform, and (*c*) flattened (Debove's membrane), rests, according to Prof. Hamilton, on a tough, homogeneous, elastic membrane, the basement membrane, which is pierced only by the wide orifices of the mucous glands. An inner fibrous coat underlies this membrane, and is separated by the muscular coat from the outer fibrous coat in which are embedded the cartilages and the mucous glands.

The adventitia or outer fibrous coat is in intimate relation with the perilobular, and therefore with the intralobular tissue of each lobule. In the case of the larger bronchi there is also a direct connexion with the interlobular stroma. The adventitia is thus the medium of extensive communications, chiefly lymphatic, between the air-tubes and the rest of the lung; and in disease it shares in all those processes to which the term "interstitial" is applied.

The muscular coat, in addition to those functions which are obvious, may also discharge other physiological duties, a knowledge of which might throw light on pulmonary pathology. Hitherto we have heard more of the perversion of the function of the bronchial muscles than of their natural uses. It is generally admitted that they are liable to tonic spasm, and that this spasm and the resulting partial closure of the smaller air-tubes enter largely into the causation of asthma, and in varying degrees complicate the respiratory difficulties special to bronchitis.

The vascular system of the bronchi consists of the posterior or main bronchial arteries originating from the descending aorta, the anterior bronchial arteries supplied by the internal mammaries, and the small branches contributed by the oesophageal, mediastinal, and pericardial arteries; these vessels accompany the bronchi, supplying not them alone, but the entire pulmonary stroma with nutrient blood, the pulmonary artery being exclusively subservient to respiration. The capillaries of both sets of arteries anastomose freely in the alveolar district, and probably also in the mucous membrane of the air-tubes. According to Zuckerkandl, "only the larger bronchi are irrigated by the bronchial arteries, the terminal tubes being vascularised by the pulmonary artery, and the intermediate bronchi by both."

A similar intercommunication exists between the bronchial veins of the smaller air-tubes (and even, according to Zuckerkandl, of the larger ones) and the pulmonary veins. The bronchial veins also anastomose in the posterior mediastinum with the venous plexus formed by branches from the oesophageal and from the diaphragmatic veins (Hamilton).

The bronchial lymphatics take their origin in the inner fibrous layer, which is in lymphatic communication with the tunica muscularis and, through the thickness of the latter, with the abundant plexus of the outer fibrous layer, where probably they are chiefly discharged into the periarterial channels. Both fibrous layers contain lymphatics in abundance; but since, according to Hamilton, these do not traverse the basement membrane, no absorption would take place from the epithelial lining, and the emunction of the latter would be effected directly into the bronchial lumen.

Before and at its entrance into the lobule, the lobular bronchiole is in lymphatic connexion with the perilobular and with the interlobular network.

Within the lobule the lymphoid tissue described by Arnold (which also occurs under the pleura) is distributed around the alveolar passage and in the bronchial wall, as well as along the blood-vessels. The peribronchial masses are said to occur on the side of the bronchus opposite to that occupied by the accompanying pulmonary artery.

The activity of the *alveolar lymphatics* is shewn by the rapid absorption of the products of pneumonia. The interepithelial spaces and their connective-tissue corpuscles communicate with interalveolar plasmatic spaces or lymph capillaries, which converge either into the superficial or into the deep lymphatic network of the lobule. The larger vessels which arise from both these networks accompany the pulmonary arteries and veins to the hilum; whilst another set reaches the latter from the superficial subpleural lymphatic network. According to Hamilton, the subpleural lymphatics have but little intercommunication with the lobular.

In the carbon-injected miner's lung (which usually is not fibrosed) the entire lymphatic scheme is displayed; and this may be studied in Hamilton's beautiful illustrations. According to Hamilton, the soot

particles lie in the perilobular and interlobular tissue, around the pulmonary artery and bronchi, in the lymphadenoid bodies of the lung and of the bronchial glands, in the alveolar walls (sparsely), in their epithelial interspaces, and in their desquamated epithelial cells.

The absence of pigment from the visceral pleura might have been expected; its absence from the bronchial mucous membrane (which retains in the miner's lung the pink hue of bronchitis) is explained, by Hamilton and others, in connexion with the impermeability of its epithelium and basement membrane, the injection of the lymphatics taking place through the alveoli only, which but few of the inhaled particles would reach. The isolating property of the basement membrane thus demonstrated has much pathological as well as physiological significance.

Classification.—The study of bronchitis has suffered from the looseness of its terminology. Clinically some of the bronchial states are sufficiently clear, but our nomenclature of them is not free from obscurity, and this has complicated their classification. Provided, however, that the list of varieties is complete their arrangement in the enumeration is not of primary importance, as that order is apt to vary with the separate standpoints of general etiology and of bacteriology, or of clinical pathology and of morbid anatomy.

For our special clinical purpose there is no need of an exhaustive classification such as that attempted by Marfan; and for the purpose of description a simple grouping will be adopted. The *primary forms* can be included in a common description in spite of their specific differences in origin. The *secondary forms*, which are seldom acute, present special features which are noted in the description of the diseases to which they belong. *Chronic bronchitis* and its varieties are also capable of being handled as a clinical unit. Pseudomembranous bronchitis in all its forms, especially *plastic bronchitis*, calls for separate consideration; and this also applies to the aggravated forms of *chronic catarrh* known as *purulent bronchitis* and *fetid or putrid bronchitis*.

Nomenclature.—For the sake of accuracy and convenience there will be room in the future for some method in the use of the original terms which are still expected to do multiple duty. For instance, the comprehensiveness of the terms bronchi or bronchia is sometimes inconvenient. They are applicable to any of the air-tubes; but they fail to express essential differences well worthy of separate registration; take, for example, the wide difference which exists between the "non-collapsible conducting tubes" and those smaller tubes, the bronchioles, which are readily obstructed by lateral pressure or by internal swelling, by secretion, or by spasm. But a much more important distinction needs emphasising—that between the "conducting" bronchiole on the one hand, and on the other the "respiratory or terminal" bronchiole, which is continuous and largely identified with the infundibulum, and reacts to irritations in a pneumonic much more than in a bronchitic manner.

Similarly a set of alternatives, if possible in single words, might be

found for "bronchitis" to describe each of the different conditions which that name covers. Such a term we already possess in bronchiolitis, the use of which is likely to become more familiar. But bronchiolitis, besides being of variable degree as an acute, subacute, or chronic process, is not always of the same kind. When the alveolus becomes inflamed and consolidated we are dealing with a very different condition from that of the simple bronchiolitis which distends the lobule with air. This condition in one of its aspects is a pneumonia, in the other a bronchitis; or more strictly it is a combination of an "alveolitis" and of a "bronchiolitis." Jaccoud used the name "broncho-alvéolite" in 1886 in recording a case of phthisis in the adult, which he described as fibrinous and haemorrhagic. Quite recently, too, in a paper on "Primary Bronchopneumonia in Adults," Dr. H. G. Melville (1906) has employed the expression "bronchiolo-alveolitis" in order to identify a distinct clinical aud pathological variety. An easier term might perhaps be found in "alveo-bronchiolitis" (from *alveus, alveolus*, a bag). Both names indicate the implication of the alveolus, which is not even suggested in the name "infantile capillary bronchitis," although it lends to the affection its special character and its gravity.

Meanwhile in the following account we shall avoid departing from the old familiar terminology, and resort incidentally only for greater clearness to any other terms. As previously stated a separate place will be reserved for chronic bronchitis, for plastic bronchitis, and for putrid bronchitis, and the secondary forms will receive some brief mention.

The ordinary acute forms will be best dealt with in the first four groups, given in the following scheme. It will be noticed that their grouping is not determined by etiological considerations, but is framed on an anatomical basis,—that of the bronchial levels chiefly implicated, from the most superficial, that of the tracheal bifurcation, to those of the deeply-seated sublobular bronchioles, and of the still more remote terminal bronchioles. It should also be understood that the varying degree of severity and duration of the attack entails a subdivision of each of these groups into acute, subacute, and chronic varieties.

The Clinical Types of Bronchitis

A.—Ordinary Acute Forms

I. Trachea-bronchitis, a bronchitis of the main bronchi, by extension from a concurrent tracheitis.

II. The ordinary "mild bronchitis" limited to the larger and to the middle-sized tubes.

III. Acute bronchitis of the small tubes, including the sublobular or subterminal tubes. It is essentially a simple "bronchiolitis"; not exclusively limited to adults.

IV. The so-called capillary bronchitis of infants and the aged, implicating the intralobular or terminal tubes, and the infundibulum and alveolus; sometimes

termed bronchopneumonia. It is essentially an "alveo-bronchiolitis"; unusual but not unknown in adults.

B.—Other Forms

Chronic bronchitis, chronic bronchial catarrh, and bronchorrhoea.

Secondary bronchitis, and the special varieties of intercurrent bronchitis.

Plastic bronchitis.

Putrid bronchitis.

General Etiology.—A. *Remote Causes.*—(i.) No age is exempt; but during early adult life the disease is much less prevalent, in spite of greater exposure. Infants and the aged are particularly liable to it, and the periods of dentition favour its onset. (ii.) Except during the working periods of life, when men are more exposed, sex is held to make little difference. (iii.) Many occupations involve direct exposure to the extremes of temperature; others are indirect causes through relaxing influences or confined air. Some trades lead to inhalation of fumes, of soot, of dust, or of irritating particles which mechanically set up bronchitis, such as particles of steel, granite, chalk, charcoal, or cotton. (iv.) Luxurious habits both in diet and in clothing, and the overheating of rooms, induce a liability which is especially regrettable in childhood, when the individual tendencies are capable of some measure of control. (v.) Heredity and temperament constitute distinct factors; a delicate bronchial membrane may be inherited, as a delicate skin or any other outward peculiarity may be. Again, acquired constitutional weakness from any cause (poverty, overwork, prolonged illness, or intemperance) has an unfavourable effect. (vi.) Certain "general" diseases favour the production of bronchitis in a special degree; such are Bright's disease, gout, diabetes, enteric fever, and, particularly, measles and rickets. (vii.) Heart disease is a potent factor, in proportion as it leads to pulmonary and bronchial congestion. (viii.) Pre-existing chest affections—thoracic, pleural, and pulmonary—also dispose to bronchitis; but none in so great a degree as emphysema. (ix.) Relative impurity of air renders the inhabitants of large towns more liable to bronchitis than country folk. The deprivation of an open-air life, and long sedentary hours in crowded dwellings, are probably still more detrimental, as those whose lives are chiefly spent out of doors, even if they perpetually breathe town air, do not suffer in the same degree. In the Registrar-General's *Sixty-Ninth Annual Report* (for 1906) the general rate of mortality from bronchitis in England and Wales to every million living, which was 1034 (males, 1044; females, 1024), was surpassed by the rate in London, where the uncorrected rate averaged 1168 (males, 1140; females, 1193). The county of Lancashire has a much higher rate even than London, 1399 (males, 1430; females, 1368), whilst Cheshire averages only 917 (males, 845; females, 988), and shews a marked preponderance in the female

mortality, which is also noted in some other counties, and is most considerable in the smaller populations of Rutlandshire and Westmorland. It has been suggested as an explanation for the great mortality from bronchitis in Lancashire, which is unequalled in any other county in England and Wales, that it may be due to the sedentary lives led by so many mill hands, to the high temperature of the factories, to the mechanical particles suspended in the atmosphere, and perhaps to the effluvia which pervade the manufacturing districts.

The climate of this country, by its humidity and variability, favours the prevalence of bronchitis. But the variations which occur year by year in the mortality cannot be wholly explained as dependent upon annual oscillations in the weather. In recent years there has been a progressive change in the recorded rate in the direction of decrease. For the following statement I am greatly indebted to Dr. John Tatham of the General-Register office. "As before stated, the death-rate from bronchitis in the year 1906 was only 1034 per million of the English population; which is below the average rate in the decennium immediately preceding by 26 per cent. In the quinquennium 1876-80 the rate had been not less than 2377 per million. These are the recorded rates; but it is unsafe to assume therefrom that the mortality from bronchitis has actually decreased to this large extent. Unfortunately there is considerable variation amongst medical men in the names employed to indicate the same morbid condition. For example, the deaths from bronchopneumonia are correctly returned by most medical men under that name; whilst some medical men name it capillary bronchitis. In the former case the deaths so described appear in the national records under the head of pneumonia, and not under that of bronchitis. Again bronchitis is now frequently returned, in medical certificates, as a fatal complication of some general disease, such as measles or enteric fever; and in that event the death is referred to the general rather than to the local affection. In earlier years the statement of complicating, or 'secondary' causes of death, in medical certificates, was less common than it is at the present day. The foregoing considerations will obviously account for some at least of the differences of the recorded mortality from time to time, without assuming great changes in the actual fatality of bronchitis."

The relative influence exercised by the seasons is such as might be expected. Bronchitis is much more prevalent during the winter months than in summer, and the liability to it extends into early spring.

(x.) Aerial impurities may be solid, fluid, or gaseous. Strongly irritating particles or vapours may act as direct exciters of bronchitis, as for instance the vapour of ammonia, of iodine, of bromine; finely powdered ipecacuanha, pepper, or tobacco; and, in the case of those specially liable, the pollen of certain varieties of flowering grass.

B. *Immediate Causes.*—The most usual proximate cause is a chill. The patient is said to have "caught cold." The precise meaning of this phrase is obscure. So long as the adaptive mechanisms are in full efficiency mere extremes of temperature do not constitute a danger to

the mucous membrane, and a strong man may pass unscathed from one extreme to the other. Even infants and old people may breathe cold air with impunity, especially if it be dry, so long as they are adequately clad and in perfect health. The liability to "catch cold" is sometimes an individual peculiarity; more often it is acquired, but it is usually intensified by sundry debilitating causes and by faulty hygiene.

Very little is known concerning any functions of the aerial mucous membrane analogous to the regulating mechanisms of the skin for temperature. Their existence is rendered probable not only by the noticeable differences in individual susceptibility, but by the interdependence of the cutaneous and of the bronchial system in the process of "chill." There are two kinds of chill—that directly applied to the air-passages by cold and damp air, the body being at the time warm and well covered; and that which is due mainly to exposure of the cutaneous surface. In both cases the sensation experienced at the time is apt to be referred partly to the skin, the patient "feeling chilly all over," and partly to the air-passages, often to the pharynx or down the trachea. A nervous link is indicated by these paired sensations. Rossbach's experiments shew that application of cold to the skin is followed in one or two minutes by a reflex contraction of the tracheal vessels, and a little later by venous congestion and an increased flow of mucus. Any fault in the regulating mechanism, and particularly in its nervous factor, would leave the mucous membrane unprotected against the physical results of continued exposure to extremes; or incapable of that rapid adaptation which is our safeguard against sudden transition from one extreme to another.

Smoke is a powerful irritant, whether by its scorching effect when inhaled hot, by the mechanical action of the suspended carbon or ash, or by the irritating nature of the volatile products of combustion.

Steam, when inhaled from the spout of a kettle by the children of the poor, usually checks inspiration, and its irritating effects are limited to the upper air-passages; but when inhalation does occur the damage to the air-tubes may be extensive.

Suspended cold moisture, as in ordinary mist, seems capable of irritating very sensitive bronchi, but it is difficult to eliminate the chilling effect of the mist on the body surface; and it is noteworthy that when an equivalent amount of moisture is inhaled in crystalline form, as in a severe frost, its mere cooling effect is not as a rule resented. The nasal passages in nose breathing would of course exercise some warming influence.

Town fogs are directly responsible for a great deal of bronchitis. Consisting as they do of a mixture of suspended moisture with varying proportions of the products of combustion, fogs differ greatly in their irritating qualities. The fog is acid, and each droplet of water is coated not only with a minute proportion of some tar-like body, but with an equally minute quantity of sulphurous acid: a combination most likely to excite inflammation of the respiratory passages in delicate persons.

Irritant gases have been classified as non-respirable and respirable.

To the first group belong chlorine, ammonia, sulphurous anhydride, and the vapours of iodine and bromine. The danger of their continuous inhalation is obviated by the intensity of the irritation causing spasmodic arrest of respiration. A single whiff of ammonia is commonly followed by a transient watery flow from the mucous membrane.

Among the mildly irritating vapours ether, so largely used for surgical purposes, deserves special mention. In the case of small children, in the aged, and in those with limited respiratory surface, its use is to be avoided. A proportion of the instances of so-called ether-bronchitis may be regarded as due to exposure of the surface during the operation, or to the cold produced by the evaporation of the ether, rather than to any direct irritation of the membrane.

As regards temperature, we know that standing in a cold draught, staying out at sunset with insufficient wraps, keeping on wet clothing after severe fatigue, or sitting long with wet or cold feet are so many modes of causation of bronchitis by cutaneous chill. When the impression of chill is confined to the mucous membrane itself, the mischief is usually due less to the intensity of the cold than to previous exposure of the membrane to hot and impure air, and to its parched condition.

Intolerance of any but the milder kinds of atmosphere is most commonly the artificial result of injudicious physical education. It also belongs to states of debility and to the extremes of age.

The popular belief in the contagious character of common catarrh has received from time to time considerable support from the prevalence of epidemic catarrh and influenza. Although the latter disease does not exclusively attack the respiratory passages, still the almost universal coincidence with it of more or less inflammation of the air-passages must give it a place among the causes of bronchitis. In many instances the irritation, whatever be its mechanism, is severe, the cough being of a harassing type which resembles that due to mechanical irritants, and is not infrequently inveterate. Ordinary bronchitis has itself been attributed to a specific contagium.

Bacteriology.—Our reference to the bacteriology of bronchitis must be limited to a few leading aspects. (1) It is generally accepted that in a fairly clean atmosphere and in pure country air the contents of the smaller bronchi and of the air-cells are sterile. (2) It is equally well known that in contaminated atmospheres even the alveolus may contain a few micro-organisms. (3) If air be heavily charged with the products of a pure culture, these will not only reach the alveolus, but may pass into the blood by penetration. This was proved experimentally by Wrzosek. (4) The larger bronchi are apt to contain any of the organisms present in the air, and in addition those that may be in the nasal cavities and accessory sinuses, the tonsils, and the pharynx, together with hyphomycetes, such as *Aspergillus fumigatus*, *Oidium albicans*, and other samples of low vegetation. (5) In this exceedingly varied flora of the upper bronchi growth is favoured by the relative slowness of the process of cleansing as compared with the salivary function in

the mouth. In bronchitis this activity is greatly increased for all the strains, and it is rare to find any approach to a pure culture. (6) Nevertheless, in the infective fevers a special proliferation and virulence may be traceable to some of them, as for instance to Pfeiffer's bacillus and to the pneumococcus in bad cases of influenza, or to the ordinary streptococci, often found almost alone, according to M'Phedran, in the infantile bronchitis of measles, of gastro-enteritis, of syphilis, and of cachexia; or, again, to the *Micrococcus catarrhalis*, and to the *Bacillus coryzae segmentosus* (Cautley) in common catarrhs. (7) Among the ordinary tenants of the upper bronchial membrane are other organisms, including the *B. coli communis*, Friedländer's diplobacillus, and Löffler's bacillus, the *Micrococcus tetragenus*, staphylococci, and others. It is assumed that their saprophytic behaviour is turned to virulence under certain vicissitudes of their host, such as chill or exhaustion, under the collateral perversions of fellow strains such as those of a streptococcus, of a *B. coli*, or lastly under the invasion of some virulent infection such as enteric fever. Where such an invasion occurs, it is not itself necessarily responsible for the bronchial complication. This would be an "homologous bronchial infection" (as, for instance, a bronchial infection from the *B. typhosus* in a case of enteric fever), but this is stated to be rather the exception, and that a "heterologous bronchial infection" by some ordinary microbe is much more common (Horton-Smith). But in diphtheria, in tuberculosis, and in influenza, the rule is for a bronchitic infection to be of mixed type. Although our knowledge of the bacteriology of acute bronchitis is not so definite as might be desired, it is important to bear its infectious character in mind, especially in children.

Morbid Anatomy.—Prof. Hamilton's researches, from which the present description is largely derived, furnish us with the most systematic account.

(i.) *Acute catarrhal bronchitis* begins with a relaxation and distension of the blood-vessels of the inner fibrous coat; a few hours after this the basement membrane becomes oedematous, much swollen, and folded: twenty to thirty hours afterwards it loses its ciliated cells in patches, and some of these may be inhaled into the smaller bronchial tubes. Immature cells are supplied in great number by the proliferation of Debove's cells, and they contribute the cellular element of the bronchitic secretion. Absolute denudation of the basement membrane may occur, but only temporarily, and over limited areas. Desquamation and active secretion of mucus take place at the same time in the mucous glands. The entire thickness of the bronchial wall is swollen, congested, and infiltrated with leucocytes. Reparative changes are initiated by a diminution in the congestion, and in the dilatation of the vessels; and the cells gradually resume their normal development and functions. Throughout the attack the normal grey colour of the mucosa is replaced by a dull red.

(ii.) *Chronic Bronchitis.*—(*a*) The common form, the result of a series of acute attacks, is usually associated with much permanent emphysema

with intervening congested areas. The lower part of the trachea and the bronchial surface in general are congested and purple, and yellowish mucopus can be squeezed out of the middle-sized and small air-tubes.

The characteristic smooth and shiny aspect of the mucosa is due to the basement membrane being laid bare, only a few ill-shapen cells adhering to it; it is not always much swollen. Some dilatations may occur in the smaller tubes; the larger ones, on the contrary, may be slightly narrowed by the great thickening of their coats. The coats are densely infiltrated with cells, among which are seen many dilated capillaries—some of which may project into the thickness of the basement membrane,—many thickened arterioles, and over-distended lymphatics; these are especially abundant close to the cartilages which are vacuolated, and in various stages of absorption. The muscular coat may be hypertrophied, or on the contrary greatly atrophied; or even absent. The mucous glands also may be destroyed by cell infiltration, or on the other hand much enlarged, with active mucous transformation of the glandular and duct cells. Atheroma is frequently observed in the middle-sized pulmonary arteries in the subjects of chronic bronchitis.

(*b*) A separate form of chronic bronchitis is characterised by the peribronchitis fibrosa chronica of Virchow, and in some cases the fibrosis extends along the pulmonary lymphatics to the entire interlobular stroma. Instead of the common atrophic, rarefying emphysema, the lung tissue then presents diffuse condensing fibrotic changes.

Peribronchitis, which occupies so large a place in pathology, is not a condition capable of clinical demonstration. We know that it must be in progress, and are also aware that this is not immaterial. In reality it is an integral part of the structural changes of bronchitis. But there is a wide range of variation in the relative proportion of the peribronchitis and of the bronchitic changes, due to the special nature and irritating properties of the exciting cause, and perhaps yet more to the relative vulnerability of the peribronchial tissues in the individual. Peribronchitis is for that reason a much greater danger, and after death a more obvious lesion in the bronchitis of children than in that of adults, in virtue of the lymphatic character of the peribronchial sheath, and of the puerile vulnerability of all lymphatic structures, a vulnerability which reaches its climax in infants and children of the "scrofulous" constitution. Thus, whilst the clinical name is bronchitis, the clinical trouble most often is peribronchitis. Peribronchitis enters largely not only into the pathology of pulmonary tuberculosis in children, but also in that of the more acute infections which are grouped under the name of "Acute Bronchopneumonia." It may perhaps be said that the structural reasons why bronchitis of the small tubes of adults should rarely, and that of infants should almost invariably turn to bronchopneumonia, are on the one hand the minuteness of the calibre and the delicacy of the inner lining of the infantile bronchiole, and on the other hand the extreme vulnerability and proliferative swelling of its lymphoid outer sheath, a conjunction which renders obstruction and consolidation almost inevitable.

Physical signs common to all forms of bronchitis are so familiar that little more than a cursory review of them is necessary.

In shape and in size the chest tends to assume the inspiratory type, without deformity, but with marked elevation of the clavicles and shoulders sufficient to deepen the suprasternal and supraclavicular fossae. In consequence of this and of the distension and emphysema of the lungs, the diaphragm, liver, and heart are more or less depressed.

The thorax moves at an increased rate, but to a diminished extent. In severe bronchitis the inspiratory efforts fail to expand the chest, except in its upper part; and there may be inspiratory recession of the lower interspaces, and in children of the lower ribs and sternum. The abdominal muscles are thrown into strong and prolonged contraction during expiration.

Bronchial fremitus is felt on *palpation* during the entire respiratory act, or may be confined to inspiration or to expiration. Vocal and tussive fremitus are not materially altered.

Percussion in most cases elicits an increased resonance, which may, however, be masked by the strong contraction of the inspiratory muscles, to which is also due the peculiar tenderness of the chest. In small children the occurrence of bronchopneumonia or of collapse may detract from the resonance, or may even cause an imperfect dulness.

Auscultation.—Except at the upper part of the thorax, where they are often exaggerated, the respiratory sounds are much diminished or may be inaudible. Their coarse and harsh character is indirectly due to the feebleness of the alveolar murmur, which no longer veils the sounds produced in the bronchioles; a condition also observed in emphysema.

The adventitious sounds arising in the chest in the course of a simple bronchitis include the two great classes of the dry and of the moist sounds. To the first belong the large or sonorous, the small or sibilant, and the intermediate or subsibilant rhonchi. The Aeolian harmony often audible seems to be specially frequent where some emphysema has resulted under the joint influence of bronchitis and of muscular spasm. Another musical sound is the rhythmic sibilus which may be set up in the neighbourhood of the heart by each cardiac systole. Considerable extension and loudness of the bronchitic sounds, although indicating the implication of rather small tubes, and compatible with severe symptoms, are not usually of anxious import in themselves, since they indicate that air passes, though not freely, through a large number of tubes. Clicks are sounds of sudden and snapping character, lacking musical quality and difficult to interpret; being occasionally suggestive of a parched, at other times of a moist, condition of the tubes. Hence they are described in different instances as moist clicks or as dry clicks, thus occupying an intermediate position between the rhonchi and the mucous rales. The moist sounds of bronchitis have a gurgling or bubbling quality. Nomenclature and description are much simplified by calling them *mucous rales* (large, medium-sized, or small), in contrast with the hard or metallic rattles, crackles, or crepitations which may occur in the same chest if

bronchopneumonia, or lobar pneumonia, or phthisis should complicate the bronchial catarrh. The fine crepitations which may become audible over limited patches in capillary bronchitis, in association with abundant mucous rales elsewhere, illustrate this distinction.

Cardiac Signs.—In fully established bronchitis a more or less distinct epigastric beat is felt, the heart being not only depressed but enlarged also. The enlargement is mainly due to an over-filling of the right auricle and ventricle, evidenced by the distended jugulars; whilst the left ventricle presents little change. At the same time the absolute dulness of the heart is lessened in its size, and the heart-sounds in their loudness by the inflation and encroachment of the sternal fringes of the lung. A relative increase in the loudness of the second pulmonary sound also belongs to uncomplicated bronchitis.

The Clinical Account of Bronchitis.—The foregoing remarks have been devoted to the general aspects of the subject. When we approach its clinical description the impossibility of dealing with bronchitis as a whole becomes obvious. Its clinical varieties, which offer every gradation, must, therefore, be grouped into the sections given on p. 75. On the other hand, there is, perhaps, a practical advantage in not splitting up the section on *treatment* (p. 110), as many of their therapeutical indications coincide.

I. Trachea-bronchitis

It would be superfluous to enter here into any separate description of the inflammatory and catarrhal conditions of the main bronchi. They are not clinically distinct from those of the lower segment of the windpipe, and are, therefore, included in the affections of the trachea. This is the only part of the bronchial tree which has hitherto been accessible to direct inspection and to the possibilities of topical treatment. It is liable to severe lesions in connexion with intrathoracic affections, including ulceration and perforation, in addition to the more trivial, but often troublesome affections of a bronchitic order. (For treatment *vide* p. 110.)

II. Ordinary "Mild Bronchitis"

This is the common ailment which is most familiar to us whether as the "acute bronchial cold," or as the "subacute stage of chronic bronchial catarrh." The following account refers to the acute attack.

Symptoms and Course.—At the onset the attack may make itself felt as a severe cold in the chest, with deep-seated rawness, soreness, and parching; or it may begin in the larynx, or in the pharyngeal or nasal region, implicating also the ocular conjunctivae, the frontal sinuses, and the upper nasal cavities. Again, there may be more or less gastric and hepatic disturbance. Individual peculiarity and local susceptibility may help in each case to determine the site of invasion. That these are not,

however, the only factors is shewn by the regularity with which special forms, such as the bronchitis of measles, begin in special situations.

In acute cases much continued or intermittent chilliness, and in children slight delirium, or even convulsions (especially during the first dentition), may open the scene.

With every variety of onset there is a uniformity in the general symptoms. The pulse and respiration are moderately quickened, and the temperature is raised two or three degrees. The patient complains of respiratory discomfort, malaise, aching pains, headache, mental and physical languor, drowsiness during waking hours, and restless sleep—the results of the sudden check to the secreting and exhaling functions of a large section of the respiratory membrane. Almost invariably the alimentary mucous membrane is involved: the appetite fails, the tongue is heavily coated, the liver inactive, and the bowels torpid.

The symptoms of the disease when in progress may be classed as general, local, and respiratory. The local pain is seldom acute. The sensation is almost always retrosternal; it is variously described as "sore," "raw," or "burning," and the cough as "tearing." Tenderness on pressure is also felt at the sternum, but greater tenderness arises later from the constant strain of cough, and is then felt over the entire chest, but particularly over the pectoral muscles and at the base of the thorax.

The general symptoms are those of slight feverishness. The dry heat of the skin which follows the stage of invasion in most cases soon gives way to moisture. The temperature oscillates in the usual manner between a morning minimum and a maximum at night, but does not often rise very high. The pulse is moderately quickened and full; at first it is excited in action and almost bounding, but subsequently, with the advent of diaphoresis, large, soft, and undulating. The tongue is furred but moist, and the appetite bad; vomiting is unusual, constipation almost the rule. The urine is of the febrile type, with rather high specific gravity; in healthy subjects it is free from albumin, but loaded with lithates, pigment, and urea; sometimes it contains less than the usual amount of sodium chloride.

Respiratory Symptoms.—The patient's complaint is of tightness and oppression at the chest, rather than of dyspnoea, though this would be brought about by any exertion. Even in the position of rest the respirations are markedly quickened and proportionately more so than the pulse; they are shallow, and ultimately become laboured. Cough sets in early, especially in the laryngeal, tracheal, and bronchial forms of onset; rather later when the pharynx is affected first, and sometimes not for a day or two when the attack begins with coryza, in which cases sneezing is more common. At first the cough is dry and irritating, and usually associated with a tickling sensation in the larynx or trachea; when these structures are involved it is much altered in tone. It is easily set up by slight irritation, and is difficult to check. At a later date the paroxysmal character is no longer due to simple irritation of the nerve-endings over a dry and parched surface, or to a congested uvula

and epiglottis, but to the difficulty in expelling the viscid and frothy secretion.

The expectoration, in all cases of bronchitis, furnishes us with indications as to the stage and progress of the affection. From the healthy state of simple moisture, free from any perceptible excess of fluid or of mucus, the inflamed membrane, after a preliminary phase of checked secretion and of dryness, quickly passes through a stage of excessive hydration, during which the mucin of the cells is matured, though little of it may find its way into the saline watery flux. After a very few hours mucus is poured out more freely, and renders the fluid ropy; but it is still transparent as glass, and free from bubbles other than those produced in the mouth or in the larger tubes. The next stage is that of purely mucous catarrh. The secretion stiffens, and, in the smaller tubes, soon offers considerable resistance to the respiratory current. This is clearly seen in the amount of air-bubbles held in the mucus, which, although in itself hyaline and colourless, forms with them a white opaque froth. This is the "crude stage" described in ancient books. In cases of rapid resolution the mucus may soon undergo a secondary hydration, losing its bubbles, and coming up with less effort and in rapidly lessening quantities.

More commonly in the ordinary case of bronchitis the sputum passes through some degree of "coction" (to use again an obsolete term), losing together with its extreme viscidity and frothiness the hyaline colourless quality, and becoming either streaked or uniformly tinged with light yellow pus, whilst continuing to form as before a confluent mass in the receiver. In more protracted cases the admixture of pus gradually increases, and imparts a greater opacity and a greenish tinge to the sputum, which becomes less hydrated, quite free from bubbles, and ultimately nummular. This is a sign that the catarrhal process is lingering in the larger tubes. There is much analogy and yet a distinction between this expectoration and the more purulent and fluid discharge which from its quantity and inveterate character has received the name of purulent bronchorrhoea, and in which the individual sputa fuse into a mawkish yellowish semi-fluid mass. In the later stage of bronchitis the sputa remain distinct.

Haemoptysis, in simple uncomplicated bronchitis, is of exceptional occurrence; but a few streaks of blood may be seen in the earlier and drier stage. They are probably due to the sudden detachment of superficial layers of the membrane under the effort of cough.

Diagnosis.—The disease carries its own diagnosis in the obviousness of its symptoms, of its physical signs, and of its expectoration. The question can only be as to the distance it may have travelled into the smaller tubes; and this is answered by the absence of dyspnoea, of fine sibili and rales, and of foamy expectoration.

Prognosis.—As to the duration of the attack, the prognosis is of necessity somewhat uncertain, and is partly governed by atmospheric conditions. In healthy children, youths, and adults, especially if not

previously affected, complete recovery under appropriate treatment may be looked for within one or two weeks, according to the severity and extent of the inflammation. Any antecedent bronchial trouble would modify and unsettle the estimate. In infants and the aged it is wise not to fix any date.

As to danger to life, it is only at the two extremes of age, and in albuminuria, or diabetes, or heart disease, or cachexia, that anxiety is likely to arise. However much they may ultimately tend to shorten life, even repeated attacks of this mild form of bronchitis are never directly fatal in subjects otherwise sound. If the respiratory muscles be feeble, as in infancy, old age, or obesity, there is risk of *bronchopneumonia a retentis*, the termination of which cannot be foretold; the other risk, peculiar to the same group of patients, arises from weakness of the heart, and especially of the right heart, which may undergo dilatation and eventually paralysis; or the bronchitis, especially in the aged, may become chronic, and prove at length a fatal drain on an exhausted vitality.

Treatment (*vide* p. 111).

III.—Acute Bronchitis of the Small Tubes

No hard and fast line can be drawn between the four levels of bronchitis; they are not mutually exclusive. Any spread of the inflammation is invariably downwards; thus trivial beginnings may usher in more serious developments, and a slight catarrh of the upper passages may be the prelude to a deep-seated bronchitis. This may never progress beyond the subacute stage; nay, a chronic form of it is a priori admissible, and we do not lack post-mortem evidence of its occurrence, for instance, in the local lesions of pulmonary tuberculosis. Nevertheless, neither of these milder stages has occupied any clinical prominence. But the acute implication of the small tubes on any large scale at once establishes an entirely new situation by its more or less urgent interference with the aerating function. This explains, though it may not justify, the limited and conventional meaning which has attached to the name in acute bronchitis. Although a previous bronchitis of the middle-sized tubes may have set in and may still persist acutely, it is the superadded inflammatory obstruction of the small tubes that constitutes the attack of acute bronchitis. The result of our imperfect terminology has been to delay the clinical analysis of the other phases of this bronchiolitis. For the clinician a small-tube bronchitis has always been an acute bronchitis; and the only other variety hitherto recognised is its more intense degree as bronchitis acutissima, in short the asphyxial or suffocative bronchitis, which will first occupy our attention.

Morbid Anatomy.—The post-mortem appearances are almost invariably those of an over-distended, non-collapsing lung, the pale pink colour of which contrasts strangely with the deep cyanosis of the body surface, and is readily explained by the influence of the residual oxygen of the

distended air-cells on the reduced quantity of blood which their overstretched capillaries accommodate. The small bronchi present, on the contrary, a swollen and deep red surface of section. Their contents vary with the duration of the cases: in early deaths they consist chiefly of mucus; they are semi-purulent in those who have survived for several days. Exceptionally here and there a pulmonary lobule may be found collapsed, but pneumonic consolidation is absent. In all cases the heart presents the asphyxial condition, and the viscera are engorged.

Acute Suffocative Bronchitis of Adults and Children; Acute Suffocative Catarrh; Asphyxial Acute Bronchitis.—*Bronchial Inflammation and Spasm.*—We must frankly acknowledge our inability to apportion the share of each of these two factors during the individual attack or after. In some subjects anxiety of breathing is soon superadded to any slight tubular obstruction. The most familiar type is that of the fit of nervous asthma, in which there is hardly any bronchitis of the small tubes, much less any terminal bronchitis, and yet a maximum of suffocative distension with air. The opposite type is the acute attack in which the alveolar distension traced after death is hardly less extreme, but is due to the mechanical obstruction of all the small tubes by frothy or catarrhal secretions and by inflammatory swelling. Between these two types lies the unknown with its scale of varying combinations between these two factors of obstruction. The outcome of the attack will be benign in proportion to the equivalent of spasm, and ominous in proportion to the equivalent of inflammation.

Simple Infantile Acute Bronchitis.—It thus happens that in infants and small children who are most prone to respiratory spasm, the acute bronchial attack so common in teething, because it is mainly spasmodic and mainly productive, as in the adult, of simple emphysematous distension without any implication of terminal bronchioles, will often end in recovery. But owing to fewer deaths and to less obviousness of the instances of bronchiolar inflammation this infantile form of simple acute bronchitis has not hitherto been allotted its proper place in nosology.

Acute Suffocative Bronchitis of Adults.—It is noteworthy that in the adult the terminal bronchioles and the alveoli are much more tolerant of infective agencies than in children. Most probably the difference is one of vulnerability rather than of relative difficulty of access or penetration, and it is the larger bronchioles which in the adult seem to be the seat of the more intense irritability.

Symptoms and Course.—Although the attack may not have been without previous warning, and may have developed as an extension of a bronchial cold, the onset is usually well defined and severe. A characteristic feature is often the exceedingly rapid and general implication of the small tubes throughout the lung. Walshe says: "I have known life destroyed in forty-six hours, reckoning from the first moment of seizure, in a middle-aged adult, who in previous years had had more than one seizure." In the adult (and it is noteworthy that young

adults are rarely attacked) orthopnoea is the rule, and, as observed by Walshe, "maintenance of the head on a low level from the first, in a case otherwise grave, is of evil augury." It is hard to say to what extent superadded muscular spasm of the bronchioles may have increased the constriction due to inflammatory swelling.

More air is at first drawn into the lung by the strenuous breathing than can be expelled by expiration. Subsequently, in spite of the powerful contractions of the muscles of extraordinary respiration, the distended chest moves comparatively little, and ultimately the character of the respiration tends more and more to become expiratory and abdominal. The lower intercostal spaces are drawn in with each inspiration, but the ribs do not usually recede. The whole chest is enlarged, and the lungs over-distended by the powerful muscular forces applied to sufficiently rigid bones and cartilages. An excess of air is, as it were, locked in by the obstruction of the bronchioles: henceforth little passes through them into the lobules, whether in the shape of air or of secretion; and the direction taken by the latter is outwards, not inwards as in capillary bronchitis. The oxygen of the imprisoned air becomes exhausted, and the turgid veins and the asphyxial complexion of the patient warn us of the degree of the obstruction to the pulmonary circulation, and of the congestion of the overloaded right heart.

Expectoration is not suppressed as often occurs in the capillary bronchitis of infants. A fine white foam resembling "whipped egg" gives in the minute size of its bubbles the gauge of the tubes affected. An analogous "whipped egg" sputum (not always quite so fine) is sometimes observed in the sudden pulmonary congestion apt to complicate an anginal attack. In the absence of angina this sputum is diagnostic of suffocative bronchitis. A change to a coarser froth with the admixture of watery, hyaline, and subsequently of purulent mucus gradually occurs in the later stages of the more favourable cases.

The asphyxiating bronchitis of the adult is not complicated with any parenchymatous inflammation of the lung. Pneumonia is perhaps mechanically obviated by the intra-alveolar pressure of gas, and by the stretching of the alveolar vessels. At any rate this immunity is attested by the pulmonary appearances after death and by the observations of every clinical observer. Walshe says: "True pneumonia, lobular or diffused, is of purely exceptional occurrence; the parenchyma is often even usually pale"; and again, "but, without meaning to deny the possibility of the fact, I must observe I have never yet seen local collapse of lobules on an extensive enough scale in simple adult bronchitis (antagonised as it is by the distending influence of the disease on the alveoli) to justify me in looking upon it as a sufficing cause of deficiency of tone"; once more he says, "Bleeding is useless for the prevention of pneumonia, seeing that, in the adult, idiopathic inflammation of the tubes does not pass on to the parenchyma."

The later course of the disease need not be detailed at full length. The symptoms are those of a progressive asphyxia—a prolonged struggle

for breath, the duration of which is measured by the patient's cardiac energy. In Walshe's unsurpassed description:—

"As long as his strength permits, the patient sits erect or bends forward; but the body gradually yields; and it is not uncommon to find patients, while still perfectly conscious, lying sidewards or forwards with the head lower than the shoulders. In rare cases, a posture of this kind is adopted from the very onset.

"The sputa gradually diminish in quantity from failure of power to expectorate; the skin, generally livid or cyanotic in tint, falls in temperature, becomes covered with cold, clammy perspiration — sometimes copious, rarely attended with formation of sudamina; the expired air grows cool, the feet and hands swell, in protracted cases the anasarca rising to the trunk, unaided by coexistent disease of the heart, or of any other organ promotive of dropsy; fitful dozes lapse into a state of somnolescence, constant, except from momentary interruptions by the cough; muttering delirium, associated in some instances with slight convulsions, precedes a comatose state which is the immediate forerunner of death."

The pulse gains in frequency as it loses in power, ranging from 120 to 150 or more. The respirations, varying from 36 to 50, may ultimately recede from the maximum rate they had attained.

The temperature is moderately elevated. Dyspnoea, oppression, retrosternal pain, restlessness, and cough are the chief symptoms complained of.

The urine is scanty and concentrated. There is occasionally a transient albuminuria, but in spite of the great diminution in the oxygen supply, there is no sugar, and usually no excess of urates.

The physical signs are those of emphysema as regards diminution of the respiratory murmur, increased bulk of the chest and of the lung, depression of the diaphragm and of the heart, and pulmonary hyper-resonance, coupled with sibili in the smaller tubes, bronchitic rales and cooing in the larger tubes owing to the ascent within them of the frothy secretion.

"*The acute suffocative catarrh*" *of Laennec* is a special variety, characterised by its abrupt onset and the urgency of its dyspnoea, which, when it does not terminate fatally within 24 to 48 hours, subsides into the ordinary acute bronchitis of the small tubes. Dr. Samuel West in connexion with a case in a young adult, in which he repeatedly found diphtheroid bacilli in the sputum, throws out the suggestion that this remarkable affection may be due to a widespread bacillary infection of the bronchial system. He draws a parallel with some of the other major dyspnoeas, and in particular with the dyspnoea of (1) acute suffocative pulmonary oedema, associated with heart disease or kidney disease, or with hyperpyrexial and infective fevers; (2) of the acute inflammatory affections of the lungs and bronchi; and (3) of collateral fluxion and pulmonary failure, such for instance as may overtake a patient during the performance of paracentesis of the thorax or abdomen.

Diagnosis.—The only affections presenting any close resemblance to

acute bronchitis are acute asthma and acute pulmonary congestion, in both of which conditions the antecedent history and the history of the attack are helpful guides. Asthmatic manifestations and probably an inherited tendency have generally preceded the former, and albuminuria is a common antecedent of the latter. Uncomplicated *asthma* is apyrexial and free from heart hurry—and this peculiarity, in its singular contrast with the intensity of the dyspnoea, at once identifies the neurosis.

As *acute pulmonary congestion* is usually accompanied with some quickness of pulse and with some elevation of temperature, it needs more careful discrimination. In its worst forms it shares with the bronchial affection the symptom of urgent dyspnoea, and the usual physical signs of a respiratory impairment by deep-seated fluid obstructions. Mere differences in the degree of the dyspnoea are not distinctive; neither is there any difference in its kind. But the physical signs are not identical. Percussion usually brings out a more resonant note in bronchitis and a less resonant one in congestion in the adult. This is an essential difference, but it does not always apply to infantile and senile bronchitis with their usual pneumonic complication. Auscultation presents us with two well-defined types: the purely bronchitic, in which fine sibili and respiratory silence are the features; and the purely congestive, in which fine rales accompanying both the inspiratory and the expiratory phases testify to the permanence of bronchial patency and to the continued penetration of some air into the lobules.

A discussion of the *mixed forms* does not belong to this section, but as they are so well known, it will suffice to name them. "Passive and hypostatic" congestion, which is usually of broncho-pulmonary nature, is characterised by the even to-and-fro of its liquid crepitations; "capillary congestion" is distinguished by the coincidence of general bronchitic sounds with fine crepitations in small patches; and in scattered "pneumonic congestion" the stiffening lung is either silent throughout the cycle, or yields its volley of fine rales only at the acme of the inspiratory expansion. None of these auscultatory signs find their exact parallel in acute bronchitis.

Lastly, the expectoration is seldom absent in acute bronchitis, though it may be scanty at first. Its fine frothing is unequalled except by that of intense congestion in the "acute suffocative catarrh" of Laennec; and this is apt to be a pink froth. The rusty or lemon-tinged hyaline sputum of pneumonic congestion, and the watery deeply blood-stained sputum of passive congestion are both equally far removed from the bronchitic type.

The prognosis is anxious even in the best subjects. The worst cases are those of pre-existing emphysema with incipient or advanced dilatation of the right heart; these subjects seldom long survive the onset of a genuine bronchitis of the small tubes. Cardiac defects or inherent debility (whether from exhaustion or atheroma), chronic albuminuria, and the various cachexias greatly reduce the chances of recovery.

The duration of a fatal attack may be reckoned in hours, or may

"drag on to the tenth or twelfth day" (Walshe). The same authority has recorded unexpected recovery after long periods of an apparently hopeless condition, with cold clammy sweat and almost complete loss of conjunctival reflex. Such cases are rare; they seem to suggest that spasm of the bronchioles had contributed to the bronchial stoppage.

Treatment (*vide* p. 113).

IV.—Capillary Bronchitis

"Capillary bronchitis" has always been known to be specially prevalent in infancy and old age. The old name indicates the predominance of the clinical features of an inflammation of the terminal bronchioles at the onset; but it cannot be gainsaid that the evolution of the lesions and their pathological importance are mainly pneumonic. A more complete description of the two types of the disease belongs therefore to the section devoted to pneumonia. It has even been suggested that the term infantile bronchopneumonia might be substituted for that of capillary bronchitis. It is significant, however, that this has not been suggested in the senile variety. At the present stage this substitution would be premature for two reasons: the pathological etiology of the alveolar changes has not yet been completely worked out; but the existence of important varieties is attested not only by bacteriological analysis, but by the difference in type recognisable on closer inspection of the minute consolidations. On the other hand, there is no uniformity in the later behaviour of the pulmonary tissues when the fatal termination has been unusually delayed. These later changes include in the case of infants suppuration, necrosis, and a vacuolation by a process of multiple breaking down, a striking instance of which was recorded by Dr. Howard Tooth. Capillary bronchitis or bronchiolitis may thus finally assume an ulcerative type. But in addition to this spurious dilatation of the bronchioles, a genuine acute bronchiolectasis (*vide* p. 161), apt to be suppurative though free from ulcerations, is one of the final results. In these directions the affection preserves an intimate relation to the bronchial system, and the bronchitic type is not entirely merged into the pneumonic. In view of this, a neutral and yet localising name such as "alveobronchiolitis" offers certain advantages.

Infantile Capillary Bronchitis.—*Infantile bronchitis* attacking the small tubes almost inevitably disables some of the respiratory districts at an early date, owing to the very unequal local resistances of the chest walls, and to the influence of decubitus. At given spots the thorax fails to draw out the subjacent lung, and is therefore dragged in. The subjacent lobules quickly become airless and collapsed, and are henceforth sealed against the entrance of gases, fluids, and solids alike; they are incapable of becoming pneumonic. Collateral emphysema results from the increased respiratory stress thrown on other parts, and, thanks to their early overdistension, these lobules also may remain free from pneumonia. It is in the remaining portions of the lung, imperfectly expanded and traversed

by enfeebled respiratory currents, that the changes occur. The secretion, failing to be expelled, sets up by its stagnation intralobular irritation and a tissue-reaction which is mainly proliferative.

Symptoms and Diagnosis.—Clinical investigation is still powerless to identify the varieties, but the history of the attack, combined with the physical signs, generally suffices to establish the diagnosis of the main affection.

The signs are those of pulmonary collapse at the anterior and lateral base of the thorax with inspiratory inward suction at the costal arch, and of emphysema of the upper part of the lung. The resonance due to the latter disguises the dulness which otherwise might have arisen from any pneumonic condensation. Nevertheless examination may reveal a lack of freedom and fulness of the auditory and tactile vibrations. Little air enters the chest in spite of the strenuous efforts of the upper inspiratory muscles and of the diaphragm, the contractions of which drag the sides of the chest inwards instead of expanding them. Sibili may be heard at first, but they are soon replaced or silenced by rales, the loudness of which, always great in the small chests of children, is intensified by any existing collapse or consolidation, and precludes the distinct perception of any bronchiolar or tubular breath-sound. In reality these rales, the only sounds audible, do not arise in the capillary bronchi, but are produced by the to-and-fro movements of the secretion within the imperfectly swept medium-sized and larger tubes.

Exhaustion is an early feature; the patients, if not too young to be able to sit up in orthopnoea, rapidly lose that power; and lie pale, livid, and helpless, with hurried respiration, dilating nostrils, and extremely rapid pulse. Expectoration does not occur in the younger children, or but rarely, and from an early period in the disease cough may be absent; but both the cough and the dyspnoea are prone to paroxysmal aggravations after remissions.

The temperature varies with the amount of pneumonic action, but probably also with the susceptibility of the individual nervous system. It may rapidly lessen with the advent of cardiac exhaustion and coma.

Prognosis.—The disease is usually fatal unless we succeed in arresting it at its earliest stage. Its later developments, except in relatively robust constitutions, are practically hopeless. The duration of the urgent symptoms varies, but, for obvious reasons, is on the average much shorter than in ordinary bronchopneumonia. The acute stage of the disease does not often exceed five or six days; it commonly destroys life at an earlier date.

Treatment (*vide* p. 115).

SENILE CAPILLARY BRONCHITIS.—*In old age* rigidity of the thorax, degenerative changes in the lung, such as widening of the alveoli and of the air-tubes, atheroma of the pulmonary artery and relaxation of the pulmonary veins, loss of inspiratory energy and considerable loss of general expiratory power, and especially of the expulsive power of individual districts, the expansibility of which may have been reduced by

pleural adhesions or by the reticular fibrosis left behind by former attacks, are some of the factors determining the special forms of capillary bronchitis. The minute diameters of the tubes and the yielding of the thoracic parietes, to which are due the pulmonary collapse and collateral emphysema distinctive of the infantile form, are conditions conspicuously absent. The character is that of passive retention rather than of primary bronchial obstruction, though this element is not entirely excluded. Gravitation has a larger share in determining the locality of the changes; and the basic and posterior regions are affected with much greater regularity than in the infant. For these and other reasons the ingravescent, slowly developing form, beginning in the medium-sized tubes, is of special frequency in senile bronchitis. Again, the tissue reaction is of a different quality. Peribronchitis and alveolar wall infiltrations are ill-developed. The consolidations are definitely lobular, or, owing to the even operation of gravitation, may become confluent. At the same time they are less dense and are usually sodden with passive congestion and with oedema, which are not features of the infantile variety.

Another important difference is the absence of the condition described as acute bronchiolectasis, and of its counterfeit pulmonary vacuolation by multiple necrosis. But bronchiolectasis of the fringes is not excluded; and sometimes it may be the recent result of a purulent bronchitis, a not uncommon event.

Course and Termination.—The affection is usually ushered in by a pharyngeal, tracheal, or bronchial cold, which more or less gradually assumes the character of general bronchitis; or it may be grafted upon a chronic catarrh. The extension of the inflammation to the bronchioles is marked by moderate pyrexia, paroxysmal cough and dyspnoea, laboured expectoration, a dusky flush changing to pallor, a rise in the rate of pulse and respiration, and great prostration. All appetite is lost, the tongue becomes dry and brown, and muttering delirium sets in, to be followed by deepening coma. In the less rapid cases, evidence of a low form of bronchopneumonia, associated with oedema and with the signs of bronchitis, may be ultimately obtained at the bases; but, as a rule, the exhausted state of the patient forbids any searching examination of the posterior pulmonary regions. In extreme old age treatment is unavailing, and the disease is almost invariably fatal.

Treatment (*vide* p. 117).

Acute suffocative pulmonary oedema, perhaps the most dramatic event occurring at the confines of the bronchial and alveolar systems, is a result of failure of the compensating mechanisms of the broncho-pulmonary circulation, when the remarkable power of the alveolar capillaries and lymphatics for the absorption and content of fluid begins more or less suddenly to fail. In Welch's opinion this is due to a loss of proportion between the power of the two ventricles, and particularly to a relative failure of the left.

In its gradual and insidious onset pulmonary oedema is a familiar termination of many chronic diseases of the circulation. In advanced

cardio-renal disease it is apt to develop with unexpected rapidity. The enfeebled heart is no longer able to keep the respiratory pump going; nothing is coughed up, and unless help should be at hand the patient is submerged by his own transudation.

But most uncommon, most strange, and hitherto inexplicable is the *acute pulmonary oedema* of clinical authors, which suddenly without any warning overwhelms persons apparently healthy or at any rate not far advanced in disease, for instance the profuse albuminous expectoration very occasionally induced by paracentesis of the pleura. The problem is why the alveolar circulation should utterly break down at a time when the cardiac energy is still equal to the expectoration of the entire load of fluid as a white or pink froth. No less strange is it that such grave attacks should not be more often fatal, and that they should be apt to recur sometimes with great frequency, or after one, two, or even three years' interval of health. Remarkable cases were recorded in 1902 (Lindsay Steven, Lissaman); and the subject has been much discussed recently (Reissman, L. Williams, West).

The diagnosis of this fulminant congestive oedema is at first difficult to make from that other rare affection the acute suffocative catarrh of Laennec. But its true nature is revealed as soon as the froth begins to be brought up by the incessant cough. Rales occupy the entire chest; but the percussion is resonant.

The prognosis turns upon cardiac endurance; it is least favourable in crippling valvular lesions, and angina pectoris.

The treatment is guided by our present view of its pathology. In the acute oedema *sine tussi* of renal disease venesection is a sovereign remedy. It should prove no less valuable in the cases of a more active struggle for life with cough and expectoration. After lightening the heart's labour, the next indication is to keep up its strength by judicious measures of support and stimulation.

Chronic Bronchitis, Chronic Bronchial Catarrh, and Bronchorrhoea

In this brief review of a wide and important subject, Walshe's division into four clinical groups will be adopted.

(*a*) *The simple winter cough*, moderate, not disabling, accompanied with the easy expectoration of a yellowish-white mucopus, is merely an expression of the bronchial irritation set up by atmospheric conditions; it is frequently observed in children and young adults, as well as in older people.

(*b*) An aggravated form of the same winter cough is peculiar to *chronic bronchial catarrh.* The health and strength suffer; and the patients are invalids, though often struggling to pursue their avocations. Decided functional and some organic change may be traced in the organs of respiration, of circulation, and of alimentation; such as short

breath, venous fulness both general and portal, and delicate digestion. The winter is spent in a succession of slight pyrexial relapses, during which the expectoration, habitually loose and muco-purulent, may, after being frothy for a while and difficult to raise, become unduly abundant and puriform. The feverish bouts may last a week or a fortnight, during which the appetite is in abeyance, the tongue, stomach, and liver are out of order, and considerable weight is lost. Between these attacks the patient regains some of the previous health and strength, but never shakes off the cough, which may even last, in a modified degree, through the summer.

These patients are protected from graver risks by their general delicacy and invalidism; but the process is progressive and devitalising through the inevitable degeneration occasioned in the lung and in the heart. Atrophic emphysema and progressive muscular disablement are its direct results, inducing premature senility and shortening life.

(*c*) *Bronchorrhoea* indicates a special group in which the constitutional factor has probably no less a share than the pulmonary changes. Two varieties need description:—

(i.) The thin mucous or thin watery bronchorrhoea is thus described by Walshe:—"In this variety paroxysms of cough and dyspnoea, which may be of almost daily occurrence, or even more frequent, are relieved by copious expectoration of a thin, watery fluid, or of a ropy, gluey, transparent substance, like raw white of egg mixed with water; a quarter of a pint of this may be secreted in the course of half an hour on the decline of a paroxysm." Though sometimes fatal in the aged, the flux is regarded by Walshe as occasionally useful in relieving pulmonary congestion due to mitral disease. This singular affection is well identified by the name of "bronchorrhoea serosa" given to it by Biermer, by that of "mucoid asthma," or by its original name "chronic pituitous catarrh," used by Laennec. The paroxysms of dyspnoea and mucorrhoea may be of isolated occurrence in the morning after waking; and the chest, after two hours, may be comparatively clear for the day: or the discharge may be repeated once or twice, producing in extreme instances a daily output of three or four pints; and this may last for years. Lebert mentions a case of survival to the age of eighty-two, after thirty years of bronchorrhoea; but Wilson Fox regards gradual failure as being the common tendency, together with increasing dyspnoea and delicacy of digestion. Pulmonary and cardiac degeneracy progressively lead to emaciation, anaemia, cyanosis, oedema, and exhaustion.

Much obscurity still attaches to the pathology of the affection; and it is still doubtful whether the disease is primarily associated with emphysema and bronchiectasis, or whether these be merely secondary changes.

(ii.) Purulent bronchorrhoea or bronchial catarrh is a severe, inveterate, and progressive affection refractory to treatment unless aided by climate. The bronchial discharge resembles in general character that observed in the diffluent stage of chronic catarrhal bronchitis during the exacerbations

noted under (*b*); but generally exceeds it in quantity, and in the semi-fluid, mucoid nature and mawkish odour of the pus. Pathologically the affection differs from simple chronic catarrh, chiefly in the extent of the bronchial and pulmonary changes. The mucous membrane is thickened, the bronchial walls infiltrated, and the calibre of the smaller tubes increased, though there need be no sacculation or extensive cylindrical dilatations such as belong to bronchiectasis. Between these two conditions there is, however, no strict demarcation, and mixed forms are met with. Emphysema is a direct and never-failing result of the loaded state of the bronchial system, and of the constant strain of cough. The atrophy of the pulmonary parenchyma contributes the progressive element in the disease, and renders it incurable after it has lasted for considerable periods.

The amount of the expectoration, which may reach one, two, or even three pints daily, is in itself a serious drain; and the cough is a severe tax on the strength. Night sweats, an habitually subpyrexial temperature, and the recurring anorexia or dyspepsia are additional depressants. In connexion with the latter, or with disturbances in the function of the liver, or with temporary retentions or inflammatory conditions in some of the bronchi, the mawkish secretion may become fetid in odour, sometimes almost gangrenous; and this reacts most unfavourably on the general state.

In spite of these distressing and wearing symptoms, the resistance of some of the patients to the fatal tendency of the disease is remarkable, and should encourage every effort to procure for them the healing effect of appropriate climate. Failing this, recurring winters bring with them steady aggravation, and life may be cut short by intercurrent broncho-pneumonia, or may lapse from gradual exhaustion and cardiac dilatation.

(*d*) In the fourth classical variety, that of *dry chronic bronchitis*, the sputum presents characters exactly opposite to those which have just been described. It is extremely scanty, and consists of semi-transparent, tough, pearl-like, roundish, small masses, apparently a highly concentrated and partly dehydrated form of hyaline mucus, in which Charcot-Leyden crystals or Curschmann's spirals are usually contained. The peculiarity of the sputum led Laennec to apply to the affection the name of "dry catarrh," although at times a little watery fluid may be expectorated. The distinctive clinical features are the distressing paroxysmal cough, causing much soreness at the chest, and the dyspnoea and oppression of breathing, intensified by the cough and in most cases kept up by the emphysema, which almost invariably complicates these cases. Laennec described this form as exceedingly prevalent; but, as pointed out by Wilson Fox, he included under "dry catarrh" not only the asthmatic cases, but all forms of nervous and sympathetic cough (gastric, hepatic, hysterical). Walshe regarded the symptoms as mainly due to active congestion of the tubes. Bronchial spasm is doubtless largely associated with the congestion; indeed, bronchial susceptibility and bronchial irritation are its unmistakable etiological factors. One of the forms of

chronic gouty bronchitis belongs to this type. Dry catarrh is also said to be prevalent at seaside places, and to occur after the cure of chronic cutaneous eruptions, and in those weakened by excesses. The physical signs are those of the dry stage of acute bronchitis.

Treatment (*vide* p. 118).

Secondary Bronchitis, and the Special Varieties of Intercurrent Bronchitis

Bronchitis is a complication common to many acute disorders; it will suffice briefly to indicate the relation which the bronchial affection bears to the several diseases.

(i.) The most important group is formed by prevalent affections such as whooping-cough, influenza, summer catarrh, phthisis, and measles; of the last bronchitis is an essential and prominent feature.

(ii.) In some of the continued fevers, but especially in typhoid fever, a varying degree of bronchitis is almost the rule; but its importance is rarely of the first order, and the same remark applies to cases of typhus fever. In enteric fever the severity of the early bronchial catarrh may occasionally mislead the physician for a day or two; and in protracted and exceptional cases the unabated persistence of bronchial rales may arouse uneasy suspicions of general tuberculosis. A malarial bronchitis has also been described.

In scarlet fever and in small-pox bronchitis is not a regular symptom. The occurrence of bronchitis in rheumatic fever, fortunately infrequent, was, before the introduction of the salicylic treatment, a most painful and dreaded complication; it still remains a serious trouble, in spite of the early relief now afforded to the articular pain.

(iii.) Gouty Bronchitis.—In most gouty subjects the bronchitic complication is local rather than general, striking at the mucous membrane rather than at the muscularis, and excited in response to surface-irritation by atmospheric influences rather than to medullary irritation by gastro-intestinal fermentations. In a minority only, that of the gouty neuro-asthmatics, the trouble is mainly spasmodic. Respiratory spasm does not usually complicate the common gouty bronchitis. The inflammation most often remains limited to the larger bronchi which share with the pharynx and with the larynx a more direct exposure to the irritation of cold, dry, or impure air. This mode of production is more likely than that from any assumed deposits of urates in the bronchial mucous membrane. At any rate the search for crystals has not led to any satisfactory result; and Bence Jones' case of sodium urate in the bronchioles has remained a solitary observation.

It is important not to overlook a third form of gouty bronchitis of mixed type and of greater acuteness, in which some of the smaller tubes are involved, and a troublesome spasmodic element may be superadded.

A correct appreciation of the etiology underlying these cases will give us the line for their successful treatment (*vide* p. 118).

(iv.) In other affections bronchitis is only an occasional complication. Among them chronic disease of the kidney probably takes the chief place, both as regards the occurrence and the gravity of secondary bronchitis. Gout is also prominent for the frequency of bronchial symptoms. Reference has already been made to the "dry bronchial irritation" so often observed in the gouty, independently of any articular seizure. In cases of retrocedent gout bronchitis may assume alarming severity, and is then probably characterised by extreme congestion. Severe bronchitis of a congestive and catarrhal type may, however, also occur as a precursor of the arthritic attack, usually subsiding with the onset of the latter. A syphilitic bronchitis was described by Graves, by Stokes, and by Munck; and Walshe bestows two pages upon its discussion. It was supposed to occur prior to the cutaneous eruption, and to alternate in gravity with the latter. Bronchitis was also described as complicating cases of syphilis between the secondary and the tertiary stages; and again during the tertiary stage, when it might be unilateral, whereas in the secondary stage it was said to be invariably bilateral. Nothing has been added to Walshe's description, which is reproduced by Wilson Fox. Indeed, syphilitic bronchitis does not now hold any independent place, and of late years has obtained no recognition; although considerable attention has been given meanwhile to the study of pulmonary syphilis (*vide* p. 420). The scrofulous bronchitis of Graves is another constitutional variety which has failed to obtain a permanent footing in the practical nomenclature of the disease. Among blood diseases, anaemia, chlorosis, and pernicious anaemia do not especially favour the occurrence of bronchitis. In scurvy, however, bronchitis is not an infrequent complication, and is often associated with haemoptysis, which does not belong in a comparable degree to any of the other forms, except the cardiac and the ulcerative varieties including phthisis and bronchiectasis.

Walshe draws attention to the occasional admixture with the sputum of substances derived from the blood; such as bile in icterus, sugar in glycosuria and diabetes, urea or its antecedents in uraemia.

(v.) A special group may be made of those forms of bronchitis which are dependent upon pre-existing pulmonary or intrathoracic disease. Aneurysm, mediastinal growths, or cicatricial stricture of a bronchus (usually syphilitic, *vide* p. 425) may give rise below the seat of stenosis to a localised bronchitis or bronchiectasis, and this may ultimately lead to disorganisation of the pulmonary substance. This result, which is very apt to follow in the rare instances of primary malignant disease of the bronchial mucous membrane, is not often observed in that of the lung, nor in secondary peribronchial malignant disease, whether generalised or occurring in single or multiple deposits. I have observed that the presence within the lung of separate malignant masses of moderate size, even in large number, may, owing to the distension of the intervening pulmonary tissue, give no signs of consolidation either auscultatory

or percussive, and yield only the common physical signs of bronchitis. Gangrenous ulceration into the root of the lung or into a large bronchus is a frequent mode of death in oesophageal cancer, and is preceded by the signs of severe bronchial irritation. Emphysema stands in the most intimate relation to bronchitis both as cause and effect. This association is fully dealt with in another article (*vide* p. 475). The close connexion existing between pleurisy, bronchitis, and catarrh is a matter of everyday clinical observation, and it will be briefly studied under a special heading. Pulmonary phthisis is invariably in part, and often to a great extent, a bronchitic process : it is enough to indicate that, in addition to the general bronchitis which is an intermittent complication of most cases, the local deposits and the local pleurisies of early phthisis determine strictly localised bronchial catarrhs which often raise the first alarm and suggest an examination of the sputum. Lastly, acute pneumonia is sometimes associated with well-marked bronchitis, which forms a most serious, though by no means necessarily fatal, complication. I have observed bronchial haemorrhage persisting for several days as a result of this combination. In the pneumonia of influenza the association with bronchitis is the rule ; but here the relation between the two diseases is reversed. Bronchitis begins and pneumonia may follow (*vide* art. "Influenza," Vol. I. p. 942).

(vi.) Another special place must be reserved for the truly secondary bronchitis of mitral disease, in which clinically, as well as anatomically, three stages may be identified : (*a*) A passive congestion of the mucous membrane, the mechanism of which has been described by every writer on valvular disease of the heart as the chief cause of the well-known "heart-cough"—short, slight, dry, and habitual, and especially common in mitral stenosis. (*b*) A mild chronic catarrhal bronchitis, easily set up and difficult to throw off, may occur in both kinds of mitral disease ; but is most frequent in mitral regurgitation. It is not, or is but occasionally, associated with streaking of the sputum. (*c*) A disabling acute bronchitis is the almost invariable agent in overthrowing the fine adjustment previously maintained between the task and the strength of the ventricles. The rest and the treatment necessitated by the cardiac breakdown may subdue for a time the bronchial trouble ; but in both forms of valvular disease the bronchial complication inevitably reappears with the relapsing failure of energy of the right heart. At this final stage the process is almost entirely passive and dependent upon the engorgement of the bronchial circulation. In cases of pure mitral stenosis previous pulmonary apoplexies may have cleared up ; but their aggravated recurrence often has a direct share in hastening the fatal event. More commonly, in mitral stenosis combined with regurgitation as well as in pure mitral reflux, the expectoration becomes watery with the onset of hypostatic pulmonary congestion and oedema ; and the final obstruction of the air-tubes with frothy mucus is the immediate result of cardiac and of general failure.

Bronchitis and Bronchial Catarrh in their Relation to Pleurisy.—(*a*) *Acute Pleurisy with Bronchitis, or Acute Pleuro-Bronchitis.*—The not

infrequent association of acute pleurisy with an acute bronchitis of the middle-sized tubes is the more worthy of attention, as there is not between these affections that necessary nexus which exists between pleurisy and acute pneumonia; and their occasional combination may be regarded as a definite clinical complex. This view finds support in the etiology and mode of onset, the two affections often arising from one and the same exciting cause and with a simultaneous invasion. I have long been in the habit of using the name "pleuro-bronchitis" to suggest something more than an accidental coincidence. The occasional occurrence of bronchitis in conjunction with rheumatic fever makes it the more probable that the rheumatic tendency, in itself so often answerable for attacks of pleurisy, may be at the root of this association, even in the absence of any arthritic manifestations; in the same way as non-articular gout is a common and fully recognised factor in the causation of bronchitis.

Cases of this kind are usually classed as "pleurisy with bronchitis as a complication"—a description justified by the relative prominence of the two sets of symptoms. When the pleurisy, as often happens, is of the dry variety, the physical signs of the bronchitis are those most easily obtained; whilst the more urgent symptoms belong rather to the pleural affection. In cases with considerable effusion this relation is reversed; extensive dulness is a prominent physical sign, but the urgency of the symptoms is largely due to the bronchitis, and is often in excess of the loudness of the auscultatory signs special to the latter. When the diaphragm is implicated in the pleurisy, the combined affection assumes unusually severe features, owing to the acutely painful dyspnoea, and to the interference with the mechanical function of cough in clearing the air-tubes.

(β) *Chronic Bronchial Catarrh associated with Pleuritic Adhesions.*—It is unusual for the acute attack to be continued into a chronic bronchitis; on the other hand, an eventual agglutination of the pleural surfaces, and especially a sealing up of the diaphragmatic groove, are fertile sources of recurring and ultimately of permanent bronchial trouble, in the shape of a localised basic catarrh. Of all local bronchial catarrhs the most common is the apex-catarrh of phthisis, or the recurrent simple apex-catarrh so often determined by the indurated and adherent scar of an old tuberculous lesion. In both cases the same mechanical influence is exerted by the adhesions in hampering the pulmonary movements and in interfering with the systematic play of the expiratory currents.

At the base, and particularly at the lateral base, distinguished in health by its active inspiratory movements, the local catarrh is apt to lead to extensive tissue changes. It is customary to speak of the affection as a "chronic pulmonary catarrh," and of the ultimate anatomical condition as a "chronic interstitial pleuro-pneumonia." We should not lose sight, however, of the essentially bronchitic origin of the mischief. The localisation and the permanence of the catarrh are primarily due to the paralysing influence of the adhesions. The combined irritations exerted within the air-passages by the retained secretion, and without by the recurring

respiratory traction, may set up a purely secondary fibrosis; and in some cases the fibrosis is mainly perilobular. Sometimes, however, the affection remains to the end essentially bronchitic with a tendency to rarefaction rather than to condensation of the pulmonary substance. Further consideration will be given to this subject in the article on "Bronchiectasis."

Plastic Bronchitis

This curious and rare disease, the earliest mention of which seems to have been made in 1697 by Clarke and Lister, has been repeatedly observed since. Biermer deals with a series of fifty-eight reported cases; but Peacock had previously given the first collection of cases on record. Lebert treats exhaustively of the same subject. In 1889 Dr. Samuel West collected fifty-two cases recorded since Lebert's article, and compiled a full bibliography. Plastic bronchitis, according to Biermer, occurs twice as frequently in the male as in the female sex, but is not confined to any age from early infancy to advanced life, though most commonly observed in the intervening period. It is still a pathological enigma.

The membranous exudations sometimes occurring in the air-passages form a large and varied group. False membranes may originate from the action of strong fumes or irritating fluids. The inhalation of steam (Parker), or of the fumes of ammonia, or of alcohol in the shape of eau-de-Cologne, are well-known instances. Again, the introduction into the air-passages of strong solutions, such as lactic acid, has been followed by plastic exudation (cf. Hoffmann); and Fritzsche describes a case in which he attributed the latter to the internal use of iodide of potassium.

As a result of disease, thin false membranes have been observed in the bronchi not only in instances of diphtheria, phthisis, erysipelas, variola, scarlet fever, measles, typhoid fever, and sewer infection (as in the cases of Picchini, quoted by Magniaux), but also in ordinary bronchitis, or pneumonia (R. Koch), in various pulmonary and cardiac diseases, in articular rheumatism (Degler), and in pemphigus (Mader).

From all these varieties of membrane, as well as from the rarer forms which have been described as primary diphtheritic and primary pneumococcic (Magniaux), the membrane of plastic bronchitis differs in its greater firmness, which allows it to be expectorated in considerable arborescent masses. The casts occasionally brought up after haemoptysis could alone compare with the latter in size and in consistence, but their origin and their composition are both sufficiently manifest. Thus whilst presenting distant affinities with the minute bronchiolar and sometimes the coarser bronchial plugs of pneumonia, with the tubular casts of diphtheria and of membranous tracheitis, and even with the occasional intratubal mucous inspissations of acute bronchitis seen chiefly in children, the formation of a continuous arborescent mould of a considerable portion of the bronchial tree stands by itself as a well-defined, although hitherto unexplained pathological process.

Whether this feature may be trusted as a sufficient indication of the pathological individuality of the affections is doubtful. Plastic bronchitis may possibly not always be of the same kind; it may be due to a variety of causes, just as there are distinct varieties of pseudo-membranous affections. Again, the fact that most of the latter have been traced to a bacterial origin, suggests that a similar causation may at some future time be made out in plastic bronchitis. In spite of this uncertainty as

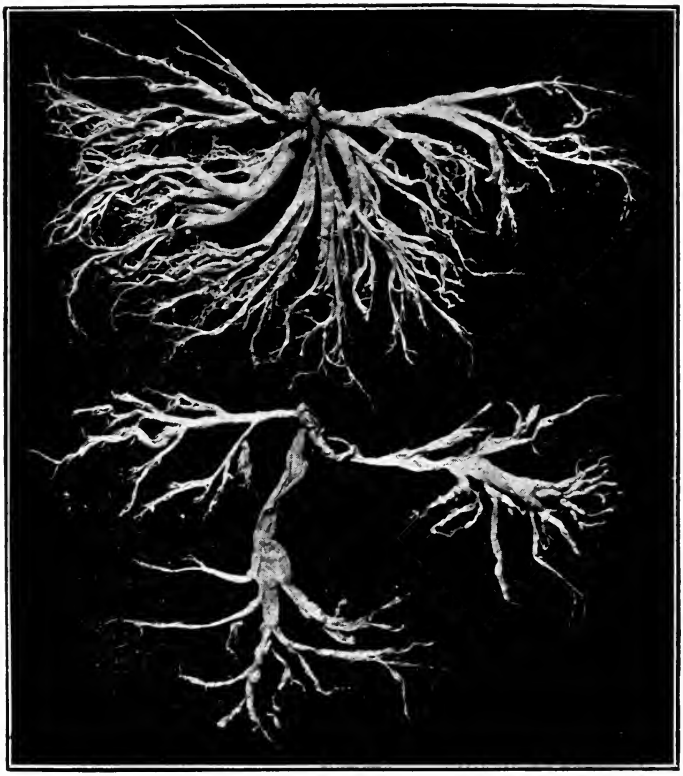

FIG. 12.—Casts expectorated by two patients suffering from plastic bronchitis. For an account of the cases see *Catalogue of St. George's Hospital Museum*, Series vii. 30A, 30B. (Size considerably reduced.)

to the unity and as to the mode of origin of the latter, we note in the cases a general agreement which binds them together into a distinct nosological group characterised anatomically by the recurring exudation, both rapid and extensive, of coagulable material in the bronchial tubes, coupled, it is said, with denudation of epithelium, and nosologically by the mechanical results of the exudation, namely, paroxysmal dyspnoea and the partial or total expulsion of the casts; or, in the more severe cases, suffocation and death.

Clinically the disease is clearly distinct from any of the affections enumerated, occurring rather in connexion with some personal idiosyncrasy than under the influence of any recognised predisposing circumstance, diathesis, or disease, and affecting robust subjects as well as those suspected of actual or of threatening tuberculosis. It was observed by Oppolzer recurrently during menstrual periods, with intermittence during pregnancy; whilst Biermer records several cases occurring during pregnancy (Wilson Fox). In its exciting causes—climatic, seasonal, and others—it is closely analogous to common bronchitis, and in its beginnings it is almost indistinguishable from the latter, the exudation supervening upon an initial catarrh.

Morbid Anatomy.—(i.) The casts may be expectorated in mere fragments or in their unbroken state. When freed from mucus, by suspension in water, undamaged specimens are found to reproduce the structure of the bronchi, from the tubes of the diameter of a goose-quill (rarely of much larger size) down to the finest ramifications, with such perfect accuracy that the site of their formation can be readily identified by comparing them with a cast of the bronchial tree obtained by artificial injection and corrosion. They are, with the exception of the smaller branchings, of firm consistence, and often perceptibly tubular; their bore being commonly plugged with mucus. "Their colour is whitish or pearly grey. They are distinctly stratified, and consist of a structureless or fibrillated basis in which are embedded inflammatory cells, mucous corpuscles, pus cells, pigmented cells, and altered gland cells, and, in their outer layers only, blood cells. They are soluble in alkalis, and also in lime-water" (Wilson Fox).

The expression "plastic bronchitis" does not define the nature of the exudation; and in this there is an advantage, since the casts are invariably mixed products, and may consist largely of mucus, as shewn by the action of the solvents just mentioned. Nevertheless they are mainly fibrinous, and owe to fibrin their characteristic consistence. Of this an indirect proof is found in the great rapidity with which fresh casts may be formed after the expectoration of previous ones. Waldenburg, and subsequently P. Lucas-Championnière, had described the occasional presence of fat in the casts. This observation has been confirmed by Model, who finds that the fat occurs as a fine granular deposit, or in droplets between layers of fibrin; it is sometimes to be seen floating in the sputum, which may contain so much of it as to suggest an escape of lymph or of chyle from the bronchial membrane.

Among the formed elements detected by the microscope in the casts should be mentioned bacteria, and occasionally haematoidin crystals, Curschmann's spirals, and particularly Charcot-Leyden crystals and eosinophil cells.

(ii.) The bronchi after death may contain casts in place, or imperfectly solidified curdy collections; or they may be quite clear and present catarrhal mucus only. The membrane may be injected, or pale, as in Biermer's case, in which the epithelial lining persisted under the cast. In

Kretschy's instance of an exceedingly rapid reproduction of the casts, the bronchi affected were deprived of their epithelium, and it was evident that the casts were not due to desquamation and transformation of cells, but to a genuine outpouring from the blood-vessels or lymphatics.

Emphysema is almost invariably present. Cases are sometimes cut short by intercurrent acute bronchitis or pneumonia. Traces of pleurisy, recent or antecedent, are sometimes found. Tubercle is present in a small proportion of the fatal cases. Model has recorded its occurrence in 10 cases in a series of 21 cases of the affection. Dilatation of the bronchi has been very rarely found.

The symptoms are those which would ensue from any extensive obstruction of air-tubes. The cough, which may have a peculiar tone, varies in intensity with the extent and consistence of the recurring thrombi; when they attain considerable size and extension their expulsion is preceded by hacking dry cough and dyspnoea lasting for hours, and in the expiratory type of the spasms resembling that of asthma. The cyanosis is usually moderate. Permanent dyspnoea is present in the proportion of the existing obstruction: during the intervals of freedom from membrane it is not complained of. Slight haemoptysis, more often following than preceding the expulsion of the casts, is very frequent—in nearly one-third of all cases (Biermer), or in one-third of the acute cases (Lebert). Sometimes it is considerable; and this has given rise to an opinion that the casts might consist merely of coagulated blood; but they contain no blood-discs, except in their outermost layers, which are frequently streaked with blood (Wilson Fox, Biermer).

Ordinary mucous sputum is apt to alternate with the casts, or to accompany them throughout when they are expectorated piecemeal; and a mucous expectoration precedes the expulsion of the larger masses, which are commonly ejected balled up in a slimy investment. Five to ten days is the most common period of retention of the casts; but this may range from one or two days to upwards of three weeks. The daily expectoration of casts may be considerable for long periods, or limited to a few fragments for a few days (Wilson Fox).

The constitutional symptoms in average cases are slight; including little or no pyrexia, except in the early stage, but occasionally a recurrent pyrexia with rigors, little emaciation, and, in a few cases only, dropsy, epistaxis, diarrhoea, or albuminuria, which may not exceed the duration of the attack. The spleen is sometimes enlarged.

A convenient division has been made between a small group of cases running an acute course (from one to four weeks or more), and a much larger group of chronic course, extending over years with intermissions and relapses of varying durations. Biermer again subdivides the acute cases into a mild variety, of shorter duration, in which the ordinary symptoms of a slight bronchitis are simply varied by the expectoration of a few casts; and a severe variety, pyrexial and suffocative, in which death may occur (six cases fatal in a series of ten) before any of the casts have been expelled The chronic form may long simulate ordinary

bronchial catarrh; or it may declare itself early. It also resembles bronchitis in its relapsing character.

The physical signs, ill-defined where the plugs are small and few, are well marked in cases of extensive obstruction. Inspiratory retraction of the chest may occur. At any rate the respiratory movement is locally impaired; and pulmonary collapse may give rise to dulness, whilst full or exaggerated resonance is elsewhere obtained. The respiratory murmur is diminished or absent; or it may be replaced by sibilant rales, by moist rales of various sizes, and, on the coagula becoming loosened, by loud whistling (Corrigan), by tubular breathing and coarse rales (van Meerbeeck), by a peculiar valve sound (Barth and Cazeaux), or by various flapping sounds described by German authors as *schmetternd*, *schnarrend*, and *flattergeräusch* (Hoffmann). On palpation a tactile fremitus may also be felt, which has been attributed to the flapping of the bronchial casts.

A unique case has been reported by Dr. S. West (147), that of a girl, aged eleven years, who during her seventh attack, which seems to have been unilateral, developed extreme displacement of the heart and mediastinum towards the left, simulating a pneumothorax. This displacement disappeared as the cast was expectorated, but recurred as each fresh cast formed.

Prognosis.—The association of the disease with pulmonary tuberculosis in a certain proportion of the cases somewhat artificially raises its mortality. Putting aside this latter group, and the unusual instances with severe onset and rapidly fatal tendency, in which grave dyspnoea coinciding with scanty expectoration and with extensive collapse of the lung are the most anxious features, the disease, as generally observed, "neither destroys life nor does grave damage, general or local" (Walshe). The liability to attacks may last for considerable periods. The case recorded by Kisch extended over twenty-five years.

The diagnosis can only be made after the expectoration of some of the coagula. The characters special to the latter, when recognised on examination, should enable us to distinguish the case from cases of intrabronchial haemorrhage and clotting, of diphtheria, of acute bronchitis, and of asthma.

Treatment of an effectual kind has yet to be discovered for the speedy removal of the casts, and *preventive* measures against their renewed formation. The solubility of the casts in lime-water, originally discovered by Dixon, which strongly suggests the presence within the casts of a large proportion of mucin, led Biermer to recommend the inhalation of atomised lime-water, and a case of its successful employment was reported by Waldenburg; but little has been heard of it since.

Emetics have also been tried for the sake of their mechanical action.

The natural process of catarrh by which the plugs are loosened tells in favour of the emollient action of an atmosphere of vapour. This measure, strongly advocated by Walshe, has the advantage of being harmless; and J. W. Ogle suggested that the steam might be medicated with tar or with other stimulating ingredients.

Internally many remedies have been prescribed and found wanting. The list includes among its more useful members creosote, tar, and turpentine. Biermer recommended the free administration of mercury in acute cases, a practice which has fortunately not been generally adopted.

Iodide of potassium, which was favourably spoken of as early as 1854 by Thierfelder and Wunderlich, has proved to be the only serviceable drug, and the published accounts of its use have been invariably favourable. Its mode of action is probably to promote the secretion of watery mucus which would tend to detach the plugs. Its recognised usefulness in this affection is an additional recommendation for its early administration in asthmatic seizures of uncertain causation.

An important precautionary measure in connexion with the severe dyspnoea to which such patients are liable, is to provide, in all ascertained or suspected cases of the disease, a portable and readily available, if small, supply of oxygen such as that provided for divers, for immediate use in the event of a sudden difficulty of breathing. Time would thus be afforded for procuring more abundant supplies, and for the adoption of other measures of relief.

Among the local measures of treatment of the bronchi the method of intratracheal injections can only be mentioned with reservations. It is obvious that bulky injections are out of place, and that any fluids capable of setting up irritation and swelling of the mucous membrane would aggravate the dyspnoea. The blandest is oil, but strong objections have been urged by Mr. Colin Campbell against it as compared with glycerin, namely, its inability to mix with the bronchial secretions, and the possibility of obstruction being set up by its insoluble sedimentations. The method has not, so far as recorded, been resorted to in plastic bronchitis. The only analogous instance was that of a case of diphtheria, in which obstruction of the trachea with membrane had been set up after a previous tracheotomy. Creosoted oil (1 in 20) dropped at intervals through the tracheotomy tube excited the desired amount of cough, and enabled the membrane to be expectorated with remarkable facility, so that the case ended in recovery (19).

The plan of breaking up the cast by corrosion or solvent action does not entirely agree with the lines of the spontaneous process of cure. Whichever be the solvents selected for injection, their concentration has to be slight; their action will therefore be slow, and their bulk must be relatively large. Moreover, their influence upon the diseased mucous membrane itself is an anxious question. Above all, we cannot forget that our object is the removal of the plug rather than its destruction. Integrity of the bronchial casts is an important help towards their complete expectoration: their fragmentation might be a doubtful gain, if the smaller branches of the cast were to be left behind.

None of the solvents at our disposal are entirely free from objections. In the case of lime-water the risk is connected with the bulkiness of the injection. Lactic acid has been credited with setting up pseudo-membranous bronchitis when accidentally dropped into the trachea, and its

employment even in dilute solutions might be open to question. The digestive ferments have been tried in diphtheria of the fauces with very unequal results. Trypsin is free from the chemical objection which may be urged against pepsin, and to a slighter extent even against the vegetable ferments papayotin and papain, which act best though not exclusively as does pepsin, in acid solutions. The results obtained with papayotin in diphtheria were not encouraging. The favourable opinion entertained by Rossbach has not been shared by other observers, the solution of the ferment having been either too dilute to be effective, or, when of a strength sufficient to destroy the false membrane, not free from damaging effects upon the mucous surface. Papain itself, the more powerful product yielded by the fruit of *Carica Papaya* (papayotin being derived from the milky sap), has been recommended ; but the success of its employment, even with the advantage of the relative accessibility of the surface to be treated, has not been such as to bring it into general use.

In conclusion, the suggestion of a local treatment of the affection, whilst opening up a promised therapeutic prospect, may prove in the event impracticable. In any case the attempt to carry it out should be made with the utmost caution. The local treatment by bactericidal agents and the hypodermic treatment by antitoxins are possibilities contingent upon the results of future pathological discovery.

During the long intervals the ordinary treatment of bronchitis is suitable for the generality of cases; and this applies also to the climatic indication, in spite of the disappointing results which have been reported.

Putrid Bronchitis

In the course of an inveterate purulent bronchorrhoea the expectoration occasionally becomes putrid; and to this condition in its worst form the name putrid bronchitis has been applied. Putrid expectoration occurs in bronchiectasis, and is probably associated with destructive lesions of the mucous surface, the result of unrelieved retentions. Instances of the uncomplicated kind are comparatively rare, the majority of the cases occurring as a late complication of long-established bronchial dilatation.

If foulness of the expectoration in itself constituted a putrid bronchitis, we might group under that name, together with many cases of bronchiectasis, all cases of pulmonary gangrene, of gangrenous tuberculous phthisis, and of putrid empyema discharging through the lung. All these, however, are removed into other categories by reason of the prevailing importance of their extra-bronchial lesions. Even here the affection is seldom, if ever, absolutely primary. The pre-existing catarrh, emphysema, pleuro-pneumonia, interstitial pneumonia, or fibroid degeneration, whilst they account for a delayed expectoration of the bronchial contents, do not in themselves explain their putrid decomposition. The cause of the latter is intrabronchial; and two views have been taken of

its etiology. According to some bacteriologists putridity is mainly due to the influence of micro-organisms, and the bronchitis is secondary to the microbic invasion—a view to which we shall presently refer. Other pathologists have regarded the bronchitis as the primary event, and have sought to trace the putrid process to definite structural changes in the bronchial mucous membrane.

The association of gangrene with bronchiectasis had been dwelt upon by Laennec. It was more definitely described in 1841 by Briguet as affecting the terminations of the dilated tubes. Marfan has recently endeavoured to apply the same explanation to putrid bronchitis. He assumes the existence of a primary *gangrene of the bronchi* which, he contends, attacks the middle-sized and smaller tubes independently of any bronchiectasis, or in association with but small terminal dilatations. Lesions of this kind have not been noticed by other observers; and in one case in which they were specially looked for after death they were reported, by Sée, to have been absent.

The view more generally accepted is that an ordinary bronchitis may degenerate into the putrid form, which may or may not be a merely passing phase, but cannot persist for long periods without progressive damage to the bronchial structures and serious risk to life.

That putridity may be set up within the air-tubes by the inhalation of septic matter is a possibility suggested by cases such as that of Tiedemann, in which this was brought about by a leakage into a pulmonary cavity from a traction diverticulum. The attempt to attach the blame to merely microbic influences is complicated by the number of microbes gaining access to the bronchi, and by the necessity of explaining this occasional failure of protective mechanisms which normally succeed even in conditions so adverse as those, for instance, of phthisis.

The bacteriology of the sputum has already grown to considerable proportions. Among the numerous micro-organisms discovered in putrid expectoration, several of which have been cultivated, J. Lumniczer succeeded in isolating a bacillus which perhaps may be the same as that isolated by Bernabei, giving, after a few days, the same odour as the sputum. Bernabei is inclined to regard putrid bronchitis as directly due to the growth of the specific bacillus which he has described. Hitzig has likewise described two bacilli not unlike the *Bacilli coli communis*, also yielding a fetid odour.

The inhalation of *Oidium albicans* was regarded as the cause of the affection in an isolated case reported by Rosenstein; and Canali has reported a case in which actinomycosis was either a cause or a complication.

The sputum sometimes presents a brownish discoloration; it is intensely fetid, either of gangrenous or of foul, sweetish odour. It separates into three layers—an upper muco-purulent and frothy layer, a middle translucent opalescent layer, and a lowermost dirty, yellowish, granular layer containing the solid constituents which have been deposited. As far back as 1850 Dittrich had described the plugging of some of the

bronchial tubes by small friable masses, varying in size from that of a millet seed to that of a bean, made up of cellular debris, pus cells, granules, oil globules, haematoidin crystals, and various micro-organisms, including the monas and cercomonas described by Kannenberg and by Streng, and *Leptothrix pulmonalis.* These "Dittrich's plugs" make their appearance in the expectoration and, together with the intensely fetid odour, settle the diagnosis. Fatty crystals (palmitic and stearic), volatile fatty acids (valerianic and butyric), leucine and tyrosine, methylamine, ammonia, and sulphuretted hydrogen are also found. *Leptothrix pulmonalis* occasions a purple, violet, or blue discoloration of the sputum when treated by iodine, a reaction observed by Virchow and by Gamgee. Jaffé's observations of the presence of minute quantities of leucine and of tyrosine are of interest in connexion with the ferment obtained from the sputum by Filehne and by Stolnikow, which they regard as analogous to pancreatic ferment. The same observers confirm the observation that Dittrich's plugs contain a substance striking blue with iodine.

Morbid Anatomy.—Pathological changes special to the affection are comparatively few. The post-mortem appearances are those of an intense bronchitis and peribronchitis with pneumonic infiltration of the surrounding tissue. Pneumonic consolidation may be found extending over more or less extensive patches; but the greater part of the lung is in a state of congestive and puriform oedema, and the bronchial glands are swollen and soft. Some of the bronchi may shew ulceration, or the mucous membrane be softened in places and deprived of its epithelium; or it may become involved with the adjoining pulmonary tissue into genuine gangrene. Cases of this kind have doubtless supplied Marfan with the basis for his separate description of a gangrene of the bronchi. The collateral changes are varied according to the morbid antecedents of each case.

The symptoms accurately given by Dittrich consist in a sudden onset of feverishness soon assuming a typhoid character, intense depression, collapse, coma, and death. The attack is accompanied or preceded by an equally sudden change in the sputum from the habitual muco-purulent type of chronic bronchial catarrh to the putrid variety. At the approach of death expectoration diminishes and finally ceases.

The long paroxysmal cough peculiar to advanced excavating disease, and the gushes of sputum of bronchiectasis are not witnessed; but the frequency of the cough and of the expectoration is often severe, particularly in the pleuro-pneumonic and fibroid cases, in which the thoracic excursions are much restricted. Fever of a remittent type is usually present throughout the putrid stage; and it may be regarded as a measure of the septic absorption.

The diagnosis is based upon the clinical history and upon the negative results of a physical examination for the lesions of bronchiectasis, of phthisis, and of pulmonary gangrene.

The prognosis varies according as the putrid condition of the

bronchial contents is grafted upon a simple chronic catarrh, or is combined with deep-seated tissue irritation and overgrowth. In the first group of cases recovery may take place after a few weeks, but relapses will be apt to occur. In the second group the fatal tendency may be hastened by catarrhal pneumonia, acute bronchitis, pulmonary gangrene, pleurisy, metastatic abscesses (including cerebral abscesses), or endocarditis.

Treatment (*vide* p. 153).

The Treatment of Bronchitis

Some account has been given of the treatment of plastic bronchitis: that of putrid bronchitis will be dealt with under the heading of Fetid Bronchiectasis (*vide* p. 153). The other varieties of bronchitis will now be considered in turn from the point of view of their abortive, curative, and palliative treatment, and of prophylaxis.

I. **Trachea-bronchitis.**—(*a*) *The abortive treatment* of simple chest cold, at its preliminary stage of coryza, has probably been more often tried than that of any other ailment, and with a greater variety of methods, most of which are based on diaphoresis and diuresis. The suppression of the coryza has, however, been sometimes attempted by a direct local action on the mucous membrane of the upper air-passages, or by way of the nervous and vasomotor systems. The direct application of powders or snuffs variously compounded of quinine, camphor, subnitrate of bismuth, morphine and astringents, and the inhalation of stimulant camphorated vapours, in which ammonia, carbolic acid, iodine, and essential oils are prominent ingredients, have often been prescribed; and remedies of this kind have at times been advertised as specifics. Of internal medication two methods have been used—the tonic and the sedative; on the one hand, liberal doses of quinine or, as employed by Sir Isambard Owen, of the tincture of perchloride of iron; on the other, large doses of potassium bromide or some of the antipyretic remedies recently brought into use, especially phenacetin and aspirin.

The diaphoretic methods do not need any detailed description: they include the traditional help of a Dover's powder, of hot grog, of blankets, of the hot air or Turkish bath, or of the vapour bath, a medicated modification of which has enjoyed some reputation in country districts. In practising this homely and doubtless efficacious method the patient stoops over a vessel of boiling water in which is infused a quantity of selected herbs, while the body is entirely covered with a sheet and blankets; after a few minutes' inhalation of the aromatic vapour profuse perspiration is induced, and a cure may result. The late Sir Andrew Clark's favourite diaphoretic treatment was the hourly administration of ammonium citrate assisted by warm drinks and warm wraps.

(*b*) *The Curative Treatment.*—If in spite of all efforts trachea-bronchitis should be established, its rapid relief can only be secured by rest in bed,

fluid diet, warm drinks, and assiduous medication, beginning with a quickly acting purge and combining diuretic and sedative action with the all-important diaphoresis. A hot foot-bath with the addition of mustard, a mustard poultice to the front of the chest, and the inhalation of steam medicated with terebene, eucalyptol, or the compound tincture of benzoin, are valuable adjuncts. As soon as decided improvement becomes manifest, iron and quinine or other tonics should be substituted for the saline remedies, and the ordinary diet resumed.

II. Ordinary Mild Acute Bronchitis of the Middle-sized Tubes.—In this relatively mild affection, the preliminary measures are the immediate administration of two to four grains of calomel followed in an hour by a black draught. Meanwhile arrangements are to be made for the steady renewal of air without any draught, combined with an equally steady regulation of the temperature of the room, at a mean of about 65° F. This often needs some planning, to suit the place, and usually involves the erection of a "half-tent" to exclude any currents of air or variations of temperature in the atmosphere immediately surrounding the exposed parts. Provision should also be made for the occasional supply of steam, and for its medication with eucalyptus, thymol, or wool-fir oil. The delay before purgation may afford time for a foot-bath or for the application of mustard leaves to the calves, to the upper sternum, or to the shoulders—or of dry cups over the back. Blisters are unnecessary, and may be inconvenient during the subsequent perspiration. The patient should be allowed to assume the position of greatest comfort, probably one of slight elevation of the head and shoulders.

The more quickly *diaphoresis* can be obtained the greater will be the hope of checking the spread of the bronchitis. The wet-pack is sometimes used; but more generally the hot air bath will be preferred, some form of which may easily be improvised. Internally the administration of ammonium acetate, of spirits of nitrous ether and of chloroform, with syrup of red poppies, and infusion of senega, will be found useful together with other means of keeping up the perspiration. In more active inflammation nothing will relieve the tightness at the chest and the hardness of the cough, whilst reducing arterial pressure and keeping the skin moist, better than antimony. Relatively small doses (not exceeding 8 ♏) of antimonial wine, perhaps combined for a few hours with small doses of Dover's powder or of bimeconate of morphine, the tendency of which is likewise to relax arterial or bronchial spasm and to reduce active congestion, afford much relief. A fluid diet of diluted milk, barley water, and hot lemonade of moderate strength, belongs to this stage.

Expectorants. — Antimony, used as indicated above, undoubtedly loosens the phlegm and promotes its expectoration; but a different combination is called for as soon as the initial discomfort has been allayed, and the skin, kidneys, and liver have been thoroughly brought into action. It is now time for the direct expectorants — squill, ipecacuanha, carbonate of ammonium, and especially potassium iodide, which, in cases presenting much spasm of the air-tubes, may be success-

fully combined with the ethereal tincture of lobelia and spirits of chloroform.

Belladonna, one of the early remedies for bronchitis, has not permanently held the position repeatedly claimed for it. That it may not be equally suitable to all cases, and that the adjustment of the dose may sometimes be of unusual importance, might have been expected with a drug possessing several powerful physiological actions. Each of the latter has in turn been credited with the remarkable results reported by observers. As the element of bronchial spasm enters in varying degrees into all cases of bronchitis, belladonna would be more useful where this factor more largely prevails; as in the bronchitis of asthma and sometimes of emphysema. In cases of this kind the remedy has, in my experience, occasionally afforded more relief when worn as a plaster over the chest than in the form of internal medication. Dr. Sydney Ringer has recalled attention to its efficacy in bronchitis in relieving the incessant cough and checking the flow of mucus, which, whether viscid and scanty or profuse and watery, is regarded by him rather as an increase of secretion than as an inflammatory product. He prescribes 10-℥ doses thrice daily or oftener. On the strength of the same property of checking the secretion he suggests its employment in ether bronchitis, and in those cases in which aspiration of the chest is followed by a profuse and sometimes suffocating amount of expectoration. The value of belladonna is also advocated by Dr. Murrell, who points out that the same advantages may be obtained by a solution of homatropine. Lastly, Mr. Davies of Sherborne has dwelt upon its "magic" effects as an inhalation, not only in asthma but in acute bronchitis. He recommends the use of 1 grain of the extract in ½ oz. of water with Siegel's inhaler, which has the additional advantage of moistening the atmosphere.

Inhalations.—To allay the irritable cough conium or chloroform may be added in the steam inhaler to representatives of the turpentine group such as thymol or eucalyptol; but, for the relief of spasm of the smaller tubes, the dry inhaler is usually found more effectual. It consists essentially of a Woulfe's bottle, provided with a long inhaling tube and mouthpiece, and packed with tow or loose cotton-wool steeped in volatile principles which impregnate the air inhaled through the bottle. The chief sedative agent to be used in all the mixtures for inhalation is undoubtedly spirits of chloroform; the other constituents may be freely varied according to indications and to suit the patient's taste.

Emetics and bleeding, formerly much in vogue and regarded as almost indispensable, are still not infrequently resorted to in some European countries; but they have long been neglected in England. Against this neglect C. J. Hare raised an energetic protest, and he specially insisted on the great value of emetics in acute bronchitis. In addition to its general and hepatic action, an emetic not only removes the existing accumulation, but, by its mechanical effect, squeezes a large quantity of effete cellular and mucous material out of the mucous membrane, thus warding

off the danger of an implication of the smaller tubes. Its early employment before the onset of this complication would be free from the risk of overtaxing the heart at a time when recovery in great measure depends upon the cardiac energy being fully sustained.

Bleeding was prescribed early in the attack in bygone days. At the present time it is not systematically used as a prophylactic, but is reserved for any more urgent symptoms which might supervene. The treatment of the catarrhal muco-purulent stage of this milder form of bronchitis is practically the same as that of chronic bronchial catarrh.

III. Acute Bronchitis of the Adult.—In all cases of threatening severity the first and all-important indication is to provide a ready supply of *oxygen*. In a dilute form oxygen cannot fail to be of use even before the onset of urgent dyspnoea; and it cannot do harm. When dyspnoea has set in, the relief its free administration will afford is limited only by the difficulties of respiration. That the choked bronchioles refuse to inspire should not discourage our efforts, for we must bear in mind how relatively small is the bulk of oxygen which corresponds to the ordinary intake of air: during the stage of urgent dyspnoea oxygen should be supplied continuously. By this method two needs are fulfilled, the pulmonary and the cardiac. The remarkable results of the local treatment of cutaneous ulcers by a diluted atmosphere of oxygen, as originally prescribed and practised by Dr. George Stoker, would lead us to expect a local beneficial action upon the mucous membrane. But there is a more important function. Final success in a protracted and severe struggle for breath is directly dependent upon the vigour of the heart and upon the endurance of the respiratory muscles, and any temporary encouragement will favour a permanent increase in cardiac and thoracic energy.

Moisture supplied as *steam* is another important agent. But an excess of steam, or still worse, of the heat used to raise it, would be injurious. Steam and oxygen work well together; the dryness of the oxygen is tempered by the steam, and the depressing effect of the vapour is relieved by the stimulation of the gas.

In the *medicinal* treatment three urgent objects must be kept in view: (i.) to uphold the patient's strength; (ii.) to relieve the bronchial spasm as much as possible; (iii.) to mature and loosen the catarrh. A preliminary dose of calomel, followed by a saline, will do good in every way; but this is the full extent to which any depressing treatment or any methods involving exertion can be countenanced. The question of an emetic should, however, be considered, and will need much judgment; it is a remedy exclusively for early employment. A large jacket poultice, made as light as it is possible in front, is of distinct advantage.

Alcoholic Stimulation.—Whenever, as in this dangerous malady, the patient's safety lies in the correctness of our estimate of the actual state of his vital powers, the early and over-zealous systematic administration of alcohol is an evil, or at the least a risk. Although a need for stimulating support exists from the first, as alcohol is not curative in suffocative bronchitis, it should not be our first resort, but be brought in rather as a

powerful reserve to carry a desperate position or to ensure its being firmly held. Its occasional use to meet an emergency is a matter of discretion, and of our estimate of the patient's actual and prospective store of cardiac energy.

Cardiac Stimulation.—The best cardiac stimulants are oxygen and speedy relief of the respiratory obstruction. With that in view a mixture containing carbonate and citrate of ammonium in sufficient amount, with iodide of potassium (3 grains), antimonial wine (3 ♏), and senega, may be administered every two or three hours at first. But unless provision can be made for the injection of strychnine, if required, we should have at hand for occasional administration, if necessary, a few doses of the following: 15 to 20 drops of tincture of digitalis, 5 ♏ of liq. strychninae, and 20 ♏ of sulphuric ether or of aromatic spirit of ammonia. The frequency of the administration of the expectorant is to be modified according to the progress of the case; and an occasional intermission of it, with some cooling acid draught as a substitute, may be welcome to the patient. Perceptible amendment should be noticeable within the first twenty-four hours. In the worst cases it will not be a discouraging result if the patient has done no more than maintain his strength.

Diet.—This should be of the lightest description. The milk should be peptonised, diluted with Vichy or some analogous water, the effervescence of which should be allowed to pass off, and supplied at intervals of three hours, and during the day only. In the night hot lemonade, which is also for use as a beverage in the daytime, and if indicated some hot grog are more suitable as affording rest to the stomach.

Mechanically aided Expiration.—As previously stated, the existence of emphysema is a specially dangerous factor, and may call for something more than medicinal treatment. I have found decidedly good results from mechanical assistance to expiration; this may be carried out by a specially trained nurse or attendant, but more safely by the physician, who places his hands, well spread out, over the axillary bases of the patient's lungs, and exerts very carefully timed pressures, judiciously adapted to the phase of spontaneous expiration. In emphysematous cases an important part of the dyspnoea and impeded expiration is dependent upon the inherent weakness of the elastic fibre of the air-sacs, over and above the mechanical obstacle produced within the small tubes by congestion, viscid secretion, or spasm. The larger the share of the first of these two factors in the individual case, so much the greater will be the relief obtained. The method may be tried in all cases, but requires to be used with considerable discretion, and with due regard to the patient's feelings, and to the effect produced upon the depth and frequency of breathing.

A case cannot remain stationary at this stage; if it do not improve it is rapidly deteriorating, and at any moment, owing to progressive congestion of the right heart, exhaustion may set in. Our duty is to apply the only adequate remedy, venesection, without waiting for the manifestations of extreme cyanosis, cold sweats, jactation, and fluttering pulse.

Direct puncture of the right auricle is for obvious reasons impracticable; but the next best means to a sudden and ample depletion of the cavity is to open the external jugular vein, from which 8 to 10 oz. should be boldly abstracted. The benefit obtained is immediate and considerable; the duration of it will depend upon the degree of remaining cardiac energy. This is the time to bring cardiac tonics to bear, and to inject under the skin $\frac{1}{30}$th to $\frac{1}{20}$th grain of strychnine. Alcoholic stimulation, if not previously pushed with improvidence, should prove a boon. Oxygen should again be inhaled, as it may afford a fresh opportunity for clearing the chest of loose mucus. After a series of mechanically aided expirations the patient should be encouraged to cough up the accumulations; and, by repeating this process, a good deal may be got rid of.

To save the right heart from a return of its previous engorgement, a liberal supply of india-rubber cups (six to eight) should be applied to the chest simultaneously, utilising any position accessible without undue disturbance to the patient. By reapplying each of them in rotation the depleting action may be kept up for a longer period. Mustard leaves to the calves are also available for a similar purpose.

Good results may be obtained from this alternation of the cardiac and of the respiratory treatment, and from the continued administration of digitalis, ether, and ammonia. If all these fail, no other measures, such as electricity in its various forms, will succeed.

The treatment to be followed in favourable cases, after recovery from the asphyxial stage, is analogous to that which has been described under a previous heading (*vide* p. 111).

IV. **Capillary Bronchitis.**—(i.) *Infantile.*—As we have no early clinical criteria to distinguish this affection from a simple acute bronchitis, there can be practically but one treatment for both; and we must regard every onset of infantile acute bronchitis as potentially the opening stage of a bronchopneumonic attack. Of no other seizure is it more true that the best, if not the only, chance of success is to check its earliest beginnings, since its fatality is most often due to late rather than to initial conditions, in particular to the ingravescent toxaemia, to cardiac exhaustion from the struggle of dyspnoea, or to the asphyxia resulting from consolidation, collapse, and emphysema. The only promising abortive treatment for the implication of the terminal tubes is a prompt combination of emesis, purgation, and diaphoresis.

Ventilation, posture, and stimulation should, however, be first referred to as primary indications which underlie the entire management of all our cases. *Stimulation* is called for early in proportion to the severity of the symptoms of invasion. In prescribing alcohol at that stage it must be borne in mind that in those cases in which it is most needed its excess might be a worse evil than its omission. Our policy should be to rely as much as possible upon the alternatives of ammonia, ether, strychnine, and digitalis, because brandy then remains for an emergency.

Open air as insisted by Northrup will largely supersede the necessity

for artificial stimulants, and is among the potent curative agents for the infection. As to the bronchitis itself, bland sedative atmospheres, like the pure air of sheltered altitudes, would in themselves be a remedy; but in our towns where the affection prevails they do not exist. In this climate the immediate essential for the bronchial inflammation is not the open air, but the combination of continually renewed fresh air with the utmost uniformity of temperature and moisture.

Steam is readily supplied with the help of the steam-tent. The latter should never form a complete investment, but be limited to the head of the bed, or to three of its sides. Oxygen will obviate the danger of rendering the atmosphere oppressive. The inhalation of oxygen needs special management in children. No attempt should ever be made to place the tube into the mouth; it is quite enough to direct the stream of gas towards the nostrils during their sleep by passing the tube through the loop of a safety-pin. Even infants will take kindly to the gas when they have experienced the relief it gives. The administration may be kept up indefinitely if needed.

Marfan, a believer in the infectiousness of these cases, urges their isolation from the other children in hospitals. He has recently recommended a solution of oil of sweet almonds, 40 grams, and menthol 0·4 gram, for daily instillations into each nostril as a prophylactic, and also the insertion of some vaseline containing 10 per cent boric acid and 1 per cent resorcin. For many years I have advocated in the medical Press the systematic use of faintly carbolised olive oil or of jasmine oil as a protecting and cleansing agent rather than as a disinfectant, in all infectious disorders of the upper air-passages, including influenza, mumps, whooping-cough. Ten to fifteen drops are slowly dropped into each nostril, whilst the head is well thrown back, twice or three times in twenty-four hours. Much comfort results in the worst cases. In bronchitis and other irritative affections the soothing and protecting influence on the mucous membrane is of much value.

Posture is too often neglected as a preventive for much pulmonary collapse and emphysema. There is less of exertion and more of efficacy in judiciously varied posture than in most artificial devices to promote pulmonary expansion. It is true that in the acute attacks of lobar pneumonia and of pleurisy infants and small children will fall into the attitudes which best suit their difficulty. But in this affection it is to an unrelieved dorsal posture that part of the difficulty is due; and in cases in which interference is admissible a resort to the prone posture on suitably raised pillows, alternating with the lateral decubitus, may be the means of rescuing from collapse large reserves of pulmonary tissue.

As to the practical details of treatment: The linseed poultice has long been discarded in favour of the lighter jacket of cotton-wool and oiled-silk, and the mustard poultice in favour of mustard compresses. Among the measures more specially directed to the pulmonary collapse and pneumonia, the flying cold compresses, the wet pack, and the cooling bath deserve special mention. Holt believes that a bath at an initial

temperature of 100° F., quickly lowered by ice to 85° or even to 80°, is more suitable for infants, and the wet pack for small children. The hot mustard bath is reserved for threatening collapse rather than to allay the nervous symptoms of pyrexia. In the latter the efficacy of Heubner's systematic *mustard pack* is endorsed by Dr. Coutts. The trunk is to be wrapped in cloths wrung out of mustard and water, mixed at a temperature not exceeding 70° F. These are removed after ten to twenty minutes, according to the action on the skin; and after sponging the latter a wet pack is applied which generally brings about comfort and sleep.

The old practice of an early induction of *vomiting* is probably one of the most effectual means of saving life, and should not in itself be a source of danger, the act being relatively easy in small children. If the case be seen before the onset of marked respiratory distress, the strength will be quite equal to this treatment, and any sign of respiratory retraction of the thoracic base should call for its immediate employment. For threatening pulmonary collapse vomiting is probably the best, if not the only, cure. It tends to fulfil two essential needs, namely, the dislodgment of the mucus from the bronchioles, and the inflation of the lobules by the deep inspirations connected with vomiting. Tartar emetic is generally considered to be unnecessarily depressing. A dose of sulphate of zinc, followed by lukewarm drinks, is a prompt and effectual agent. Dr. Rolleston has found good results from the hypodermic injection of apomorphine $\frac{1}{30}$ gr. with liq. strychninae ℥ $\frac{1}{2}$ to prevent collapse.

Leeching is a valuable method, but must be employed with the utmost care; it cannot be recommended as a routine treatment in infants.

Medicinally the principles to be followed are almost identical with those indicated for the adult: (1) to increase, to loosen, and to remove the bronchial secretion whilst relieving spasm, no remedies compare with antimony and iodide of potassium administered at first in hourly doses, as they are free from the risks attaching to pilocarpine; and (2) for diaphoresis and diuresis the simple addition to the dose of enough ammonium citrate or acetate and of a little potassium citrate is all that is needed. Belladonna was recently held up as a sovereign remedy in the capillary bronchitis of infants and of young children. Dr. March, who recommends it in minim doses every four hours for infants of six months, reducing the dose on the slightest indication of improvement, ascribed its value to its stimulant action on the respiratory centres. This view is to be set against the objection sometimes made that the action of the skin and the bronchial secretion, both of which we have been taught to promote, are checked by belladonna. But this drug cannot be regarded as a specific.

(ii.) *In senile capillary bronchitis* neither emetics nor bleeding are admissible in ordinary circumstances. The treatment must consist in careful feeding and stimulation, the saving of energy, the promotion of expectoration, and constant and judicious nursing. Oxygen is

indispensable; and the regulation of the temperature and of the moisture of the atmosphere is also a point of much nicety.

Theoretically, mechanically-aided expiration would seem to be specially indicated; but the rigidity of the senile cartilages, although not always so great as might be expected, is an apparent objection to the method. Moreover, the other conditions are not quite simple, and aged patients are often intolerant of any mechanical interference with the thorax.

Among internal medicines the stimulant and balsamic expectorants are specially appropriate, and, up to a certain point, successful. Quinine or caffeine may have to be associated with carbonate of ammonia, although they are not in themselves remedies for the cough. Digitalis and strychnine must also be called to aid if necessary. Strong counter-irritation cannot be recommended without reservation, and blisters are not advisable. A milder form of stimulation of the skin may, however, be obtained from the application to the front of the chest of flannel sprinkled with a dram or two of terebene, which also serves the purpose of an insensible inhalation.

As previously explained, capillary bronchitis at an advanced age is a most fatal affection, and the chief aim and result of treatment may be but a short prolongation of life.

Secondary Bronchitis.—The treatment of the bronchitis associated with the infectious fevers, sometimes, as originally observed by Laennec, throughout their course, does not often call for separate attention. The management of the bronchitis of asthma and of hay-fever, of mechanically induced bronchitis, of the bronchitis of phthisis, and of that incidental to other parasitic diseases, will be considered in other sections of this work.

Acute Gouty Bronchitis.—In the treatment of a serious form of acute bronchitis occurring in gouty subjects, sometimes as a precursor, at other times as a phenomenon of recession of the arthritic trouble, the special indication is the relief of the pulmonary congestion and irregularity of the heart. The sudden subsidence of these grave symptoms on the re-appearance of the arthritis suggested the old treatment of applying mechanical irritation to the great toe or other joints with a view to calling back the local inflammation. If this attempt should succeed, pulmonary relief may follow, but the remedy is an uncertain one. Moreover, the bronchitis does not always stand in this relation to the articular paroxysms; it may be independent of them; and it should be borne in mind that its gravity is sometimes the expression of a complicating renal difficulty. The requisites in the more urgent stage are stimulation and derivation. Among derivatives the most convenient are mustard foot-baths and dry cups freely applied; whilst a rapidly-acting purge, such as calomel and senna, should be followed up by mild doses of colchicum and of an alkali, if no special contra-indication should exist.

Chronic Bronchitis.—The varieties of chronic bronchitis call for some detail in their treatment; but for all of them our therapeutic

agents may be arranged in four groups: (i.) the atmospheric treatment, including the climatic; (ii.) the topical, including counter-irritation; (iii.) the medicinal, and (iv.) the constitutional, including the balnear treatment.

(i.) The value of *climatic treatment* is demonstrated by the rarity of chronic bronchitis among inhabitants of more temperate zones, and by the improvement experienced by invalids from the North. For the larger number distant journeys are impracticable, and artificial atmospheric conditions must therefore be devised. The essentials in an artificial atmosphere are purity of the air-supply, freedom from suspended particles, and due regulation of temperature and moisture. The dryness of artificially-heated air being specially noxious in chronic bronchitis, a constant renewal of air without oscillations in the temperature, and with a proper supply of moisture, are problems claiming earnest attention in practical hygiene. Evenness of temperature and of moisture, if they can be secured, will enable the chronic bronchitic to remain in this country without serious detriment, spending indoors the periods of more wintry weather, and occasionally enjoying exercise in the open during warmer spells. But this after all is merely protective treatment, rather devised for safety than for cure.

(ii.) *Topical Treatment.*—Atmospheric therapeutics aim at something more than mere prophylaxis, and are needed in the more active stages. Strictly, the term should be limited to the volatile agents, which can be used to impregnate the air at the normal temperature. Members of the turpentine group—terebene, pinol, cresol, eucalyptol, myrtol, creosote, tar,—carbolic acid, iodine, and the like are all in some slight degree volatile; though not to the extent observed in the case of chloroform, alcohol, and ether. Chloride of ammonium vapour, supplied by means of a special inhaler, may be combined with some of the vapours enumerated. All these substances may be inhaled in greater concentration when combined with steam, and this method has the most beneficial effect. The practical means of volatilising carbolic acid and other agents at varying temperatures have received much attention from Dr. Robert J. Lee.

Reference has already been made to the "dry inhaler" by means of which the more volatile, as well as a slight proportion of the less volatile, substances can be directly inhaled with the inspiratory current. The fine atomising or nebulising sprays, for which some excellent apparatuses have recently been introduced, enable us to add to the list of the atmospheric agents almost any of the non-volatile substances, provided they be soluble. Common salt, bicarbonate of sodium, chloride of ammonium, alum, tannin, and various astringents may be thus used as required. A proportion of the spray probably passes the glottis, though doubtless the greater part is condensed on the pharyngeal walls. To this minimum introduced into the lung we cannot fail to attribute a share in the marked benefit obtained; and we recognise in it a first step towards the more vigorous topical treatment by intralaryngeal injections, from which excellent results may be expected in a large number of cases. The laryngeal

insufflation of fine powders is less commonly used, and, owing to the ciliary function, it is doubtful whether their action would extend much below the trachea itself.

Counter-irritation is of undoubted value in most forms of chronic bronchial catarrh, for the treatment of the exacerbations. Its usual modes of application are the irritating liniments and applications, such as croton oil, blistering, and the actual cautery. The latter is extensively used in France under the name of "*pointes-de-feu*," for the relief of cough, of local pain, and of profuse expectoration. For the same objects blistering is invariably useful. In *putrid bronchitis* blisters may prove of decided service in checking both the fetor and the amount of the expectoration; and in those cases in which, owing to fibrosis of the lung, Dr. Chaplin's treatment by creosote inhalation is not successful, this mode of relief might be tried (*vide* p. 157).

(iii.) *Internal treatment* has regard not only to the immediate relief of the bronchial trouble, but also to constitutional requirements. The list of those drugs which are beneficial to the membrane need not be given in full; their active constituents are usually such as can be exhaled from the blood into the lung, so as to take effect on the bronchial membrane. Many derivatives of tar, and tar itself, the turpentines, and the balsams are valuable in the treatment of chronic bronchitis. The more direct expectorants are also sometimes needed, especially when tonics, which are otherwise to be preferred, act as a source of irritation. The preparations of conium, squill, ipecacuanha, senega, in combination with mild salines, will prove of value in these irritable forms; and if there should be much spasm, morphine, belladonna, hydrocyanic acid, lobelia, and like agents may be required. Of the internal remedies taking special effect on the secreting function of the membrane four groups may be especially mentioned: (*a*) Certain balsams, such as balsam of Peru, of tolu, and the compound tincture of benzoin; among the oleo-resins copaiba, and among the tar derivatives creosote and guaiacol (to be taken in capsules). These remedies stimulate the membrane and tend to diminish the catarrh. (*b*) Iodine in all its combinations, and particularly as iodide of potassium, has the opposite tendency, and is especially useful when the mucous membrane is dry and the expectoration scanty and difficult, as in the so-called dry catarrhs. (*c*) Sulphur and the sulphides have long enjoyed a reputation for the relief of suppurative conditions, and their checking influence on the profuse muco-purulent discharge of bronchorrhoea and the worst forms of catarrhs is striking. When this can be combined with the tonic effect of a bracing air and with thermal treatment, results may be obtained such as have established the reputation of Harrogate in this country, and of Eaux Bonnes, Cauterets, Luchon, Aix-les-Bains, Royat, Mont Dore, La Bourboule, and other stations abroad.

At all thermal stations patients are subjected to a limited course of treatment by baths, mineral-water drinking, and exercise in the open air. When sulphur is administered to a patient treated at home the same

attention should be given to a limitation of the period of administration, lest irritability of the mucous membrane or irritability of the skin should be induced. Lastly, (*d*) cod-liver oil, when tolerated, is an invaluable remedy.

(iv.) *Constitutional Treatment.*—As a rule, a slightly purgative plan is of great value; indeed this is one of the favourable aspects of the treatment by sulphur. Various mineral waters may be used, and, with the same object, patients are sent to various medicinal springs.

The cardiac indication is usually obvious. The right heart needs not only to be cured of its dilatation, but if possible toned up. Strychnine, digitalis, strophanthus are thus direct agents in relieving chronic bronchitis by reducing the pulmonary congestion. We should not forget that an excellent way to strengthen the right heart is to strengthen the left. In chronic bronchitis shortness of breath leads to muscular inertia and atrophy; for this there is a remedy in oxygen inhalations, or in their equivalent, systematic purposive hyperpnoea. Patients would gain much by training their breathing in the direction of the utmost mechanical advantage, and by cultivating general muscular exercise, at first purely passive, but ultimately active. A general recovery of neuro-muscular energy, other circumstances being favourable, will act most beneficially upon the chest through the great improvement in cardiac strength. For artificial methods of lung gymnastics the reader is referred to the article on Aero-therapeutics (*vide* p. 34).

Lastly, haematinic remedies are wanted in a large number of cases; this is a special indication in the groups of protracted muco-purulent and of all severe purulent catarrhs; and these are also the cases which most benefit under cod-liver oil. The administration of iron is not to be limited to those patients whose anaemia and wasting are obvious; iron and quassia, or some other bitter, and particularly cinchona, are not only well tolerated, but of direct value as stimulants to the relaxed and congested bronchial membrane in cases in which venous embarrassment gives rise to a deceptive appearance of plethora.

In all cases of inveterate catarrh, but particularly in those which from their severity deserve the name of bronchorrhoea, a warm and equable climate during the winter is indispensable. Various sheltered stations have been recommended in this country, such as the Undercliff, Torquay, Falmouth, Ilfracombe, Minehead, the Scilly Isles, and others. Some patients will derive great benefit from a winter's residence in the bracing atmosphere of Thanet. Nevertheless, whenever this is possible, the Mediterranean seaside resorts are to be preferred; and among them the more sheltered, such as Mentone, San Remo, Alassio, Rapallo, the Riviera di Levante, Capri, Malaga, Corfu, Egypt, and suitable resorts on the North African coast. This large subject is fully treated in the article on "Climate in the Treatment of Disease" in the first volume.

Unless the membrane be protected from irritation for prolonged periods no lasting improvement in the condition can be looked for.

Permanent residence for some years in a favourable district is the only really curative treatment; but this may with benefit be combined with a summer visit to one of the hot sulphur springs; or to Ems, Soden, or any of the saline muriated and carbonated springs, suitable for the individual case. The opportunities for permanent residence in eligible climates are widening year by year.

Prophylaxis.—(i.) *Prophylactic Measures between the Attacks.*—No risks should be incurred by the chronic bronchitic patient. Sudden changes of temperature, as at sunset, or from walking out of heated rooms into the cool of the night, or into cold and damp buildings after exposure to the sun, cold winds, dampness of air and soil, dusty localities and occupations, great variations in the amount and thickness of clothing, chill from damp underclothing after perspiration, and, almost above all, inactivity of the liver should be sedulously guarded against. The merely passive avoidance of obvious dangers is, however, a lame policy; we should be prepared for those which are apt to fall upon us unawares. Bracing resorts help us in this by toning up the nerves and tightening the membrane. A great deal can be done by the patients themselves in utilising the opportunities afforded by protective climates for the combined development of muscular energy and of respiratory activity. Systematic and graduated respiratory exercises, based upon the performance of effective expirations, would appreciably relieve the passive emphysematous distension. Much of the hepatic and of the local bronchial congestion will also be corrected by the greater activity of circulation thus initiated; and increased oxygenation will promote the growth of a less delicate and irritable epithelium.

The same tonic system can profitably be applied to the skin by means of a well-planned course of rubbing, bathing, and douching. All these measures need long perseverance before their beneficial effects can be fully secured; but their sedulous employment will bring with it an almost assured reward.

(ii.) *Prophylaxis in Early Bronchial Delicacy.*—Yet more important is the subject of prophylaxis in infancy and childhood. The bronchial tubes are apt to suffer early in life; worst of all is the mischief arising from a severe attack of whooping-cough. Inherited family tendencies may in some children point also to a future liability to bronchitis. Moreover, in the case of all children, and especially of town-bred children, we have to deal with the liability induced by climate. All infants in this country, but in special and varying degrees the offspring of delicate, asthmatic, bronchitic, and gouty parents, stand in need of the help of preventive measures. If this were thoroughly understood and our practice regulated accordingly, a vast saving of life and health would be secured. The prophylactic plan suggested can be summed up in one word. It is a "hardening" plan carried out with vigilance and discretion; its essentials lie in the management of respiration and atmosphere, of temperature, of clothing, and of the skin.

Respiration and the Atmosphere.—It is not sufficiently recognised

that the bronchial tubes and lungs are constructed for the air we live in, and not conversely. Specially strong is the prejudice against night air, which in itself is exceedingly beneficial. The innocuousness for the bronchial membrane of the higher temperatures of atmospheric air needs no demonstration; the innocuousness of extremely cold air, though it is not usually brought home to us, is evidenced by the ease and comfort with which respiration is carried on in arctic temperatures. Much of the objection to night air is generally directed against the dampness of it; but moisture need not in itself be detrimental; indeed, as we have seen, it is often used as a remedy. Nevertheless any of the normal atmospheric peculiarities may cease to be beneficial and may be turned into a source of irritation by a systematic substitution of artificial atmospheres for that provided by nature.

The best prophylactic method is to see that infants and children live and sleep in the open air as much as possible during the day, and enjoy as much free ventilation from the outer air at night as may be compatible with prudence. The full measure of this fresh-air treatment may be attained by degrees only; but it should be persistently aimed at. In towns this rule is of much greater importance than in the country. The extraordinary amount of health enjoyed in London by the children of the poor, in spite of so much that is depressing, is in great measure to be explained by the out-door life they are obliged to lead in their dark streets and alleys.

The Skin and Temperature.—More serious still than the neglected training of the aerial mucous membrane is the neglected education of the heat-generating function in relation to the skin. An excessive amount of clothing by day and by night, with wraps round the neck and wool next the skin, excludes too completely the oscillations of the outer temperature which should act as stimuli to the cutaneous surface. Moreover, the constant moist heat which is thus maintained tends to make the skin delicate and to depress its power of reaction. Flannel underwear is the best and safest for subjects too feeble to keep up their body heat; and it is an invaluable provision against unusual variations in the atmospheric temperature or in cutaneous action, as in athletics, campaigning, rapid journeys through extremes of climate; but its constant use is not part of the systematic training of the skin. In healthy children and adults it is as a rule superfluous at night, although indispensable for children suffering from rickets, restlessness in sleep, or enuresis. When it is worn during the day the outer garments should be made proportionately lighter. To pile up heavy outer clothing over thick flannel undergarments is bad hygiene, and cannot fail to weaken growing children.

Hygienic Treatment of the Skin.—Active means of promoting a vigorous habit of the skin should not be neglected. Massage is almost superfluous in children, whose life is perpetual movement. The chief indication is the sponge bath or the douche and rubbing. Few children will fail to take kindly to the cold bath if trained with sufficient tact to its use. As a rule, there will be no difficulty in obtaining the glow of

cutaneous reaction after the bath by friction with a coarse towel. In some constitutions the cutaneous circulation is slow to recover itself, and some special modification of the bath is called for. An essential precaution is the application of plenty of warmth immediately before and immediately after the cold sponging. The child may be placed for a minute or two into a warm bath, transferred to another bath for cold or tepid sponging, and again put into the warm bath for an equally short time, before towelling. An alternative, and in some ways a better, method is to sponge the surface rapidly with warm water while the child is standing in a warm foot-bath. After the cold sponging he is to stand again in hot water while the body is being rubbed dry. The latter method is extremely simple and very effectual. Adults also who otherwise might be debarred from the boon of the cold bath are in this way enabled to resort to it with perfect safety and with enjoyment. In nurseries a bright fire should be burning before the cold baths are given on winter mornings. The daily cold affusion is of the greatest value as a direct protective against "catching cold"; and its systematic use must be reckoned among the most powerful helps in training a habit of resistance and of ultimate indifference to all ordinary bronchial or cutaneous impressions where debility or inherited predisposition might otherwise have led to ever-recurring risks of bronchitis.

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Consult also Biermer (*v. supra*) and Riegel (*v. supra*).

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BRONCHIAL DILATATION: BRONCHIECTASIS AND BRONCHIOLECTASIS

By WILLIAM EWART, M.D., F.R.C.P.

DILATATION of the air-tubes is a pathological result arising from various causes. But in spite of the diversity of its origin, it lends itself for clinical purposes to a most simple division into two groups: Bronchiectasis, or dilatation of the bronchi; Bronchiolectasis, or dilatation of the bronchioles, which will therefore be described separately.

I. Bronchiectasis

Morbid Anatomy.—Since the time of Laennec, to whom we owe the first anatomical and clinical account of the disease, three main varieties of dilatation have usually been described: (i.) the regular or cylindrical, (ii.) the fusiform, and (iii.) the globular or sacculated. A modification of the *globular* is the *bead-like* variety, in which a tube may present at intervals a normal calibre between successive distensions. Sacculated dilatations, with that exception, are terminal. The *cylindrical* expansions, on the contrary, affect the tubes as they pass towards the periphery. If a further dilatation should occur at their peripheral end, and cause the latter to become bulbous, the *fusiform* variety is brought about.

The largest and most extensive bronchiectases are found in more or less fibrotic lungs. Dilatations occurring in emphysematous surroundings are usually either fusiform or bulbar dilatations of single tubes, or cylindrical expansions of sets of smaller bronchial tubes which may be filled with catarrhal secretion.

Congenital bronchiectasis, the varieties of which constitute a distinct group, may be regarded as a malformation, or as resulting from some intra-uterine disease, perhaps syphilis. Usually one lung only is affected, and may present a large cyst with a central space branching into a peripheral set of intercommunicating secondary and tertiary cysts with serous contents. Instances of this kind have been described by Grawitz, Kessler, Meyer, and by Fränkel. In another variety described by Grawitz, numerous separate cysts are formed on the bronchi of the third and fourth order; some of them communicating with the bronchial lumen, others being entirely closed. Goitre was found associated with this malformation.

In the atelectatic bronchiectasis described by Heller, there is an abnormal growth of the bronchial cartilages, together with remnants of unexpanded, non-pigmented fetal lung tissue; and the epithelial lining is not of the columnar ciliated, but of the pavement type. Cases have also been described by Gairdner, Francke, Herxheimer, Neisser, and others.

Lastly, congenital bronchiectasis may be due to a *dermoid growth* invading a bronchus, as in the almost unique specimen described by Dr. Cyril Ogle. The patient, a male aged twenty-eight, had suffered intermittently for five years with cough and haemoptysis, and ultimately died from profuse haemorrhage, after a period of hectic temperature, fetid expectoration, and physical signs suggesting empyema or bronchiectasis, both of which were found after death. The dermoid mass, consisting of cheesy sebaceous material which contained loose hair and a tooth, was attached to the internal surface of a primary division of the right bronchus; this division was much dilated, and continuous with a large cavity in the substance of the lower lobe. A similar hairy mass,

growing in the upper lobe of the left lung, in communication with the bronchus, is depicted in Albers' Atlas.

Situation of the Dilatation.—Bronchiectasis may be limited to one lung. Lebert found in fifty-four autopsies implication of a single lung in 52 per cent, and of both lungs in 48 per cent. Even when restricted to one lung the dilatations are usually multiple, and they may occur in any situation. Lebert's figures are interesting in this respect; in his twenty-eight cases of unilateral bronchiectasis, six (21 per cent) presented an affection of the upper lobe; one (4 per cent) of the middle lobe alone; nine (32 per cent) of the middle and lower lobes; and twelve (43 per cent) of the whole lung. The view held by Laennec, Stokes, and others, that the apex is the commonest site of bronchiectasis, may have arisen from an imperfect distinction between tuberculous and bronchiectatic lesions. In a further series of fifty-five cases, observed only during life, fifteen (27 per cent) presented bilateral signs. In the remaining group of unilateral cases the upper lobe suffered in six (11 per cent); the lower lobe in fifteen (27 per cent); and the entire lung in fifteen (27 per cent).

Spurious Bronchiectasis.—The distinction between tuberculous cavities and simple dilatation occurring at the apex never presents any difficulty, except in chronic phthisis, or when a vomica has emptied itself of all caseous matter, and presents a smooth and relatively dry surface. This latter condition was described by me in the Goulstonian Lectures on Pulmonary Cavities in 1882. Close inspection will shew: (i.) that the bronchus opens into the cavity too abruptly for bronchiectasis; (ii.) that the bronchial membrane can only be followed over a small surface immediately adjoining the orifice of the bronchus; and (iii.) that the wall of the cavity presents none of that sculptural detail which identifies the original structure of a bronchus even in extreme dilatation.

In a section through a much contracted fibrotic apex, bronchi of normal size may appear to be enlarged owing to the disproportion between the atrophied lobe and its larger air-tubes, which are shortened and slightly widened by its retraction. Moreover, excavation of any part of the lung renders a progressive dilatation of tubes belonging to the same bronchial set improbable, the damaged portion of the bronchial tree having become leaky, as it were, and unlikely to sustain much pressure. In the softening of phthisis the tendency is to an early ulceration and destruction of the tubes; and, as stated in my Goulstonian Lectures on Pulmonary Cavities, although during the progress of excavation the blood-vessels may persist for a long time in the trabeculae, the bronchi—even those of large size—which traverse the diseased region are laid open and removed by ulceration at an early stage.

In the emphysematous tissue surrounding very chronic and practically healed lesions of the apex it is not uncommon to find unimportant dilatations of the peripheral air-tubes due to a rarefaction of the lung substance; these, however, are hardly to be dignified with the name bronchiectasis.

The Changes in the Mucous Membrane and in the Outer Bronchial Coats.—So long as the mucous membrane escapes destruction—and it is remark-

able how long it will remain intact—it presents the signs of catarrh. In its later stages, however, it loses the velvety look, and assumes rather a smooth and shiny appearance consistent with atrophy of the epithelial layer. Most probably the atrophic changes prevail in all cases; although in some they may be limited to the internal coat, the adventitia taking on an inflammatory action which explains the thickening described as the alternative change. In Walshe's words, "The walls of such dilated portions of tube, commonly thick, and exhibiting the several characters assigned to tubes affected with chronic bronchitis, are, on the contrary, in rare instances thin and almost transparent." In general the instances of thickened bronchial membrane are those in which the inflammatory process extends around the dilated tubes into the pulmonary and interstitial tissue; whilst the bronchiectases with thin walls belong to the emphysematous group.

The condition of the mucous membrane differs much in the several varieties and stages of the disease; it is swollen and congested in the acute form (as in the acute cases of childhood), and in those chronic cases which remain free from much accumulation; congested and atrophic in cases of an opposite process; and, lastly, sometimes ulcerated or even gangrenous in the later stages of extensive retention, when septic inflammation has supervened. Marfan devotes a special chapter to "gangrene of the bronchi," which he regards as distinct from pulmonary gangrene and from putrid bronchitis.

Hanot and Gilbert have connected the occurrence of haemoptysis in bronchiectasis with the marked alterations described by them in the blood-vessels, which may form in the submucous tissue an extensive cavernous network, interspersed with numerous minute aneurysms.

According to Professor Hamilton the basement membrane of the original bronchus seldom gives way, but becomes stretched and attenuated. "On the basement membrane stratified columnar epithelium in a wonderful state of preservation may sometimes be found."

The Changes in the Surrounding Pulmonary Tissue.—As stated by Walshe, "The surrounding tissue is either slightly condensed by pressure, hardened by chronic pneumonia, rarefied by emphysema, or perfectly natural." Ulceration occurring in a sacculation is prone to set up fatal pulmonary gangrene. This was observed in twelve cases out of twenty-four by Rapp; in three out of forty by Barth; and in five out of fifty-four by Biermer. The gangrene, as in an isolated case mentioned by Lebert, may perforate a branch of the pulmonary artery. Perforation of the pleura would probably be less rare than it is but for the adhesions which so commonly exist and check the production of pneumothorax and of subcutaneous emphysema. Both these conditions have, however, been observed.

Sir T. Grainger Stewart has described the process of absorption by which bands are left stretching across bronchiectatic cavities; or the latter may become multilocular, as is often seen at the pulmonary base.

Inflammatory changes in the pulmonary tissue in the vicinity of

the lesions are common. Acute pneumonia was recorded in twelve cases by Biermer, and in five by Lebert. Some inflammation also extends to the air-tubes in general. Hypertrophy of the bronchial cartilages, and a calcification of the walls of the dilated tubes—which is stated by Biermer not to be uncommon in the bovine species—have been described in isolated cases.

A cystic form of bronchial dilatation has sometimes been described (Biermer, Briquet); the cysts, which average the size of a walnut, being associated with a bronchial stenosis situated higher up. The contents may be serous, mucous, caseous, or even calcareous.

The secretion found in the dilated bronchi at different stages varies in its fetor, and in the proportion of its fluid and of its solid constituents. Among the latter may be found: (*a*) recent mucus; (*b*) small casts, described by Dittrich and by Grainger Stewart, sometimes presenting epithelial flakes; (*c*) stale, opaque mucus undergoing granular and fatty degeneration; (*d*) micro-organisms of putrefaction (including sometimes sarcinae and *Leptothrix pulmonalis*, to which is due the purplish colour reaction of the bronchial casts on the addition of iodine), but no tubercle bacilli. Influenza bacilli may be constantly present in the sputum, either in mixed or pure culture (Lord, Boggs). Occasionally the contents are blood-stained. Very frequently, though not always, crystals of the fatty acids and of cholesterin are found, especially in the fetid stage. Calculous concretions have also been observed (34,106).

Pathological Changes in Distant Organs.—Various accidental complications have been described, such, for instance, as cancer, which Barth recognised in 8 out of 43 cases. The associated changes special to the disease are chiefly those connected with the obstructed circulation through the lungs; secondary dilatation of the right side of the heart, and venous congestion in the portal and in the systemic circuits. Valvular lesions may coexist, but do not appear to be traceable to the disease; pericardial adhesions sometimes occur as an extension of the pleuro-pulmonary fibrosis. The liver is almost always congested; it may present fatty change, and is sometimes lardaceous. Lardaceous degeneration also occurs in the kidney; and catarrhal nephritis has been recorded. Abscesses may be set up in various situations; the brain is not an uncommon site.

A subacute arthritis, analogous to gonorrhoeal and other forms of infective arthritis or to that sometimes following dysentery, was described by Gerhardt in two of his cases as secondary to the bronchial trouble. It is one of the recognised consequences of an infected state of the dilatations.

The well-known *skeletal changes*, not limited to this disease, described by P. Marie and by Souza-Leite under the name of Hypertrophic Pulmonary Osteo-arthropathy, had been previously noted by Bamberger [*vide* Vol. III. p. 64].

General and Clinical Causation.—The insidious beginnings and the chronic course of bronchiectasis are not favourable to a study of its

causes. Statistics of the disease at *various ages* can only deal with approximations. Lebert, in a series of 83 cases, found 47 per cent occurring before, and 53 per cent occurring after, the age of 40.

7	per cent occurred	under	the	age of	10
8	„	„	„	„	20
20	„	„	from	the age of	20 to 30
12	„	„	„	„	31 „ 40
18	„	„	„	„	41 „ 50
11	„	„	„	„	51 „ 60
24	„	„	„	„	61 „ 85

In Dr. Acland's series of 60 cases 46 or 76·7 per cent occurred before, and 14 or 23·3 per cent after the age of 40.

The congenital dilatations are exceedingly rare.

The male *sex* is more often affected than the female, according to Trojanowski and Bamberger; but Biermer and Williglk have not traced any difference. *Occupation* does not influence the production of the disease in any direct way, though it may act indirectly by setting up pulmonary and bronchial changes favouring a dilatation. Depressing circumstances of all kinds might also have an indirect effect.

Clinical Antecedents.—We have no proof that the change ever arises spontaneously during extra-uterine life. In children we are able to trace its acute form to bronchitis. Fatal cases of this kind furnish us with the only direct evidence in favour of a definite causation from acute inflammatory disease; but clinical observations, although less conclusive, lend their support to the same view. When not traceable to an acute attack, dilatation is probably secondary to some chronic bronchial or pulmonary affection, and the precise time of its onset becomes difficult to determine. Influenza certainly gives rise to acute bronchiectasis as shewn by post-mortem examination. Some cases of this kind may recover, others become chronic.

As regards the immediate etiological factors Lebert's results are probably trustworthy. In a quarter of his series there had been previous emphysema; in another quarter an acute pleurisy or an acute pneumonia had preceded the disease; and in a large number the history was one of long-continued bronchitis with intercurrent acute attacks (Wilson Fox). Thus, bronchitis in all its forms, but especially when complicated with spasmodic cough, as in whooping-cough (Laennec) and in asthma (Hyde Salter), contributes a well-marked etiological group; pulmonary diseases, whether acute or chronic, rarefying or condensing, forming a second group; and pleuritic affections a third. A fourth group is that in which a temporary or permanent narrowing of a large bronchus, as by an aneurysm, has led to increased strain or to accumulations within its subdivisions.

In forty cases of bronchiectasis verified by necropsy Dr. Acland found that the causes or antecedent conditions were as follows:—Chronic bronchitis (*e.g.* cough, onset gradual), in 18 or 45 per cent; chronic cough since childhood, in 6 or 15 per cent; pleurisy, in 5 or 12·5 per cent;

pneumonia, in 4 or 10 per cent; tumour, in 3 or 7·5 per cent; foreign body, in 2 or 5·0 per cent; aneurysm, in 2 or 5·0 per cent.

The relation to tuberculosis has been much discussed. Some, including Rokitansky, have regarded the two diseases as almost incompatible, and as mutually protective. Nevertheless, true bronchiectasis may occur in the subjects of chronic tuberculous disease; for instance, at the base of a lung with an indurated apex. And, conversely, sufferers from chronic bronchiectasis may end in tuberculosis, though this is rare.

Wilson Fox suspected that the fibrotic induration around the tubes was probably tuberculous in its origin, the other tuberculous deposits in the same lungs having been slight and obsolescent: but this opinion does not appear to have had the support of any direct evidence.

Biermer, who quotes Trojanowski as reporting tuberculosis in 21 out of a series of 68 cases, could only find 3 in his own collection of cases. As pointed out by Wilson Fox, discrepancies of this magnitude can only be explained on the score of some confusion between tuberculous lesions and those due to bronchiectasis.

Pathological Etiology.—The history of the subject is a record of hypotheses as varied as the associated intrathoracic conditions; but they may be briefly classified as attempting to identify the causation (1) with changes limited to the tubes themselves, (2) with changes in the pulmonary tissue, (3) with changes in the pleura, or lastly (4) with a combination of the bronchial, pulmonary, and pleural changes.

Apart from the congenital group, some cases carry their own explanation of the mechanism of production. Cicatricial stricture, lateral pressure from aneurysms or morbid growths, internal obstruction due to tumours, and particularly the impaction of foreign bodies are all occasional causes of bronchiectasis. But those needing elucidation form a much larger group.

Laennec regarded the dilatation as due to an accumulation of mucus. Andral accepted this view only for the bead-like form, and attributed the other dilatations to a process of hypertrophy analogous to that of other hollow organs; this was also in part the view of Louis. Rokitansky, and subsequently Hasse, assumed a stenosis of the larger and an obliteration of the smaller bronchi, with compensatory dilatations elsewhere. Stokes and Williams traced the production of dilatation, under stress of cough or of accumulating secretion, to impairment of elasticity and of muscular contractility by inflammation. Atrophy of the bronchial muscles has been described by Bamberger, by Trojanowski, by Lebert, and, as a primary and probably constitutional defect, by Sir T. Grainger Stewart. Lebert also suggested that dilatation might be due to atony dependent upon defective innervation. Various other pathologists (Beau and Maissiat, and Mendelssohn) have insisted on the share taken by cough in the production of dilatation.

Wilson Fox considered all forms, except those secondary to a constriction, as essentially inflammatory in origin; the loss of elasticity and muscular contractility of the tubes themselves being the only essential

changes, and sometimes the only changes found; whilst on the other hand the dilatation would be favoured by the coexistence of a pneumonia, or of a bronchopneumonia, or by pulmonary collapse or tuberculous indurations in the surrounding tissue. The acute bronchiectasis of infantile bronchitis he regarded as due to cough pressure rather than to any inspiratory mechanism or to any indirect effect of collateral collapse; but the proofs upon which he based this view were not fully stated by him. As an explanation of the infrequency of bronchiectasis, in spite of the great frequency of bronchitis, Wilson Fox alleged that the dilatation is readily recovered from in children; and that in adults chronic bronchitis tends to hypertrophy rather than to weaken muscular fibre, in contrast with its action upon the pulmonary parenchyma.

It is noteworthy that Biermer traces as many as a quarter of the aggregate cases to acute pneumonia. The strict priority of the pneumonia is in many cases difficult to establish, and therefore open to some doubt.

Biermer is also a believer in the influence of pleural adhesions, which, according to Wilson Fox are more easily explained as a secondary process. A compression of the lung by fluid was regarded by Buhl as most likely to lead eventually to bronchial dilatation. In this connexion it may be pointed out that in simple pulmonary collapse no dilatation can occur in previously healthy tubes, so long as they receive evenly from all sides the strong support of carnified tissues; and that on the other hand the appearances of dilatation are very apt to be simulated by the shortening and retraction of tubes within a collapsed portion of the lung.

The explanation given by Sir Dominic Corrigan of the mechanism of the dilatation in cirrhosis of the lung, though it may not be correct, has become classical. It was subsequently adopted almost unaltered by Rokitansky and by Lebert. The latter based the etiology, at least in fibrotic cases, on some antecedent *pleuritis profunda* setting up a proliferative irritation in the pleuro-pulmonary connective-tissue. Owing to the rigid connexion of the surface of the fibrosed lung with the chest wall, not only will the spontaneous shrinking of the fibrous tissue lessen the distance between the chest wall and the bronchial wall, but every inspiratory effort of the former will take effect in dilating the cavity of the bronchus. It has been objected that in reality the opposite mechanical effect results, and that it is the thorax which is drawn in instead of its drawing out the lung. It should not be forgotten, however, that a considerable divergence must arise between the lines of retraction of a general or *massive* fibrosis, and those, apt to be multiple and less uniform, of a scattered *reticular* fibrosis of the lung.

Dr. David Drummond's views on the production of bronchiectasis from *pleuro-bronchitis* are suggestive:—

"The common form begins as an acute bronchitis and pleurisy, to which the name pleuro-bronchitis is fairly applicable. The process leads early to blocking of some of the larger tubes by hypertrophic thickening of the mucous membrane, and in consequence to collapse of lung and

diffuse bronchopneumonia. This form of pleurisy is essentially progressive. The fluid becoming absorbed, fibrous thickening of the pleura sets in. Tube after tube becomes blocked and subsequently dilated from pent-up discharge, which in time bursts away. After death the tubes first attacked are found surrounded by fibrous tissue; but those affected later are devoid of fibrous tissue, and only nuclei and collapsed lung can be found in their vicinity, shewing that the fibrous tissue is developed after the dilatation of the tubes."

Most of these hypotheses are summed up and criticised by Sir T. Grainger Stewart and Dr. Gibson under the headings of:—(1) Direct pressure of stagnating secretion—a mechanism in which they do not believe; (2) Concentrated air-pressure, as in cough (Reynaud, Williams), an explanation which they regard as inadequate apart from another factor, that of an essential debility of the bronchial wall; (3) Extra-bronchial traction—which they recognise only in cases of pulmonary cirrhosis, but not in all, since in as many as 20 per cent of them Dr. Bastian did not find any dilatation; (4) Inflammation of the bronchial wall causing loss of elasticity, of contractility, and of ciliary movement (Stokes)—a view which, according to them, leaves unexplained the infrequency of bronchiectasis in spite of the great prevalence of bronchitis; (5) Dilatation as a result of defective innervation and loss of tone, as alleged by Lebert, an origin which they regard as unproved; (6) Lastly, Sir T. Grainger Stewart's hypothesis, first published in 1867, refers the origin of a large proportion of the cases to a constitutional, or possibly, as held by Leroy, to an hereditary weakness, a "primary atrophy" of the bronchial wall, unfitting the bronchi for stress even within the physiological limits of powerful inspiratory efforts, of cough, and of violent exercise. Once originated in an insidious manner, this *primary bronchiectasis* progresses to the fully developed forms with the well-known symptoms.

In another large group—that of the *secondary bronchiectases*, including a *general* and a *local* variety of dilatation—the same authors recognise among the determining causes the influence of pertussis, of capillary bronchitis, of bronchial stenosis or impaction, of pulmonary cirrhosis. Most of the explanations hitherto attempted have, according to them, been limited to these secondary varieties. Here again individual delicacy or inflammatory impairment of the contractility or of the elasticity of the bronchi may be frequent factors in the result.

The Mode of Origin as viewed by the Writer.—The first essential for a comprehensive hypothesis of bronchiectasis is a sufficiently broad basis. There is one feature which is common to all; namely, the faulty distribution of space between the air-tubes and the pulmonary tissue. In health the intrathoracic space is suitably distributed between its several contents; the functions of which are regulated for the avoidance of undue stress on any one of them. Any excessive stress ultimately finds out the least resistant tissue, and this is most often the pulmonary tissue which becomes emphysematous. In exceptional instances of sustained intra-

pulmonary pressure, the bronchi suffer instead of the pulmonary tissue. Disorderly nutritive changes may have occurred at an early period of development as a result of some vascular disease. On the whole, however, there is little support for the view that bronchiectasis is developed independently of any local disease, as a progressive deterioration due to an innate local delicacy.

In disease, mechanical factors arise which are entirely foreign to the natural play of the organ, and which do not necessarily seek out the weakest part. To these belong, within the tubes themselves, an accumulation of mucus and the antecedent or the resulting degenerative changes in the bronchial wall.

A second influence is that of changes induced in the lung tissue. In a rather large proportion of cases bronchiectasis is accompanied by more or less emphysema. Much of this is clearly a result rather than a cause, since the ordinary vesicular emphysema does not carry with it any accessory bronchiectasis.

Another frequent accompaniment of bronchiectasis is pulmonary collapse. When occurring unevenly, at one side of a bronchial tube, this may act as one of the agents of dilatation. Not only in advanced bronchiectasis do we often observe a proportionate amount of condensing fibrosis of the lung, but in any recent dilatation, such as that witnessed in the infant after bronchitis or whooping-cough, the incipient bronchial bulgings occur side by side with considerable lobular collapse.

A further set of structural changes contributing, in a large proportion of the cases, to faulty allotment in space, are those of the pulmonary stroma, which includes the subpleural, the perilobular, and the interlobular systems.

As to the *general mechanism* of the dilatation we must again look for some elementary factor common to all varieties; and this we find in "obstruction," understood in the broadest sense of the word.

In the alimentary tract and in most animal tubes the obstruction is invariably situated forward, beyond the dilating segment. In the bronchial tract no such local restriction obtains. Neither is the nature of the obstruction necessarily limited to stenosis or to impaction. Owing to the alternating direction of the respiratory air-currents, an obstruction may lead to dilatation either on its proximal or on its distal side. Again, the dilating force is not usually, as in other tubes, the pressure of an accumulation within the dilating bronchus. This mechanism may occur in the bronchial system: an instance in point is the thin-walled sacculation, completely filled with stiff gelatinous mucus, sometimes found beyond a bronchial stenosis. But much more often the obstruction has its seat on the distal side of the dilatation and is not a bronchial stenosis, but a terminal occlusion of a respiratory district of the lung; and the dilating force, far from being exclusively due to the pressure of an internal accumulation, is then applied to the outside of the tube; it is an aspirating, not a forcing pressure.

If we bear these elementary data in mind we shall find that the

details of the problem work out. Thus, whereas in the normal state each pulmonary constituent preserves its relative position and its allotted space, the local failure of any individual constituent to perform its respiratory function would interfere with the perfect adjustment of other parts during the phases of respiration. How readily bronchiectasis might result from this disturbance will be seen from a consideration of the forces which normally protect the weaker non-cartilaginous tubes against the dilating influences of atmospheric pressure. The elasticity proper to the inflated pulmonary tissue through which they pass tends to widen them; but this tendency is counteracted by the inspiratory elongation of the lung, and probably never goes further in health than to ensure their patency, thus acting in the depth of the lung in lieu of a cartilaginous armature. On the other hand, both during inspiration and during expiration, the small tubes receive lateral support from their closely fitting environments. Let this support be withdrawn at any one spot by the persistent inspiratory inactivity of one of the adjacent lobules, even though this were merely a delay in the fulfilment of inspiratory inflation, then the imperfectly resisted intrabronchial pressure would gradually bulge out the yielding wall into the space rendered available, and thus establish the first stage of a progressive dilatation. Or, to put the matter more clearly, the inspiratory traction made by the chest wall, if it should fail to expand an obstructed lobule, might be transmitted to the delicate air-tube adjoining the latter, and might dilate it.

Owing to the solidarity existing between all parts of the lung, this *encroachment of bronchial space into the vacated pulmonary space* may occur at a distance from the original collapse. The same mechanism might therefore be concerned in some measure in the production of almost every variety of bronchiectasis. Its more strictly local operation is probably alone concerned in the early stages of the affection when the pulmonary tissue is still free from induration. In some instances bronchiectasis remains permanently uncomplicated with any pulmonary fibrosis, or with any peribronchial thickening. It is in these cases that the bronchial membrane preserves its delicate and transparent thinness. The plug of semi-gelatinous mucus which sometimes fills simple dilatations of this kind in the midst of soft spongy lung tissue suggests that the mucus itself was originally the obstacle to the free inflation of the collateral lobules, whilst its accumulation eventually assisted in producing the distension.

The progressive increase in the dilatation may conceivably be brought about by the various mechanisms assumed by the so-called inspiratory and expiratory hypotheses; although much that has been advanced in connexion with them is lacking in strict proof. Thus:—

(i.) *The inspiratory hypothesis* of Laennec asserts that the abnormal inspiratory effort preceding cough throws damaging stress upon the weakened parietes of the bronchial tube. In the diagram (Fig. 13) which illustrates this supposed agency, if we imagine the shaded zone to remain unexpanded, the arrows would represent the inspiratory traction thus transferred from the alveolar to the bronchial walls.

The same explanation has been applied to the condition which may result from a proximally situated stenosis, when the impeded removal of the products of catarrh from the terminal districts has led to an irregular lobular collapse with consequent disturbance of the balance of pressures.

(ii.) *The expiratory hypothesis* has also been pressed into the service of bronchiectasis as well as of emphysema. Were it not that one of the chief functions of man in earning his bread by manual labour is the performance of *muscular strain with closed glottis*, and that his organs are specially constructed for that purpose, the wonder would be that bronchiectasis and emphysema are not universal.

As a fact, nothing gives way within our visceral cavities under the high pressures due to muscular strain so long as every part is sound and works true. The extent to which we are dependent for this immunity

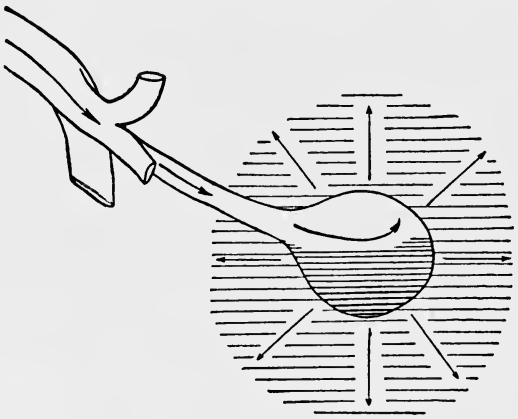

FIG. 13.—Illustrating the alleged mechanism of dilatation, according to the inspiratory hypothesis.

upon a perfect distribution of pressures is illustrated by some of the delicate valvular membranes of the heart which could not perennially resist the stress to which they are exposed, were not the pressure exerted upon one of the two surfaces neutralised by equivalent pressure of support on the other. So must it be also with the delicate bronchial membrane. The range of pressures to which it is exposed is not so great, but the risk is multiplied by the number of the subordinate districts. A loss of the even balance between the intra- and the extra-bronchial pressure occasioned by imperfect inflation of any of the latter might in delicate and predisposed subjects cause the bronchial wall to yield to progressive dilatation.

Cough is a special instance of muscular stress; it is often complicated by the mechanical influence of the secretion which excites it. The diagram (Fig. 14) illustrating the mechanical hypothesis of expiratory pressure will also serve to explain this point.

The cough which may be powerless to dislodge and evacuate the contents may yet propel some of them far enough to cut off the dilated chamber from the main bronchial channel. The moment represented is that of the explosive expiration, when the air accumulated under high pressure leaves the chest without any further hindrance. Alone in the dilated tube the pressure, indicated by the curved arrows, will remain at that moment nearly as high as during the period of closure of the glottis; and its dilating effect is but feebly counteracted by the released elasticity of the immediately surrounding lung tissue. Slowly, with the ensuing inspiration, the plug may be sucked in again; and this suction is the most likely explanation of the long-drawn, semi-musical, or croaking rhonchi and rales of bronchiectasis.

The practical results of a recurring valvular obstruction of this kind

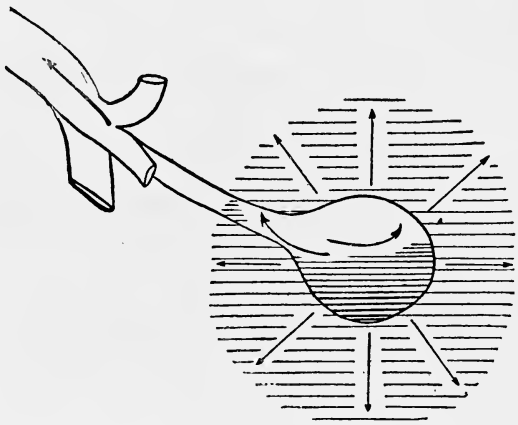

FIG. 14.—Illustrating some of the effects of cough in bronchiectasis. (From *Clin. Journal*, 1894, iii. 280.)

would be not only a continued fulness of the dilatation, whilst the surrounding tissues are being relieved of much of their air, but a maintenance within it of the highest air-pressure at the time when the air-pressure in its vicinity is at its minimum. Neither should we lose sight of the possible injection into the tributary bronchioles and lymphatics of some of the bronchiectatic contents.

Most cases may begin and progress after the mode suggested; but, except in fatal cases of bronchitis and whooping-cough in children, where these etiological relations are well displayed, an opportunity of examining the lung at this stage is not often afforded; and ulterior changes of a very different kind usually obscure, more or less completely, the original mechanisms.

The influence of catarrh seems entitled to be regarded, as it has been by most writers since Laennec, as the chief and earliest etiological factor of bronchiectasis. The inflammatory softening and weakening of the

bronchial wall, the changes in its muscular and fibrous coats, whether in the direction of atrophy or of overgrowth, are all possible accessory agents; but the special action of catarrh consists in the mechanical plugging of bronchioles. When a bronchiole becomes occluded the amount and the pressure of the air within its district are rapidly altered, and the balance of pressures will be disturbed to the special detriment of the tube from which the bronchiole sprang. If the pressure can be speedily readjusted by collateral expansion in the vicinity any strain or dilatation thus induced will be corrected. Failing this adjustment, however, the existing catarrh will aggravate the dilatation by a tendency to accumulation and by the impairment of the respiratory mechanisms of relief.

The successive obliteration by catarrh of many tributary bronchioles is probably the mode of extension of bronchiectasis. The greater the stretching of the dilated bronchial membrane and the accumulation within it, so much the greater will be the number of collateral bronchioles obliterated by stretching or by plugging, and so much the greater the extent of the resulting atelectasis.

A direct influence aiding the dilatation is that of any impairment of the muscular coat, whether in its structure, as in the atrophic fibrosis described by Lebert, or the simple atrophy of Grainger Stewart; or in its function, as in atony from defective innervation, or from insensitiveness of the mucous membrane.

Indirectly, the process of dilatation by accumulation and retention might be favoured, as in pertussis and in acute bronchitis, by the opposite condition of bronchial spasm, since this would lead to a narrowing and to a more ready plugging of the smaller tubes. This is most probably the history of bronchiolectasis.

The Influence of Interstitial Pneumonia and Fibrosis.—In whatever way it may have arisen, a sacculation of a small bronchus is fatally prone to accumulate secretion during periods of catarrh, and to resulting irritation not only within its own terminal divisions, but probably, by overflow and by inhalation, in collateral lobules also. This is the beginning of an interstitial pneumonia, the ultimate result of which may be a conversion of the pulmonary substance into structureless fibrous tissue. The loss of expulsive power is progressive, and the shrinking of the chronically inflamed parenchyma favours the encroachment of the sacculation; whilst the implication of the lymphatics of the lobule causes an extension of the changes along the perilobular system. In this way the pulmonary degeneration is promoted along two lines, by intralobular and by perilobular agencies. How far it may extend will depend upon the varying ability of the remaining pulmonary tissue to replace by its increased expansion some of that which has atrophied. Dense adhesions would largely interfere with this compensatory process.

The Influence of Pleuro-pneumonic Fibrosis.—The close relationship existing between the pleura and subjacent stroma and the lymphatic system of the lung explains the influence which agglutination of the pleural surface exercises on the course of the interstitial pneumonia,

and on the etiology of bronchiectasis. Extensive pleuritic thickening at the base, with obliteration of the groove and agglutination of the surface of the diaphragm, cripples the lung. The respiratory function of the base is almost entirely lost, or can be carried on only by considerable mechanical effort on the part of the diaphragm, and of the inspiratory muscles; an effort which must tell on the pulmonary tissue as a constantly recurring and irritating traction. The lymphatic circulation may also be impeded. The result is usually a considerable shrinking of the side affected, and a compensatory hypertrophy of the sound lung, with visible distension of that side of the thorax, and some curvature of the spine.

The process which has just been sketched is essentially that originally described by Corrigan under the name of "cirrhosis of the lung."

The Influence of Stenosis.—Dilatations are by no means the invariable result of bronchial stenosis. When a bronchiectasis occurs beyond the stenosis its mechanism is generally held to be analogous to that of emphysema from a partial obstruction of tubes, which allows a slow entrance, but unduly delays the escape of air. Syphilis, being a well-known cause of bronchial stricture, should be allotted a place among the recognised factors of bronchiectasis. It is not improbable that in some cases the occurrence of a late ulceration of the dilated tubes may be due to the same influence.

Hoffmann believes that sufficient attention has hardly been paid to the probably frequent origin of bronchiectasis from *inhalation of solid particles*; and he refers to the experiments of Cohn which shew that dilatation occurs not beyond but at the seat of impaction, around the impacted foreign body.

Lichtheim's experiments go to prove that total closure of a bronchial tube leads within twenty-four hours to atelectasis of the pulmonary district, with purulent accumulation within the tubes. After several weeks the obstructed bronchi become more or less dilated at the seat of impaction, the surrounding tissue being completely compressed by the bronchial distension, or expanded by collateral emphysema.

Beyond any valvular obstruction micro-organisms which easily penetrate through the stenosis may set up fermentation, and the secondary results of putrid decomposition will follow.

Symptoms.—The severity of the disease varies greatly in different individuals and at different stages in each. Its course and its symptoms are largely determined—(*a*) by the mechanical factors, such as induration or persisting elasticity of the surrounding tissue, position of the dilatation, its single or multiple character; (*b*) by constitutional factors special to the individual or to phases of his general health; and (*c*) by climatic and atmospheric factors, including not only temperature and humidity, but also purity of air, in the sense of relative freedom from septic germs.

It has already been stated that in exceptional instances bronchiectasis may be latent for some time after its commencement: in a few cases also there may be periods of quiescence during which it might pass unobserved.

These are the milder forms, of a catarrhal and emphysematous type—non-indurative, non-septic, non-ulcerative, progressing but slowly, and compatible with relative longevity. All cases are liable to exacerbations in the symptoms, to occasional or periodical increase in the expectoration, to recurring intervals of fetidity of the sputum, and to intercurrent attacks of general bronchitis or catarrh.

Constitutional Symptoms.—For long periods the flow of expectoration, sometimes even when fetid, may proceed without making any obvious impression upon the general nutrition or functions; but these are gradually involved as the diminution of respiratory surface and consequent loss of energy advance; and ultimately the system is contaminated by the septic matters inhaled, absorbed, and swallowed. The constitutional symptoms set in at different stages, and at first may not be permanent, but coincide with transient periods of fetor of the sputum. In the worst forms these deteriorations are lasting. Sooner or later the pulse and respiration become permanently accelerated, and the temperature moderately hectic, or at the least remittent, with an evening rise to 101° or 102°, and in a few cases with associated night-sweats. Diarrhoea may be among the septic symptoms, and sometimes vomiting also. Vomiting as a mechanical result of cough is not so common in bronchial dilatation as in phthisis.

Failure of cardiac energy lies at the root of the final cachexia. In addition to the previous lividity and cyanosis oedema supervenes, and the patient becomes a bed-ridden invalid. At this stage, or prior to it, intercurrent albuminuria may be observed; or in association with lardaceous disease it may become permanent. Various complications may cut short the gradual process of exhaustion; low pneumonia, putrid bronchitis and gangrene, septicaemia or pyaemia, cardiac or renal disease, and cerebral abscess are among the most common. In the more favourable cases, especially when helped by the advantage of climate and treatment, the sufferers may live with their trouble for years, and die from other causes. Those who reach a relatively mature age are more and more exposed to catarrh and emphysema with their attendant symptoms, and the disease, whether directly or through its complications, is usually responsible for death.

Pulmonary Symptoms.—Under this heading we must briefly review pain, dyspnoea, and some other modifications of the respiratory function such as cough, expectoration, and haemoptysis.

Pain.—In spite of the profound changes within the lung, pain does not appear to be set up in it by the distension of the tubes or by their irritation. The existence of pain is an individual rather than an essential feature in the course of the affection, and therefore variable. When it occurs, as it probably does incidentally in all cases, it may be intercostal or pleural from cough-strain, or pleuritic (of congestive, pleuro-pneumonic type). In some cases it may possibly be rheumatic, in connexion with thick pleural adhesions.

Dyspnoea.—There is often a cardiac element in the dyspnoea observed

in bronchiectasis. Much cardiac and nervous depression is induced at times by septic absorption from the bronchial tubes and through the breath, especially in ulcerative cases. As a rule, during the major part of the clinical history the dyspnoea is not excessive; but it varies much with the degree of emphysema or of fibrosis, and with the amount of intercurrent catarrh. In the ultimate stages dyspnoea becomes a prominent feature.

Cough.—A leading peculiarity of the cough of uncomplicated bronchiectasis is its intermittence. It would seem as though the sacculated membranes lost their sensitiveness, and that cough were excited only when the tide of accumulation reached the level of some healthier part of the bronchial tubes. It is often observed that for long periods, during which a patient preserves the posture which acts as a protection, no cough is set up; but change of position will bring on severe spasmodic cough and profuse expectoration. The severity of the cough and its paroxysmal character are explained by the irritating quality of the secretion which has to be forwarded through the sensitive upper passages; and also by the difficulty, or impossibility in some cases, of complete relief on account of the position of the sacculations. Whereas an overflow relief of the surplus of the bronchial contents is comparatively easy, nothing short of an inversion of the patient could empty some of the ultimate dilatations, especially when surrounded by fibrous tissue. The creosote inhalation method introduced by Dr. Chaplin has demonstrated that the fetor of this residual material is much in excess of that of the tidal output, a point of the utmost importance in treatment.

Expectoration.—The sputum in bronchiectasis varies considerably in amount and in character. Sometimes it remains sweet and almost purely mucous for long periods; more usually it is muco-purulent throughout; in most cases it becomes fetid at times; or lastly this may be the habitual condition. Very often, when ulceration has taken place or after severe paroxysmal cough, it is slightly blood-stained. A dirty lemon tinge indicates that the secreting membrane is in a state of haemorrhagic congestion.

A third of a pint or half a pint is not an unusual daily quantity; but this amount is often much exceeded. The way in which the expectoration pours out of the mouth in some cases is almost distinctive, though the same peculiarity may be observed in phthisis. At intervals the expectoration may be much lessened or completely absent. Complications, especially bronchitis or pneumonia, commonly reduce the amount.

The sediment deposited by the expectoration, which may separate into an upper frothy mucus and a lower puriform layer with an intervening opalescent watery layer traversed by strings of mucus, presents, besides bronchial epithelia, numerous pus-cells, granular debris, bacteria and vibriones, fatty-acid crystals, and occasionally sarcinae, leptothrix, Dittrich's plugs, and Charcot-Leyden crystals. The presence of elastic fibre would be a proof of ulceration. The fetor is apt to be great, but it is often more marked in the cough-breath than in the sputum itself.

Haemoptysis was among the symptoms described by Laennec. Walshe failed to observe haemoptysis except in the presence of mitral disease or of tubercle. Lebert observed haemoptysis, of varying degrees but decidedly more marked than that which belongs to ordinary pneumonia, in one-sixth of his cases. Biermer reports one case of fatal haemorrhage in non-tuberculous ulcerative bronchiectasis. Wilson Fox, who quotes these authors, refers to it as not being rare. It may occur early and independently of any ulceration. On the whole, it is to be regarded rather as a frequent complication than as an invariable symptom. This is borne out by Dr. Acland's experience of the incidence of haemoptysis in 25 cases of bronchiectasis verified by autopsy at the Brompton hospital; in 5 or 20 per cent it was absent; in 8 or 32 per cent there was streaky, and in 5 or 20 per cent moderate haemoptysis (℥ii-℥vi); and in 7 or 28 per cent haemoptysis was profuse (a pint or more).

The respiratory symptoms vary with the degree of the pulmonary atrophy. Among them are to be noted frequency of breathing and dyspnoea on exertion, and, in severe unilateral cases, inability to lie on the sound side.

Physical Examination of the Chest.—*Inspection.*—There is no distinctive chest shape common to all cases of bronchiectasis. The thorax does not present the characteristics of phthisis, even though one side may be much retracted. Whatever amount of flattening may be present locally, this is compensated elsewhere by active thoracic expansion. The immunity of the apex in the majority of cases and its compensatory expansion, coupled with the fulness of the neck, establish at first sight a distinction from the ordinary case of phthisis. Often, on the other hand, the deformity peculiar to emphysema may be more or less fully established. The unilateral character of the group of cases described by Corrigan as cirrhosis of the lung is usually made obvious by the cardiac displacement, and by the extreme disproportion both in the size and in the respiratory movements of the two sides of the chest. But in some unusual cases, owing to considerable encroachment of the sound lung across the middle line, the thorax on the side affected is much less collapsed than the lung which it contains. Cases of this kind are deceptive, and need, for an accurate determination of the size of the lung, a very careful percussion of the boundaries of the cardiac dulness. I have described a case of this sort. This cirrhosis of the lung without thoracic deformity is much less readily distinguished from phthisis or from chronic bronchitis than the usual form.

Among the bilateral cases the emphysematous variety is to be diagnosed from phthisis, on mere inspection, by the dusky and congested complexion, the prominent veins and deeply coloured lips, the high, deep, and broad chest, and the relatively good nutrition.

In the remaining groups the diagnosis may be assisted by a knowledge of the following points:—(*a*) A bronchiectatic lesion, if solitary, is seldom localised at the apex; this is the customary site for the tuberculous lesion. (*b*) The supraclavicular area is usually not implicated in any

dulness due to bronchiectasis; it is invariably implicated in the apex dulness of phthisis. (*c*) In phthisis, as pointed out by Stokes, consolidation precedes, excavation follows; in bronchiectasis this is otherwise. And again, extension of the excavation is peculiar to phthisis (Stokes), whilst a stationary size belongs to bronchial dilatation (Walshe). (*d*) The almost daily alternations between the signs of fulness and those of vacuity greatly help the diagnosis of sacculation. This peculiarity is usually absent or inconstant in excavating phthisis. (*e*) The normal site for tuberculous disease is the apex; it hardly ever involves the base. The site of predilection for bronchial dilatation is the base; but bronchiectasis also favours the middle and lower thirds of the back and may affect various other situations without any hitherto ascertained regularity of order; it is specially uncommon in the district of the vertical bronchi ascending to the apex. (*f*) It is unusual in phthisis for multiple excavations to form in the same lung with the intervention of sound pulmonary substance, except in the situations described in my Goulstonian Lectures for 1882, and in Dr. J. Kingston Fowler's *Dictionary of Medicine*. Even these secondary cavities are commonly almost continuous with the upper zone of disease. In multiple bronchiectasis a truly sporadic arrangement is the rule. (*g*) Unilateral indurative tuberculous phthisis invariably excavates and condenses the apex first, even if later it should extend downwards. The fibroid change associated with bronchiectasis originates as a rule at the base and spreads upwards. (*h*) The displacement of the heart towards the diseased side of the chest in the usual cases of unilateral phthisis follows an oblique direction upwards; a horizontal displacement is exceptional and suggests some complicating basic-pleural factor. In unilateral bronchiectasis the displacement is, practically speaking, always horizontal; not only by reason of the basic origin of the disease, but largely also owing to the lowering of the diaphragm on the sound side, with extension of the cardiac beat into the epigastric notch.

Attention to these general guides may often prove of greater value than a close search for points of difference in the auscultatory and percussive sounds.

Percussion in advanced cases may yield different results in the same chest at brief intervals of time, according to the amount of retained secretion; and this variability is perhaps the most distinctive feature obtainable by the method. If in an otherwise resonant chest patches of dulness be found scattered in the middle and lower thirds, and particularly over the back, and if some of them yield a cracked-pot sound, a strong suspicion of bronchiectasis will arise. The high-pitched, the tympanitic, the amphoric, the splashing, and other varieties of percussion note which have been described cannot be expected in every instance. Much emphysema may almost preclude a diagnosis by percussion alone; although with a previous knowledge of the existence of sacculations their site could in most cases be made out by an expert percusser. The strong element of dulness in the fibroid variety of the

disease, coupled with the boxy note obtained over the cavities when empty, is a much more definite guide; although the diagnosis from a basic cavity of tuberculous origin would still have to be made.

Auscultation, although not always capable of establishing a diagnosis between slight bronchiectasis and bronchial catarrh, seldom fails to identify advanced dilatation, from a joint observation of the respiratory sounds and of the rales.

As regards the respiratory sounds, the peculiarity of the emphysematous variety of bronchiectasis is the intimate blending of the tubular with the vesicular breath-sounds; the fibrotic variety is distinguished by the local absence of the latter.

The rales occurring in small dilatations, and in those which are mainly cylindrical, do not differ from ordinary catarrhal rales of medium and of large size. A distinctive character belongs to those produced in the sacculations, and when heard it indicates that the latter are not thoroughly relieved of their contents. The sound, which is best described as "croaking," is partly due to the valvular action of the viscid and confluent secretion, and partly to the free communication and continuity subsisting between the sacculations and the corresponding bronchus. The undiminished length of the latter, and the branches which open into it above the terminal sac, are probably additional factors. An explanation of the mode of production of this sound is suggested above in connexion with Fig. 14. The croaking sound is most distinctly produced in sacculations surrounded with more or less spongy tissue. In the fibrotic variety the solid medium through which it is conducted to the ear imparts to it a more metallic character.

It is unnecessary to dwell upon the common catarrhal sounds, the sibili and the rhonchi, which may spread over the lung as a result of general bronchitis. They may complicate the diagnosis by veiling to a certain extent the diagnostic sounds which have been described, although they seldom mask them entirely.

The voice-sounds sometimes supply definite data. Bronchophony and aego-bronchophony are yielded by the extensive and multiple sacculations of a partly cirrhosed lung, and sometimes by those not surrounded with fibrous tissue, if sufficiently large and superficial. Hollowness of the voice-sound would, however, disappear if the cavity were to fill completely. The vocal fremitus varies considerably in different cases, the pleura being unaltered in some, in others greatly thickened.

Diagnosis.—The diseases most likely to be mistaken for bronchiectasis are the various forms of bronchitis and phthisis. Less commonly the difficulty may be to distinguish it from emphysema, pulmonary gangrene, and cancer.

When originating in a *general bronchitis*, dilatation in its earlier stages can only be inferred. Subsequently fetor of the sputum necessitates a diagnosis from fetid bronchitis or bronchorrhoea. Except with the help of some previous knowledge of the case, the distinction may be extremely difficult if a general catarrh should coexist. In the absence of the latter,

dilatation would be known by the localisation of the large rales in the situations which present some alteration of the percussion note; and the same observation would also be a help in the more complicated condition. Again, the mode of the expectoration, even more than the nature of it, might throw light on the case; although in fetid bronchorrhoea the expulsion of the bronchial contents may often be sudden and paroxysmal.

Pulmonary gangrene, occurring in aged or broken-down subjects and preceded by a history of chronic bronchial catarrh, might be attributed to bronchiectasis culminating in ulceration. Most commonly the onset of pulmonary gangrene is sudden and marked by extreme prostration; that of gangrenous ulceration of a bronchiectasis is gradual. As pulmonary tissue is expectorated in both cases, our guides must be the clinical data and the clinical history. But in bronchiectasis a quasi-gangrenous odour may occur apart from any massive necrosis; and a fruitless search for elastic fibre would strengthen any direct evidence of bronchiectasis otherwise obtained, and any negative evidence as to the existence of bronchopneumonic or tuberculous processes such as lead to gangrene.

Ulceration of an *empyema* into a bronchus may closely simulate bronchiectasis. Its presence will be sufficiently indicated by the absence or insignificant amount of any expectoration prior to the bursting; and of the considerable relief given by the latter to the cough, dyspnoea, pain, and thoracic deformity. The expectoration of an empyema is usually distinguishable at first sight, by its freedom from mucus, from that of bronchial dilatation. According to Biermer, it contains crystals of cholesterin and of haematoidin. In any special case a physical examination of the chest would probably remove any lingering doubt.

Prior to the discovery of Koch's bacillus the diagnosis from *phthisis* had to be made almost exclusively from physical signs, and was often very difficult for persons unfamiliar with the physiognomy of bronchiectasis. A microscopical examination of the sputum now decides the question; and the tuberculin tests are an additional help. Still, the old-fashioned diagnosis by means of (*a*) the clinical history, (*b*) the general clinical state and aspect, and (*c*) the physical signs—is too important to be neglected.

(*a*) In most cases phthisis can be traced back to characteristic beginnings, the constitutional effects of the invasion being out of proportion to the pulmonary symptoms existing at that time. This is not the history of bronchiectasis, which begins with a definite bronchial affection, or with a pneumonia or a pleurisy; the worse constitutional symptoms being relegated to the late stages. Again, when the patient's affection begins with a profuse haemoptysis the probability of its tuberculous nature is great.

Moreover, the duration and the progress of the two diseases are strikingly different. Cough and expectoration of many years' standing, in a subject not markedly marasmic, would not be features of the common phthisis; though we should not forget that unilateral phthisis may, and often does, run an exceedingly protracted and mild course. In

such a case the signs would be unmistakable and strictly apical, and therefore unlike those of bronchiectasis which, when single, hardly ever implicates the pulmonary summit.

(*b*) Between ordinary pulmonary tuberculosis and ordinary bronchiectasis a very marked contrast in the general clinical appearances is at once perceptible. In the ultimate stage of pulmonary consumption there is no difficulty in the diagnosis; the patient carries it written large in every feature. At a rather earlier period in the complaint, when doubt might be possible, the same peculiarities are apparent, although not yet so manifest as to strike the superficial observer. They are briefly these—wasting of the subcutaneous fat in general, and in particular of the fat of the orbit and of the cheek; wasting of the muscles; visible loss of energy; pronounced anaemia in the strict sense of the word, namely, reduction in the total amount of the blood, the patient being bloodless and withered. These are not features of bronchial dilatation, uncomplicated with tubercle, at a like interval after the beginning of the affection: emaciation usually exists, but it is not extreme; there may be slight anaemia also, but it does not confer the characteristic wan look of phthisis. The hollow orbit, with undue exposure of the sclerotic, the sunken cheek with projecting malar eminence, and the thin, drawn lip are all conspicuously absent. In contrast with all this, bronchiectasis often presents outward peculiarities of its own; a certain fulness of the eye, of the lip, and of the features, and a slight duskiness of the complexion suggestive of congestion rather than of anaemia: and the veins, the jugulars in particular, are commonly conspicuous, if not turgid. On analysis these peculiarities will be found correlated with the state of fulness of the right side of the heart, which in advanced phthisis is never surcharged, in spite of the great obstacle to the pulmonary circulation. In short, the bulk of the blood is not reduced in proportion to the pulmonary destruction, as is the case in phthisis. For the same reason also the depressed and devitalised aspect peculiar to phthisis is not noticed in this disease.

Another striking peculiarity is the unusually bulbous expansion of the finger-tips, associated with a very marked incurvation of the nails. In phthisis the nails are aduncate, but the finger-ends are seldom much clubbed; nay, the pulp of the finger is atrophied and tapers, and the incurved nail is thin.

A diagnosis from *bronchiolectasis* will not be possible until we attain to a clinical identification of the latter; but we should not forget that the two conditions may coexist.

An interesting attempt has been made by Neisser to define the lines of a diagnosis between the congenital and the acquired forms.

Prognosis.—Spontaneous cure, such as occurs in acute bronchiolectasis in the growing lung of infants, cannot be expected in bronchiectasis; and a restoration of the integrity of the damaged lung is impossible. In rare instances, in which the dilatation is single and is no longer the seat of catarrh, as in the exceptional case of the cicatricial closure

of its bronchus higher up, the disease may become obsolete. Lebert quotes a case of Bamberger's, in which the formation of an external fistula eventuated in a cure; and a similar result might be hoped for from the surgical treatment of a solitary dilatation. Dr. T. Redmayne has published a successful case of this kind. In the great majority of chronic cases, so long as the original conditions persist, the disease, if left to itself is inevitably progressive, and as time goes on more difficult to relieve. A relative quiescence of the trouble is all that can be expected in inveterate cases. The more favourable achievements are reserved for active treatment applied in early life and quite early in the disease.

Whilst so much depends upon the activity and the early date of our treatment, the individual factor has to be reckoned with as regards virulence, resistance, and external influences. The great diversity in the kind, degree, and multiplicity of the lesions, and of their bronchial, pulmonary, and pleural complications, must in itself establish a wide difference between the individual chances of duration of life. Of this some idea is given by the figures obtained by Lebert in a series of fifty-two cases. The period of survival was :—

Of one year	in	21·1 per cent.
Of one to two years . . .	„	7·7 „
Of three to five years . . .	„	30·7 „
Of six to ten years . . .	„	15·5 „
Of upwards of ten years . .	„	25·0 „

In those favoured cases which remain free from all serious complications life may not be greatly shortened.

So difficult is an exact determination by physical examination of the extent and number of the lesions that the physician's forecast in the individual case must be based on very broad considerations: such as the age, temperament, antecedents, energy, nutrition, and general circumstances of the patient; the mode of origin, unilateral or bilateral character, and the cirrhotic, emphysematous, or stenotic type of the affection; the presence or absence of lardaceous disease and albuminuria, or of heart, kidney, or liver disease; the present and the previous state of the expectoration, and the effects of treatment on the catarrh.

The worst prognosis will probably always belong to the bilateral cases and to the unilateral cirrhotic variety especially when associated with some defect of the other lung or pleura. Haemorrhage is occasionally a fatal complication; it is apt to be profuse in cases of valvular disease or of secondary cardiac dilatation. The occurrence of perforation and pyopneumothorax, or of ulceration with the attendant dangers of gangrene, of putrid bronchitis, of pyaemia, and of septicaemia, would justify a grave prognosis. Mere fetor of the expectoration is not in itself an alarming sign.

When all has been taken into account, great uncertainty must still surround the prognosis, and it will be wise not to venture upon

too precise a statement of the probabilities. In the future much may be expected from an improved diagnosis, and from the earlier adoption of improved preventive, palliative, and curative measures, although surgical interference does not seem likely to prove more successful than in the past.

Treatment.—*In children* the responsibility and the scope of treatment are even greater than in the adult, for it is specially in them that a permanent cure may possibly be brought about, and that it might conceivably be missed by delayed or by inadequate treatment. Treatment has the best chance when employed in the larval period of imperfectly developed symptoms. In the vital interests of our patients we must learn to suspect the presence of the affection, as in the case of bronchiolectasis we are compelled to do, independently of any physical signs. If we should be so fortunate as to forestall its evolution the task of treatment will be simplified almost to one of prophylaxis. This opportunity is comparatively rare except in childhood. But in all other respects the treatment of the puerile type of the disease is practically identical with that of the adult type. In the adult also early treatment is the more to be urged, since there is less opening for prophylaxis.

Inveterate bronchiectasis was formerly the only stage recognised for treatment. Its incurability was to be expected: and its therapeutical record is merely one of palliation of late pathological results and of severe complications. This is still too often the earliest stage accessible to the physician, as at first, and for long periods, it does not disable the patient completely. Before approaching the curative treatment which is more closely akin to prophylaxis, the *general* or *constitutional* treatment and that of the *complications* in the confirmed affection, will be considered.

The constitutional treatment, an essential adjunct of the pulmonary treatment, need not detain us long, since its climatic and hygienic aspects are included in the account to be given of the latter. It cannot be regarded as curative, nor even as being aimed at the cause of the affection; but it undoubtedly promotes the patient's chances and the results to be obtained from symptomatic treatment. The only instances in which it might claim to be in any sense specific are those in which the disease has been traced to syphilis, and in which mercury, a drug possessing also general advantages as an antiseptic, should have a trial. Iron, quinine, and cod-liver oil perseveringly administered with intervals of rest and interludes of alterative treatment are still, so far as we know, the best means to the end of strengthening both fibre and function. Syrup of the iodide of iron in liberal doses, or the hypophosphites of calcium, of sodium, and of iron also freely administered, are remedies specially adapted to counteract the exhausting effect of catarrh on the serous and glandular elements. A liberal, varied, and nutritious diet, and a moderate allowance of burgundy or of port wine are indicated. Much general tonic effect may also be obtained by systematic treatment of the skin and by salt-water baths—subjects to be discussed presently.

Neither should we lose sight, in cases shewing a tendency to venous stasis and to cardiac dilatation, of the great value of derivative, alterative, and mildly laxative treatment. Much might be effected in early stages by hygienic and medicinal measures of this kind; but too often the opportunity of recommending them is not afforded until it is almost too late for their successful employment.

The Treatment of Complications.—As in other chronic affections, medical advice may at first be called in for the treatment of aggravated symptoms, of complications, and of emergencies. Among the latter, haemorrhage—fortunately rare in its worst form, that of the ulcerative perforation of an arterial branch—calls for immediate action, and must be treated on the usual principle of reduction of blood-pressure, by the inhalation of nitrite of amyl, by subcutaneous injections of nitro-glycerin, and if necessary of morphine, by calomel by the mouth, and by an enema of glycerin (not of a large bulk of fluid).

The febrile exacerbations of the bronchial catarrh, the complications of pneumonia and of pleurisy, the severe symptoms attendant upon absorption of septic material, and the occurrence of ulceration, with threatenings of gangrene, will need measures adapted to each event. In all of them a supporting plan of treatment will be necessary, and in those last mentioned, stimulants, both medicinal and alcoholic, must be freely administered.

The curative treatment of bronchiectasis is still in its infancy; but it has been fairly started on rational lines of a causal and symptomatic treatment of the disease, and of a physiological management of the respiratory organs and function.

The methods previously employed had acted as palliatives; but their inability to check the progress of the worst cases was one of the reproaches of medicine, and had led to a desperate resort to surgical measures, the hopelessness of which has now been made apparent.

We are now guided by the following indications, which until recently had been very imperfectly fulfilled: (i.) the emptying of the cavities; (ii.) the reduction of the catarrh; (iii.) the relief of the fetor; (iv.) the protection of the membrane from further irritation; (v.) the diminution of the size of the dilatations, and (vi.) an increase in the volume of the healthy pulmonary tissue by the improvement of the respiratory function in general.

The Postural Treatment.—The bronchial treatment is in the first place essentially postural. Sufferers often discover at an early stage the value of posture as a mechanical aid to the bronchial outflow. With the majority, lying down or turning to one side or to the other will bring on more or less cough and expectoration; but in others, when the dilatations are situated at the back, it is the change to the sitting posture which induces the paroxysm of cough. In this disease, even more than in phthisis, lowering the head, either over the edge of the bed or whilst standing, will allow the accumulated secretion to gravitate out of the sacculations and into the receiver. Some patients are in the habit

of practising this method of relief. Its regular employment should be suggested whenever no contra-indications exist.

Instead of this primitive method I have advocated a systematic postural treatment, of which the following is a brief account.

(A.) The Intermittent Postural Method.—A. Quincke first definitely suggested the prone postural treatment by the intermittent use of the inclined plane. Although it had often been noted that sputum flowed more abundantly in given positions, the practical therapeutical conclusion had never been drawn, or at any rate insisted upon abroad except perhaps by E. Apolant, who recommended for abscess of the lung the method long familiar to chest physicians in this country for the relief of accumulations in basic cavities, that of systematic bending over to promote cough and expectoration. O. Jacobson in 1900 dealt with the practical applications of Quincke's idea, and pointed out that even a slight acceleration of the secretion towards the trachea imparted simultaneously in all the bronchial tubes might have the effect of clearing the entire lung by stimulating the mucous membrane above the insensitive and atonic zone and of reopening obstructed alveolar districts. *Systematic prone recumbency* was prescribed for one or two hours morning or evening or both, in order to ensure at least once a day the evacuation of the 24 hours' secretion.

(B.) The continuous postural method includes nocturnal as well as diurnal treatment. It was planned on the principle of not allowing any retrogression or interruption in the operation of the curative process. The bronchus was not only to be emptied, but to be kept empty:—the compressed pulmonary tissue not only to be re-expanded, but to be kept re-expanding. The first step (1901) was the nocturnal treatment by means of the "slanted bed" (devised in ignorance of Quincke's previous suggestion). The patients were to keep to their bed for a given period of treatment, or on an uptilted sofa during the daytime, but were encouraged to practise respiratory and other exercises. The second step was the "respiratory jacket," or in children the costo-abdominal elastic belt, as a means of keeping up steadily a stimulation of the respiration. The third instalment was the systematic diurnal treatment by exercises in the prone and slanting posture. For this purpose the wheeled "Convalescent machine" is available for adults, and the "All-fours exerciser" is likewise capable of regulations for different sizes. During the period of "thorough treatment" the slanted position is to be maintained without intermission alternately on the bed, on the couch, and on the exerciser. Later, when the catarrh has subsided the diurnal treatment may be made intermittent, but it will be desirable not to discontinue for a long time the nocturnal treatment which after a while ceases to be a discomfort.

In carrying out the nocturnal treatment attention to a few points is necessary. The blocks for raising the foot of the bed should be at least 10 inches high; but this declivity would be rendered illusory but for two essential precautions. A large pillow or bolster should not be

allowed to extend under the shoulders, the head and neck only being raised above the level of the mattress. In order to ensure this, particularly with children, it is well to provide a specially narrow bolster and to secure it at both ends to the head rail. Children may also need to be placed between sand-bags to keep them from lying across the mattress. Another requisite in the "bronchiectasis bed" or the "bronchiectasis cot" is the fracture-bottom. Without that unyielded foundation the slant of the bedstead is likely to be neutralised. Moreover, the fracture-bottom makes it possible to dispense with the blocks. By resting its foot against an upright board, which is secured to the end of the bedstead and furnished with two stout pins and a double vertical row of holes, the inclination can be varied with great ease. A much simpler arrangement may be improvised by slinging the foot end of the fracture-bottom on a rope secured to the foot rails of the bedstead or cot. A makeshift for the "all-fours exerciser" is also easily extemporised by padding a high stool, cutting down its legs to the extent desired, and finally mounting it upon wheels. And for the adult we may adapt for our purpose, with slight modifications, Dr. Tucker Wise's "Inclined Plane for Phthisis."

Expectorants constitute an important adjunct to the postural treatment. Howsoever contradictory it may sound to increase secretion when we are engaged in combating its excess and retention, there is, on the basis of the "empty bronchus" treatment, no inconsistency, but great benefit in doing so; and this is the first stage in the treatment of the mucous membrane. The object at this stage is to wash out the glands and the gland ducts with their own secretion, in imitation of lavage of the stomach and bowel. It can be carried out by a quick or by a slow method, but a more thorough plan is the combination of the two, which I originally described in 1901. The procedure is: (1) to secure free drainage by posture, as tested by the thermometer, for in uncomplicated cases the effect upon the temperature is the same as that of establishing efficient drainage for an abscess; (2) to set up a slight drug-catarrh, in order to clear away if possible the causes of fetor, which drainage alone may not remedy, by administering every four hours a little iodide of potassium and antimonial wine in an expectorant mixture, and with it increasing doses of ichthyol in a capsule or, for children, disguised in the mixture by some liquorice; and (3) after three or four days to squeeze out the secretion by an emetic. Vomiting appears to contract the muscularis mucosae in a degree not attainable by simple cough. In children in whom treatment aims at being curative and must therefore be quite thorough, emesis should not be omitted, and it may be repeated with advantage so long as indications recur for its use. In other subjects it may also be adopted with equal safety and benefit unless the results of the simple expectorant treatment should justify us in dispensing with the emetic.

The Treatment of the Bronchial Fetor.—For the relief of the fetor two methods have hitherto been adopted alternately or combined: (*a*) the

inhalation, and (*b*) the internal administration of deodorising and antiseptic agents.

(*a*) Inhalations as a rule fail to influence the bulk of the accumulations, though they may reach the uppermost layers. A noteworthy exception must be made in favour of those inhalations which set up cough and copious expectoration.

Theoretically, oxygen was expected to fulfil a double purpose, as an aid to respiration and as a disinfectant; but it has really proved of little service, partly perhaps because of its tendency to diminish rather than to increase the activity of the respiratory movements.

Inhalation, from a jug, of vapour impregnated with thymol, eucalyptol, pine oil, or other antiseptics may be arranged so as not to be a discomfort.

Inhalation may also be practised, as in the case of oxygen, through a tube from the "dry inhaler" bottle, through which air is drawn over a sponge or small pieces of blotting-paper mixed with horse-hair and steeped in the solution to be used. Since only those constituents are inhaled which are volatile at the ordinary temperatures, substances such as carbolic acid, creosote, tar, terebene, can be used fairly concentrated. Iodine can also be used with proper precautions.

Lastly, inhalation may be conducted on the principle of the spray. Steam sprays, at one time much in use, have their drawbacks, but in some respects are convenient as a vehicle for a great variety of medication. The discomfort of steam is avoided in the mechanical spray-producers which "atomise" the solutions to be inhaled, by forcing them through the minute orifice of the outlet with a jet of compressed air worked by an india-rubber hand-ball. In this case the solutions are not diluted by steam, and must be prescribed of an appropriate strength. The dripping and dampness inseparable from the steam are avoided; and the nozzle of the instrument can be introduced into the nose or mouth, thus almost ensuring actual inhalation of a large proportion of the remedies. The finest subdivision is obtained in "nebulisers" which combine strong pressure with smallness of orifice. The latter condition unfortunately limits the supply of the medicated atmosphere (*vide* p. 31).

(*b*) The internal administration of creosote, tar, terebene, the essential oils, the oleo-resins, and the balsams has long been in use. Only of late years, however, have the improvements in pharmaceutical detail enabled efficient doses of the more powerful of these agents to be taken with comfort. Copaiba, tar, and especially thymol, eucalyptol, guaiacol, and creosote, can be administered in the shape of capsules at frequent intervals throughout the day; and, by the persistent action kept up on the respiratory mucous membrane, may be of great benefit. Fifteen centigram capsules of myrtol, taken every two hours throughout the day, are well spoken of in Germany, and are worthy of trial in cases in which none of the measures about to be described can be carried out.

The fault of most of these methods is their inadequacy; they do not deal with the evil at its chief seat in the depths of the lung. A new era in the prognosis of bronchiectasis has happily been opened up by the

more thorough methods associated with the names of Vivian Poore, A. Rosenberg, Sir T. Grainger Stewart, Mr. Colin Campbell, and Dr. Arnold Chaplin; these methods consist respectively in the internal administration of garlic, in the intralaryngeal injection of disinfecting solutions, and in the systematic inhalation of the vapour of coal-tar creosote.

Poore's method was based upon the penetrating properties of some of the volatile constituents of garlic, and upon their stimulating and antiseptic as well as deodorant powers. Garlic probably acts as a general tonic as well as a local stimulant. Its local effect is produced at the surface of the mucous membrane by exhalation; but the fact that the smell of garlic is also given off by the skin suggests that the constitutional influence of the drug may be widespread and important. The favourable results reported by Poore were obtained from the continued administration of sufficient garlic to render the odour permanent in the breath. In the cases to which he refers the original fetor of the expectoration was replaced by a pungent smell reminding one of that of syringa; the discharge was greatly diminished; and a remarkable improvement took place in the health, in the strength, and in the weight of the patients. The treatment is generally well borne, and, if the remedy be taken with meals, patients submit to it without much inconvenience. A clove of garlic is chopped up and mixed with the beef-tea, or preferably enclosed in gelatin capsules. I have administered as much as eight capsules daily, each containing 30 grains of chopped garlic. An extract might also be used. Poore suggested that sulphide of allyl, which is contained in the essential oil of garlic, is probably the remedial agent. The oil of allyl has an exceedingly penetrating smell. It should be taken immediately after meals. I have prescribed it in 3-minim capsules three times a day; but this dose is too large, and soon disagrees. Capsules containing half a minim of the oil will be found more convenient. The remarkable results obtained by this method are not limited to cases of bronchiectasis, but have also been obtained in phthisis. The chief theoretical objection to the treatment by garlic is that, whilst it provides for the disinfection, it does not ensure the complete clearance of the dilated bronchi, nor directly assist their contraction. The practical objection is the smell.

The Intratracheal or Direct Treatment.—Intratracheal injections of menthol and olive oil through the glottis for the treatment of pulmonary and laryngeal phthisis were first practised by A. Rosenberg in 1885. His method was tried in Scotland by Jamieson, Downie, Byrom Bramwell (1889), Sir T. Grainger Stewart (1893), and others. Since 1893 it has been extensively practised and elaborated by Mr. Colin Campbell (23*a*), and in its present form may be spoken of as his method. The experimental data were worked out in 1886 by Sehrwald by means of percutaneous intratracheal injections in dogs, and by Reichert. Reichert's experiments, made on calves and sheep, proved that the fluid injected found its way even into the finest bronchioles. Sehrwald's

conclusions were: (1) That large quantities of fluid could be injected without discomfort. (2) That the fluids not only passed into the alveoli, permeating the surrounding tissues, but also reached the peribronchial and pleural fibrous structures, and even penetrated the cartilages. (3) That the lungs absorb more rapidly than the digestive tract, or even the subcutaneous tissue, the rapidity of absorption corresponding with the extent of the absorbing surface; so much so, indeed, that the lung of a dog can absorb four times its own weight in less than five days. (4) That medicines thus introduced act in smaller doses, and more rapidly, than when introduced in any other way.

Mr. Colin Campbell's earliest improvement consisted in substituting Price's distilled glycerin for olive oil, as the latter neither dissolves nor mixes with the mucous secretions, and is not so good an expectorant. Other glycerins were too irritating for use. Menthol (8 to 12 per cent) as an anaesthetic and anti-bacterial remedy, and guaiacol (2 to 4 per cent) he continued to use after trying various substitutes such as benzosol, turpentine, terebene. More recently he has employed izal. As to the bulk of the injection, he finds it best generally to empty a syringe holding about 100 minims at each squirt, and to repeat this dose two or three times at each sitting. But as much as 4 or even 6 drams have been injected, or a total of 3 oz. in one day.

Technique.—Mr. Colin Campbell recommends that "the tube should be rapidly passed into the larynx, and should fit the curve of the base of the tongue, and lie tightly against it, thus fixing the epiglottis and preventing spasm. The squirt should be delivered like lightning—either with inspiration, or during a slightly prolonged interval following expiration. If the operation be properly performed, the taste of the fluid injected should not be perceived by the patient." The patient learns to hold the tongue, and the operator to introduce the syringe without a laryngeal reflector. It is essential that the patient should sit or stand straight at the time, even though as in cases other than those of general bronchitis or asthma, the purpose be to reach some definite region of one or both lungs. There is no cough, pain, or asphyxia when the operation is properly performed, and care is taken to avoid the three following mistakes, namely:—(1) touching the fauces, base of tongue, epiglottis, or rima glottidis with the nozzle of the syringe; (2) squirting down the oesophagus; (3) squirting during expiration. The first mistake would occasion retching; the second, gastric pain and unpleasant eructations from the remedies used; the third, a feeling of suffocation causing the fluid to be returned into the mouth. These unpleasant results can best be avoided by great care in passing the tube through the mouth and fauces.

The postural factor has been elaborated by Mr. Colin Campbell by the use of an ingenious machine "the revolving chair" (24). Thanks to this mechanical advantage, and to the employment of large injections (2 to 3 oz.) of 10 per cent izal solution, he has recently obtained most encouraging results in confirmed bronchiectasis. The possibilities opened

up by this therapeutic innovation are obviously great, and its applicability is not restricted to the disease under discussion, nor to the stated formula. Chronic and excavating pulmonary tuberculosis, chronic bronchial catarrh, putrid bronchitis, and bronchorrhoea, especially of the purulent variety, are suited for its adoption.

Although in common with those who have tried this method I have wondered at the facility with which the pulmonary lymphatics dispose of the injected solution, we are left too much in the dark as to the destination of the latter. It is much if, by carefully directing the nozzle of the syringe and subsequently adjusting the patient's posture, we can ensure the treatment of one lung rather than of the other; but we are unable to control the injected fluid in its course down the tubes.

No objections of this sort can be urged against Dr. Arnold Chaplin's creosote method, which theoretically and in its results is rational and efficient. Its principle is to obtain an amount of coughing sufficient to squeeze out every remnant of the noxious secretion, and to keep up local disinfection by inhalation for a sufficient time, and in sufficient strength, to enable the mucous membrane and the lung itself to be completely purified. These indications once fulfilled, nature may do the rest. Living in an atmosphere of the disinfectant would carry out an important part of the treatment; and Dr. Chaplin originally noted the tradition, which exists among workmen constantly employed in an atmosphere of creosote, that the fumes "clear the chest of phlegm," and confer an immunity from "asthma" and consumption. But in bronchiectasis the object is to bring about a complete expectoration of the bronchial contents; and with this view the creosote atmosphere has to be made almost intolerably strong, so that it can be inhaled for short periods only. The concentration of the vapour is the irksome side of the treatment; but the hardships are not resented when the patients have experienced the remarkable relief from its use. In addition to the intense cough, which has the advantage of leading to inhalations of the disinfecting agent proportionately deep, the discomforts are chiefly the irritating action upon the other mucous surfaces and the eyes, the strong smell which clings to the hair and clothing, and the diffusion of the smell into the surrounding space. It is desirable to provide an entirely separate inhalation chamber at some distance from the doors and windows of other buildings. The remaining difficulties are met by loosely plugging the nostrils with cotton wool, by wearing over the eyes watch-glasses framed in bandage or sticking-plaster, and by covering the garments and the head with oiled silk or mackintosh.

The inhalation chamber should be of small size, 6 or 7 feet wide by 8 feet high, suitably ventilated, but capable of being made air-tight for short periods if necessary. In vaporising the creosote proper care must be taken to prevent a conflagration. A fair-sized metallic evaporating dish is the best, and in this it is convenient to place some dry sand. Some more stable support than the common tripod should be used, and gas flames must be avoided.

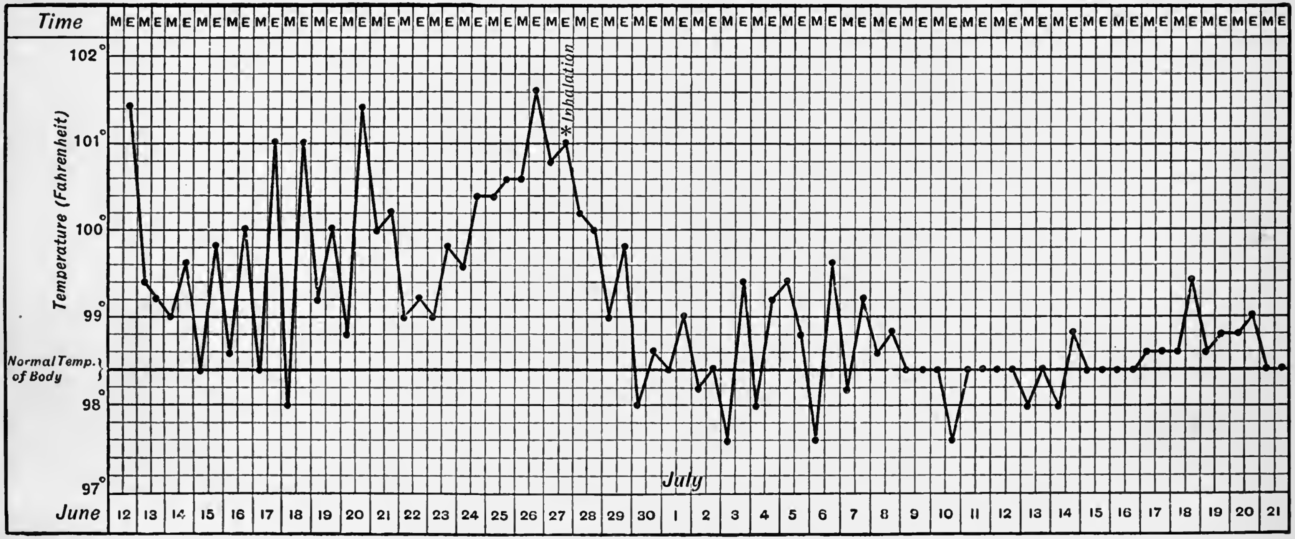

CHART. 1.—Reproduced from Dr. Brian Dobell's report of Dr. Devereux's case of bronchiectasis, shewing the influence of the creosote inhalation treatment upon the pyrexia.

The duration of the exposure is gradually increased from a quarter of an hour to an hour or more. The residual phlegm dislodged by the searching cough is exceedingly offensive; but the fetor is partly covered by the strong creosote odour. The treatment, unless contra-indicated, is to be continued daily until little is coughed up in the chamber, and until no expectoration is brought up spontaneously the next morning. In an average case this will imply a treatment of from four to six weeks.

In itself the ordeal is a valuable respiratory exercise. Expansion of the lung is induced by the cough, and a gradual contraction of the sacculations is promoted. A remarkable improvement ensues in the general health and strength, as well as in the respiratory capacity. In the seven cases originally reported by Dr. Chaplin excellent results were obtained. Notes of equally successful cases have been kindly communicated to me by Dr. Devereux of Tewkesbury. A full account of one of his cases has been published by Dr. Brian Dobell. Through the kindness of Dr. Dobell and of the Editor of the *British Medical Journal* the temperature chart of this case is reproduced as a striking illustration of the reduction of temperature which is obtained in pyrexial cases.

In conclusion we are now in possession of three efficient methods each of which holds out some curative prospect. The capabilities of the intratracheal treatment are still an imperfectly known quantity. They may prove such as to surpass the other methods in curative power and in rapidity of action. A combination of all three methods is quite conceivable as the ideal treatment. But a satisfactory approximation, within the reach of every patient, will probably be found in a combination of the other two forms. When drainage and pulmonary expansion are provided by the postural method, the severity of the creosote treatment may possibly be relaxed without any loss of efficiency, by lessening the strength and increasing the duration of the inhalations; and in this way perhaps the trials of the creosote chamber may become a thing of the past. Thanks to these methods and to others which may accrue, it is not improbable that in the future, when cases are treated sufficiently early, bronchiectasis may cease to be regarded as an incurable disease.

Surgical Treatment.—An attempt was made some years ago to treat the lesions by injecting weak solutions of carbolic acid, of iodine, and of other antiseptics through the chest wall into the surrounding pulmonary tissue. No good results were obtained by this method, which has since then been almost forgotten.

Treatment by incision and drainage was proposed and attempted as a last resort a few years prior to the recent advances. The few cases reported in this country and elsewhere are not encouraging. Hofmockel, who gives a review of 80 cases of operation for abscess, for gangrene, or for bronchiectasis, finds that the worst results were obtained in the cases of bronchiectasis. Schmidt's recent report on pulmonary surgery tells the same tale.

A disastrous experience has shewn that success can be looked for only when a single dilatation exists. These are, however, the cases in which the

symptoms are least urgent as well as least refractory to the ordinary measures. Where help is most needed—in the instances of multiple sacculations—surgery is doomed to failure. To attempt multiple incisions is to multiply the risks of septic infection of the pleura; and to open only one of the sacculations is not only to leave a great part of the disease unrelieved, but to place its remaining foci in a worse position than before, by weakening the expulsive mechanism of cough by direct leakage of air, and by unavoidable interference with the freedom of the thoracic movements.

The *mechanical hygiene of respiration* and the *climatic treatment* may be considered under one heading. They are both necessary adjuncts to any method of treatment, although in the future their relative importance will probably be less than it has been heretofore.

For the control of the catarrh and for the protection of the mucous membrane from further irritation we had until recently looked with greater confidence to the effect of climate than to medicine. The great indication was to strengthen the clogged and sodden mucous membrane by constant contact with the purest air, whilst invigorating the system by prolonged residence in a warm and equable climate, where patients might live in the open. The dry and stimulating climates to be found on the table-lands of South Africa, in South California, on some of the slopes of the Andes, or at high elevations in islands, as in the West Indies, or even in the Mediterranean, as at Ischia or Capri, are specially indicated; and along the shores of the Mediterranean there is a large selection of suitable sites.

Patients who at a sufficiently early date adopt and adhere to this thorough treatment by climate might hope for a permanent arrest of their catarrh, and, thanks to the increasing pulmonary expansion due to open-air life, might ultimately secure a degree of improvement almost equivalent to a cure. For this happy result a life-long treatment is now less indispensable, nor need we expatriate our patients. The climatic treatment is henceforth, as in the case of other diseases, an after-cure. A suitable climate for the winter retains its importance; but its selection is no longer limited as formerly when the consequences of any incidental catarrh were much less within our control. We might, for instance, without serious risk, in the case of some convalescents not advanced in years, recommend the dry cold atmosphere of the Alpine winter and the outdoor life and physical exercise, which are not the least of the advantages of the Alpine cure; whilst for those unable to travel, our home resorts and seaside places afford eligible climates, among which Thanet, Folkestone, Eastbourne, and Brighton deserve special mention.

Warm sea-water baths may be of considerable value. For some patients a stronger effect might be sought from the artificial Nauheim salt-water baths. In any case the temperature and the duration of the bath must be adapted to the individual. An important part of the balnear treatment is the tepid, and ultimately the cool or cold affusion terminating the bath, followed by strong friction of the surface.

Among the *medicinal springs* the sulphurous thermal waters enjoy a deserved reputation in the treatment of this affection. Harrogate, Moffat, Challes, Aix-les-Bains, Eaux Bonnes, Eaux Chaudes, Cauterets, Bagnères-de-Luchon, and other spas including Royat, Mont Dore, and La Bourboule, might be visited with profit; but for patients unable to leave home a substitute may be found in tonic baths combined with the internal administration, for recurring periods, of some preparation of sulphur.

At most of the foreign health stations and at some of our own various *hygienic measures* are recommended in addition to the use of baths or waters. Among them special value attaches to the following:—

(*a*) The inhalation of an oxygenated and terebinthinated atmosphere; (*b*) systematic exercise, at first passive only, of the thoracic muscles and of the abdominal muscles, including the use of dumb-bells or clubs, and a variety of postural exercises; (*c*) systematic respiratory gymnastics, such as deep inspirations followed by deep expirations in various attitudes, reading aloud or singing; (*d*) general massage and passive resistance movements followed by brisk rubbing. An improved circulation through the skin and a general bracing of its nerves are special objects of this form of treatment; another is the tonic effect on the right heart and pulmonary circulation, and the help which the mucous membrane may derive by sympathy from a healthier cutaneous surface, and from its improved reaction to atmospheric influences.

The importance of these systematic methods lies in the regularity with which they can be enforced; but the benefit they can confer might equally well be secured by a perpetual outdoor life in a really suitable climate, and by progressive exercise gradually pushed to the extent of slight breathlessness.

The contraction of the sacculations and the general improvement of the respiratory function, which are the final aims of our treatment, are directly promoted by all the measures which have been detailed; and in none of the ordinary cases, nor even in fibrotic cases if one lung be perfectly sound, need we despair of their partial attainment.

II. Bronchiolectasis

Dilatation limited to the smaller tubes is best expressed by this word, which is less open to misunderstanding than that of "capillary bronchiectasis" or of "acute bronchiectasis." Clinically the bronchioles also liable to chronic and subacute dilatation, and bronchiolectasis may be described as acute, subacute, or chronic.

Dilatation of the bronchioles seems to have been originally viewed as a first stage, though death might occur too rapidly for any implication of the larger tubes to follow. These severe cases, standing for an aggravated and hurried form of the normal evolution of a full-sized bronchiectasis, have been styled, with some verbal inconsistence, acute bronchiectasis, in spite of the absence of that result. Dilatation of the

larger tubes is not always preceded by a dilatation of the smaller ones; and as some of its other modes of origin also are relatively rapid, the expression acute bronchiectasis must apply to them. For that reason and also because it is still doubtful whether a dilatation of the smaller tubes, acute or chronic, necessarily passes into a progressive dilatation of the larger tubes, a separate designation is wanted for the striking puerile affection which was first described by Andral, and has been more recently referred to as acute bronchiectasis.

In the few cases which have been published, the pulmonary disease was extensive and associated with more collateral pneumonia or bronchitis than was compatible with recovery. We should not, however, assume that this is the only degree of which the affection is capable. Milder cases may occur. The repeated post-mortem recognition of a dilatation of the small tubes in connexion with certain clinical symptoms noted during life led to the inference that in other cases also, which presented the same symptoms but ultimately recovered, the same lesions might have existed. Hence a current belief that children may completely recover from acute bronchiectasis. But, granting that recovery is possible, it might sometimes be partial only; and persisting dilatations might grow in the course of years into the common bronchiectasis of the larger tubes.

Classification and Nomenclature.—The data available do not yet fill in the clinical and the pathological picture; but they may supply a temporary framework for future elaboration.

A. *The clinical classification* of the cases can only be attempted on a very broad scale. Bronchiolectasis may be *acute*, *subacute*, or *chronic*:—

Chronic bronchiolectasis is a local affection not invading the entire lung. It is most commonly an associated lesion induced by chronic catarrh whether simple or bacterial. Subacute bronchiolectasis occupies a position intermediate in severity and in extent between this and the acute variety.

Acute bronchiolectasis may occur in two forms:—(1) local, (2) general. The local form is least known to us pathologically, because it is not necessarily fatal when it is active. The general form is least known to us clinically, because it is too rapidly fatal to admit of much observation during life. The pathological anatomy of its terminal lesions is beginning to be known; but its early etiology and mechanism are still obscure. In the interests of future study it would be well always to refer to this variety under its full name, generalised acute bronchiolectasis.

The clinical grouping of the fatal cases hitherto recorded agrees with the pathological and with the etiological grouping. There are two main clinical forms: the pneumonic and the bronchitic, to which other forms may have to be added. Miliary tuberculosis may conceivably coincide with either of these main forms, but its presence has not been noted in the most genuine cases.

B. *The pathological classification* endorses from post-mortem observation these two main forms of acute bronchiolectasis. We might have

expected a third type, the pleuritic or pleuro-pneumonic; but no clear instance of that kind has been observed. The existence of a congenital variety is only conceivable as a malformation.

The bronchitic form, by no means uncommonly recognised in the mortuary, is probably much more frequently overlooked while under our clinical observation. In the less severe cases recovery may perhaps take place; for as the fatal cases, chiefly in severe whooping-cough or measles, do not present during life any distinctive signs or symptoms apart from the bronchitic, it is not unreasonable to suspect that other severe cases differing from them apparently only in their eventual recovery may have been the subject of acute bronchiolectasis. The morbid changes are characteristic. There may not be an entire freedom from bronchopneumonic deposits or congestions, indeed this would be an unlikely result; but the lung as a whole is not a pneumonic lung, and in particular the dilated bronchioles are not surrounded by much consolidation. On the other hand the air-tubes are the seat of an intense and widespread bronchitis. The dilated bronchioles present two striking features which are diagnostic: (1) the inflammatory swelling of their inner, and the fibroid thickening of their outer coats; and (2) the purulent semi-fluid secretion with which they are loaded and which can be squeezed out of most of the bronchioles. This engorgement affords ample explanation for the ultimate asphyxia, and also for the alternating areas of pulmonary collapse and emphysema which are found after death. These are cases of genuine, simple, non-ulcerative, acute bronchiolectasis in their stage of inflammation and suppuration. The subvarieties which doubtless exist in this bronchitic group await further investigation.

The pneumonic form is probably less common in its clinical occurrence, and seems to be much less capable of recovery. Its etiology and its clinical history are immature, and cannot yet be written. What little is certain suggests that the disease may not be necessarily associated with any of the common zymotics; that it is probably always infective, though not always due to the same infection; and that it appears to be an exceedingly acute process. Anatomical examination confirms the clinical conclusion that we have here a composite group to analyse. The common feature is the presence of bronchopneumonic consolidation, and the striking occurrence of the multiple dilatations within the consolidated areas themselves, a circumstance which opens up a theoretical question, the accepted mechanical view having hitherto been that dilatation begins through the withdrawal of solid support by a resolution of the pneumonia. Part of that question is whether the appearances of the dilatations can identify them as prior or as secondary to the consolidation. The cases of this form have been published by Drs. Walter Carr (1891), Sharkey (1893), Kingston Fowler (1898), and Morley Fletcher (1901), and shew that neither the bronchiolar nor the pulmonary conditions are in any way uniform.

Spurious Bronchiolectasis.—What to the naked eye may appear to be the section of a dilated bronchiole may be nothing more than

the cavity left by a small necrosis in the centre of a bronchopneumonic area and lined, with deceptive smoothness, by a thin layer of the retracted fibro-elastic remnants of the melted tissues. Close inspection is needed to differentiate between this and the true bronchial lining. We should therefore hesitate to diagnose bronchiolectasis when a lining membrane fails to present that bold outline which was described as characteristic of the bronchitic type, and is filmy instead. Thus, in Dr. Tooth's specimen of multiple cavities in bronchopneumonia, the aspect of the lungs was that of bronchiolectasis, but microscopic examination shewed that this was not the case. Dr. G. Carpenter described a similar appearance as a case of "Acute Leucocytic Pleuropneumonia with extensive Fibrinous Plugs visible to the naked eye in Enlarged Lymphatics." The deceptive vacuolation was described as really due to the dropping out of plugs of fibrinous deposits. Enough has been said to shew that the pneumonic etiology of bronchiolectasis will require considerable elucidation.

The nomenclature of bronchiolectasis can only be based with security upon searching anatomical observation, as an acute "pneumonic" bronchiolectasis, for instance, may be "genuine" or "doubtful."

The nomenclature of the various stages in which a bronchiolectasis may be found is almost the same as that which applies to bronchiectasis. But as regards shape we are familiar with two types only, the *cylindrical, and the saccular dilatation.* Any bronchiolectasis is capable of the following conditions: (1) distension or collapse; (2) congestion and inflammation, with or without capillary haemorrhage; (3) thinning or thickening of the wall; (4) ulceration which may lead to haemorrhage; (5) necrosis or gangrene. The destructive processes (4 and 5) are capable of demonstration when a bronchiolectasis secondary to chronic indurative phthisis is overtaken by extensive softening.

The clinical account of bronchiolectasis at present available is meagre. It is deficient in all the divisions of the group. (1) In its chronic variety bronchiolectasis occurs in childhood as well as in the adult, and is sometimes partly saccular, but is chiefly cylindrical. (2) The local or limited acute variety is known to occur in the adult although it is much more common in children, in contrast with the *Generalised or Universal Acute Bronchiolectasis* which is not known to have ever occurred in the adult. (3) The general acute bronchitic variety of the latter differs from that mentioned under (2) in that it implicates in extreme cases the entire lung. (4) The general acute "pneumonic" variety is even more rare than the bronchitic variety, and may lead to destructive changes of almost equal degree.

(1) *In its chronic form* bronchiolar dilatation is relatively of small importance. It is a local lesion secondary to the respiratory inactivity of a pulmonary district disabled by bronchial obstruction, or hampered by adhesions; in short, to imperfect expansion of the lung with resulting accumulation of mucus. A common seat is the apex of the lung in phthisis, where, although an old vomica may have undergone considerable

contraction, the collapsed alveolar substance in its vicinity has failed, owing to surrounding fibrous changes, to expand again completely. Small thin-walled bronchi, distended with clear or purulent mucus, may often be seen in these partially aerated and inactive remains of healthy lung tissue.

The same change may, however, be met with in an opposite association, in emphysema due to chronic bronchial catarrh. In this variety the seats of election are the lower anterior pulmonary fringes. Where the emphysema tends to become bullous the dilated bronchioles may take a share in the formation of the bullae, and occasionally perhaps in the production of pneumothorax.

In the adult, localised dilatations of bronchioles are frequent in chronic bronchial catarrh, and may follow an acute purulent bronchitis. So far as I have observed, their accompaniment is not atelectasis, but chiefly emphysema. Their value is rather that of a complication than of a disease. Since, however, their symptoms do not distinguish them from catarrhal bronchitis nor add largely to the fatality of the latter, it is conceivable that acute dilatation of the smaller tubes may occur more often in the adult, and more often be the origin of true bronchiectasis than is commonly thought.

(2) Among the *acute varieties* clinical importance attaches to the local or limited variety, particularly in children. In them it is probably exceedingly common in its milder degrees and in its bronchitic form as a temporary condition, which may leave behind it only slight pulmonary and bronchial impairment; too frequently it contributes to a fatal termination in cases of measles or whooping-cough complicated with capillary bronchitis.

Great clinical interest attaches to the extreme cases described as "generalised or universal acute bronchiolectasis" of bronchitic or of pneumonic type, and to the *honeycomb lung* change to which they give rise. Illustrations of both these types are appended. Dr. Morley Fletcher's case in which the vacuolation is extreme presented no trace of consolidation, and may have been of purely bronchitic origin, representing the bronchitic type. The condition was unsuspected during life, and the case presented the usual clinical features of intense catarrh of the bronchioles.

The pneumonic type is well displayed in the drawings reproduced, from Dr. Sharkey's paper on acute bronchiectasis. The lesion is essentially the result of an acute catarrhal pneumonia and peribronchitis, with multiple and widely diffused secondary collapse. The course of the disease and its clinical features are not very distinctive, as may be gathered from the brief account given by Dr. Sharkey of his two cases. The cases were not diagnosed as bronchiectasis during life.

In the first patient, aet. 2 (Fig. 16), there was no previous record of illness except measles. The lungs after death were pale and curiously dotted with black pigment spots, hard to the touch. The centre of each of these was occupied by a small bronchus. The bronchioles were everywhere dilated, and scattered here and there were what appeared to be

small miliary tubercles; but the other organs were free from tubercle. Microscopically acute peribronchitis was found, accompanied with ex-

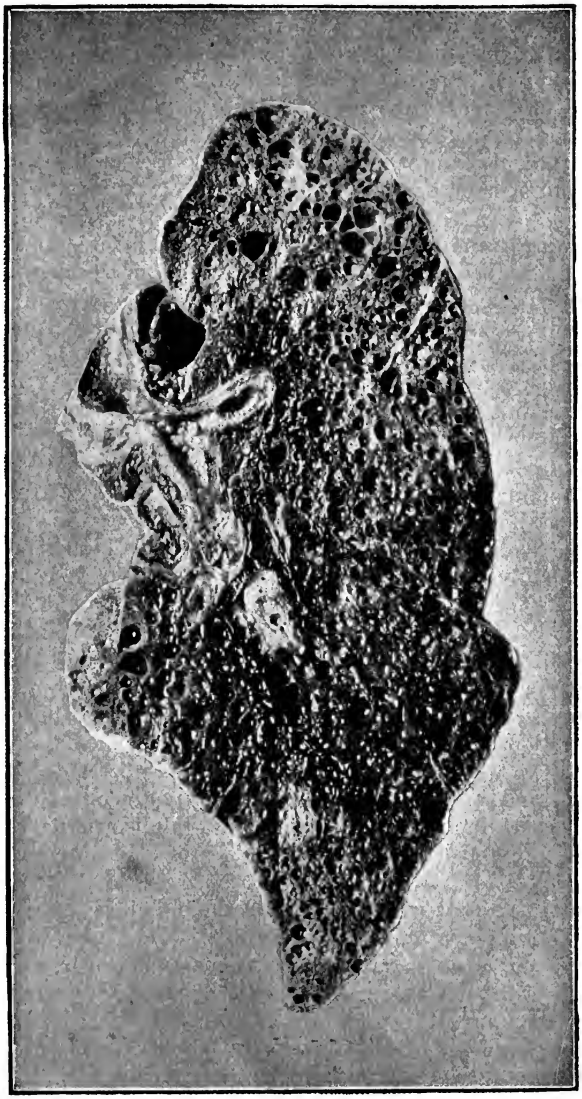

FIG. 15.—Honeycomb lung illustrating the extreme results of generalised acute bronchiolectasis of the bronchitic type. (Dr. H. Morley Fletcher's case, *Trans. Path. Soc.*, London, 1901, lii. 195.)

treme bronchiectasis, and a little, but very little, emphysema. No genuine tubercles were seen.

The other patient, a child aged 4, was under observation from May 7

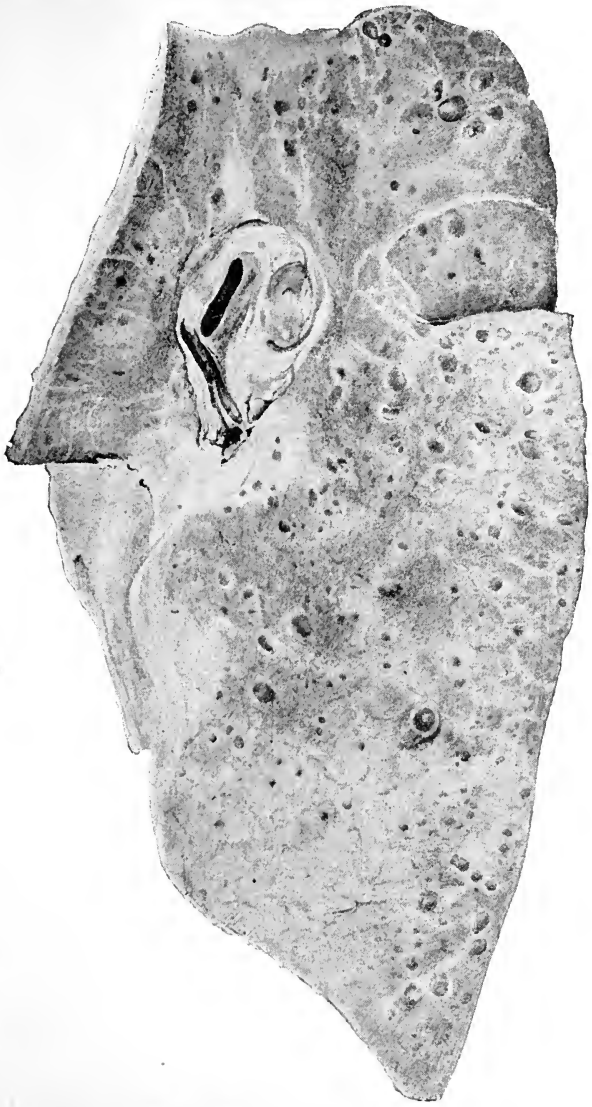

FIG. 16.—Generalised acute bronchiolectasis of the pneumonic type. Reproduced from Dr. Sharkey's Plate I. The figure represents the external surface of the lung, which is seen to be dotted with vesicles. In the fresh state they projected boldly on the pleural surface.

to June 10, 1893. He had always been healthy till cough began, two months prior to admission. Since then he had spat up thick phlegm, and

had vomited three or four times a day; but he was able to attend school until admission. At that time he presented a dusky flush, rapid breath-

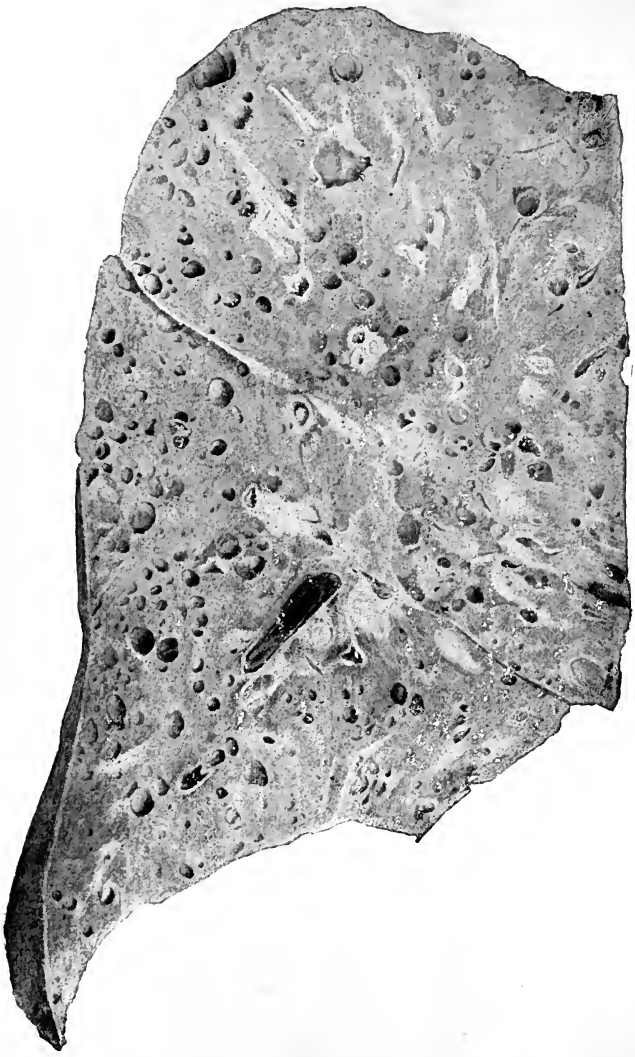

FIG. 17.—Generalised acute bronchiolectasis of the pneumonic type. Reproduced from Dr. Sharkey's Plate II. A vertical section of the same lung as in Fig. 16, shewing dilated bronchioles distributed over the whole surface.

ing, no marked dulness on percussion, no tubular breathing, but crepitations over the whole of both lungs. The pulse-rate was 136; the temperature 102·6°; the respirations 44 per minute. The temperature

gradually fell, but on June 3 subcutaneous emphysema occurred; otherwise no material change took place till death. The lungs were found bulky, their surfaces thickly strewn with soft, round, transparent, bladder-like elevations, the cavities of which were perfectly smooth, and either empty or full of frothy mucus. Scattered through the lungs these small cavities, the largest of which was about the size of a pea, gave a worm-eaten appearance. The larger tubes were not perceptibly dilated or diseased, but there were numerous patches of bronchopneumonia of small size, and here and there some collapse; but no tubercle. The microscope detected widespread acute bronchitis, peribronchitis, bronchopneumonia, and pulmonary collapse. The bronchioles were extremely dilated, and there was also considerable emphysema.

The clinical diagnosis of dilatation of the bronchioles cannot be made with any certainty, even in children; not even when, as in these cases, the change is general and extreme. At most its presence can be guessed at. Neither percussion nor auscultation can fasten upon any trustworthy sign, and the character of the expectoration does not differentiate the most acute affection from severe catarrh. In its limited and localised form in the adult and in children, acute dilatation of the small tubes is still less capable of recognition.

Prognosis.—The acute puerile form, as shewn by the cases narrated, is sometimes the result of a catarrh so severe as to be in itself fatal. In other cases, perhaps, the bronchiolar affection may be limited to a portion of the lung; and the catarrh getting well, the small tubes may lose their dilatation. That this does occur is the view generally held; but, so long as a diagnosis of capillary bronchiolectasis by physical signs is impossible, this must remain an unproved opinion. Considerable likelihood has recently been added to it by the successful results obtained in cases of bronchiectasis in the adult.

The treatment of an affection incapable of diagnosis cannot be laid down with any definiteness. In the chronic form none may be needed, the general symptoms being themselves chronic and sometimes unimportant. Treatment of the chronic and localised acute and subacute forms should be conducted on the lines laid down in the treatment of bronchiectasis (*vide* p. 150). In the acute affection the presence of the bronchitis and of the catarrh supplies all the important indications; and these are sufficiently dealt with elsewhere. The great object in bronchitis being to prevent stagnation in the bronchioles, of which this form of dilatation is one of the results, the treatment of both diseases is practically identical.

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NEW GROWTHS OF THE BRONCHI

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BENIGN TUMOURS.—Examples of lipoma (arising in the submucosa), papilloma, adenoma, chondroma, and even osteoma have been recorded.

MALIGNANT TUMOURS.—Sarcoma is very rare; it usually forms a large growth and invades the lung. Carcinoma, though more often seen than sarcoma, is still rare.

Morbid Anatomy.—Their favourite *site* is the main bronchi, but they occasionally occur in the smaller; and cases have been reported of carcinoma arising from the wall of bronchial dilatations (Letulle). The starting-point in the bronchi is more often the mucous glands of the wall than the lining epithelium, the microscopic structure of the former being that of a carcinoma forming acini lined by cubical cells from which mucus is secreted, of the latter a columnar-celled, or not infrequently, by a curious metaplasia of the epithelium (Benda), a squamous-celled carcinoma: cornification is then common, and cell-nests and prickle-cells can be seen.

In appearance these growths sometimes form papillomatous projections encroaching on the lumen of the bronchus; in other cases the wall may be thickened and infiltrated for a considerable distance by growth limited externally by the cartilages (Handford (7)).

Spread and Metastases.—Clinically we must distinguish (1) a group which remains strictly limited to the neighbourhood of the original site, spreading only to the glands just outside the bronchial wall; and (2) a group of wider metastases in the bronchial, supraclavicular, and mediastinal glands, the lung, and the pleura, making it difficult to decide in

which part of the thoracic organs the growth originated, as well as in distant organs, the liver, kidneys, and brain. In the second group the extensive and widespread secondary growths often form a striking contrast to the insignificant primary growth, which in life may have been latent and completely overlooked. A most interesting point about these secondary growths is that, like metastases of primary carcinomas of the thyroid and prostate glands, they are particularly prone to occur in bones (Turnbull and Worthington). Large growths in the bones may be widely disseminated, and the whole picture may be the well-known one of intense pains with albumose in the urine. In 119 consecutive autopsies on malignant disease at the London Hospital, including 3 of primary bronchial growth, the bones were the seat of secondary deposits in 8 cases in all, 3 of which were the bronchial cases.

Symptoms.—The special feature of a growth of the bronchus, whether benign or malignant, is to cause stenosis. Collapse of the affected area of lung with bronchial dilatation going on to excavation of the lung will result; in rare instances gangrene of the lung and empyema have resulted. The chief physical signs are diminished entry of air on the affected side, dulness of varying degree, and tubular breathing. Rales depending on the presence of dilated tubes or caused by destruction of the lung may be present. Other signs, peculiar to the malignant growths, may arise from invasion of the pleura and from the metastases in distant organs such as those just mentioned in the case of the bones; symptoms due to pressure on the thoracic nerves and vessels have been reported. In these cases of more extensive spread the picture becomes so like that of a *primary tumour of the lung or mediastinal growth*, that the reader is referred to those articles for full details. Cough with expectoration, catarrhal at first and purulent or fetid later from the effects of the stenosis, slight fever, and cachexia are commonly present. The sputa are often blood-stained, but serious and even fatal haemorrhage (Handford (6)) has occurred from ulceration of the growth and erosion of a vessel.

Diagnosis.—Aneurysm or a large mediastinal growth pressing on the bronchus will be excluded, at any rate in the localised cases, by the absence of their special physical signs and by examination by the *x*-rays. The diagnosis will then lie between malignant and syphilitic stricture of the bronchus. Enlargement of the supraclavicular glands, which is common in carcinoma of the bronchi, will be decisive; in one case malignant cells were found in the sputa. Bronchoscopy bids fair to be a great aid (*vide* Vol. IV. Part II. p. 310).

Treatment is purely palliative.

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J. J. P.

ACUTE LOBULAR PNEUMONIA AND BRONCHOPNEUMONIA

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LOBULAR pneumonia, as an anatomical change, includes such different conditions as the caseating pneumonia of tuberculosis, hypostatic pneumonia, and the infective pneumonia which follows embolism or the aspiration of food into the lungs. None of these conditions will be dealt with here. There remains a group of cases of acute lobular pneumonia which is difficult to define, with the exception that it attacks children far more frequently than adults. This group is well recognised clinically, but from the pathological point of view it is only one form of acute lobular pneumonia.

This disease in children and adults varies much in its clinical symptoms and course, and it cannot be doubted that these variations are largely due to different bacteria producing the same anatomical lesion. The bacteriology of lobular pneumonia is still imperfectly worked out; that is to say, it is not yet possible from the course of the disease to say in all cases what bacterium or combination of bacteria is responsible for the intoxication. It is therefore advisable to adopt a classification of cases based not upon bacteriology alone, but upon clinical and pathological distinctions, and, when possible, to correlate the clinical course with a definite bacterial cause.

Unfortunately, classification is complicated by the fact that different authors have not always referred to the same clinical groups of cases, although they appear to have adopted the same classification. The confusion arises from the use of bronchopneumonia as a synonym for

lobular pneumonia. Dr. S. West pointed out the existence of cases of lobular pneumonia which are identical with lobar pneumonia in their symptoms, course, and pathological appearances, and differ from lobar pneumonia only in the distribution of the pneumonia being lobular instead of lobar. He suggests that these pneumonias are due to a pure pneumococcal infection of the lung, and calls them primary broncho-pneumonia, as opposed to secondary bronchopneumonia, in which a bronchitis or acute specific fever precedes the pneumonia. If, as seems probable, the pneumococcus produces an inflammation primarily in the alveoli, and not primarily in the bronchial mucous membrane with a secondary extension to the alveoli, these pure pneumococcal cases of lobular pneumonia should not be included in bronchopneumonia, but should be called primary lobular pneumonia, in contradistinction to bronchopneumonia or secondary lobular pneumonia. Other authors (Holt, Dunlop) include in primary bronchopneumonia all cases of lobular pneumonia which are not secondary to pre-existing disease. Their group of primary bronchopneumonia, therefore, includes the cases designated as such by Dr. S. West, and, in addition, those cases in which, apart from antecedent disease, the inflammation in the lungs has the form of a bronchial catarrh leading to lobular consolidation,—in other words, a true bronchopneumonia. Holt, it is true, states that there are cases of lobular pneumonia which are not pathologically bronchopneumonias, but he does not classify them separately.

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Bacteriology.—As has just been pointed out, a clear distinction must be drawn between the inflammation resulting from the direct invasion of the tissues of the infantile type of lung by the pneumococcus, and that associated with, dependent upon, and an extension of, an acute or chronic inflammation of the bronchi. The former is a true pneumonia, not a bronchopneumonia, and is due to a specific organism—the pneumo-coccus—(*vide* p. 198): and that the lesions observed after death in cases of this nature are lobular rather than lobar, is due to the operation of factors which are purely anatomical. The latter is, as its name implies, an inflammation of the lung tissue adjacent to an infected bronchus, or bronchi; it may be primary, or occur secondarily during the progress of some other and general infection, such as tuberculosis, measles, diph-theria. The bacteriology of such a bronchopneumonia is to all intents and purposes that of the bronchitis from which it derived its origin, and hence may be due to any or many of the pathogenetic organisms that are able to gain entrance to the upper air-passages; for bronchopneu-monia can fairly be described as an auto-infection by direct extension from the bucco-pharyngeal cavity, and caused by pathogenetic microbes which have probably been residing in that situation for some time previously. No one organism has been found with such a degree of constancy in cases of bronchopneumonia as to warrant any claim to specificity; indeed, in nearly half the observed cases there is clear

evidence that the lesions described depend on the combined action of two or more species of bacteria.

Analysis of a few of the recorded observations, the chief of which were carried out during the last decade of the nineteenth century, and of a short hitherto unpublished series by the late Dr. Washbourn and myself, shews

TABLE I.

Observer.	Total Cases investigated.	Single Species of Micro-organisms observed.	Mixed Infection.
Mosny	17	11	6
Netter	95	64	31
Wollstein . . .	33	13	20
Eyre and Washbourn .	30	15	15
	175	103	72

this clearly (Table I.); these observations also shew that the organisms present either alone or in association are usually as follows: *Diplococcus pneumoniae*, *Streptococcus pyogenes longus*, *Staphylococcus pyogenes aureus* and *albus*, the pneumo-bacillus of Friedländer, and the bacillus of influenza. Summarising the results obtained when a single species of micro-organism was present in the above observations, we obtain the following table of relative frequency. The details of the mixed infection noted by some of these workers are not sufficiently full to enable the total results to be displayed in the same manner.

TABLE II.

Observer.	Pneumococcus.	Streptococcus pyogenes longus.	Pneumobacillus.	Staphylococcus aureus and albus.	B. influenzae.
Mosny . . .	4	6	1	...	...
Netter . . .	25	20	11	8	...
Wollstein . . .	11	2	...	...	...
Eyre and Washbourn .	4	5	3	1	2
	44	33	15	9	2

As already remarked, the various series of cases of bronchopneumonia investigated post-mortem were studied at a period when our ignorance of the nutritional requirements of many of the parasitic bacteria was even greater than it now is, and in all probability the actual percentage of mixed infections is much larger than is indicated in Table I. Eyre and Washbourn's series, comprising 30 cases completed in 1901, pointed to mixed infection in 50 per cent. Further, in many

of these mixed infections *Bacillus influenzae* was present, an organism which is practically never recovered from the infected tissues save by the use of special culture media containing mammalian blood in some form. Hence it is conceivable that in the early recorded cases this bacillus was sometimes present, but as many cases were examined by ordinary cultural methods only, the associated organism was recorded as present in pure culture. Again, *Micrococcus catarrhalis* is very frequently present either in pure culture, or associated with other and better-known pathogenetic bacteria, but it is only within recent years that the importance of this coccus has been sufficiently appreciated to ensure its presence, when recognised, being recorded. In a further series of 99 cases which I have examined, as opportunity offered, between 1902 and 1909, a percentage of 62 per cent mixed infections was noted. The results of the series may be tabulated as follows:—

Total number of cases examined, 99 (all cases between the ages of 2 months and 6 years, with three exceptions, aged respectively 10, 12, and 18 years).
,, ,, ,, yielding pure cultivations, 37
,, ,, ,, ,, mixed ,, 62

Micro-organisms isolated.	In pure Culture.	In Association with one or more Pathogenetic Bacteria.
Diplococcus pneumoniae	12 times	39 times
Streptococcus pyogenes longus	13 ,,	29 ,,
Staphylococcus pyogenes aureus and albus	4 ,,	25 ,,
Micrococcus catarrhalis	1 ,,	12 ,,
Micrococcus tetragenus	0 ,,	7 ,,
Bacillus of Friedländer	4 ,,	7 ,,
Bacillus influenzae	3 ,,	15 ,,
Bacillus pertussis	0 ,,	2 ,,
Bacillus pyocyaneus	0 ,,	1 ,,
Bacillus typhosus	0 ,,	1 ,,
Bacillus diphtheriae	0 ,,	3 ,,

[*Bacillus coli* was isolated in all the mixed infections in which the interval between death and necropsy exceeded twelve hours, 23 in all, and in 20 of the so-called pure cultivations in which a similar interval had elapsed.]

Although no other extended series of observations upon the bacteriology of *unselected* cases of bronchopneumonia has been carried out during recent years, many investigations have been instituted upon the bronchopneumonia associated with special infections, as, for example, that by Jochmann and Mollrecht, who record the isolation of the *B. pertussis* (Eppendorf) in a series of 23 cases of whooping-cough out of a total of 25 examined, and Meunier, who records 10 cases of infantile bronchopneumonia as due to the *Bacillus influenzae* out of a total of 15 examined.

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I. Primary Lobular Pneumonia

Synonyms.—*Pneumococcal lobular pneumonia; Primary broncho-pneumonia* (West).

It has already been pointed out that the clinical course of a pneumonia depends upon the kind of micro-organism which is infecting the lungs, and not upon the distribution of the pathological changes which it produces there. It follows that when the pneumococcus, apart from other bacteria, produces a pneumonia, the symptoms and course of the disease will be the same, no matter whether the pneumonia be lobar or lobular in distribution.

In adults pneumonococcal pneumonia is always lobar; in children it may be either lobar or lobular. No satisfactory explanation of this difference can be offered, but it may possibly depend upon some anatomical peculiarity of the lungs of young children, because the younger a child is the more likely is the pneumonia to be lobular, and after about five years of age it will almost certainly be lobar. It is not very uncommon to find at a necropsy on a child that the pneumonia is lobar in one lung and lobular in the other or in another part of the same lung; or that in the middle of the lobar pneumonia there are patches with a lobular distribution. The age of the child, however, is not a safe clinical guide to the distribution of the pneumonia, because even in the youngest infants the pneumonia may be entirely lobar.

The relative frequency with which pneumococcal pneumonia is lobar or lobular at different ages in children is not accurately known. In order to classify a given case of pneumonia during life two points must be known about it; in the first place the distribution of the pneumonia must be determined; in some cases this is obvious, but in others it is not; and there can be no doubt that it may be impossible by physical signs to diagnose between a lobar and a confluent lobular pneumonia. In the second place we must know the bacteriology of the pneumonia,—whether it is caused by a pure infection by the pneumococcus or other micro-organism, or by a mixed infection. In some instances this can be inferred from a careful consideration of the clinical symptoms of the disease, but in others it is quite impossible, for in children sputum is seldom available for bacteriological examination.

Incidence.—The statistics which have been published up to 1907 in regard to the incidence and mortality of pneumonias in children have been collected and reviewed by Dr. F. Taylor, but it cannot be said that the results point to any very definite conclusions. It is clear that the statistics published by various authors are not comparable; for different authors adopt different classifications and base their classification on different criteria. Some authors deal only with cases observed during life, and one writer classifies every case ending by crisis as lobar. Others

deal only with cases verified by a necropsy; and in this connexion it must be remembered that pneumococcal pneumonia has a very much lower mortality than bronchopneumonia. In spite of statistical uncertainties, there can be no doubt that pneumococcal lobular pneumonia is by no means an uncommon form of pneumonia in young children. Of 500 cases of pneumonia in children Dr. Dunlop classified 147 as lobar, and 120 as primary bronchopneumonia. In 13 of these 120 cases the pyrexia ended by crisis; the infection therefore was certainly pneumococcal; and in all probability there would be other pneumococcal cases terminating by lysis. Of the 147 cases classified as lobar, 55 were less than two years old, and 42 were between two and five years of age. It may be safely inferred that some of these cases were suffering from confluent lobular pneumonia which could not be distinguished from lobar pneumonia. In the statistics quoted by Holt dealing with 100 cases of pneumonia other than lobar in children, the pneumococcus was found to be the only organism present in 31 cases. It must be pointed out that the pneumococcus is frequently found in bronchopneumonia in conjunction with other organisms, and that it is only when it is the sole organism present that the distinctive features of primary lobular pneumonia are produced.

Morbid Anatomy.—In this disease the patches of consolidation may be widely distributed through both lungs without any obvious relation to the bronchi, and are often confined to one lung or even to one lobe. Frequently they coalesce and become confluent, forming a large area of solid lung, which, however, on section has not the uniform granular appearance of lobar pneumonia, but is obviously made up of solid lobules. The solid lung is covered with pleurisy. Microscopical examination shews that the lesion is identical with that of lobar pneumonia, and widely different from that seen in bronchopneumonia.

The clinical course, symptoms, and complications are the same as those of lobar pneumonia (*vide* p. 205).

The only point which remains to be discussed here is the **diagnosis** of this disease on the one hand from lobar pneumonia and on the other from bronchopneumonia. From *lobar pneumonia* the only method of distinction is by physical signs. If the pneumonic patches are disseminated, but otherwise the case is like one of lobar pneumonia, the diagnosis is obvious. If, however, the lobular pneumonia is confluent and confined to one or two lobes, the physical signs are, we believe, indistinguishable from those of lobar pneumonia; thus, in one case, the necropsy shewed that the pneumococcus had produced a lobar pneumonia in one lower lobe and a confluent lobular pneumonia in the other; and yet during life there was no difference between the physical signs on the two sides. Judging by the infrequency with which a diagnosis of primary lobular pneumonia can be made during life, it seems probable that this kind of pneumonia is generally confluent and diagnosed as lobar.

From *bronchopneumonia* these cases differ in their symptoms, course, and physical signs. The following points serve to distinguish them:—

Their sudden onset, with high temperature and severe nervous symptoms; the duration is shorter, the pyrexia is more regular and sustained, less remittent, and often ends by crisis; recovery is rapid, there is no tendency to relapse, and the mortality is small and probably not more than between one-half and one-quarter of that of bronchopneumonia at the same age; bronchitis is absent both before and at the time of the onset, it may appear later, but is clearly secondary.

II. Bronchopneumonia

Synonyms.—*Pulmonary catarrh; catarrhal pneumonia; capillary bronchitis; secondary lobular pneumonia.*

Bronchopneumonia, as the name implies, is not a primary affection of the alveoli of the lungs, but a widespread catarrhal inflammation of the small bronchi, which in places spreads to the alveoli, producing pneumonic consolidation. In many cases the pneumonia is definitely preceded by bronchitis of the large tubes, or occurs in the course of an acute specific fever; such cases may be referred to as secondary. When there is no antecedent illness the bronchopneumonia may be called primary. Secondary cases in children, according to the published statistics, are at least two or three times as numerous as the primary cases. This is probably an underestimate of the disproportion, because it is probable that not only the pneumococcal cases already described, but also many cases really secondary to influenza are classified as primary. In adults primary cases are very unusual, nearly all cases being secondary.

Etiology.—*Age.*—Bronchopneumonia is essentially the pneumonia of infants and young children; at least 70 per cent of all cases occur within the first two years of life. Of primary cases, a majority are less than two years old, and after four years of age the disease is infrequent. Of secondary cases, nearly half are more than two years old, and they may be found throughout childhood as a result of specific fevers. But as age advances this complication of bronchitis and specific fevers becomes less and less frequent, until in adult life bronchopneumonia is a rare disease, and when it occurs it more frequently complicates influenza and bronchitis.

The *season* of the year has considerable effect upon the incidence of bronchopneumonia. It occurs throughout the year, but is very much more frequent during the cold months of the winter and spring.

The *primary diseases* to which bronchopneumonia is most often secondary are measles, whooping-cough, and bronchitis of the larger tubes; less frequently diphtheria, scarlet fever, acute gastro-enteritis, enteric fever, and influenza. In regard to influenza, as has already been pointed out, it is probable that many cases which appear to be primary are really influenzal.

Morbid Anatomy.—The disease affects both lungs in about 80 per cent of all cases, and the bases about six times as often as the apices. The inflammation in secondary bronchopneumonia may begin in the larger tubes and gradually spread down to the smaller bronchi and alveoli in which these tubes end, and through the walls of the smaller bronchi to the surrounding alveoli. In the more acute primary cases the inflammation seems to affect the smaller bronchi and alveoli almost simultaneously. Often several adjacent lobules are affected together so as to form a patch of solid lung, which may coalesce with similar patches and form a considerable area of solid lung.

Bronchopneumonia, unlike lobar pneumonia, does not run a definite clinical course, nor does the pathological process necessarily pass through the series of changes denoted by congestion, hepatisation, and resolution. In the most acute cases, which die within the first two or three days of what appears to be capillary bronchitis, the lungs may not look very abnormal to the naked eye, excepting that the bronchi contain mucopus and the lungs in parts are acutely congested, red, and oedematous. And it is only on microscopical examination that the alveoli are found to be affected; they are seen to be partially filled with desquamated epithelium, a few leucocytes, and perhaps in places some red cells.

When the disease has lasted as long as fourteen days the cut section of the lung shews areas of grey or reddish-grey mottling. These grey areas of consolidation surround the small bronchi, and vary much in size. The smallest and most recent may be but little larger than miliary tubercles. The older ones are large, and produced by the inflammation spreading to adjacent alveoli. These areas may again coalesce and produce solid areas of any size, even up to that of an entire lobe. However large these areas of consolidation may be they never present the nearly smooth, finely granular, uniform surface of lobar pneumonia; they feel lumpy to the finger, and can be seen to be made up of discrete patches separated by congested or collapsed lung. The bronchial tubes contain mucopus, the front of the lung is often emphysematous, the areas of consolidation may be covered by pleurisy, and posteriorly dark depressed areas of collapse are frequently present. Under the microscope the walls of the small bronchi are seen to be thickened and infiltrated with leucocytes, and the bronchial epithelium is desquamating. In the grey areas of consolidation the alveoli are filled with leucocytes and desquamating epithelium; and where the process is in its earliest and most acute stage the vessels are congested and the alveoli may contain, besides leucocytes and epithelium, a few red cells, and sometimes fibrin. In the more protracted cases which have lasted several weeks there may be, in addition to the appearances already mentioned, well-marked inflammatory changes in the septa between the alveoli.

Symptoms and Clinical Course.—Bronchopneumonia has not any characteristic clinical course, and the symptoms and signs of the disease are more variable and less striking than in lobar pneumonia.

The *onset* in secondary cases is generally gradual. The symptoms,

due to bronchitis or the primary infectious disease, pass slowly, or less often suddenly, into those of bronchopneumonia, the actual onset of which is shewn by a rising temperature, more rapid respirations and cough, and an increase in the general constitutional disturbance. In primary cases the onset is often sudden and not unlike that of lobar pneumonia. It is marked by a high temperature, vomiting, less often convulsions, together with rapid respirations, cough, some cyanosis, and rapidly increasing constitutional disturbance.

The *temperature* is generally high, not sustained, but marked by daily remissions of 3° F. or more; it may be intermittent. The pyrexia ends gradually by lysis and never by crisis. Hyperpyrexia is not very uncommon, and when occurring late in the case generally indicates the onset of a rapidly fatal septicaemia. The absence of a high temperature is not necessarily a good sign. Weakly infants and marasmic children may die and have never had a pyrexia greater than is usually seen in a mild attack of bronchitis; the temperature in the worst of these cases may even be subnormal throughout.

The *respirations* are rapid, and generally more than fifty a minute; they increase in frequency in proportion to the extent of lung affected. The alae nasi are working obviously, and there is conspicuous dyspnoea. Very often the respiratory rhythm becomes inverted in children, so that the pause is at the end of inspiration, instead of following expiration. With inspiration a deep depression is seen to form above the clavicles, and another between the trachea and manubrium. The epigastrium is thrust in, and even the lower ribs and ensiform cartilage yield to atmospheric pressure. Marked orthopnoea is uncommon in children as compared with adults.

The *cough* is frequent, sometimes almost continuous, and generally distressing. The cough in children is a much less effectual means of emptying their tubes than in adults; the same feeble and ineffectual cough is sometimes seen in aged patients. A vigorous cough and strong respiratory movements are always a good sign, indicating that the medulla is not too poisoned to respond energetically to reflex stimulation. Unfortunately for diagnosis young children never expectorate, but swallow their sputum. In adults the expectoration is usually scanty, and consists of thin mucus without much admixture of air; occasionally it is streaked with blood. In most cases, however, there is always present the frothy muco-purulent expectoration of pre-existing bronchitis.

The *pulse* is always frequent, at first bounding, then small and compressible, and finally weak and irregular. Dilatation and engorgement of the right heart are not infrequent in children, and more so in adults. General cardiac dilatation and failure, however, are not nearly so early and marked, even in severe cases, as is failure of the respiratory mechanism.

The *skin* is usually moist and sweating, sometimes dry and hot, but it does not have the pungent feel characteristic of lobar pneumonia. The face is generally flushed at first, and the expression is anxious and

distressed. Herpes is not uncommon, although more so than in lobar pneumonia.

Cyanosis due to imperfect aeration of the blood, and later to right-sided cardiac failure as well, is present in all severe cases. It is usually first seen in the lips and ears, then in the fingers and toes, next in the face, and finally over the whole surface of the body and mucous membrane of the mouth. Even when slight it indicates severe and extensive mischief in the lungs. The prognosis becomes very grave indeed when cyanosis gradually disappears and its place is taken by pallor, with a cold and clammy skin. This pallor appears to indicate that the vasomotor centre is failing, and that the whole circulation is in danger of coming to a standstill.

Nervous symptoms at the onset are generally less prominent than in lobar pneumonia; vomiting is common, but severe convulsions are less so, and consequently confusion with meningitis is less likely to occur. Towards the end of severe cases fits are not uncommon and generally fatal. Most severe cases shew much peevishness, restlessness, mental excitement and sleeplessness, and often some delirium. The younger the patient the more likely are these symptoms to be marked. Before death most children pass gradually into a stuporous condition; and nothing is more serious than to see a patient gradually sliding down in bed, breathing less vigorously and hardly coughing at all, although the bronchial tubes are full of secretion, becoming cold, pale and clammy, and taking little or no notice of what is going on.

Digestive disturbance is common; the appetite is much impaired and there is great thirst. Some children refuse food and require nasal feeding. More marked gastro-intestinal disturbance is not uncommon in young children; there is vomiting and diarrhoea with green stools containing undigested food and mucus. In infants and weakly children the vomiting and diarrhoea add greatly to the gravity of the condition. Most children lose flesh and strength rapidly and look very ill; in prolonged cases emaciation may become extreme.

The *urine* is generally scanty; sometimes it contains a small quantity of albumin. Acute nephritis is very uncommon in bronchopneumonia, and when present can generally be ascribed to the specific fever of which the bronchopneumonia is a complication.

The *duration* of the disease, as judged by the pyrexia, is extremely variable; it may be any period between one or two days and three or four months, and even longer cases than this have been observed. The commonest duration is about a fortnight; about 70 per cent of all cases in children last between 7 and 21 days, about 10 per cent a shorter time, and about 20 per cent for a longer period. In cases which have lasted longer than about a fortnight the course of the pyrexia generally becomes extremely irregular. For two or three days the pyrexia becomes less and may even disappear, to be followed by another outbreak of high temperature for a week or more. Such cases in fact are prolonged because they suffer from a series of relapses.

The *physical signs* vary in different cases; they are necessarily influenced by the degree of general bronchitis present, and by the number of the pneumonic patches, few or many, and by their distribution, widely disseminated or confluent. In general it may be said that auscultation is by far the most valuable and fruitful method of examination. Definite signs of consolidation are absent in about a third of the cases, and even when present it may be necessary to examine every portion of the chest systematically inch by inch in order to detect them. In a great majority of the cases in which signs of consolidation are observed these signs are noticed for the first time between the fourth and seventh days.

In the first few days of the disease the physical signs are those of bronchitis and congestion. There is no change to percussion, the breath-sounds may be feeble and there may be coarse and fine sibilant rales due to general bronchitis. The first distinctive sign of bronchopneumonia is localised fine rales, heard generally over some part of one or both lower lobes. As consolidation advances these localised rales become louder, sharper and, like the breath-sounds, of higher pitch; and at the same time the sounds produced by the voice and cry are increased. Not infrequently the auscultatory signs of consolidation cannot be heard as long as the child is breathing quietly, because the corresponding tubes are blocked by secretion; the physical signs appear, however, when the child cries and has a fit of coughing. The signs of general bronchitis of the larger and finer tubes may be very obvious. At this stage there may still be an absence of dulness, and only a general and slight impairment of resonance.

When consolidation is complete the physical signs heard over the patches are bronchial breathing with numerous crackling rales and increased voice-sounds, and perhaps a pleuritic rub. There may be very definite general impairment of resonance over the lower lobes due to congestion of the lungs and collapse; and at the same time the anterior portions give a hyper-resonant note due to emphysema. Only when many patches have coalesced to form a comparatively large area of consolidation, can definite localised dulness be made out. The physical signs heard over such a dull area are in certain particulars different from those heard in lobar pneumonia. In bronchopneumonia there is no prolonged stage of loud bronchial breathing and bronchophony unaccompanied by any moist sounds whatever, excepting perhaps a few pneumonic crepitations at the spreading edge. Again the true pneumonic crepitation is not heard in bronchopneumonia, the rale present is always and at all stages coarser and more crackling. Further, there is a considerable difference in the rate at which the signs of consolidation disappear in typical examples of the two diseases. In bronchopneumonia it is unusual for these signs to disappear in a few days; more often it takes several days or even weeks. The physical signs of bronchitis may persist for still longer periods. The longer the disease has lasted, the greater is the time taken in clearing the lungs. Convalescence, too,

is generally much more tedious than after even severe cases of lobar pneumonia.

There are certain acute and atypical cases of bronchopneumonia which must be mentioned. They are referred to by various authors as acute congestion of the lungs, suffocative catarrh, capillary bronchitis, or acute congestive bronchopneumonia. They are uncommon cases and generally seen in infants. They may be primary or secondary. The usual history is that the child is suddenly taken ill with a high temperature, rapid breathing, cyanosis, little or no cough, and prominent cerebral symptoms. Within a few hours the patient is in a condition of extreme toxaemia and very seriously ill. The physical signs in the chest may be confined to a few moist sounds, and the diagnosis may be uncertain. Infants may die within one day of the onset of these symptoms; others rapidly improve and are well within a week. In other cases the fine sibilant rales of capillary bronchitis appear early together with incessant cough; death may take place in a few days, or the more severe symptoms may subside and be followed by those of ordinary bronchopneumonia.

Complications.—Although the mortality of bronchopneumonia is high, cases, which do not end fatally, recover completely as a rule and complications are uncommon. Pleurisy is comparatively frequent and may lead to adhesions. Pleural effusion is rarer than with lobar pneumonia, and is nearly always purulent. Gangrene and abscess of the lung may both occur; but they are rare, although less so than after lobar pneumonia.

Cases of protracted bronchopneumonia generally die. Of those who survive, a majority recover completely in the course of time. But in others the inflammation of the lung does not resolve and fibrosis of the lungs and bronchiectasis are the result.

A large number of septicaemic lesions have been observed as rare complications; such are pericarditis, endocarditis, purulent meningitis, and nephritis.

Some authors express the opinion that the most frequent and formidable complication is tuberculosis, either as miliary tuberculosis of the lungs or as chronic phthisis. There can be no doubt that bronchopneumonia may light up a quiescent tuberculous lesion in the lungs or bronchial glands. Nevertheless, it seems almost certain this is not the usual sequence of events, and that cases which run on from apparent bronchopneumonia into chronic pulmonary tuberculosis, or which at the necropsy shew bronchopneumonic consolidation with miliary tuberculosis, were really tuberculous from the outset.

Diagnosis.—Bronchopneumonia does not often present difficulties in diagnosis. A high temperature, cough, and rapid respirations, together with cyanosis and prostration, obviously suggest acute pulmonary trouble of some sort. It is only in the acute atypical cases that there may be a doubt whether the symptoms are due to pulmonary disease or not; and in them the rapidity of the respirations and cyanosis are the symptoms which would have to be relied upon until physical signs appeared in the

chest. The acute diseases of the lungs from which bronchopneumonia has to be distinguished are bronchitis, lobar pneumonia, and tuberculosis.

From *bronchitis* the diagnosis is obvious when the signs of commencing consolidation appear. Localised bronchitis in children always suggests bronchopneumonia or tuberculosis. Apart from the physical signs, a high temperature and severe constitutional disturbance lasting more than one or two days point to bronchopneumonia rather than to simple bronchitis.

From *pneumococcal lobar* and *lobular pneumonia* the diagnosis is generally easy, and has been already considered (*vide* p. 180).

From *tuberculous bronchitis* and *bronchopneumonia* the diagnosis is often most difficult. Neither the severity and duration of the symptoms nor the physical signs and their localisation offer any presumptive, much less certain, evidence in favour of either diagnosis. The possibility of tuberculosis should always be considered when a case has lasted more than a month or six weeks. The ophthalmo-tuberculin reaction is of no help, because cases of such acute tuberculosis do not give it. The only moderately certain method of diagnosis is to pass a stomach-tube well down into the oesophagus after the child has been coughing up sputum, and to stain a portion of the sputum adhering to the tube.

Pleural effusion offers few diagnostic difficulties. The physical signs and their distribution over the lungs, the displacement of the heart and mediastinum are usually sufficient. In case of doubt, the chest should be explored by puncture.

Prognosis and Mortality.—The mortality in hospital practice is high, and therefore the prognosis is always doubtful. The most divergent estimates of the mortality in children have been given by different authors, the extremes being about 25 per cent and 75 per cent. It is impossible to explain these differences satisfactorily.

The points on which the prognosis of each case has to be based are numerous and may be summarised as follows:—(1) Primary cases have a very decidedly lower mortality than secondary cases. (2) Secondary cases have different death-rates in accordance with the nature of the primary disease. The death-rate among children suffering from a specific fever, such as measles, whooping-cough, diphtheria, scarlet fever, and summer diarrhoea, is probably double that of bronchopneumonia following bronchitis of the larger tubes. (3) The previous health of the child is important. In private practice the children are as a whole better nourished and developed, and come under treatment earlier than hospital patients. In private cases the mortality has been put as low as 10 per cent; but amongst rickety, ill-nourished children it is very high indeed. (4) The age of the patient; the mortality varies directly as the age, being greatest in the first year of life and decreasing steadily as the age increases. (5) The symptoms which have to be taken into account are the extent of the lung involved, the height, course, and duration of the pyrexia, the presence or absence of cyanosis, late nervous symptoms, and gastro-intestinal disturbance. A temperature over 105° F. is serious,

because it points to a virulent infection: but a low or subnormal temperature is even more serious, because it indicates a feeble and weakly child. A high irregular pyrexia with remissions of many degrees and relapses is an unfavourable type of chart. When the pyrexia has lasted more than a month the prognosis is much less good; but cases have continued for five months and recovered.

Death appears clinically to be caused in one of the three following ways:—(*a*) Suffocation and toxaemia in the early stages; (*b*) heart failure which is often sudden; (*c*) increasing exhaustion in the prolonged cases. In many cases the real cause of death is septicaemia.

Treatment.—The fact that secondary bronchopneumonia is so common, severe, and fatal in hospital patients, and just the reverse in private practice, suggests that much could be done to prevent its onset by taking greater care of children suffering from bronchitis or from specific fevers liable to produce bronchitis (*vide* p. 122).

The curative treatment of bronchopneumonia by injections of serums or vaccins may be said to be almost impossible in the present state of our knowledge, because of the difficulty of ascertaining the bacteriology of individual cases during life. In the protracted relapsing cases which are known to be frequently due to streptococcal infection, I, and probably others, have tried injections of polyvalent antistreptococcic serum without any very striking improvement being obvious. It is only in the treatment of empyema after bronchopneumonia that vaccination could be easily applied.

The object of the symptomatic treatment of bronchopneumonia, as of every other infective disease, is to put the patient in the best possible position to withstand the toxaemia and to deal with the infection of his tissues. With this object in view, the chief points which require attention are the ventilation and temperature of the patient and the room, and the feeding; further it is necessary to keep the central nervous system alive to the reflex calls for cough and respiratory exertion, and to prevent the bronchial tubes from becoming waterlogged with secretion, which renders the proper aeration of the blood impossible; the heart and circulation also require attention.

Children should be kept in bed; infants will necessarily have to be nursed for a considerable part of the day. The position of the child should be changed frequently, in order to promote coughing and the emptying of the tubes. The room should be well ventilated night and day by open windows, and the patient should be protected from direct draughts by a screen. The chest should be covered by a loose jacket of Gamgee tissue under the flannel night-dress, because it is difficult to prevent children from exposing themselves. Tents and steam-kettles do harm; a hot atmosphere saturated with moisture is oppressive and greatly curtails the power of the body to get rid of heat, and therefore to keep down its temperature. Poultices are objectionable because of their weight and heat, and, moreover, like local applications of mustard and the like to the chest, are useless; for there is not any evidence that local

applications of heat, cold, or irritants to the surface of the chest can influence an acute inflammatory lesion of the lungs.

The food should be given at regular intervals, which may have to be short on account of the small quantity taken at each feed. It will generally have to be liquid and well diluted. Plenty of water or other fluid should be given between the feeds if the child is thirsty. If food is refused or taken in insufficient quantities nasal feeding at regular intervals should be resorted to early.

Alcohol is valuable in severe cases. It is best given as brandy or whisky in a spoon and not too much diluted with water, the dose being about 15 or more minims every two or four hours, according to the age and condition of the patient. In case of need the dose may be pushed considerably for a short time. Alcohol is not a stimulant to the heart, the circulation, or the central nervous system; but it is the only food, except dextrose, which does not require digestion, it is readily absorbed, easily oxidised, and further, it helps the appetite and aids digestion. It is therefore of great value when the appetite and digestion are failing and when vomiting and diarrhoea are present. It is invaluable in infants whose general metabolic activity is too feeble to respond to the infection by a satisfactory pyrexia. In addition alcohol is a hypnotic, and is of use in combating the restless, excitable, and sleepless condition which is often difficult to deal with.

Expectorants are only of value in loosening the hard dry cough of the large-tubed bronchitis which may precede or accompany bronchopneumonia; and in children as soon as this result has been obtained the expectorant should be stopped altogether. In a great majority of cases expectorants are not only useless but actively harmful; the younger the child and the more extensive the small-tubed bronchitis the more dangerous they are. Not only do all expectorants when given in large doses act as emetics, and therefore upset appetite and digestion, but of all drugs they are the least required in the treatment of the disease of the lungs. When once the secretion in the tubes is fluid, the question is not how to produce more secretion, but rather how to empty the tubes and prevent the accumulation of secretion. It is no exaggeration to say that many children die drowned in their own bronchial secretion; and this is hardly to be wondered at, since the only mechanism for emptying the finer bronchial tubes is the ciliated epithelium, which is extensively destroyed in the inflammatory process. Emetics, such as vinum ipecacuanhae, are of value when the secretion first begins to accumulate and the cough is feeble; but they must be used early. When once stupor and weakness of the body and pulse have set in they are useless, because they fail to stimulate the medulla and produce vomiting.

Opium, heroin, and similar drugs, which act by reducing the excitability of the cough centre in the medulla, should be avoided as long as secretion is abundant. In all serious cases the safety of the patient depends largely upon the excitability of the cough and respiratory centres.

Inhalations are of decided value in relieving the cough. The most useful way of giving them, because it does not disturb the patient, is either to burn a cresoline or creosote lamp in the room, or to sprinkle oil of eucalyptus on the front of the night-dress, or on a handkerchief placed near the patient's head.

Of circulatory stimulants the most valuable for prolonged use is strychnine. It may be given in minim doses of the liquor every few hours; the mistake which is frequently made is to give it far too sparingly. In all cases of serious circulatory failure, it should be injected hypodermically with a liberal hand. In the presence of diarrhoea strychnine may have to be stopped. The best substitute for it is tincture of strophanthus, which is better than digitalis because it is less irritating to the stomach. A far more potent drug, but one only to be used for emergencies, is adrenalin. It should be given in doses of 1 minim of 1 in 1000 solution for every year of age, and must be repeated every hour for not more than 24 hours. It must be injected hypodermically, because it is not absorbed from the alimentary canal. Inhalations of oxygen are indicated whenever cyanosis is present. Here again the mistake is often made of giving it too late and for too short a time.

Of respiratory stimulants the most valuable are strychnine, belladonna, or atropine, oxygen together with warm mustard baths. Belladonna and atropine are useful not only for the stimulatory effect upon the respiratory centre, but also because they help materially to decrease the outflow of bronchial secretion. We do not possess any means of stimulating the cerebrum and medulla more efficient than stimulating an enormous number of sensatory nerve-endings in the skin. Hot mustard baths are therefore invaluable for treating the convulsions, the stupor, and the attacks of sudden collapse which are frequently seen in severe cases.

Antipyretic drugs should never be used to reduce pyrexia; so long as the temperature does not exceed 104° F. there is no necessity as a rule to reduce it. When the temperature rises to 105° F. or more it must be reduced, and for this purpose the most efficient and safest method is the application of cold. In infants a tepid bath is best, and for older children a cold pack or sponging. The process of abstracting heat must be far more carefully watched in a child than in an adult. Bathing together with alcohol are the best means of reducing the restlessness and loss of sleep which are so often seen in children with flushed faces and a hot dry skin.

In weakly infants with low temperatures an exactly opposite course has to be pursued. The child's limbs and body should be wrapped in cotton wool, hot bottles applied, and a deliberate effort made to raise the temperature and increase the metabolic activity of the body, in the hope that the tissues will respond more energetically to the infection.

The treatment of bronchopneumonia in adults does not require any separate description; it follows on the same lines as in children. The only measure which is not applicable to young children but is of value in adults is venesection. Whenever orthopnoea is prominent and coupled

with lividity and distension of the right heart, venesection is urgently necessary.

Convalescence requires patience. When the fever has disappeared the child should be taken into the fresh air. A change of air from the town to the country or from the country to the seaside does more good than many bottles of tonics. This is especially the case when the physical signs persist after the pyrexia has ceased. Such a patient should be treated by the open-air method just as if he had pulmonary tuberculosis, and it is remarkable how often the signs clear up.

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LOBAR PNEUMONIA

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SYNONYMS.—*Peripneumony*, *περιπνευμονία*. Hippocrates and later Greek writers, *Pneumonia*, *πνευμονία* (Attic form *πλευμονία*, used by Plutarch). *Peripneumonia vera* (Sydenham), as distinguished from *Peripneumonia notha*, "obstruction of the lungs by a heavy, viscid pituitous matter," that is, in modern nomenclature, bronchitis. *Pneumonic fever* (Huxham). *Pleuro-pneumonia; Acute* or *Sthenic pneumonia; Croupous* or *Fibrinous pneumonia; Pulmonary fever.*

Definition.—An infective disease of the lung, running a short and characteristic course, directly resulting from a general infection of the blood, and the subsequent localisation and multiplication within the pulmonary tissue of a specific micro-organism, the pneumococcus. Other pathogenetic micro-organisms, the *Streptococcus longus*, *Bacillus tuberculosis*, and *B. typhosus*, may produce a similar lesion in the lungs, but this is associated with a different clinical course.

Introduction.—Inflammatory consolidation of the lung—pneumonia—is either lobar or lobular in distribution; and each of these anatomical varieties may be acute or chronic in its course.

The clinical course of an acute pneumonia does not depend primarily upon the anatomical distribution of the consolidation, but upon the

micro-organism which is producing the inflammation. Thus, the pneumococcus may cause either a lobar or lobular pneumonia, as is shewn by clinical investigation and the experiments of Washbourn and Eyre and of Wadsworth; nevertheless, the clinical course, complications, and sequels of the disease are the same in either case. In fact in every infective disease all the anatomical lesions and all the clinical symptoms are due to changes produced in the body by the corresponding bacterial toxin; and since each pathogenetic bacterium has a specific toxin, it follows that two pneumonias due to different micro-organisms cannot have exactly the same clinical course and symptoms, although their anatomical distribution in the lungs may be identical. Thus, it is recognised that the course of the local lesion and the symptoms of a pneumonia produced by the tubercle bacillus differ from those due to the pneumococcus or streptococcus.

These considerations indicate that the pneumonias should be classified in accordance with the micro-organisms which cause them, and in practice we separate from other pneumonias those caused by *Bacillus tuberculosis*, *B. pestis*, *B. anthracis*, and so on. But unfortunately the bacteriology of pneumonia as a whole is by no means fully known. It is uncertain how far some of the clinical forms of pneumonia have a constant bacteriological cause; indeed, it seems probable that two or more micro-organisms may produce pneumonias which are at present clinically indistinguishable. And, further, the whole subject is complicated by the occurrence of double or multiple infections, and by the fact that the bacteriology of many of the specific fevers, which are liable to be complicated by pneumonia, is not known or uncertain. For these reasons a bacteriological classification of acute pneumonias is not attempted here.

The term pneumonia without qualification is frequently used in clinical medicine, generally as synonymous with an acute inflammatory consolidation of the lung, the particular form being inferred from the context. When an adult is described as suffering from "pneumonia" we picture to ourselves an acute lobar pneumonia probably due to the pneumococcus. And the word will be used in this sense throughout this article. But a child suffering from "pneumonia" following whooping-cough would be considered to be the subject of an acute broncho-pneumonia of uncertain bacteriology.

History.—Before morbid anatomy was studied, or physical diagnosis invented, acute inflammations of the chest, whether affecting the parietal pleura alone or the lung with its pleural covering, were described under the name *peripneumonia*; that of "pleurisy" being applied to the sharp characteristic pain in the side which accompanies both diseases. Charlemagne is said to have died of a "fever, with a pain in the side which the Greeks call pleurisy." We now recognise the pain as due to inflammation of the pleural membrane, and the name of the symptom is applied to the anatomical change which it accompanies; pleurisy always accompanies acute lobar pneumonia, although it is often present independently; and the name pleuro-pneumonia is therefore superfluous.

The characteristic clinical features of pneumonia were identified with solidification of the lungs by Morgagni; and Baillie described the lungs as sometimes converted into a solid mass very much resembling liver ("hepatisation"). But Laennec, Cruveilhier, and Rokitansky completely described the anatomy of the disease. The diagnosis of pneumonia by auscultation was one of the most important results of Laennec's great discovery. The chief steps since made in advance have been the proof by Addison that the exudation of pneumonia is not into the "interstices" of the lung, but into the air-vesicles themselves; the distinction between fibrinous or lobar and catarrhal or lobular pneumonia, which is due to Rokitansky; and the discovery of a specific pathogenetic microbe, which has been the work of numerous observers.

Etiology.—Lobar pneumonia, as seen in this country, is a sporadic and endemic disease. It is common all over temperate Europe, in the United States, Canada, and in the inhabited parts of the south temperate zone, in Australia and New Zealand, at Buenos Ayres, and in South Africa. It is less common in the Tropics; but in the hill-stations of India it is far from infrequent during cold weather. It is also common in the highlands of Central Asia; in Pekin, Cabul, Baluchistan, it is ascribed, as in Italy, to the sudden change from the scorching heat of the day to the severe cold after sundown.

Pneumonia has been described as occurring in an epidemic form. From the Middle Ages downwards we have accounts of acute epidemic disorders, which seem more like pneumonia than any other disease; and from time to time circumscribed epidemics in the same village or house have been reported in this country and in other parts of Europe. But there is not sufficient evidence to shew that these epidemics are pneumococcal pneumonia rather than influenza or some similar infection.

In the case of a micro-organism, such as the pneumococcus, which is so frequently present in the fauces of healthy persons, it is very difficult to prove direct infection from person to person. Nevertheless, hospital practice provides evidence that persons suffering from pneumococcal pneumonia or its suppurative complications may be sources of contagion and infect other patients. It is usually assumed that pneumonia is an infection of the lungs necessarily by way of the air-passages, but it is probable that infection of the blood can take place by way of the alimentary canal, the genital passages, or the skin, and that pneumonia may develop sometimes as an infection of the lungs from the blood.

Season.—The frequency of pneumonia is greatly influenced by the time of year. About 15 per cent of the cases occur in the summer quarter and about the same number in the autumn; the proportion is doubled in the winter months and undergoes a further slight increase to about 35 per cent in the spring months. The seasonal incidence is almost the same as that of bronchitis and of bronchopneumonia. The climatic conditions which seem to be of importance are sudden changes of temperature, cold winds, and dampness; and these are the conditions which are likely to cause sudden chilling of the surface of the body.

Sex.—The disease is at least twice as common in men as in women. Doubtless this is to be ascribed to the greater exposure of males to changes of weather. The difference is most marked in early adult life, least in children, and disappears in the statistics of prisons, where both sexes are under similar external conditions. It has been shewn that pneumonia is more common in outdoor workers than in those who follow an indoor occupation.

Age.—No period of life is exempt from pneumonia, but no age seems to be especially susceptible to it. In this respect it differs from broncho-pneumonia, which is comparatively rare after childhood. The age-incidence of pneumonia corresponds roughly to the relative numbers of persons living at different ages. A possible exception is childhood; but here the diagnosis between lobar and lobular pneumonias may be sufficiently difficult to make statistics unreliable. Dr. Dunlop has analysed 500 pneumonias occurring in children of all ages; 147 were lobar and 353 lobular pneumonias. Under two years of age the respective figures were 45 and 233, and above two years 102 and 120. These figures shew that in infancy lobar pneumonia is not uncommon, but far less so than lobular pneumonia. As the age increases lobar pneumonia becomes equally and then more common than lobular pneumonia.

Susceptibility.—Pneumococcal pneumonia does not confer a prolonged immunity after recovery; relapses are therefore not very rare. We have seen a child recover from one attack by crisis and then a fortnight afterwards have another characteristic attack in the other lung which ended by crisis on the fourth day. From 10 to 30 per cent of patients give a history of one previous attack; and cases are recorded in which the attacks have been numerous; these are apparently instances of a natural or inherited susceptibility greater than the average. An increased susceptibility may also be acquired. The defensive mechanisms of the body which enable the tissues to put an end to an infection, are the same as those which prevent infection. It follows that in the case of a micro-organism so universally present as the pneumococcus, the conditions, such as alcoholism, diabetes, and other general diseases and intoxications, which prejudice the power of the tissues to end an infection, must also render the body more liable to attack. It is often said that one attack makes the patient more susceptible to a second at any future date. The evidence brought forward is statistical. This notion that recovery from an infection may be followed by prolonged decrease in immunity against the micro-organism in question is opposed to our knowledge of infective processes in general, and is probably untrue.

Injury.—It is a debatable question how far injury may determine an attack of pneumonia. The point is not unimportant in relation to the Employers' Liability Act. When the chest has received a severe blow without fracture of the bones, and then pneumonia begins within a day or two beneath the part injured, it is hard to believe and impossible to swear, that there is no causal relation between the two events.

Morbid Anatomy.—Pneumonia begins with an infection of the

alveoli by pneumococci which set up an intense and acute inflammation there. The inflammatory process shews the usual series of changes observed in all inflammations; nevertheless, when taken as a whole, it is fairly characteristic of its specific cause. The first change is vaso-dilatation which produces an intense hyperaemia or engorgement. At the same time the capillaries in the walls of the alveoli begin to pour out into the air-spaces an exudate which coagulates; white corpuscles migrate and red cells are squeezed into the vesicles, and in a few hours the inflamed lung is solid and airless. The hepatised lung, originally red, undergoes changes which alter its colour to grey; and finally the inflammatory products are removed and the affected lung becomes healthy. It is usual for purposes of description to divide the pneumonic process into four stages, namely engorgement, red hepatisation, grey hepatisation, and resolution. These, however, are not separate changes, but only the four most striking features in one continuous process; this point is frequently overlooked, and can not be too strongly insisted on.

In the stage of *red hepatisation* the affected tissue feels heavy, looks distended, and readily sinks in water. Its surface is covered with pleurisy. The cut surface of the lung is seen to be dark red and the colour of liver; the advancing edge of the inflamed area is red and engorged, but not yet solid. The surface of the solid part is granular, uniform, and dry, compared with most other morbid states of the lung. It is friable and readily breaks down under pressure. A scanty blood-stained liquid, characteristically free from froth, issues from the squeezed tissue, and red fibrinous plugs may be seen filling the smallest bronchial tubes. On microscopical examination the alveoli are filled with a fibrinous network, the meshes of which contain large numbers of red and white corpuscles. The infundibula and minute bronchi also are filled with fibrinous exudation.

In the stage of *grey hepatisation* the older parts of the inflamed tissue have changed in colour to a pale or yellowish-grey; the spreading edge shews the stages of engorgement and red hepatisation. The change in colour from red to grey is seen on microscopical examination to be due to an alteration in the contents of the alveoli. The red cells have been removed by the phagocytic action of the leucocytes, which have increased greatly in number. The mesh-work of fibrin has nearly disappeared; it has been liquefied and digested by unorganised ferments and the products removed by way of the blood-vessels and lymphatics. In fact resolution has already begun, and the plugs in the infundibula and minute bronchi have disappeared.

During *resolution* the process of autolysis or peptonisation of inflammatory products by unorganised ferments continues, and in this way the abnormal contents of the alveoli are removed by absorption into the lymphatics and circulation. Finally, the vascular changes retrogress, and the lung returns to its normal condition. The period, which elapses in a favourable case, between the crisis and the completion of resolution is

not accurately known, but it is probably never less than a fortnight. The weight of inflammatory products which may have to be removed is very considerable; a pneumonic lung often weighs 2 lbs. more than the healthy organ. One of the most remarkable features of pneumococcal pneumonia is that the pulmonary tissue itself, with the exception of the capillaries, is scarcely, if at all, affected. There is no alteration of the elastic fibres and no infiltration of the interalveolar connective-tissue, such as commonly occurs in bronchopneumonia. Correlated with this freedom of the tissue from inflammatory changes are the rapidity with which the lung clears and the rarity with which lobar pneumonia is followed by fibrosis (*vide* p. 255).

Anatomical Distribution.—The statistics bearing upon this point are given in full by West, Holt, and J. M'Crae. It is sufficient to indicate here the general conclusions to which they point.

One lung is more frequently attacked than both, the right lung than the left, and the base than the apex. In about 50 per cent of cases the right lung alone is affected, and in from 10 to 20 per cent both lungs. The pneumonia begins at the base in about 75 per cent of the cases, and at the apex in about 20 per cent. There is said to be a third site which is still more seldom selected, the deep part of the lung near its root; it is difficult to detect this "central pneumonia" before it has advanced to the surface. Occasionally the anterior tongue-like process of the left lung is alone affected on that side. One lobe alone is affected in about 40 per cent of the cases, and when this is the lower lobe it is but little more common on the right than on the left side; but if it is an apex, then it is twice as often on the right as on the left side. Two lobes are affected in about 40 per cent of the cases, and three lobes in another 20 per cent; pneumonia in more than three lobes is rare. When two lobes are diseased, the most common combination is both bases. Double apical pneumonia is very rare. In children apical pneumonia is more frequent than in adults. Under five years of age more than 40 per cent of cases are apical; but after that the proportion steadily declines. In Holt's tables the right apex is affected twice as often as the left. The parts of the lungs which are not solid are seldom normal throughout. Emphysematous distension is common; and not infrequently there is some bronchitis and hypostatic congestion at the bases.

At necropsies it is rare to find other organs diseased. The bronchial glands are large, swollen, and red or grey in accordance with the stage of the hepatisation; although acutely inflamed, they seldom suppurate. The spleen is soft and pulpy, and, according to M'Crae is rarely enlarged unless the infection is either not pneumococcal at all or mixed.

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Bacteriology.—As pointed out in the definition on p. 191, acute lobar pneumonia is an infective disease directly resulting from the localisation within the lung tissues, and the subsequent multiplication in that

situation of a specific micro-organism commonly referred to as the pneumococcus and also known as *Diplococcus lanceolatus*. Other pathogenetic micro-organisms, for example the *Streptococcus longus*, the *B. influenzae*, the pneumobacillus (of Friedländer), the *B. pestis*, are also found in lung tissue, producing acute inflammation, but of the broncho-pneumonic rather than the lobar pneumonic type.

Historical.—The ultimate factor in the causation of acute lobar pneumonia—the pneumococcus—was first discovered by Sternberg (1880) in saliva, and almost simultaneously (1881) described by Pasteur; but its real importance escaped notice for some time, although Koch and Eberth (1881) demonstrated capsulated diplococci in the lungs from cases of lobar pneumonia, and v. Leyden and Günther (1882) found them in fluid drawn from the hepatised lung during life, results which were confirmed by Matray and Ziehl (1883). At this stage, however, the issue was temporarily confused, for Friedländer (1883) described an "oval coccus," also capsulated, which he had isolated from cases of lobar pneumonia and cultivated upon gelatin at the room temperature, which he regarded as the causative factor; Talamon (1884) obtained from pneumonic exudates cultures of an organism which would only grow at the body temperature, but when injected into laboratory animals gave rise to fatal septicaemia, sometimes accompanied by a lobar pneumonia; the blood and exudates of these fatal cases always contained cocci, and yielded pure cultures capable of producing similar inoculation-results. He had also found the coccus in fluid drawn during life from the hepatised lung in man in eight cases. In one fatal case it occurred in the general circulation at the moment of death.

Friedländer and Talamon, however, were working with two distinct organisms, but some time elapsed before this became apparent. Thus, Sternberg, in April 1885, read a paper before the Pathological Society of Philadelphia, pointing out the identity of the coccus which he had discovered in 1880 in his own saliva with the coccus which he had more recently isolated in cases of lobar pneumonia, but fell into the error of supposing it to be identical also with Friedländer's micro-organism. Fraenkel's contributions to the discussion in the following year cleared the ground somewhat, for he independently recognised the identity of Sternberg's coccus of sputum septicaemia with the pneumococcus, and quoted three cases of lobar pneumonia from which he had cultivated it on *solid media*. In other communications (1886) he published fuller accounts of his observations and gave differential descriptions of the pneumococcus and Friedländer's "oval coccus," which he pointed out was in truth a bipolar-staining bacillus, and differed from the pneumococcus not only in the luxuriance of its saprophytic growth, but also in its inability to retain the stain when treated by Gram's method. In May 1886 Weichselbaum reported that he had examined the exudate from 129 cases of pulmonary inflammation, of which 94 were undoubted lobar pneumonia and from which he cultivated the pneumococcus, and that from 9 cases only had he obtained Friedländer's pneumobacillus.

The chain of evidence establishing the causal association of the pneumococcus with lobar pneumonia was not, however, completed until Gamaleia (1888), working in Pasteur's laboratory, was successful in reproducing experimentally the characteristic pathological lesions of acute lobar pneumonia by inoculating sheep and dogs with cultures of the pneumococcus.

Characteristics of the Pneumococcus.—*Morphology.*—The pneumococcus is an aerobic, facultative anaerobic, non-motile, highly parasitic coccus, occurring in the body fluids in pairs, of which the individual members are lanceolate or "candle-flame" shaped, with the rounded bases in apposition, and surrounded by a mucinous capsule which can be positively demonstrated by MacConkey's, Muir's, or one of Hiss's staining methods; or as short chains, also capsulated; occurring in artificial cultivations as more nearly spherical bodies in pairs or short or long chains; staining with the ordinary aniline dyes and not decolourised by Gram's method.

Cultural Characters.—The pneumococcus grows upon artificial nutrient media at the temperature of the body (*i.e.* 37° C.), but not upon gelatin at 20° C. Certain saprophytic forms which are devoid of virulence, or practically so, are, however, capable of multiplication at temperatures approximating to what is spoken of as room temperature—namely, 20° to 22° C. The coccus will multiply in broth of reaction varying from + 12 to + 16 (Eyre's scale) with the production of a uniform turbidity but without the formation of indole; in litmus-milk it grows and gives rise to the formation of an acid reaction, occasionally accompanied by clotting of the medium; when cultivated upon agar or upon inspissated serum as discrete, translucent, circular, hemispherical or slightly flattened colonies. The appearance of the growth upon agar, over the surface of which sterile rabbits' or human blood has been smeared, is of considerable importance, for although the colonies resemble those upon ordinary agar, the growth is much more vigorous, and accompanied by a discoloration of the blood (due to the transformation of the oxyhaemoglobin into methaemoglobin), which is an almost pathognomonic feature of the growth of this coccus; and in old cultures upon this medium the colonies themselves frequently acquire a canary-yellow colour. In the serum of animals immunised to the pneumococcus, the growth of the organism itself assumes the form of a flocculent deposit in an otherwise clear fluid, the flocculi being composed of felted masses of long and convoluted chains of pneumococci, a peculiarity first pointed out by Washbourn.

Interesting, but of minor importance from the point of view of identity, is the power possessed by the pneumococcus of splitting up certain carbohydrate substances when these are dissolved in the medium in which the organism is growing. The substances generally used in these tests are dextrose, laevulose, galactose, lactose, saccharose, maltose, mannite, dextrin, and inulin. The first six of these are always acted upon by the pneumococcus, and the activity of the pneumococcus is indicated by a change in the reaction (originally neutral) of the medium

to acid. The remaining three compounds are sometimes but not invariably "fermented" by the organism under discussion; hence the contention of some American observers that the fermentation of inulin by the pneumococcus is such a constant character as to be of the highest value in diagnosis is not borne out in everyday work.

Finally, and most important of all, is the fact that a pneumococcus isolated *from a definite lesion* in the human subject is markedly pathogenetic for the rabbit. Speaking generally, if injected into the peritoneal cavity of this animal such a pneumococcus will produce an acute septicaemia and cause the death of the animal in one, two, three, or four days, whilst the organism can be recovered in a state of purity from the blood of the general circulation and from all the organs.

Animal Experiments.—The pneumococcus is pathogenetic in varying degrees for all the usual laboratory animals—the rabbit, mouse, guinea-pig, dog, cat, and monkey; fowls and pigeons enjoy an absolute natural immunity. By varying the factors in experimental inoculations—namely, the size of dose, virulence of organism, site of inoculation, and resistance of animal—the pneumococcus can be made to produce various lesions ranging from acute septicaemia to localised abscess formation. It was noted by Washbourn and myself that although all strains of virulent pneumococci produced a rapidly fatal septicaemia when introduced into the peritoneal cavity of the rabbit, yet if the injection was made into the subcutaneous tissue the various strains frequently presented such striking differences in the histological characters of the local lesions they produced as to point to the existence of two distinct types. Thus, sometimes fibrinous exudation formed the bulk of the material at the site of inoculation; at other times the local reaction consisted mainly of accumulations of polymorphonuclear leucocytes. These two types of cocci are referred to as the "fibrinous" and the "cellular" types respectively. To instance the results obtained by infection of the subcutaneous tissue of the abdomen of the rabbit, the following points may be noted:—(*a*) If a young rabbit is selected for the experiment, a small dose of either of these types of the pneumococcus will cause death within 48 hours from acute pneumococcic septicaemia. At the seat of inoculation the reaction, usually small in amount and limited in area, is practically always oedematous in character, and either of the serous, sero-haemorrhagic, or more rarely the haemorrhagic type. (*b*) If, however, a half-grown rabbit is substituted and a similar dose of the cultivation of either type is injected, the animal survives for a much longer period, say three or four days, or even a week. Now the local reaction at the seat of infection is a much more extensive process and clearly indicates by both its macroscopical and microscopical characters the particular "type" of pneumococcus that has been employed to produce infection. If the fibrinous type has been injected the local lesion will be a firm gelatinous exudation consisting of fibrin and leucocytes, together with red blood-discs, thrown out and occupying the subcutaneous cellular tissue for a considerable distance round the needle puncture, frequently, indeed,

extending down to the peritoneum below; but if the cellular type has been inoculated a dense, opaque, yellowish exudation consisting almost entirely of small round cells will result, fibrin being almost entirely absent. (*c*) Finally, if a fully-grown animal be infected with a similar dose of either type the local lesion at the seat of inoculation consists of a larger or smaller circumscribed oedema, usually noticed within 24 hours of infection, which enlarges slightly during the next few days, though remaining strictly localised, becomes soft, and in about ten days contains pus and can be made to fluctuate. If untreated the skin over the abscess undergoes necrosis, sloughs, and gives exit to a thick, creamy yellowish pus literally teeming with pneumococci, and the animal dies from exhaustion in a fortnight or so, or in some few instances completely recovers.

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J. E.

CLINICAL COURSE AND SYMPTOMS.—The clinical course and symptoms of pneumonia are so familiar that a characteristic case need not be quoted and described at length. Fortunately for clinical medicine, variations from this type are of frequent occurrence, as will become obvious when the individual symptoms are described. Before dealing with these symptoms in detail it will be well to consider what processes are taking place in the body in a characteristic case, and why the disease runs the course which it does; and then in the light of this information to describe and explain the variations.

In a characteristic case the following changes take place. When the lungs become infected by pneumococci a local inflammatory reaction is set up; but before this is capable of localising the infection, a septicaemia, accompanied by a general inflammatory reaction, is always produced. This septicaemia calls forth the usual responses from the defensive mechanisms of the body. These responses are phagocytosis and the production of anti-bodies, and are measured clinically by enumerating the leucocytes in the blood and estimating the opsonic index. A reference to Chart 3 on p. 244 will shew that a large leucocytosis is produced at once, and a large increase of opsonin after the necessary latent period. By means of anti-bodies and phagocytosis the septicaemia is successfully dealt with, the intoxication is brought to an end, the symptoms caused by the toxaemia stop suddenly, and the crisis takes place. In the meanwhile, probably during the first day, the infection in the lungs has been localised, except at the spreading edge of the inflammation. At this spot the absorption of toxin and a fresh septicaemic invasion of the blood will constantly be taking place. In the otherwise isolated space, the inflamed lungs, a battle between the multiplying pneumococci and the phagocytes is fought out. When the phagocytes have won, peptonising ferments are liberated; the digestion and absorption of inflammatory products begins, and the inflamed area as a whole ceases to be shut off from the circulation. This process in point of time begins before the crisis. During the digestion and removal of dead pneumococci much toxin must be liberated and absorbed; but provided that an excess of antitoxin has been produced in response to the original toxaemia, no fresh signs of intoxication are seen. The course of the crisis is not interrupted, and no constitutional disturbance is produced. After the crisis the temperature remains normal; the leucocytosis and the quantity of opsonin in the blood slowly diminish; and the infection of the body as a whole has been put an end to.

The **onset** is generally very sudden and without any premonitory signs. The symptoms which mark it are those common to many acute infections, namely, a chilly sensation, headache, vomiting, and fever, and in addition pain in the chest and cough. The pain and cough are observed in about 90 per cent of cases, headache and vomiting in about 40 per cent. The patient rapidly becomes prostrate, and has to take to his bed. In some cases, probably less than a quarter of the whole, the onset is either less sudden, or marked by less severe constitutional disturbance; in hospital practice it is not unusual to find that a patient admitted with advanced consolidation, though feeling ill, has been sufficiently well to be up and at work. The chilly sensation is present in about 70 per cent of cases. Definite and severe rigors are much less common; M'Crae's estimate was as low as in 6 per cent of the cases. The initial rigor occurs within the first few hours; as a rule it is single, but occasionally it may be repeated during the first day, and much more rarely during the second. One or more very severe rigors point to an acute and virulent infection.

In older children the initial symptoms are the same as in adults. In younger children the most frequent symptoms are vomiting and pain, which is referred to the abdominal muscles more often than to the chest; the abdominal muscles become rigid, and this may lead to error in diagnosis. Convulsions or delirium may take the place of a rigor, and are followed by headache and drowsiness. Dr. Dunlop observed these cerebral symptoms in about 25 per cent of 147 cases in children of all ages. Convulsions are uncommon in children over two years of age, and extremely rare in adults.

When twelve or more hours have passed, the patient's aspect is characteristic. The face is flushed, the eyes bright and on the watch, the expression that of constraint and apprehension. He usually lies on his back without marked orthopnoea. The breathing is short, frequent, and shallow, deep and efficient respiration being hampered by the sharp pain. The pulse is quickened and full. The skin is dry and pungent to the hand. As the disease progresses, much can be learned about a patient's condition by noting changes in his general appearance, his attitude in bed, the character of his respiratory movements, and the effectiveness of his cough.

It is convenient to divide the symptoms which follow the onset into two groups, general and localising. The former are caused by the toxaemia, and are therefore the same in primary pneumococcal pleurisy or peritonitis as in pneumonia. The latter are characteristic of the organ in which the infection is being localised.

A. **General Symptoms.**—*Temperature.*—A careful study of the course of the pyrexia gives valuable information both as to diagnosis and prognosis. The characteristic chart is usually divided into periods of rising, of continued, and of falling temperature. The rise is abrupt and rapid; and within twelve hours the temperature will have reached 102°-104° F. Not infrequently the initial pyrexia is very high, above 104° F.; and although evidence of an acute septicaemic infection, it also shews a good reaction on the part of the patient. A very high temperature is of very much less serious import at this early stage than at any other period. A more gradual and moderate rise is sometimes observed in cases in which pneumonia begins during the pyrexia caused by some other disease; it is seen also in aged and cachectic patients, and is then a bad sign, indicating a feeble power of reaction.

The continued fever in a characteristic case is high, between 102° and 104° F., with daily remissions of not more than 1°-2°. Variations from this type are common, and must be described and their significance discussed. Fever is caused by toxaemia, and the degree of pyrexia produced in a given case is the resultant of two variables, the dose or virulence of the infection and the power of the patient's reaction. Thus, on the one hand a continuously high temperature, over 104° F., may indicate either a severe infection with a correspondingly vigorous reaction, or an infection altogether in excess of the patient's resistance. And on the other hand a continuously moderate fever, less than 102° F., may

point either to a mild infection with a correspondingly reduced reaction, or to a power of reaction quite inadequate to meet the infection. These considerations shew that it is impossible to judge of the severity and progress of a case from the height of the pyrexia alone and without reference to the patient's reaction. We judge of the latter either from the other constitutional symptoms, or from estimations of the leucocytes and opsonin in the blood. Reaction by cells takes time; the latent period of the response by leucocytes may be measured in hours, but in the case of the formation of anti-bodies, in days. For this reason a high temperature and severe constitutional symptoms at the onset are not necessarily serious, provided that at the end of the necessary latent period they are followed by improvement.

Cases with a continuously low temperature are not common. If the other constitutional symptoms are slight and a leucocytosis is present, the prognosis is good; this type of case is more frequently seen in older children and healthy young adults. But when the opposite state of affairs is present, it is equally obvious that the patient's protoplasm is being killed by the toxaemia; this is not infrequently seen in elderly and cachectic patients. In some recorded cases the pneumonia has been apyrexial throughout; the prognosis is then generally hopeless.

There is another type of chart which exemplifies the point that a low temperature may be a very bad sign; it is seen not infrequently in alcoholic patients. The pyrexia is at first high and the constitutional disturbance severe, then follows a slow and steady fall of temperature, accompanied by the same or an aggravated constitutional disturbance. These patients usually die at the end of the first week, just when the temperature has reached a normal level. In such cases a leucocytosis and a rise in the opsonic index are absent. The fall of temperature means that the protoplasm is slowly being paralysed by the intoxication; and the earlier the fall begins the worse is the prognosis. Occasionally the slow fall is interrupted towards the end of the week by a rise of temperature; and the pyrexia may then continue at a higher level for days or weeks. It is in such cases that purulent infiltration of the lungs without death is most frequently seen.

There are falls of temperature during the period of continued fever which do not affect the prognosis. Not infrequently the course of the temperature is suddenly interrupted by a deep remission of several degrees, or even by an intermission. The remission is most frequently seen on the day before the crisis. It can be distinguished from the crisis by the absence of any material improvement in the constitutional disturbance.

Cases with a continuously high pyrexia are comparatively common; they are always severe, but not necessarily serious. The degree of the patient's reaction determines the prognosis, and when it is deficient we get the following types of chart. From the first the temperature is high and continuous, and the constitutional symptoms very severe; the temperature may begin to fall a little, but towards the end of the first

week one of two events happens; on the one hand the temperature may rise suddenly and rapidly, and the patient dies of hyperpyrexia. On the other hand the temperature may fall within a few hours to the normal or below it; there is no improvement in the constitutional symptoms, and death takes place within a few hours of the fall. An example is given in Chart 4. It is this type of case which seems to be the foundation of the belief that patients not infrequently die of exhaustion soon after the crisis. These grave cases are found amongst robust adults. Reference to Chart 4 shews an absence of leucocytosis and a low opsonic index throughout. Such a patient failed from the first to cope with the septicaemia; the drop of temperature marks, not a crisis, but a final intoxication of the patient's protoplasm.

The fall of temperature begins in a characteristic case on about the seventh day of the illness. Two types of fall are recognised; an abrupt fall by crisis and a more prolonged one by lysis. The dividing line between the two is arbitrary, and is usually placed at about twenty-four hours. Of the cases which recover 60 per cent fall by crisis, about 30 per cent by lysis, and in the remaining 10 per cent the fall is atypical. In children under three years of age the termination by a short lysis is as common as one by crisis.

The crisis most frequently takes place on the seventh day; and then on the fifth, sixth, and eighth in the order named. In more than 90 per cent of cases it is complete before the end of the ninth day. It may occur as late as the twenty-sixth day, or as early as the second. The exact date of crisis in any given case depends upon the degree of toxaemia and the length of time taken by the patient's tissues to react. As has already been pointed out, every acute fall of temperature is not a crisis. The critical fall marks a sudden diminution in the toxaemia, and is necessarily accompanied by a great improvement in the constitutional disturbance, and by a rapid increase in the rate of resolution; the pulse and respirations are slower, the distress and discomfort less, and the skin becomes moist. After the crisis the temperature may remain subnormal for a few days, and some prostration may be obvious.

The group of cases in which the temperature falls by lysis is a more varied one. In some cases the fall is not continuous, but shews interruptions spread over about two days. In other cases the temperature begins to fall slowly, and may reach normal on the morning of the third day, but is up to 100° F. at night. This short and imperfect lysis is frequently followed by a secondary gradual rise, which marks the onset of some septicaemic complication, such as pleural effusion or pericarditis. In yet other cases the fall by lysis is slight and imperfect or almost absent; and about the twelfth or fourteenth day of illness the temperature is still further raised by the onset of some complication.

When we compare the two extreme types, a rapid crisis and an imperfect lysis, it is obvious that they represent cases with a very different prognosis. They correspond roughly to two of the types of opsonic index shewn in Chart 2. In the one case ample quantities

of immunising substances have been produced, and in the other there has been up to a certain point an altogether insufficient quantity. The practical result may be expressed by saying that the more rapid and complete the crisis, the less likelihood is there of any septicaemic complication ensuing and the more quickly will the lungs clear; and on the other hand the slower and more imperfect the lysis, the more certainly are such complications present and the greater will be the time taken by resolution. Cases, however, do occur in which an empyema or some other similar complication appears after a satisfactory crisis. The explanation seems to be that in such a case, although the general septicaemia has been successfully dealt with, more toxin has been liberated during the early stages of resolution than there is antitoxin to neutralise; the opsonic index therefore shews a rapid fall and a definite negative phase, during which pneumococci unkilled in some tissue take on a new lease of life, and produce a localised suppuration. At the other end of the scale is the patient who has not put an end to his general septicaemia before a local suppuration develops. When estimating the prognosis of a septicaemic complication, such as empyema, it is necessary to consider whether the local suppuration is only the residuum of a septicaemia already over, or is part of a general septicaemia still existing.

The Heart and Circulation.—The rate and character of the pulse is of considerable importance in pneumonia. In adults the rate is not increased out of proportion to the pyrexia so long as the patient is doing well. Thus, with a temperature ranging between 102° and 104° F. the pulse should not be more than 110. If the rate is continuously over 110 the case must be considered a severe one; if over 120 a doubtful one; and over 130 a dangerous one. In young and healthy adults the pulse may not reach 100, and may even be scarcely accelerated at all. A decidedly slow pulse is much less common in pneumonia than in enteric fever. In children the rate is faster; it is generally 130 to 150; it may rise to 160 or 170 without being very serious, but when continuously over 180 it makes the prognosis doubtful or grave. At the crisis the rate falls rapidly to the normal. The fall may lag behind that of the temperature, but it does so much less often than that of the respirations. If the pulse-rate remain high for several days, although the temperature is normal, some cardiac lesion is probably present. Dr. Dunlop draws attention to "the extreme slowness and irregularity of the pulse sometimes present during convalescence, indicating the profound toxaemic influence of the pneumococcus on the cardiac muscle. On two occasions a pulse-rate of 40 is noted, and it is quite a frequent occurrence to find it between 50 and 60 a minute, certainly a very slow pulse-rate for a child." This is also seen in adults after pneumonia, just as it is after rheumatic fever, and other infective diseases. Extreme slowness without irregularity is not uncommon soon after the crisis, and generally lasts for a week or so; it is presumably due to some toxic action upon the cardiac muscle, but it may certainly occur without any associated dilatation or other discoverable abnormality of the heart. It is impossible to explain why poisoning

of the heart should cause sometimes a rapid and in other cases a slow pulse. Irregularity, weakness, or dilatation of the heart are more significant of serious damage than slowness alone. Nevertheless, it is a good rule during convalescence from all acute infections not to allow the patient to get up until the pulse-rate is normal, no matter whether it is too fast or too slow.

The character of the pulse in pneumonia, as in other fevers, is at first forcible, sustained, and bounding. When the exaggerated action of the heart begins to pass off the pulse is shorter, smaller, often dicrotic, and the up-stroke less energetic; the arterial blood-pressure is still good. When the heart begins to fail seriously the pulse becomes more rapid; it is small, feeble, very short, and may be irregular in frequency and force; ultimately it becomes running in character and almost uncountable. It cannot be too frequently repeated that the arterial blood-pressure cannot be deduced from observations on the rhythm, size, force, and rate of the pulse; it must be estimated separately by the finger or an instrument. When a heart begins to fail slowly, the arterial blood-pressure does not fall, because the vasomotor centre is stimulated to greater activity, and thus by increasing the peripheral resistance compensates, and generally more than compensates, for the loss of cardiac power. An appreciable fall in arterial blood-pressure is in fact only a terminal phenomenon.

The *heart* is more often the cause of anxiety than any other organ. In all specific fevers associated with high temperature and toxaemia it undergoes some slight and general dilatation, which is most often made out in children owing to the thinness of their chest wall; when present in a slight degree it is of no importance. Two types of severe and serious cardiac dilatation are observed in pneumonia, namely, that which is limited to the right side, and that which affects the whole heart. The former is much the more frequent, and on the whole the less serious. Failure of the right side alone must be due to causes which are special to it and not common to both sides. The probable causes are cough, rapid and shallow respirations, and mechanical resistance in the pulmonary capillaries. It seems that the greater the area of lung involved the more likely is the right side to fail. The failure is shewn by change in the pulse, increased dulness to the right of the sternum, swelling of the liver, and a decreased output of urine; and further by three clinical signs of great importance, orthopnoea, cyanosis, and laboured respirations. Cyanosis is a common feature in bronchopneumonia, but not in lobar pneumonia unless either the right side is failing or much bronchitis is present. There is only one change in the patient's colour worse than lividity, and that is the pallor which ultimately succeeds it in most fatal cases. This pallor is due to failure of the vasomotor centre, and represents the inability of the splanchnic resistance to keep blood in the superficial parts of the body. This change is more often seen in children than in adults. Orthopnoea is almost always present until the terminal stage of cardiac failure. It is an unconscious effort on the part of the

patient to bleed himself by the aid of gravity into his own abdominal veins, and thus to limit the blood sent into the right heart so as to prevent its over-distension. The significance of the laboured breathing in right-sided failure is often not appreciated. Pyrexia, toxaemia, and diminution of the respiratory surface by consolidation cause an increased rate of respiration, but not laboured breathing. The respiratory movements are a circulatory pump auxiliary to the action of the heart. When the heart begins to fail seriously, the activity of the auxiliary pump presided over by the respiratory centre is increased to a visible extent. The bearing of this upon the use of opiates in cases with right-sided failure is obvious. The same forcible use of the respiratory pump is seen in pericarditis when the fluid is under positive pressure. Failure of the right heart is frequent and serious when the organ is previously healthy; it is all the more so when the right ventricle is already overworked by pre-existing disease of the lungs or mitral valve. In 100 fatal cases M'Crae found chronic endocarditis in 23, emphysema in 8, and chronic bronchitis in 6.

Severe dilatation of both sides of the heart is much less frequent, and is due to causes affecting the whole organ; but when it occurs it is a very serious symptom. It is rare in the acute stage, unless the cardiac muscle is previously diseased or overworked. It is therefore found to occur in patients suffering from mitral or aortic disease, in cases of chronic nephritis and of myocardial disease caused by toxaemias, degenerations or infiltrations, and in old people with degenerated arteries. Of 100 fatal cases M'Crae found that 32 had chronic nephritis, 8 had severe general arteriosclerosis, and 8 chronic myocarditis. In the later stages of pneumonia acute dilatation of the heart is indicative of acute myocarditis with or without pericarditis. It is a symptom which necessarily causes anxiety. Frequently it passes off more or less completely in the course of time; convalescence is delayed, and the heart must be watched when the patient is at last allowed up.

The Blood.—Bacteriaemia is constant in the early and acute stage of pneumonia. Prochaska found the pneumococcus in the blood in every one of 50 cases, and Rosenow in 132 out of 145 cases. In cases which run a favourable course the septicaemia is put an end to by the processes of phagocytosis and bacteriolysis, and the toxaemia terminates by crisis. In less favourable cases the septicaemia is imperfectly attacked, and septicaemic complications follow. In rapidly fatal cases the septicaemia kills the patient before local suppurative complications have time to develop.

Leucocytosis is very important in pneumonia. It is a manifestation of positive chemiotaxis, and represents the special response of the leucoblastic tissues to certain toxaemias. Certain leucocytes carry out phagocytosis; they provide the unorganised ferments for the process of resolution, probably also the opsonin, and possibly other antibacterial substances. In a severe but favourable case the leucocytosis begins at once, and within a very few hours may be high, over 40,000. During the period of

continued pyrexia, as is shewn in Chart 3, the leucocyte count is on the whole high; it presents daily variations which do not correspond with those of the temperature. It must be remembered that the leucocytes in the peripheral systemic circulation alone are estimated. And it is probable that the decrease in leucocytosis which is frequently observed in the middle part of the week, is due not to a decreased formation but to the abstraction of leucocytes from the systemic and their accumulation in the pulmonary circuit. The leucocytosis does not decrease during a pseudo-crisis; but at about the time of the crisis it begins to fall, and like the opsonin-curve, more slowly than the temperature. The degree of leucocytosis observed during the first week of illness is of great importance in prognosis; but more than a single observation may be required in order to obtain the necessary information. The cases may be divided into three groups in accordance with the degree of the leucocytosis and its interpretation. (1) A mild infection with a vigorous reaction gives a slight leucocytosis of not more than about 15,000. Such cases are rare and constitute about 10 per cent of the whole. (2) A moderate or severe infection with a vigorous reaction produces a leucocytosis of between 15,000 and about 60,000. (3) A severe infection with a feeble reaction is either not accompanied by leucocytosis or produces leucopenia; such cases almost invariably die of the acute septicaemia. It might be thought that it would be possible to confuse the leucocyte counts of the first and third groups; but in practice there can never be any difficulty in distinguishing between an extremely mild and a necessarily fatal case. With the advent of a local septicaemic complication, such as empyema or suppurative pericarditis, the leucocyte count shews a secondary rise. When there has been no crisis, and delayed resolution or purulent infiltration of the lung is present, a slight leucocytosis may continue for weeks.

Two other changes in the blood may be mentioned, although their significance is not known. The antitryptic power of the serum is increased up to the onset of the crisis and then rapidly diminishes. Conner and Roper have found in fatal cases that within three days of death the bilirubin disappears from the blood and urobilin appears. They did not find urobilin in the blood in any disease other than fatal pneumonia; and as they could not prove that the urobilin was produced from either haemoglobin or bilirubin as a result of bacterial activity in the blood, they suggest that the changes are of hepatic origin.

The Nervous System.—Symptoms caused by the intoxication of the central nervous system are very frequent in pneumonia; but may be nearly absent. The most common are headache and sleeplessness. Headache occurs in the early stage of about 50 per cent of cases. Unlike the headache of enteric fever it is usually not severe nor does it continue for more than a day or two. Its severity bears no relation to that of the case. Insomnia is usually present; few patients can sleep soundly on account of pain, cough, or dyspnoea. And the greater the general distress of the patient becomes the more fitful and less refreshing

is his sleep. There is another type of sleeplessness seen in severe cases. The patient may have no very great distress and yet he cannot close his eyes and sleep. This condition of cerebral excitement appears to be akin to delirium or to the mental state of patients with chronic failure of the cerebral circulation; and in pneumonia it is frequently associated with failure of the right heart. It is in these patients that the question is so often raised, whether it is safe to give them opium in order to procure the sleep which is so urgently needed.

Convulsions are a misleading symptom unless the age of the patient and the time of their occurrence are taken into account. In children convulsions are not infrequently seen at the outset of the disease. Dr. Dunlop observed this mode of onset seventeen times in 147 cases; and since early convulsions rarely occur in children over two years old, and only 45 of his cases were younger than two, convulsions cannot be uncommon in infants. The convulsion may be repeated more than once on the first day, and is followed by headache and drowsiness, and sometimes by active delirium and even by coma. These cerebral symptoms may include rigidity of the neck and back, contracted or dilated pupils, squint, Kernig's sign, retraction of the abdomen, and irregular pulse; they may continue for several days, in fact until the crisis. Cases which begin in this way do not necessarily become very severe, and the prognosis may not be materially altered; Holt records only 1 fatal case out of a total of 7. Convulsions beginning late in the attack generally indicate the onset of meningitis, and both in children and adults are nearly always fatal. There appears to be no truth in the statement that nervous symptoms are more common in pneumonia at an apex than elsewhere.

Delirium is a symptom the significance of which depends upon the age and previous history of the patient, the time of onset, and the kind of delirium. In children over five years old delirium takes the place of the initial convulsion of infants. Dr. Dunlop noted the symptom twenty-five times in 147 children of all ages. During the course of the disease slight delirium at night is common, when the temperature is high. The delirium is either active or of a muttering type, associated in the worst cases with muscular twitching, tremor of the tongue, picking at the bed-clothes, and diarrhoea. In only 2 of Dr. Dunlop's 25 cases did death occur.

In adults the place of the early cerebral symptoms seen in children is taken by a rigor. A boy aged fifteen years under our care survived an attack of coma during the first two days of what turned out to be pneumonia of moderate severity; such a case is quite exceptional. In adults all cerebral symptoms are of serious but by no means necessarily of fatal significance. During the first week or so many severe cases are somewhat light-headed at night or by day as well. M'Crae noted delirium in 35 per cent of his cases; and of the 157 delirious patients 93 did not drink alcohol and 64 did. In aged or alcoholic patients the delirium is frequently more marked; in alcoholic patients the delirium may be very active, and either maniacal in form or indistinguishable from delirium

tremens except by the temperature. These patients may recover; but more frequently they pass either into coma or into a low muttering delirium in which they die. Although delirium and death are common in drunkards, it must not be thought that every drunkard who contracts pneumonia develops even delirium. In M'Crae's statistics 60 per cent of 63 drunkards were delirious, and 41 per cent of the 154 patients who drank alcohol in quite small quantities. In aged patients the delirium is generally low and muttering from the onset; and the prognosis is almost hopeless. Muscular tremors of the lips, tongue, and hands similar to those seen in drunkards may occur in pneumonia with and apart from delirium. In adults all nervous symptoms make the prognosis less good than it otherwise would be; and the extent to which they do so can be expressed by the statement that the more severe the cerebral symptoms and the earlier they appear the worse is the prognosis.

After the crisis some patients are in a state of mental excitement which appears to be associated with the prolonged want of sleep. An injection of morphine and twelve hours' good sleep will remove the symptom. Other patients are exhausted, prostrate, and wander at night; this condition is generally cured by warmth and alcohol.

The *pupils* are generally dilated; but when cyanosis begins they contract, and dilate again when the patient is either recovering or moribund.

The Urinary System.—The urine shews changes similar to those seen in other infective diseases. The quantity excreted in twenty-four hours is decreased. This is due to two causes: (1) excessive quantities of water are evaporated from the skin and lungs; (2) the rate of blood-flow through the kidneys is lessened, and this is especially marked when the heart begins to fail. The diminution in the quantity excreted makes the urine very concentrated in comparison with what it would be in a healthy person on the same low and fluid diet. This concentration in the urine may entail two results which are often overlooked. In the first place the kidney is the main exit from the body of bacterial toxins. Until the production of toxin has been stopped or the toxin has been neutralised by antitoxin, the kidney is the organ whose duty it is to remove the toxin circulating in the blood. Nothing can be more serious in a severe case of pneumonia than a fall in the quantity of urine to a few ounces in the day. And in the second place the kidney is a site at which a very great concentration of excretory substances takes place. When the quantity of urine is small the concentration of toxin in the excretory cells may be such that the cells are damaged and an early stage of acute parenchymatous nephritis is produced. This toxaemic nephritis is common in pneumonia as in other acute toxaemias, such as diphtheria and diabetic coma. The clinical symptoms of it are a great increase in the number of granular casts and slight albuminuria; probably it is never sufficiently severe to produce haematuria. Albuminuria was found at Guy's Hospital in 15 per cent of 727 cases; at other hospitals in London in 1 per cent of 988 cases; and M'Crae observed it in 26 per

cent of 450 cases. It is probable that all these statistics are gross underestimates, and that if the urine were examined every day albuminuria would be found in about 70 per cent of cases. As soon as the toxaemia ceases the albuminuria comes to an end; because it is not possible to conceive of an inflammation continuing or becoming chronic in the absence of an irritant. Another and severe kind of nephritis may occur in pneumonia, namely, septicaemic nephritis, which is due to the growth of pneumococci in the renal tissues and will be described amongst the complications (p. 229).

The excretion of chlorides may be normal in pneumonia, but in about half the cases it is reduced or absent during the acute stage. The same phenomenon is observed in other fevers, such as enteric, but it is more frequent in pneumonia than in any other. The food in fever is generally very deficient in chlorides—a point which should be remembered in treatment—and when there is much diarrhoea or copious expectoration the deficiency is all the more marked. Nevertheless a shortage of chlorides in the food is not the whole explanation. The body actively retains chlorides together with sodium; and when sodium chloride in measured quantities is added to the food, some or all of it is kept back and not immediately excreted in the urine. It is not known why a fevered body should require more chlorides, and though there are many hypotheses, none of them are satisfactory. After the crisis the retained sodium chloride is excreted.

Albumosuria has been frequently observed in severe cases during the period of resolution or when a suppurative complication is present. Albumose absorbed from the lung or from a local abscess may reach the circulation and be excreted by the kidney. It is not of clinical importance, except that albumose may be mistaken for albumin by the cold nitric acid test.

The skin generally feels hot and pungent, not because it is hotter than in other diseases, but because it is drier. In about a third of the cases the skin is damp and loses its burning character. When sweating is associated with lividity, coldness of the skin, and other severe constitutional symptoms the prognosis is grave. At the crisis profuse sweating is frequently seen.

In about a quarter of all cases an eruption is seen upon the face; this consists of a group of small clear vesicles on a reddened patch. This herpes is most commonly seen on the upper lip in the neighbourhood of one or other nostril; but it may be seen on the lower lip at the angle of the mouth, or upon any part of the cheek, chin, or jaw. It has been described on the cornea, chest, upper arm, mucous membrane of the mouth, and round the anus. It usually appears during the febrile stage, but it may come out or recur after the crisis. The vesicles cause no pain, become purulent, and dry up with the formation of dark crusts, which drop off and do not leave any scar. Herpes is not diagnostic of pneumonia, but is probably commoner in it than in any other fever. The pneumococcus is said to have been found in the vesicles round the anus.

Dr. J. Mackenzie suggests that this may be true of herpes in other situations; and that the favourable prognosis, which herpes is supposed to indicate, may have a solid foundation and be due to auto-vaccination. It has yet, however, to be proved that herpes is a local pneumococcal infection, and many observers deny that cases with herpes do run a specially favourable course.

The Alimentary System.—There is nothing characteristic about the digestive disturbance in pneumonia; it is that common to all fevers, namely furred tongue, loss of appetite, and thirst. In children vomiting and diarrhoea are frequent early symptoms; more so in infants than in older children. Vomiting soon stops unless it is kept up by drugs which irritate the stomach, such as ipecacuanha, carbonate of ammonium, digitalis, and squill. The state of the bowels in the cases analysed by J. M'Crae was normal in 60 per cent; constipation was present in 30 per cent, and diarrhoea in 10 per cent. Pseudo-membranous colitis is a very rare and fatal complication, but when it occurs severe and intractable diarrhoea is its most prominent symptom.

The general nutrition, even in children, is not severely affected, except in prolonged cases associated with purulent infiltration of the lung or other severe complications. Convalescence in the absence of complications is rapid and complete.

B. **The Localising Symptoms.**—*Pain* in the side or abdomen is an early symptom in most cases. It is due to pleurisy, and is therefore absent in deep-seated pneumonia. The pain is caused by the movements of the two inflamed surfaces of pleura on each other, and is in consequence less marked or more frequently absent in apical than in basal pneumonia. In basal pneumonia it may be absent if the patient scarcely moves the affected side of his chest and does not cough violently; when the diaphragmatic pleura is inflamed the pain is usually severe. The pain is of the referred visceral type, and is usually felt on the same side of the chest or abdomen as the pneumonia. It is therefore a localising symptom. But in rare cases it may be referred to the opposite side or to both sides. It may be felt in any part of the abdomen from the epigastric angle to Poupart's ligament.

Cough is another early symptom. At first it is short, dry, and restrained by the patient. It may be severe and painful, especially after taking food or talking, and adds greatly to the subjective distress. Later when resolution is taking place or when bronchitis or hypostatic congestion have supervened, the cough becomes loose and is of great importance to the patient. There is no more serious symptom in any acute pulmonary disease than a gradual disappearance of cough in spite of an accumulation of secretion in the bronchi.

The *sputum* which the patient coughs up is fairly characteristic. It is not abundant, not very frothy, and is unmixed with saliva or with pus. It consists of clear, tenacious mucus with a few air-bubbles, and is more or less deeply-stained with blood. The colour when most characteristic deserves its traditional name of rusty; it is bright orange-brown,

resembling the burnt sienna of the colour-box. When the sputum is abundant and thin, it loses its bright chestnut colour, and has been aptly compared to the juice of dried prunes when stewed. As the blood pigment undergoes change the reddish tint is lost and replaced by a greenish-yellow; the sputum is then compared in colour to the fleshy part of ripe greengages. When the amount of blood is scanty from the first, a bright lemon colour is no less characteristic than the usual rusty sputum; when on the other hand it is excessive, the yellowish-brown is replaced by a more decided red. Rusty sputum is seen in a high proportion, in about 50 per cent, of the cases. It is generally present within the first two days, but its advent may be deferred to a later date, and, it is said, even until convalescence. In less than about 10 per cent of cases pure blood is spat up. This *haemoptysis* usually occurs in the early days of the attack, and may be repeated on several days; it is sometimes very free, consisting of several ounces of pure bright blood, and denotes unusually intense congestion. It does not appear to have an unfavourable import, and certainly it does not necessarily point either to existing or subsequent tuberculosis or to cardiac disease. On microscopical examination the sputum consists of mucus from the bronchial tubes mixed with the contents of the alveoli and infundibula. Besides structureless mucus there are abundant red cells and leucocytes, together with a few epithelial cells and fibrinous plugs from the smallest bronchioles. When treated by appropriate stains the pneumococcus is revealed.

It is well known that children do not expectorate. Even as late as the age of eleven and twelve years the patient may be unable or unwilling to bring up the phlegm. When a child vomits after coughing, characteristic rusty sputum may sometimes be seen in the basin. Old patients as a rule are like children in this respect; they seem too feeble to expectorate. In adults the sputum is not more than about one or two ounces in a day, and like the cough may be entirely absent. It is obvious that the sputum never amounts to more than a small proportion of the inflammatory products poured out into the lung. Rusty sputum always strongly suggests lobar pneumonia, but is not diagnostic of it in the absence of a microscopical or bacteriological examination, as it occurs in acute pneumonias due to micro-organisms other than the pneumococcus, and in infarction of the lung. Complications may alter the character of the sputum. When bronchitis or oedema of the lung supervenes, the sputum becomes more abundant and frothy. An empyema or abscess may be coughed up; and when gangrene sets in the sputum becomes fetid and contains disintegrated pulmonary tissue.

The respirations undergo many important changes in character. They are generally rapid and shallow and often jerky, painful and distressing to the patient. The rate of the respirations is altered in a way that is of diagnostic and prognostic value. During the pyrexial period the rate is increased, but the magnitude of the increase is not the same in all cases. In an adult suffering from an attack of moderate severity the respirations are usually about 40; they may be less, and in mild attacks

associated with but little disturbance may be considerably under 30. They may number 60 or more in very severe, and generally fatal, attacks. A respiration-rate over 50 causes anxiety. In children the rate is necessarily higher, being ordinarily 55 to 60; a rate about 70 causes anxiety, but the recovery may occur in a case in which the rate was 80.

The causes of this change in the respiratory rate must be analysed so as to appreciate its significance in different cases. The causes are both local and general, because pneumonia is an acute septicaemia and toxaemia as well as a pulmonary disease. The general causes are the pyrexia and toxaemia, and subsequently circulatory failure and imperfect aeration of the blood due to cardiac dilatation or bronchitis. It may be stated at once that the pyrexia, as a rule, has little influence on the rate; that circulatory failure influences the character of the respirations much more than their rate; and that the toxaemia is the one important factor. The only local cause of importance is the pleurisy, which by making the respirations shallower, increases the rate. Pleurisy alone may raise the rate to 30 or 40, and does so in proportion to the pain. It is clear, therefore, that in any given case the first point to decide is how much of the increased rate is due to shallow breathing and how much to toxaemia. This can only be done by watching the respiratory movements; if they are markedly shallow, painful, and jerky, then we may calculate that the respirations might be about 35-40 from the pleuritic pain alone; and that any excess in rate over that figure is to be ascribed to toxaemia. Almost more important than the actual respiratory rate on any one day is the amount by which the rate may have increased during the course of the disease. Such increase is rarely caused by an aggravation of the pleuritic pain, and is generally due either to increased toxaemia or to circulatory failure. The respiratory rate does not follow the pyrexia, except in so far as the latter is a gauge of the toxaemia. When the toxaemia becomes excessive the pyrexia may begin to decrease; and in such a case the rate does not fall, but remains high or increases. Again, the respiratory rate is independent of the extent of the local lesion in the lungs, excepting in so far as it is generally true that very extensive consolidation is associated with a severe toxaemia. Thus, a drunkard with a patch of pneumonia so small and early that it can scarcely be discovered may have a rate of 60, whilst a patient with the whole of a lower lobe solid may have a rate of 30; the one patient cannot cope with his septicaemia, the other can. The bearing of the respiratory rate on diagnosis and prognosis may be summarised as follows. An increased rate due to causes local in the lungs is important in diagnosis and unimportant in prognosis; and when it is caused by toxaemia, exactly the opposite is true.

At the crisis the respiratory rate decreases. The fall is frequently less rapid and complete than that of the pulse-rate. Not infrequently the respirations are 30 or more for days after the crisis; but this high rate does not necessarily indicate the presence of a pulmonary complication, provided that at the end of a few days it begins to diminish. When, however, it begins to rise again, a suppurative complication, such

as empyema or pericarditis, should be suspected, even although the temperature remains normal.

Considerable stress has been laid upon the *pulse-respiration ratio* both in diagnosis and prognosis. In health the ratio is about $4\frac{1}{2}$ to 1; and in pneumonia 3 to 1, 2 to 1, or even less. This ratio, however, is subject to so many exceptions and qualifications that it is of little value. The following general statements will suffice: There is no other febrile disease in which the respirations are so frequently increased out of proportion to the pulse. In enteric fever a low ratio may be produced by a slight increase in the respirations and an actual slowing in the pulse; this is rarely seen in pneumonia. A very low ratio in pneumonia, less than 2 to 1, indicates a severe attack; thus a pulse of 90 may be accompanied with respirations of 54. When, however, such a ratio goes up because the pulse becomes faster, the condition is more serious. The larger the figures which give any particular low ratio, the more serious is the condition; thus, with a ratio of 2 to 1, a pulse of 120 and respirations of 60 is much more serious than a pulse of 80 with respirations of 40. A high ratio may be a very good or a very bad sign; for instance, a pulse of 90 and respirations of 30 is good, but a pulse of 180 and respirations of 60 is very serious.

Young children often shew an inversion of their respiratory rhythm, in such a way that the pause follows inspiration instead of expiration. Frequently, too, they make a grunting or groaning noise with expiration.

Orthopnoea and the laboured breathing which accompany right-sided failure or pericarditis have already been considered among the circulatory symptoms (p. 211).

Cheyne-Stokes breathing is a very grave sign both in adults and older children. It is seen towards the end of cases fatal from toxaemia or circulatory failure. This peculiar rhythm shews that the respiratory centre is becoming too poisoned to respond regularly to the usual percentage of CO_2 in the blood. During apnoea CO_2 accumulates until it reaches a concentration in the blood, which will stimulate the centre; respiration then begins again, and continues until enough CO_2 has been pumped out of the blood to reduce it below its stimulatory value. Cheyne-Stokes respiration can be temporarily abolished either by raising the excitability of the centre or by increasing the stimulus. The former effect can be produced to a slight extent by strychnine and atropine; and to a much greater extent by oxygen, which, however, must be given undiluted with air through an anaesthetic mask. The latter effect can be obtained by giving the patient air or oxygen to breathe containing a small percentage of CO_2.

The Physical Signs.—The pneumonic lung yields physical signs characteristic of the different stages into which the inflammatory process is artificially divided. We can distinguish between engorgement, consolidation, resolution, and purulent infiltration.

Inspection shews the side and part of the chest to which the pain is referred, and in a majority of the cases indicates the site of the lesion.

The movements of this part are impaired or abolished. These points can be confirmed or discovered by palpation.

The stage of engorgement is of short duration, and lasts less than 24 hours, often less than 12 hours. If the part of the lung involved is sufficiently large, an area of diminished resonance will be found. The breath-sounds are altered; but the nature of the alteration depends upon whether this part of the chest is moving freely or not. If it is, the breathing is noisy; if it is not, the breath-sounds are feeble. Very soon the breath-sounds lose their vesicular character entirely; their pitch begins to rise; and a few crepitations may be heard during inspiration, and less often during expiration also. In the healthy parts of the lung the breathing is puerile or compensatory; and so loud and harsh may these breath-sounds be in children that the inexperienced may feel inclined to diagnose the lesion on the wrong side of the chest. Occasionally the signs over the pneumonic lung are strikingly different from the picture just described; the site of the pneumonia may be marked by a tympanitic note in comparison with which the healthy lung may seem deficient in resonance, and in apical pneumonia a cracked-pot note may sometimes be obtained in children and in adults with thin chests. The same peculiar tympanitic note is not infrequently heard over the spreading edge of the consolidation.

The Stage of Consolidation.—Within 12 hours of the onset the signs of complete consolidation may be present. Tactile vocal resonance is increased, if the area of consolidation be sufficiently large; the note is dull; there is loud bronchial breathing and bronchophony, and a pleuritic rub may be heard. At the very earliest period of this stage pneumonic crepitations may still be present, but they disappear in a few hours; and from this time onwards until resolution begins, no moist sound of any kind should be heard over the original site of consolidation. In adults, crepitations are sometimes not heard, and in children, according to Dr. Dunlop, they are as frequently absent as present. At the spreading edge the signs of engorgement are obtained.

Not infrequently at the very beginning of consolidation the signs are altered in such a way as to resemble fluid. The bronchioles are occluded by fibrinous plugs or secretion, no air reaches this part of the lung, and the breath-sounds and voice-sounds are completely absent. Theoretically therefore the physical signs in pneumonia may simulate those over a pleural effusion or a primary pneumococcal empyema; but in practice the difficulty offered to diagnosis is not great. For, if the patient's pain allows him to cough powerfully several times the tubes are as a rule freed sufficiently to enable faint bronchial breathing to be heard. Further, in pneumonia the dulness is less absolute, the mediastinum is not displaced towards the opposite side, and the tubes become freed spontaneously in about 24 hours' time allowing loud bronchial breathing to be heard.

Another not uncommon peculiarity, especially in children, is delay in the appearance of the signs of consolidation. They may appear for the first time several days after the onset, even after the crisis or never at

all. Of 86 cases Holt found that in 25 per cent consolidation did not appear until the fifth day or later; in 6 cases it was delayed until the seventh day or later, and in one case until the twelfth day. The usual explanation of this delay is that the pneumonia begins in a central position and therefore gives no sign of its presence, and skiagraphy lends support to this solution (*vide* Vol. I. p. 498). It must, however, be remembered that central pneumonia is unknown at necropsies. It is possible that in some of these cases the primary infection was not through the lungs at all, and that the lung became infected from the blood as a complication of a pneumococcal septicaemia. There can hardly be any doubt that this sequence of events may take place in the case of the pleura, as was first pointed out by Washbourn. A patient has all the constitutional symptoms of pneumonia, but no abnormal physical signs in the chest, ultimately the physical signs of fluid appear and pus is found.

A third peculiarity in the physical signs of consolidation is that sometimes they appear to extend for a short time after the crisis. In some cases this may be due to unplugging of bronchioles in what was the spreading edge. It is, however, not inconceivable that the pulmonary inflammation might really extend. The crisis marks the cessation of general intoxication and might not coincide exactly in time with the victory of the local inflammation over the localised infection.

The physical signs obtained over the healthy parts of the lungs are, increased movement, a hyper-resonant or even tympanitic note, and loud compensatory breathing. There are no moist sounds in the case of a previously healthy chest, unless either hypostatic congestion or bronchitis is developing as a complication.

The onset of resolution is marked by the appearance of redux crepitations, which are first heard about the time of the crisis, or sometimes about twenty-four hours earlier. After the crisis the signs of consolidation diminish rapidly and disappear in about four days to a week. In children this process may be as short as two or three days. At the stage when bronchial breathing has finally disappeared the signs over the affected area are, some impairment of resonance with feeble high-pitched breath-sounds, and some rather coarse moist sounds. These rales disappear in two or three weeks and the breath-sounds become vesicular. The last sign to disappear is the impairment of resonance. Skiagraphy may shew evidence of consolidation after all physical signs have gone (*vide* Vol. I. p. 496).

When the pyrexia has disappeared by crisis, resolution is more rapid than after lysis; and the slower the lysis the greater is the delay in the clearing of the lung. When a suppurative complication begins within a few days of the crisis the process of resolution is slowed and may even be temporarily inhibited.

Purulent infiltration, as will be seen later, should be regarded as a complete inhibition of resolution, accompanied by oedema and a local or general bronchitis. Some observers consider that it takes place only in

fatal cases. We do not agree with this opinion, and believe that purulent infiltration can be diagnosed during life by the signs taken in conjunction with the symptoms; that such patients may recover after a long illness; and that the solid lung may clear up in the course of time completely. The following is a typical case: An alcoholic patient slightly delirious at night, with a temperature of 104° F., respirations of 55, and a pulse of 120, has loud bronchial breathing over the solid lung, unaccompanied by any moist sounds. Perhaps on the fourth day of the disease it is discovered that fine moist sounds, like redux crepitations, can be heard over the solid lung; and yet it is clear from the symptoms that resolution cannot have begun. This premature appearance of moist sounds is the first sign of purulent infiltration, and may precede any obvious change in the symptoms by twenty-four hours. Gradually the solid lung becomes moister; and besides crepitation fine bubbling rales are heard over it; signs of oedema and general bronchitis appear over the previously healthy parts of the lungs. Such a patient generally dies within a few days; but he may struggle on for a week or two with a high irregular pyrexia, and then begin to improve slowly although the pulmonary signs appear to be unchanged. In the course of weeks or even of months the lungs gradually begin to clear, and finally do so completely. The earlier the day of the disease on which purulent infiltration begins, the worse the prognosis.

Complications.—The complications of pneumonia are extremely numerous, but fortunately only a few of them are common. In fatal cases it is not unusual to find several complications in the same body. A discussion by Dr. H. Mackenzie and others on the complications of pneumonia has provided an elaborate series of statistics dealing with 7868 cases treated in the hospitals of London; and from this source a majority of the following statistics has been obtained:—

I. *Pulmonary Complications.*—Emphysema of the healthy parts of the lungs is frequently observed during life and at the necropsy. The lung is healthy, but distended with air, and has in fact undergone a compensatory hypertrophy. The condition is physiological, not pathological, and has no connexion with the disease called emphysema. Hypostatic engorgement of the bases is of frequent occurrence in severe or fatal cases.

Bronchitis can only be termed a complication when it begins in the course of pneumonia, and affects the healthy as well as the diseased parts. Such bronchitis is a very serious complication, and is due, not to the pneumococcus, but to some secondary infection. Cases in which it is present may recover. As a rule it forms part of the clinical picture which we associate with purulent infiltration of the lung. J. M'Crae found acute bronchitis in 61 per cent of fatal cases. The onset of bronchitis increases the quantity and alters the character of the sputum. Bronchitis and emphysema antecedent to the pneumonia do not affect prognosis unless they are throwing much strain on the right heart.

Gangrene is extremely rare; in 7868 cases it occurred 37 times,

with 29 deaths and 8 recoveries. The acuteness of the inflammation in the hepatised area may be so great as to cause thrombosis in the blood-vessels and necrosis of the pulmonary tissue. This gangrenous area may be diffuse, in which case recovery is hardly possible; or it may be circumscribed and end in an abscess. If the necrotic area becomes infected by putrefactive micro-organisms, fetor of the breath and sputum is noted. Pneumothorax has followed gangrene.

Abscess is another very rare complication. Some authors say that it is more common than gangrene, and others that it is less so; the difference is one of nomenclature. Some observers would classify an irregular ragged cavity with purulent and necrotic contents as an abscess, and not as gangrene unless it were fetid; others confine the term abscess to a pus-containing circumscribed cavity lined with pyogenic membrane. Abscess is usually single, generally fatal, and discovered for the first time at the necropsy. The diagnosis, like that of gangrene, will depend upon the continuance of severe constitutional symptoms together with localised signs of consolidation. Help might be obtained from a microscopical examination of the sputum and from a blood-count. The *x*-rays have demonstrated such cavities when they contained gas as well as pus. An abscess in the lung may be indistinguishable from an interlobar empyema; both may burst through the lungs, and both, like gangrene, are amenable to surgical interference.

Purulent Infiltration.—In 100 fatal cases J. M'Crae found that the lung was in the stage of red hepatisation in 23, and grey in 55. A majority of these 55 grey lungs were in a state of purulent infiltration, which differs from grey hepatisation in that the lung is much more moist, juicy, and friable. Some authors look upon purulent infiltration as a distinct and uniformly fatal complication, and, as the name implies, akin to abscess formation. We have already expressed our belief that purulent infiltration need not be fatal, but may end in complete recovery. Histologically it is indistinguishable from grey hepatisation; the lung tissue is not undergoing necrosis and liquefaction, and is not in a condition having any resemblance to abscess formation. We believe that purulent infiltration is nothing more than an acute oedema of lung in a stage of grey hepatisation, and that it marks the complete arrest of the process of resolution for the time being. This arrest might be due to either or both of two processes: namely, a secondary infection of the lung by pyogenetic micro-organisms, or an arrest of the processes which induce resolution. In regard to the first possibility, streptococci have been found in purulent infiltration; it is recognised that double infections by pneumococci and other pyogenetic micro-organisms produce a pneumonia which runs a protracted course and does not clear up with the extraordinary rapidity shewn by pure pneumococcal cases; and during the stage of purulent infiltration until resolution finally begins considerable pyrexia is present. Nevertheless, it is difficult to believe that this is the whole explanation, because purulent infiltration undergoes resolution far more slowly than any pneumonia caused by a double infection. In other words purulent

infiltration must be associated with a failure of the processes which determine resolution, that is of the general defensive mechanisms of the body. And we know that this is so. Such cases shew an almost complete absence of leucocytosis and of a rise in the opsonic index. As resolution is carried out by unorganised ferments, the arrest of resolution can be explained by supposing that the ferments are either absent or inoperative. The former is the more likely. The ferments are certainly derived from leucocytes; we know that leucocytosis has failed; and possibly the tryptic power of such phagocytes as are present is abnormally low. Ferments could be inoperative only if the corresponding anti-ferment or anti-kinase were being produced in excessive quantities; and there is no evidence that such is the case.

Induration is closely associated with purulent infiltration. It was stated by Addison that occasionally a pneumonic lung never recovers its permeability to air and may gradually pass into an unnaturally firm, pale, solid state, containing an excess of fibrous tissue, a state which he described as "marbled induration." It consists essentially in the gradual organisation of the inflammatory products contained in the alveoli. The complication is so rare that some authors seem to doubt whether it ever occurs, and when the condition is found at a necropsy whether it can be ascribed to a previous attack of lobar pneumonia which they did not see. One of us (A. P. B.) has had two patients under his observation from the original attack of pneumonia to their death. Both patients were considered to have had purulent infiltration; the physical signs of consolidation and a high irregular pyrexia persisted: and death took place within four months of the original attack. The lungs were in the condition described by Addison, and this was confirmed by microscopical examination. (*Vide* art. "Chronic Interstitial Pneumonia," p. 254.)

II. *Pleural Complications.*—Pleurisy is frequently not diagnosed during life, but it is found in over 90 per cent of fatal cases, and is in fact always present when the consolidation has reached the surface of the lung. The pleura loses its polish and is roughened; the lobes adhere together and to the parietal pleura. It is frequently covered with flakes of lymph or with a complete fibrinous membrane which can be peeled off. These inflammatory products rapidly disappear during resolution and leave at most a few adhesions. Fibrotic thickening of the pleura is not infrequently diagnosed in order to explain the impaired resonance, which may persist for a few weeks after the crisis. A thickening of the pleura sufficiently great to give evidence of its presence seldom or never follows pneumonia except as a result of a long-standing empyema.

Serous effusion was observed 125 times, 1·6 per cent, in 7868 cases; 13 of these 125 cases were fatal. The effusion is frequently small, does not require to be tapped, and disappears spontaneously and often with rapidity. It must not be forgotten that fluid found to be serous on one occasion may become purulent later; and pus should be suspected if the effusion does not disappear and the pyrexia persists. Further, the

association of a serous effusion with an interlobar empyema must not be lost sight of.

Empyema.—The frequency with which empyema complicates pneumonia is curiously variable even in large series of cases. In 7868 cases above ten years of age it occurred in 3·7 per cent, or 290 cases, of which 88 were fatal. This gives an incidence more than double that of serous effusion. In other collections of cases exactly the reverse has been found. At different London hospitals the percentage varies from 1·2 to 7 per cent. Empyema is much more frequent in children than in adults; and the frequency varies inversely as their age. A considerable increase is found also at the other end of life. At the East London Hospital for children Dr. Gossage found amongst 759 cases of lobar pneumonia with a mortality of 14 per cent, that 12 per cent of the cases developed empyema, with a mortality of 33 per cent; and that death from empyema represented 29 per cent of the total deaths. Empyema and other septicaemic complications are much more frequent in some years than in others; and this suggests variations from year to year in the virulence of the pneumococcus.

The site of the empyema is generally over the hepatised lung, but not necessarily so. It may be bilateral and the pneumonia unilateral; or it may be on the opposite side to the pneumonia. These data seem to prove that at least some empyemas are caused by a septicaemic and not by a local infection of the pleural cavity. The possibility that empyemas may have a septicaemic origin is shewn by the not infrequent occurrence of pneumococcal empyemas apart from pneumonia. Dr. Gossage records 60 such cases of which 22 died. Empyema is the most frequent complication except pleurisy, which indeed is almost part of the disease. It should always be suspected when the usual rapidity of recovery is interrupted. The diagnosis is based both upon symptoms and upon physical signs. If there has been a crisis, the onset of empyema is marked by a slow rise of temperature, which begins in one to four days after the crisis. This secondary pyrexia is very seldom absent or delayed. Another and important symptom is that the respiratory rate either fails to fall at the crisis, or shews a marked secondary rise. In cases in which the temperature is falling by lysis, the secondary rise may still be obvious; but in other and rare cases the temperature has never fallen and no secondary rise can be made out. The physical signs of empyema are those of localised fluid in the chest. Occasionally in adults and more frequently in children the physical signs are more like those of solid lung than of fluid; and this is especially the case when the empyema has formed over pneumonic lung. Instead of the characteristic absence of breath-sounds, there are feeble or loud, rough breath-sounds and even bronchial breathing, together with bubbling and sharp crackling rales. In such cases the shifting of the mediastinum towards the opposite side is a great help in diagnosis. The localisation of the empyema is easy, except when it is interlobar or between the lung and the diaphragm. When empyema is suspected, but cannot be localised with certainty, it

may be necessary to give an anaesthetic, and puncture the chest in a systematic way before either the pus may be found or empyema excluded. The selection of the sites for puncture would be guided by any physical signs which did exist, by finding a spot tender to firm pressure, and sometimes by an *x*-ray examination of the chest.

The pleural inflammation may spread to surrounding structures. Inflammation of the muscle of the diaphragm is common, and causes the abdominal viscera to lie about one rib higher than usual on the affected side. J. M'Crae found mediastinitis twice in 100 necropsies. Suppuration of the bronchial glands has occurred.

III. *Septicaemic complications* form a numerous and important group. They are not infrequently multiple, and taking them as a whole are more common in children than in adults. The death-rate from septicaemic complications compared with the total death-rate from pneumonia is very much greater in children than in adults. The explanation of this would appear to be that adults, who fail to cope successfully with the septicaemia of pneumonia, generally die before there has been time for them to develop a septicaemic complication. The commonest time of onset of these complications is from the eighth to the twelfth or fourteenth day of the illness.

Pericarditis is the most frequent of these complications. In 7868 cases, of which 1722 were fatal, it was present in 10·6 per cent of the fatal cases, and in less than 1 per cent of the cases which recovered. It is, however, probable that pericarditis is three or four times more frequent than 1 per cent in cases which are not fatal. The reason for this statement is that pericarditis, unsuspected during life, is not infrequently found at a necropsy. This is particularly true with regard to children; in 100 cases of suppurative pericarditis, the great majority being pneumococcal, a diagnosis was made in 6 only (Poynton). It is therefore next to pleural effusion the most common complication. The uncertainty as to its frequency of occurrence makes it impossible to state the mortality with accuracy. The mortality is about 80 per cent in cases in which the condition is diagnosed. It usually begins at about the same period as empyema, and in 54 of Dr. Poynton's 100 cases was associated with empyema on one or both sides. It is slightly more common in pneumonia of the left than of the right side; and empyema is slightly more frequent in the left than in the right chest. These two points suggest that the pericardium may be infected from the surrounding structures by direct extension. Probably it is far more often septicaemic, and this is supported by the frequency with which pericarditis is associated with septicaemic complications other than empyema. The inflammation is not necessarily associated with either a serous or purulent effusion. The effusion, when present, is seldom so large as to demand tapping for mechanical reasons, but occasionally a purulent effusion is present and requires to be drained. The high mortality of pericarditis is probably due to the severe myocarditis which frequently accompanies it. The occurrence of sudden and acute dilatation of the heart should always suggest myocarditis and pericarditis.

Endocarditis is much more frequent than is generally supposed. According to Preble it occurred 126 times in 11,243 cases, that is, in about 1 per cent; in fatal cases the proportion was nearly 5 per cent. Diseased cardiac valves become infected more often than those previously healthy. The aortic valve is affected in 50 per cent of cases, and the tricuspid in 10 per cent. The constitutional symptoms accompanying it are the same as with empyema; and when these are present, and no other complication can be found, endocarditis should always be suspected. The patient may die of the septicaemia before the endocarditis has lasted long enough to be accompanied by bruits. The endocarditis is always of the infective form; and if the patient live long enough, embolism of various arteries may take place. The diagnosis in the later stages is made by physical signs and by blood cultures. The cases have been almost uniformly fatal up to the present; but treatment by a vaccin may alter the prognosis.

Suppurative Peritonitis.—Out of 7868 cases peritonitis occurred in 22 or 0·3 per cent of the whole; 5 of the cases recovered and 17 died. The peritonitis begins at the same period of the disease as empyema and pericarditis. The most important point about these cases is their diagnosis; and this as a rule does not offer serious difficulty. The simulation of acute abdominal disease by pneumonia in its early stages is very real, and is discussed under diagnosis; but at the stage at which peritonitis may begin it will be obvious that the patient has pneumonia. The onset of abdominal symptoms, such as pain, rigidity, and distension, should always arouse suspicion. The liver, spleen, and intestines should be carefully auscultated for a rub, the rectum examined, the loins palpated for rigidity and percussed for impaired resonance. A leucocyte count might help. The abdominal rigidity caused by the pain of pleurisy disappears as a rule within the first few days; sometimes it may persist, but it could hardly simulate peritonitis, because it would have been present throughout.

Arthritis is far from common. Statistics shew that it occurs only in about 0·1 per cent of cases, in a degree which makes it obvious. Like other septicaemic complications, it is most frequent in children, and begins about the twelfth day of the illness. It affects chiefly the larger joints of the limbs. The joint is very painful, tender, and distended with purulent fluid. It is probable that mild cases are not very infrequent, and recover spontaneously. But when the joint is distended and the constitutional disturbance is severe, surgical interference is necessary, and the prognosis is grave. The mortality is about 50 per cent (*vide* also Vol. III. p. 55).

Meningitis is a complication which is said to occur in about 0·1 per cent of cases above ten years of age, and in about 1 to 2 per cent of cases in children below that age. It may come on within the first week of very grave cases, or about the tenth day, together with other complications, in less rapidly fatal cases. It is usually purulent and uniformly fatal. It is most often over the vertex, in which case it is frequently

undiagnosed during life, the symptoms being ascribed to toxaemic delirium; it may be basal, in which case it is more readily diagnosed. Dr. Gossage has suggested that pneumococcal meningitis may sometimes be serous instead of purulent; and that it may disappear spontaneously like the corresponding pleurisy. He records a case in which head-retraction, twitching, and optic neuritis were observed; and yet the patient recovered. In all doubtful cases of meningitis a bacteriological and cytological examination of the cerebrospinal fluid, withdrawn by lumbar or cerebral puncture, should be made. The whole question of the incidence of meningitis in pneumonia requires investigation, because Dr. F. Buzzard has shewn that the brain and spinal cord may appear healthy, although microscopical examination proves that meningitis is present. Purulent meningitis may come on at a later stage altogether in cases suffering from infective endocarditis. A chronic serofibrinous variety, resembling posterior basic meningitis, has been described.

Nephritis.—In addition to toxaemic nephritis, which has been described in connexion with the symptoms, there is a much more severe affection of the kidney, caused by the infection of the renal tissues with pneumococci. Septicaemic nephritis is rare, and occurs in about 1 per cent of the cases; it is more common in children than in adults. The symptoms begin at about the same time as the other septicaemic complications, and are similar to those of scarlatinal nephritis. The mortality is high; but if the case is not fatal the nephritis generally disappears. There can be no doubt that a septicaemic nephritis, which does not clear up, is within the range of treatment by a vaccin.

Abscesses and suppuration in bone, muscle, the brain, and subcutaneous tissues have been observed.

Thrombosis occurs in about 1 per cent of the cases. It affects the femoral veins more often than any other vessel, and, as in enteric fever, the left more frequently than the right. It has been observed in other vessels, such as the external jugular, axillary, and internal saphenous veins, in the superior longitudinal sinus, and the cerebral vessels. It has generally been observed in the early stages of convalescence; it begins with the usual symptoms, accompanied by a rise of temperature. The prognosis is naturally influenced by the situation of the vessel affected; but when it is the femoral vein, the prognosis is good. J. M'Crae found ante-mortem clots in the heart in 42 per cent of his necropsies. It is therefore not surprising that sudden death from pulmonary embolism has been noted both during the illness and after apparent recovery.

IV. *Local inflammations* of parts in connexion with the upper air-passages and alimentary canal are rare. They may occur as primary diseases and apart from pneumonia; but it is not surprising that the pneumococcus should set up acute inflammations of the various passages, which it frequently infects, during the prolonged negative phase seen in many cases of pneumonia. Suppurative otitis media is the most frequent of these complications; it is much more often seen in children than in adults. It was noted in about 0·5 per cent of 7868 cases above 10 years

of age, and in 3 per cent of cases in children under that age. It runs the same course and is liable to the same complications as the primary disease caused by the same and other micro-organisms. Acute membranous inflammations of the mouth, tonsils, fauces, pharynx, trachea, nares, conjunctiva, stomach, colon, and rectum have been observed in pneumonia as well as independently of it. Those affecting the stomach and colon are rare, but usually fatal.

V. *Toxaemic Complications.*—Severe epistaxis occasionally marks the onset of pneumonia, and may recur during its course. Except in elderly patients this is not a serious symptom. It is noted in about 2·5 per cent of the cases. Petechiae are not infrequently seen on the pericardium and pleurae of acutely fatal cases. But nothing approaching the general haemorrhagic condition seen in some cases of pneumococcal septicaemia is ever seen in pneumonia; the patient would be dead long before he could develop signs of pneumonia. Petechial rashes have been seen in severe cases. Ulceration of the stomach (Dieulafoy) and of the duodenum (Griffon) has been described. One of us (A. P. B.) has seen a man with pneumonia and pneumococcal peritonitis, who, though in all probability he had neither cirrhosis of the liver nor gastric ulcer, developed a petechial rash and recurrent attacks of haematemesis during the most acute stage of his illness; he ultimately recovered.

Jaundice is an occasional complication of pneumonia. It is stated to be more frequent with a right basal pneumonia, but it must be remembered that pneumonia is more frequent in that situation. It is said to be more common in some outbreaks of pneumonia than in others. It most often begins during the pyrexial period and is slight in amount; the motions contain bile and the complication is unimportant. Deep jaundice with catarrhal obstruction of the bile-duct may occur without altering the prognosis. Jaundice may accompany the septicaemia or pyaemia of pneumonia as of any other disease; it is of importance only because of its cause.

Acute dilatation of the stomach or intestines is a rare but very grave complication; 3 out of 44 cases of acute dilatation of the stomach analysed by Dr. Campbell Thomson were in pneumonia. It may occur with great suddenness and be extreme. One of us (A. P. B.) has seen a case mistaken for perforation of the stomach, owing to the rapid onset with pain and complete absence of liver dulness. The patient was dead at the end of three hours from the onset. It appears to be a toxaemic paralysis, and is generally fatal in a few hours.

Peripheral neuritis has been described as following pneumonia. In its mildest form the only evidence is absence of the knee-jerks; many good observers have reported that these reflexes are generally absent in lobar pneumonia and present in bronchopneumonia. Of 125 cases of pneumonia in St. George's Hospital, the knee-jerk was present in 90 and absent or diminished in 35. A more severe form of neuritis is described as beginning with paresis and pain in the muscles of the arms and legs.

The Duration.—In cases which recover, a crisis occurs in about

60 per cent. It may be as early as the second day or as late as the twenty-sixth. In another 30 per cent of the cases the pyrexia ends by a lysis, which may be short or slow. It is generally true that, however slow the lysis may be, the illness does not often last more than a fortnight unless some complication is present. Complications delay recovery for various periods. Purulent infiltration is the one which causes the greatest delay; recovery may be deferred for many weeks or months.

Short or *abortive* attacks of pneumonia are not very infrequent. About 14 per cent of the cases which end by crisis terminate before the beginning of the fifth day; and the crisis has been described as taking place at the end of one day's illness. Such short cases are open to the obvious fallacy of errors in diagnosis. Nevertheless, there is no doubt that very short cases are met with; and there is nothing surprising in it. The date of the crisis is determined by the resultant of two factors, the dose or virulence of the infection, and the rapidity and degree of the reaction of the patient's tissues. If both factors are very favourable to the patient, an early crisis is the result. The lungs in these very short cases may not become inflamed sufficiently to give the physical signs of consolidation, but pass from a state of engorgement rapidly into one of resolution. It is probable that some cases of acute congestive bronchopneumonia described in the article on Bronchopneumonia are of this kind. The onset is extremely sudden, with very severe constitutional symptoms and signs of acute engorgement; but within two or three days there is a crisis and the child is convalescent. Abortive cases are the ones which most frequently have *relapses*. The crisis is followed by an apyrexial period of about three to fourteen days; and then another attack of pneumonia begins in some other part of the lungs. In an abortive case the original infection has been mild and has called forth a slight but adequate reaction. If pneumococci subsequently gain access to healthy pulmonary tissue, there may not be sufficient general immunity to prevent a second infection of the blood from taking place.

In fatal cases, other than those which die from local complications, death rarely takes place before the fourth day or later than about the tenth. These cases are rapidly fatal, because the patients are unable to cope with the septicaemia; and the general toxaemia gradually poisons the cardiac muscle and the central nervous system. The patient sinks down in bed, taking less and less notice of anything around him, or passes into a state of low muttering delirium. Signs of general circulatory failure are obvious; the pulse becomes weak, rapid, and irregular; the skin becomes cold, clammy, livid, and finally pale; and the respirations are feeble, and the cough is infrequent or disappears.

Some patients, however, die in less than four days, and even in less than one day. They may die so rapidly that the lungs at the necropsy appear perfectly normal to the naked eye; but on microscopical examination the earliest stages of inflammatory reaction are seen. A remarkable case of rapidly fatal pneumococcal septicaemia, due to infection through the lungs, is recorded by Holt. The child died in thirty hours; and the

pneumococcus was cultivated from both lungs, the heart's blood, the spleen, and both kidneys. Such a case is only one degree less acute than a case which dies within twelve hours of haemorrhagic pneumococcal septicaemia.

Mortality and Prognosis.—The average *mortality* in 7868 cases over ten years of age admitted into the hospitals of London in the ten years, 1897-1906, was 21·8 per cent. The mortality is affected in a very important way by the age of the patient. In general it is above the average in infants below two years of age; it is lowest in children and youths; it reaches the average in the period between twenty to thirty years of age, and then increases continuously with the age. Dr. Gossage in 986 cases under ten years of age found an average mortality of 13·8 per cent; but below two years of age it was 26·4 per cent; and above two years only 6·2 per cent. In old age, on the other hand, the mortality may be double or treble the average. It is said to be less in general private practice than in hospitals, and slightly higher in women than in men; but all statistics do not confirm the latter point. There is no doubt that the mortality varies from year to year, like the liability to septicaemic complications; and that this is to be ascribed to variations in the average virulence of the pneumococcus. The average mortality is not the same in all countries. It is much higher in drunkards and heavy drinkers; but it is difficult to express the greater mortality in figures, because of the impossibility of defining a heavy drinker for purposes of statistics. If we say that chronic alcoholism doubles the mortality, we are well within the truth.

The immediate *prognosis* in pneumonia must depend upon the resultant of two variable factors, namely, the resistance of the patient and the dose or virulence of the infection. We have no means of measuring directly either of these factors. We can, however, roughly estimate, by the opsonic index and the degree of leucocytosis, the actual response which the tissues are making to an unknown dose of toxin. But in order that these methods may give data on which to found a prognosis, it would be necessary to have estimations made almost daily. And since this is not possible in a majority of cases, we are reduced to basing our prognosis, not upon certainties, but upon probabilities. In the first place, we gauge the likelihood of the patient's resistance being greater or less than the average by observing his age, and whether his tissues were previously healthy or subject to diseases and intoxications; and if the latter, we gather from clinical experience whether these are such as to diminish his power of dealing with a pneumococcal infection. We have already seen that infancy and old age, chronic alcoholism, diabetes, general arteriosclerosis, chronic nephritis, chronic circulatory failure, and any considerable degree of ill-health have this effect. In the second place, we observe the changes which the toxaemia induces in the functional activity of various organs and systems. And we judge of the degree of the toxaemia and of the power of the tissues to withstand and combat it actively by the magnitude and duration of these functional

disturbances. All these points have already been dealt with, but we may repeat here that the most important are: the course, degree, and duration of the pyrexia; the condition of the heart; the character and the rapidity of the pulse and respirations; and symptoms which indicate severe poisoning of the central nervous system. In the third place, we judge by the onset of local complications that the body has failed to some extent, it may be very partially or almost completely, to neutralise the toxaemia or to put an end to the infection of the blood, of the lungs, or of other tissues. And we judge, from the situation and nature of the local complication, whether it is likely by itself, or as a part of a more general condition, to influence the prognosis.

The relation between the extent of the pulmonary lesion and the prognosis remains to be discussed. J. M'Crae found that of fatal cases, 2 lobes were affected in 38 per cent, 3 lobes in 31 per cent, 1 lobe in 21 per cent, and 4 lobes in 9 per cent; and that of non-fatal cases, 1 lobe was affected in 40 per cent, 2 lobes in 33 per cent, 3 lobes in 20 per cent, and 4 lobes in 1 per cent. The only deduction which can be drawn from these figures is that the extent of the consolidation has a very direct bearing upon prognosis, and for obvious reasons. At the growing edge neither the bacteria in the lungs nor their toxins are shut off from the blood; and the more numerous and extensive the spreading edges of the disease, the greater will be the dose of toxin and bacteria absorbed into the blood. And again, at the growing edge, and probably there only, the bacteria are subjected to the influence of anti-bacterial substances circulating in the blood. A rapidly-spreading edge, therefore, indicates that there is comparatively little anti-bacterial substance present in the blood; and this in turn points to a deep and prolonged negative phase caused either by a large dose of infection or by a poor reaction of the tissues.

Diagnosis.—The presence of the physical signs of a lobar consolidation of the lung and the accompanying constitutional disturbance enable us to distinguish pneumonia from other conditions easily and certainly. There are, however, difficulties in diagnosis both before and after the pulmonary signs have appeared; these must now be considered.

(1) *From other Varieties of Lobar Pneumonia.*—The definition of lobar pneumonia indicates that there are at least three micro-organisms other than the pneumococcus, which can produce a pneumonia with a lobar distribution. Up to this point we have considered only pneumococcal pneumonia. It is therefore necessary to inquire whether in any given case of lobar pneumonia the bacterial cause can be ascertained during life. A certain diagnosis could be obtained by a proper bacteriological examination of the sputum, the blood, or material removed from the solid lung by puncture. In the absence of such information a diagnosis must be founded upon either the course of the illness or the physical signs in the chest or the probabilities; and we have now to inquire if it is possible to do so. There are no statistics which give the exact comparative frequencies of these four forms of pneumonia; but we

know that the probability that any given lobar pneumonia is due to the pneumococcus, alone or with other bacteria, is almost overwhelming.

Lobar pneumonia caused by *Bacillus typhosus* is so rare that the case reported by Drs. S. Phillips and Spilsbury is unique in England, and even this case is not above suspicion; for the organism found in the lungs was not cultivated, but was recognised by its morphological appearances and staining reactions only. Pneumococci and tubercle bacilli were shewn to be absent. The *B. typhosus* may produce either a lobar pneumonia or a bronchopneumonia. When lobar pneumonia occurs in the course of enteric fever it is usually due to the pneumococcus; and this complication runs the ordinary course of a pneumococcal pneumonia. The lobar pneumonia caused by the *B. typhosus* is said to be characterised by its early onset in the course of the typhoid attack, by very rapid development, and by resolving extremely slowly. The last point is the most important, and was well shewn in Dr. S. Phillips' case; the patient died seventeen days after the onset of the cough and of the expectoration of sputum; the symptoms of enteric fever had begun to decline in severity, those of pneumonia had not; and at the necropsy the lung was still in the stage of red hepatisation and contained multiple small abscesses. The physical signs were not in any way peculiar.

Tuberculous lobar pneumonia is a well-established condition, although it is the rarest form of tuberculosis of the lung. The patient may die in a fortnight; and in this event the clinical course and physical signs may be indistinguishable from those of pneumococcal pneumonia. More frequently, however, the case is more prolonged; and the hectic fever, progressive wasting, complete absence of signs of resolution, and the presence of the signs of excavation suggest that the pneumonia is not pneumococcal. The detection of tubercle bacilli and the absence of pneumococci are the only data on which a positive diagnosis could be based (*vide* p. 332).

Streptococcal lobar pneumonia is the most frequent of the three rare varieties; but here again there is great uncertainty as to the frequency of its occurrence. In J. M'Crae's fatal cases the streptococcus was the main agent in 8 per cent of the cases. The combined statistics of Prochaska and Rosenow shew that pneumococci were found in the blood in 182 cases out of a total of 195; that is, in 93 per cent. At present there is no certain clinical distinction, other than a bacteriological one, between pure pneumococcal and pure streptococcal pneumonias. It is probably safe to conclude that all cases which end by crisis are pneumococcal. The whole question is made difficult by the occurrence of mixed infections, which certainly run a longer and more irregular course than pure pneumococcal pneumonias.

(2) *From other Acute Pulmonary Diseases.*—The points of distinction between lobar pneumonia and a pleural effusion or primary pneumococcal empyema have already been considered (p. 226); the distinction is one of physical signs. In children lobar pneumonia must be diagnosed both from confluent lobular pneumonia and from confluent bronchopneumonia; this has

been considered in the article in which these conditions are described (p. 180). In adults, influenza is generally considered to be the disease which most frequently simulates lobar pneumonia. Influenzal pneumonia is either a disseminated pneumonia or a bronchopneumonia, and differs from lobar pneumonia both in its clinical course and in the physical signs. A lobar pneumonia following influenza has generally been found to be caused by the pneumococcus.

(3) *From other Acute Infections.*—The sudden onset of illness associated with high fever and vomiting in a child suggests one of the exanthematous fevers or influenza just as much as pneumonia. Before the physical signs of pneumonia appear, the diagnosis is founded upon the presence of pain and cough, and upon the increased rate of the respiration in relation to the temperature and pulse. It must, however, be remembered that this early rapidity of the respiration is special to the pneumococcal toxin, and is seen no matter whether the primary pneumococcal infection falls on the peritoneum, pleura, or lung.

(4) *From Acute Abdominal Diseases.*—When the pleuritic pain of pneumonia is referred to the belly, the abdomen may be as rigid and tender as in acute abdominal disease. It is impossible to repeat the statement too often, that abdominal pain and rigidity do not necessarily indicate abdominal disease; for the responsible cause may be in the thorax, spine, or in fact in any viscus innervated from the corresponding posterior nerve-root. Pneumonia at the onset may simulate acute abdominal disease to perfection; and the diagnosis may be so difficult that laparotomy is not very infrequently either proposed or performed in cases of early pneumonia. It may copy any acute condition below the diaphragm; but mistakes are most frequently made between pneumonia and appendicitis in children, and between pneumonia and perforated gastric ulcer or appendicitis in adults.

From Appendicitis.—The following symptoms are common to pneumonia and appendicitis; a sudden attack of pain in the right iliac fossa or loin, associated with high fever, vomiting, increased pulse-rate, rigidity and tenderness, constipation, and leucocytosis. The correct diagnosis is made by carefully examining the chest for limitation of movement on one side and for the early signs of pneumonia; by counting the respirations and considering the rate in comparison with that of the pulse and with the temperature; and by making a rectal examination.

From Perforated Gastric Ulcer.—An early pneumonia may present the following points in common with perforated gastric ulcer. The history of the onset may be very similar in the two conditions. The patient after getting up in the morning and starting to work is seized with violent pain in the epigastrium, followed by vomiting and collapse. When the patient is examined some hours later the abdominal wall is more or less rigid and tender all over, especially in its upper part, and moves badly on respiration; the respirations are shallower and therefore more frequent than normal, and painful. The following points must be considered in order to reach a correct diagnosis. The temperature may

be raised in cases of perforated ulcer after the first shock has passed off; but it is very moderate and about 100° to 101° F. The pulse may not be more rapid in the one condition than in the other, but its character is very important. In pneumonia the pulse is bounding; in perforated ulcer it is generally small, the artery is contracted, and the blood-pressure raised to 130-140 mm. of mercury. The respiratory rate is of importance; in perforated ulcer it may certainly be raised and is frequently about 25 to 30; but a rate of 40 or more would point strongly to pneumonia. The physical examination of the chest may reveal definite signs of early pneumonic consolidation. The presence of a rub may be difficult to interpret; because it may not be obvious whether the rub is above or below the diaphragm. If the rub is heard only over the intestines, the liver or spleen in front, it may just as well be peritoneal as pleural; but if it is heard only over the base behind, it is more likely to be pleural. Too great reliance, however, must not be placed upon an increased pulse-respiration ratio coupled with a rub over a base behind; otherwise it may lead to the converse mistake of diagnosing a case of perforated ulcer as one of pneumonia; in a case in which this mistake was made the patient when seen eight hours after perforation had a pulse of 100, respirations of 40 and a temperature of 101° F. The physical signs of free gas below the diaphragm are conclusive, when they can be obtained. We have found the following procedures of help on more than one occasion; with the patient lying on his back, diminution of the hepatic dulness in front is not necessarily evidence of free gas. A decidedly tympanitic note over the liver in front, and not in the axilla, is very suggestive of the presence of free gas. The patient should then be rolled over on to his left side; if now the right lower axillary region becomes tympanitic, and at the same time the hepatic dulness in front increases, there is free gas under the diaphragm. We have also noticed that, when there is not enough free gas to give movable resonance, if the stethoscope be placed over the lower ribs in front and the skin of the chest be gently stroked with the finger, a clear and distinct bell-note may be obtained. Not infrequently the general appearance of the patient is more helpful and diagnostic than the symptoms or physical signs. Less importance should be attached to the previous medical history than to anything else. There are few patients from whom a history of painful digestion cannot be obtained; and it must be remembered that a patient with a perforated ulcer may never have been conscious of indigestion. If there is a reliable history of haematemesis or melaena, it is suggestive, but nothing more. Nevertheless, in spite of the most careful examination there are cases in which it is impossible to give a dogmatic opinion at once; they are few; but in such a case it is proper to operate without delay. It is much less serious to perform laparotomy upon a case of pneumonia than to hesitate in dealing with a perforated ulcer.

(5) *From Meningitis.*—In young children pneumonia, as we have seen, may begin with severe cerebral symptoms, which may continue for days. The symptoms are due to irritation of nerve-cells by the toxins circu-

lating in the blood. In meningitis also the nerve-cells are irritated by the toxin; but there may be in addition symptoms due to an increase of the intracranial pressure or to localised inflammation of the brain and cranial nerves. The symptoms of toxaemic cerebral irritation common to the two conditions are general convulsions, delirium, drowsiness, unconsciousness verging even on deep coma, Kernig's sign, retraction of the abdomen, rigidity of the neck and back, vomiting, and a pulse which may be irregular and vary widely in rate from hour to hour. Meningitis undoubtedly may be present and not give rise to any symptoms but those of cerebral irritation. A definite diagnosis in such a case could be made only by a cytological and bacteriological examination of the fluid removed by lumbar puncture. The symptoms of increased intracranial pressure, which if present would be diagnostic of meningitis, are slowing of the pulse or respirations, very deep coma, Cheyne-Stokes respiration, and a very considerable rise of arterial blood-pressure. The symptoms which would point to an inflammation of the central nervous system and its nerves are, optic neuritis, monoplegic or hemiplegic paresis, paralysis or rigidity, and great and constant rigidity of the neck or spine. Squint is of value only when it is marked and constant for several hours. Many infants, when delirious, develop slight and variable squints. The general statement may be made that in pneumonia the temperature is generally higher, the respirations are rapid and never slow, stupor is less profound, localised paralyses are absent, and the cerebral symptoms do not get progressively worse, but are generally more marked at first than at the end of one or two days.

Acute and severe cerebral symptoms beginning during the course of pneumonia either in children or adults should be ascribed to a septicaemic lesion of the central nervous system, and not merely to the general toxaemia.

In adults the cerebral symptoms may simulate delirium tremens. A correct diagnosis can be made by observing the temperature and by finding physical signs of pneumonia. In uncomplicated delirium tremens the temperature is raised but little, if at all.

Treatment. — *Historical Sketch.* — Acute pneumonia is so striking and so severe a disease that as soon as it was definitely recognised it was attacked by all the resources of medicine. During the whole of the past century the treatment of pneumonia has reflected the various theories of disease and the changing practice of therapeutics.

The conception of pneumonia current in the first half of the nineteenth century was that of an acute inflammation, directly produced by cold, and attacking a healthy subject. The business of the physician was to combat the enemy by the potent weapons of bleeding, blistering, and starvation, aided by purgative and alterative drugs. The high fever, the flushed face, the acute pain and the burning skin were evidence of a "sthenic" inflammation. The physician felt confident that by antiphlogistic remedies he could subdue the disease; and his only fear was lest the patient's strength should fail under the necessary treatment,

that he might die, not of the disease, but of the weakness attending its cure—*mort guéri*. The "corroborant" practice of the Brunonian school of medicine never obtained such vogue in England as on the Continent. It was as baseless as the iatro-chemical or the iatro-mechanical systems which prevailed earlier in the eighteenth century, and had deservedly fallen into disrepute. During the first half of the last century the antiphlogistic treatment of pneumonia and of other acute inflammations continued to be the only one followed in civilised countries—in Dublin as well as in Edinburgh, in Vienna as well as in Madrid; and precisely the same treatment was adopted by surgeons for compound fractures, inflammations of the eye, and for what we now call pyaemia. To realise the confidence and energy with which this absurdly called "heroic" treatment was carried out, one must have seen, as might be seen so late as 1863-64, the treatment not only of pneumonia and pericarditis, but of rheumatic and enteric fever, by a learned and experienced physician, Prof. Bouillaud at the Charité; or one must read the lectures of Peter Mere Latham (1845), in which with admirable rhetorical skill he enforces the dogmas of that day.

The only important modification of the antiphlogistic treatment of pneumonia introduced during the period between 1790 and 1850 was the introduction of large and repeated doses of antimony by Rasori (1808), a practice much followed for a time both in Italy and France. The undoubted effects of this drug, in producing nausea and disinclination to food, lowering the blood-pressure, and causing diaphoresis, were quite in harmony with the effects of bleeding, purging, and salivation.

It was and still is true, when a patient is suffering from acute pain in the side with fever and a frequent, strong, and hard pulse, that venesection and free purging will relieve the pain, reduce the arterial tension, and give him grateful relief from his sense of fulness and oppression. It was no doubt from observation of these effects, which were well known to Sydenham, Mead, and Boerhaave, that the antiphlogistic practice began; and when the discoveries of Laennec made it possible to recognise pneumonia from the first, and to trace its daily progress, it seemed right to continue and to reinforce a treatment apparently so appropriate.

The mistake lay in having no control-observations. Physicians saw patients in an illness apparently desperate, and under treatment by bleeding and antimony they saw most of the symptoms relieved; frequently, after a battle of several days, the disease was subdued and the patient convalescent; but they did not know, because they never ventured to try, what would happen if these remedies had been omitted. It is a humiliating but instructive fact that the possibility of recovery from acute disease without active treatment was established by the assumed success of a demonstrably futile system of therapeutics, the last, we may hope, of attempts to answer the absurd question, "On what universal principle should disease be treated?" When it could not be denied that persons suffering from pneumonia and other acute disorders did recover when

treated with infinitesimal doses of useless drugs, it could not be long doubted that some acute diseases might get well of themselves.

The report of some cases of pneumonia which recovered in the Homoeopathic Hospital at Vienna awakened thought on this subject, and an article by Sir John Forbes, which appeared in the *British and Foreign Medico-Chirurgical Review* (1846), pressed the lesson home. Skoda had given fair trial to other methods of treatment, and found that under the so-called expectant treatment the mortality of his patients from acute pneumonia was much less than when treated by bleeding, blisters, and antimony. These facts were made known in England by Geo. Balfour, who had followed Skoda's practice in Vienna. Hughes Bennett of Edinburgh also published a series of cases of pneumonia treated without bleeding, antimony, or mercury with unusually small mortality (1848); and he gave an interesting account of the arguments of Alison, Watson, Christison, and Markham. Discussion followed, but it was less prolonged than might have been supposed; as so often happens, general opinion had been gradually altering, and was ready to turn at the first summons. Moreover, the advocates of antiphlogistic treatment threw away their case by the assertion that they were right in bleeding before, and right in doing nothing afterwards—not because their opinions but the nature of the disease had changed; and a presumed "sthenic type" of fevers and inflammations, with a successful heroic treatment corresponding thereto, was dwelt upon with the same satisfaction that an old man contrasts the hard frosts and heroic exploits of his youth with the mild winters and feeble powers of his contemporaries. For a long time the antiphlogistic treatment held its ground in books and lectures; but those who taught it always found in practice an excuse for disobeying their own precepts. By 1860, however, the change in treatment was nearly universal; and during the latter half of the nineteenth century, English physicians, under the guidance of Jenner and of Gull, gave up the "heroic" treatment of pneumonia.

General Treatment of Uncomplicated Cases.—The treatment of an infective disease may be of two kinds, curative and symptomatic or expectant. The former, so far as it relates to the use of serums or vaccins and is capable of application to pneumonia, is dealt with on p. 241. We do not possess a curative drug for pneumonia, in the sense in which mercury and iodides are specific in syphilis, quinine in malaria, or thyroid extract in myxoedema. Whether pneumonia can be cut short or not, it may be successfully guided. The terms "expectant" and "symptomatic" as applied to treatment are unfortunate; we should neither wait to see what occurs in the case, nor treat symptoms merely because they are present in disease and not in health. The underlying principle of treatment is to put the patient in the best possible position to withstand and overcome the infection. The patient has to cure himself, and it is our duty to help him to do so. With this object in view our aim should be to foresee the dangers special to the disease and the case, and to ward them off or minimise their effects. It is important to realise that the

reaction of the body to an infection is a single process involving a complicated series of changes, both general and local; that these changes can alone effect a cure; and that in order that they may do so, they must be orderly and mutually balanced. Many constitutional symptoms, such as fever, are a part of this reaction, and unnecessary interference with them may upset the curative process. A symptom of reaction should never be interfered with, merely because it accompanies a diseased state, unless it is either prejudicial to recovery or in itself dangerous to life.

The treatment of a child suffering from pneumonia, in so far as it differs from that of an adult, is detailed in the article on Broncho-pneumonia (p. 188).

A case of pneumonia in a youth or young adult often requires but little active treatment. Our first care should be to satisfy ourselves from day to day by careful examination of the patient that the disease is running a favourable course, as only by so doing can we scent danger from afar. After the crisis, the minuteness of our examination of the chest, the chart, the pulse- and the respiration-rate should not be relaxed; otherwise the onset of empyema and other complications may not be diagnosed at an early date.

The patient should be put to bed in a room well ventilated by night as well as by day. The temperature of the room should not be raised artificially above 60° F., and may be allowed to fall considerably at night, unless the patient is an infant or elderly and infirm or is suffering from bronchitis. The bed-clothes should be light and may be kept off the patient by cradles, when the pyrexia is high. It is often difficult to persuade the laity that a pneumonic patient should neither be kept in a room warmed to 70° F. from which fresh air is excluded as far as possible nor have more bed-clothes the more fevered he is. Plenty of fresh air is of importance during the acute attack just as much as during convalescence; but the proposal to treat pneumonia in the open air is perhaps scarcely wise in our climate, excepting in the case of very vigorous patients. The bed should be protected from direct draughts by a screen. Frequent sponging with tepid water adds greatly to the comfort of the patient and promotes sleep and appetite.

Diet is not as a rule the important question in pneumonia that it is in enteric fever. The patient should be allowed to eat whatever food he fancies provided it is adequate in quantity and does not upset his digestion, but generally he has no appetite. If he will take two pints of milk or its equivalent in twenty-four hours he will not starve. The disease lasts so short a time that in well-nourished adults there is no necessity to force food upon an unwilling and often flatulent stomach. Young children who refuse to eat must be fed at regular intervals through a nasal tube. Elderly and weakly patients also require considerable quantities of nourishment, which is generally best given in small quantities at frequent intervals. If the patient fancies solid food and can digest it, there is no reason why he should not have it. Many patients with flatulent indigestion do better on a dry than on a liquid

diet. The shortage of sodium chloride in the diet should be corrected if possible. If the urine gives little or no precipitate with a solution of silver nitrate, salt should be added to the food. It may be given in beef-tea; but in most cases the quickest and best way to supply the want without increasing thirst is to give a few rectal injections of salt and water, of the strength of two drams to the pint.

The thirst, the parched tongue, the fever, the scanty and concentrated urine, and the hot and dry skin all call for drink. The patient should be allowed to take as much fluid as he pleases, and should be urged to take from three to five pints a day in addition to his food.

With regard to drugs it is advisable to give a purge at the beginning of an acute disease; it helps to cure the headache, the loss of appetite, and the flatulence. Alcohol should not be given unless required by some special indication. It aids appetite and digestion; and to patients accustomed to it, small quantities of brandy or whisky may be given from the onset with this object in view. A mixture may be necessary in order to satisfy the patient and his friends; and the most generally useful is an acid and bitter mixture containing dilute nitro-hydrochloric acid with strychnine and quinine, because these drugs aid appetite and digestion. A simple diaphoretic mixture is harmless, but useless; because the nervous mechanism which controls sweating is far too upset to respond to it. Expectorants are unnecessary, because the alveoli and not the bronchial tubes are affected. The cough is not as a rule troublesome; and, if it is, the discomfort is due to pleuritic pain. An empty condition of the bronchial tubes, procured by coughing, should always be encouraged, unless severe haemoptysis has taken place.

The pain in the side can usually be relieved by hot or cold poultices, by counter-irritation, or by leeches; the patient should be allowed to choose whichever makes him most comfortable; and if he prefers to be without, he may. The pain is referred to the skin; and we can swamp or inhibit this sensation of pain by starting other sensory impulses from the same area of skin. The removal of pain by poultices or counter-irritation is no more curative of the inflammation which causes it, than is relief of pain by an injection of morphine. The notion that the course of an acute infective inflammation in the alveoli, can be modified by doing something to the skin of the chest, is pathologically untrue and physiologically impossible. Even the much-abused nervous system cannot be invoked as a means of communication between the skin and the pulmonary blood-vessels; because the latter are not under the direct control of the vasomotor system.

H. P. P.-S.
A. P. B.

Bacterial Therapy.—The bacteriological therapy of pneumonia has hitherto proceeded along two distinct lines, namely, serum treatment and vaccine treatment. Many of the earliest students of the life-history of the pneumococcus—the Klemperer brothers, Foà and Carbone, and in this country, Washbourn—shewed that the blood-serum of immunised animals

protected other animals from the effects of pneumococcal inoculations, if injected simultaneously or even subsequently. Washbourn, early in 1897 immunised the horse, and about the same time Pane immunised the donkey and the goat, in order to obtain potent serums for the treatment of pneumonia and pneumococcic infections in man. Such serums, however, have never been really extensively tested in this country, and therefore no very definite opinion can be expressed as to their value. In a small series of six cases of pneumonia Washbourn considered that the serum exerted a powerful and beneficial effect upon the temperature and upon the pulse- and respiration-rates in three; in one case it appeared to have no effect whatever, and in another it was powerless to avert the fatal issue; the dosage he recommended was 20 c.c. twice daily until the temperature falls to and remains at the normal. Pane, in reporting 29 cases with two deaths and a further series of nine severe cases of epidemic pneumonia (in Naples) with one death, insists on the rapid improvement that follows the injection of serum.

Antipneumococcic serum, however, has not achieved results in lobar pneumonia in any way comparable to those obtained in the serum treatment of diphtheria, and it has never gained the confidence of the physician, whilst in chronic and suppurative pneumococcal infections the serum is quite useless. There are many reasons for its failure; in the first place, the pneumococcus elaborates but very feeble toxins *in vitro*, and the serum which is obtained from immunised animals is antibacterial only; hence it would appear probable that its administration would only be effective during the very early stages of infection, or in cases of pneumococcic septicaemia. But the symptoms in man do not appear and the diagnosis cannot be made until the pneumococcus has obtained a firm foothold; consequently to be of value a very powerful bactericidal serum is needed. Unfortunately such is not available, for, experimentally, serum with the capacity to protect against some 300 minimal lethal doses per cubic centimetre of serum is the most potent at present prepared. Many of the symptoms observed in pneumonia are, moreover, often those of profound toxaemia, and in such circumstances a purely bactericidal serum would appear to possess very little therapeutic value; against this must be set the statement of Pane that though his antipneumococcic serum is bactericidal, it does not act directly upon the pneumococcus itself, but produces its beneficial effects by establishing a true active immunity. Then again, Washbourn and I shewed that varieties exist among strains of pneumococci which can only be appreciated by the failure of a particular serum to protect animals infected with them, for in testing Pane's serum we found that it protected against four out of five of these strains but was absolutely powerless against the fifth. Finally, the various brands of serum vary considerably, even in their bactericidal power, probably owing to the fact that the bleeding of the immune animal is usually carried out at a date determined by purely clinical observation, and it is just possible that if the animal's blood was examined frequently and the amount of some anti-body—say pneumococcus opsonin

—estimated and the bleeding performed when that body was present in maximum quantity, vastly superior clinical results might follow the administration of such serum.

Turning now to the other phase of bacterial therapy, the employment of "killed cultivations" or "vaccins" in the treatment of pneumonia, a considerable measure of success is obtained, and in order to appreciate the rationale of the method it is necessary to refer to the behaviour of the infected individual towards the pneumococcus so far as relates to the elaboration within his blood of those anti-substances which Sir A. E. Wright has designated opsonins. My observations in this connexion, which fully confirm those of Dr. Macdonald, shew that the resistance of the individual,

CHART 2.—The Opsonin-index in pneumococcic infections: three leading types.

so far as can be measured by the movements of his "pneumococcus" opsonin-index, conforms to one of three main classes which are represented by the three curves in Chart 2. Two of these curves are compiled from estimations carried out in connexion with two clinical forms of lobar pneumonia, namely, that in which crisis takes place and that which recovers by lysis, in order to contrast them with the curve obtained in the acutely septicaemic form (see also Chart 4) which in the instance selected terminated in death. In the third, represented by the dotted curve, the process by which opsonins are elaborated is completely paralysed, as a result possibly of an extremely heavy dose of infective material, of infection by an extremely virulent pneumococcus, or of infection directed originally towards the blood stream, or more probably of a combination of all of these factors. In the second (continuous

line) the production of pneumococcus opsonin is temporarily suspended, perhaps owing to the existence of, say, any two of the factors just enumerated, but after a time recovery of tone takes place, production of opsonin goes on in excess of expenditure, and, finally, sufficient opsonin is produced and thrown out into the circulation to ensure the defeat of the invader. Incidentally it may be mentioned that this type of case is most frequently the one in which the pneumonia is associated with some suppurative lesion. In the first (thick continuous line) the immunising machinery promptly responds to the call made upon it, at once elaborates

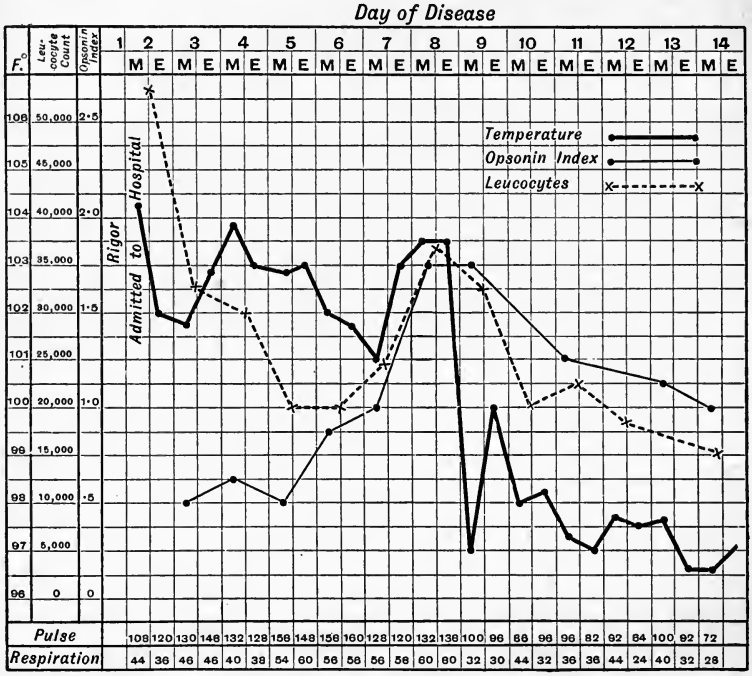

CHART 3.—Case of pneumonia terminating by crisis.

opsonin in excess, with the result that the pneumococcus is rapidly destroyed, the pyrexia terminates by crisis on the seventh to eleventh day, and recovery takes place. Occasionally, be it noted, this type of curve after returning to the normal suffers a further fall, and some few pneumococci remaining in some far distant spot, in an almost moribund condition, take on a fresh lease of life, and some small localised suppuration results. In such circumstances the opsonin curve would be expressed by tacking the beginning of the second curve in the chart on to the end of the first. In other words, in the third instance the immunising machinery is badly overstrained, in the second understrained, and in the first severely but not unduly strained.

The first curve in Chart 2 represents then the movements of the pneumococcus opsonin-index in a case of lobar pneumonia undergoing the natural process of cure, but the actual sequence of events is more readily appreciated by a study of Chart 3, in which the opsonin-index curve is plotted on the patient's temperature chart. From this it will be seen that a marked rise in available opsonin precedes the crisis by some hours, and so constant a feature is this in uncomplicated cases, that having noted this rise in the opsonin content of the serum we can foretell the occurrence of the crisis and almost fix the hour at which the temperature will

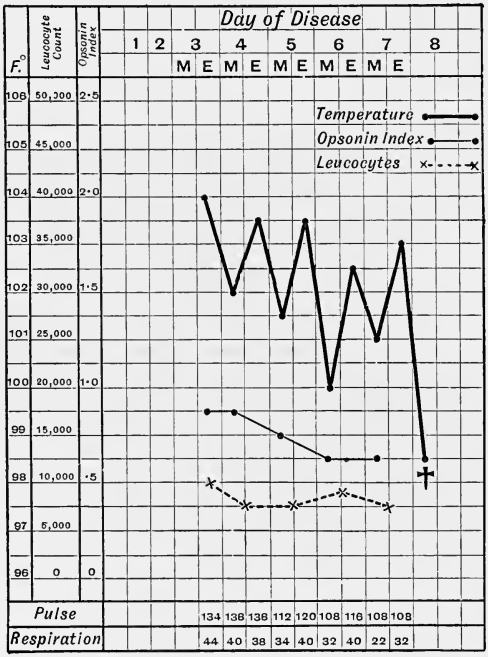

CHART 4.—Fatal case of pneumococcic septicaemia.

suddenly fall. I have elsewhere insisted on the rule that a considerable leucocytosis precedes the appearance of a large amount of available pneumococcus opsonin in the serum, and that when this leucocytosis does not occur, opsonin is deficient in quantity; and in this and the following chart the leucocyte count has also been plotted to shew its suggestive relationship to the opsonin curve. In Chart 4, which refers to a fatal case, it is seen that a gradual uninterrupted fall in the opsonin-index proclaims the gravity of the case. By contrasting and comparing these two charts we arrive at the main principle underlying the treatment by vaccin, namely, the necessity for the stimulation of the opsonin-elaborating machinery in order to provide a larger supply of available pneumococcus opsonin. With the methods of estimating the opsonin-index and

the preparation of the vaccin we are not at the moment concerned, though it must be noted that the results obtained by employing a vaccin prepared from the actual pneumococcus responsible for the infection are far superior to those following the use of a "stock" vaccin. Here it will be sufficient to say that an initial dose varying in size, according to the age and physique of the patient and the severity of the infection, from five millions to twenty-five millions of pneumococci should be injected subcutaneously at the earliest possible moment, and the effect upon the index carefully watched. As soon as the positive phase is well established, usually from thirty-six to forty-eight hours after the first injection, a second dose of two, three, four, or five times the size of the first should be administered. By this means the marked rise in available opsonin that naturally precedes the crisis, and the consequent fall in temperature and disappearance of physical signs, may be considerably antedated, and the process of cure correspondingly hastened.

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Treatment of Special Symptoms.—*Pyrexia.*—The rise of temperature is caused by the toxaemia, and is part of the inflammatory reaction of the body. It may be so high as to be dangerous to the life of protoplasm; it may be so low as to indicate that the protoplasm is moribund. Both of these conditions call for active and energetic treatment. But in the present state of our knowledge there is no evidence that a patient is better for systematic reduction of moderate pyrexia, or even as well off as when left alone. The benefits obtained by the cold-bath treatment of enteric and other fevers are largely independent of the reduction of the pyrexia.

In pneumonia the pyrexia is often too high and sometimes too low. The exact temperature at which interference is demanded is not the same in all cases. In deciding that a given temperature is too high or too low, the constitutional disturbance and course of the temperature, as well as the actual height of the pyrexia, must be considered. As has been

pointed out, a temperature of 104° F. may indicate either a vigorous reaction or an excessive dose of toxin; it is satisfactory in the one case and ominous in the other. In an adult, speaking generally, a temperature continuously over 103° F. should be reduced periodically. Sudden hyperpyrexia, 105° F. or more, is not infrequent in very severe cases in robust adults, and calls for energetic treatment. Antipyretic drugs should never be used to reduce the pyrexia in pneumonia; they are inefficient except in toxic doses and their effect is transient. Temperature should always be reduced in adults by abstracting heat from their bodies by cold air or water. Cradling combined with ice-bags will often do much to keep down a continuously high temperature. If this is ineffectual, or the temperature begins to rise suddenly, more drastic measures are necessary, such as a cold bath or pack, frequent sponging with ice-cold water, or rubbing with ice. In children and elderly patients the cooling process must be performed with caution and watched most carefully; tepid sponging combined with cradling will generally suffice. Infants may be given a hot bath and then wrapped without drying in hot blankets and left to sweat.

The temperature is not infrequently too low in aged, weakly, or alcoholic patients, who are slowly succumbing to pneumonia. The want of pyrexia is due to the severe toxaemia; and as their cells become poisoned and lose their functional activity the prospect of their manufacturing immunising substances becomes more and more remote. If we can artificially raise the temperature of such patients, we increase the functional activity of their protoplasm and the chance of recovery. With this object in view the rate at which heat is lost to the body through the skin must be reduced, and the tissues must be provided with readily oxidisable food. The limbs should be wrapped up in cotton wool, hot water-bottles placed about the body, the temperature of the room raised, and more bed-clothes given. The two food-stuffs which should be added to whatever nourishment the patient is able to take are alcohol and dextrose; because both are absorbed without previous digestion, and are utilised by the tissues in the form in which they are absorbed. Dextrose is best given by continuous rectal infusion of a 10-20 per cent solution in water kept at a temperature of not less than 100° F. When using alcohol in large doses, it must be remembered that it is an antipyretic; it dilates the cutaneous blood-vessels and increases the rate at which heat is lost from the body. In patients, whose temperature is already too low, this effect of alcohol must be counteracted by hot bottles and additional coverings to the body.

Cardiac and circulatory failure call for active treatment more often than any other symptoms in pneumonia. A moderate increase of pulse-rate is part of the general reaction to infection, and is of value, because it brings about a more rapid circulation of blood through the tissues. Systematic attempts to reduce the pulse-rate, when the heart is not failing, are fortunately futile, otherwise they would be mischievous. When, however, the pulse-rate begins to rise still further, because the

heart is failing, the physician should step in early and energetically. Failure of both sides of the heart may be considered first, although it is less frequent than that of the right side alone. The failure is due either to the toxaemia acting upon muscle previously healthy or diseased, or to an acute inflammation of the muscle. The object of treatment is to keep up the arterial blood-pressure and therefore the circulation, by acting upon the heart, the peripheral resistance, or upon both. The means at our disposal are three, namely, drugs, baths, and cold applied to the surface of the body. Digitalis, strophanthus, and squill have far less good effects upon poisoned or diseased muscle than they have upon tired, overstretched, but otherwise healthy muscle. Nevertheless they are of some value in pneumonia. The best preparations are physiologically standardised tinctures; those in the present pharmacopoeia are of uncertain strength and therefore unreliable. Digitalis is the most valuable of the three drugs; but it is also the most likely to irritate the stomach and to produce toxic symptoms. It should be given well diluted with water; and when used in full doses, its effect upon the pulse must be most carefully watched; otherwise, with a pulse already rapid or irregular, the onset of toxic symptoms may be easily overlooked. Digitoxin and digitalin are potent when active, but very uncertain in their activity. Strychnine is a valuable drug; it acts upon the peripheral resistance through the vasomotor centre, and has but little direct effect upon the heart itself. It must be given subcutaneously and in ample doses, which may have to be increased as the patient becomes accustomed to the drug. An adult may begin with 5 minims of the official liquor every six, four, or two hours. The largest dose which we have given to an adult is 15 minims of the liquor strychninae every two hours for a fortnight. If the patient's fingers begin to twitch slightly the drug should be stopped for a few hours. Its administration must never be stopped suddenly and completely if large doses have been given, because if it is, severe diarrhoea sets in. Adrenalin chloride is a still more potent drug, and is, in fact, by far the most powerful circulatory stimulant which we possess. It acts upon the heart and the systemic arterioles. It is not absorbed when given by the mouth, excepting in cases of Addison's disease. It must therefore be administered either intravenously or subcutaneously. Theoretically it is not absorbed from the subcutaneous tissues; but in man small vessels are pricked by the needle, and a subcutaneous injection scarcely ever fails to act. The effect of a single injection is obvious within five minutes, and has disappeared in less than an hour. The dose for an adult is 20 to 30 minims of a one in a thousand solution given subcutaneously every hour. The injections may be repeated for twenty-four hours, but not for longer, because they are liable to lead to the production of necrotic areas in the liver. Injections always produce a transient glycosuria.

Many other drugs have been recommended and may be mentioned briefly. Alcohol and ether have no stimulatory action either on the heart or circulation. Alcohol may, it is true, slow the pulse; but this

is due entirely to its hypnotic action in reducing delirium. Musk is almost prohibitive in price and most uncertain in action. Injections of camphor are in our experience most disappointing or useless. The administration of calcium salts has been recommended. It is well known that the perfusion of blood, enriched with calcium salts, exerts a digitalis-like action upon the heart; but there is no evidence that the administration of calcium salts by the mouth to a patient who is not suffering from any deficiency of them, will raise the percentage of these salts in the blood and exert any action upon the heart.

A bath helps the circulation, because the hydrostatic effect of the water aids the venous return. And when the stimulating action of cold is added to this, we have an explanation of the value of cold baths in fevers. Cold applied to the skin stimulates sensory nerve-endings, and is one of the most powerful stimulants to the circulation, the respiratory centre, and the cerebrum, which we possess. When a pneumonic patient with a high temperature and failing circulation is livid and delirious, no therapeutic measure is comparable to the use of cold water or ice. A somewhat similar effect can be produced in young children by the use of a hot mustard bath.

Right-sided cardiac failure, associated with orthopnoea, laboured breathing, cyanosis, and contracted pupils, is the cardiac condition which most frequently calls for treatment. So far as drugs and baths are concerned, the treatment is on the lines which have just been considered. There are two measures, however, which are especially indicated when engorgement of the right heart and cyanosis are present. Venesection is of the greatest value in such cases. It is not applicable to children and aged patients; but in full-blooded and robust adults its usefulness cannot be overestimated. Ten to twenty ounces of blood should be withdrawn from the arm as rapidly as possible. Venesection should be performed directly the symptoms of right-sided failure become obvious; and if the case is suitable it is seldom necessary to repeat it. The second measure is the use of oxygen. It should be used in a severe case as soon as ever lividity appears, and long before the patient is deeply cyanosed, with contracted pupils, a clammy skin, and deficient respiratory effort and cough. It should be continued until the patient is of a good colour, and repeated as often as is necessary to maintain that colour. It is best given through an inverted glass filtering funnel (*vide* p. 28). Some patients object strongly to the noise, dryness, and coldness of the gas, and to the sense of suffocation which they think that they suffer from having something held close to their faces. The dryness and coldness of the gas may be obviated by passing it through a Woulfe's bottle containing hot water. In a serious case its use should be insisted upon, except when the patient is trying to get to sleep; and if sufficient of the gas is given, most patients feel the benefit which they derive from it.

Respiratory Failure.—Many patients appear to die of failure of the respiratory and cough centres quite as much as from failure of the

heart. In spite of the toxaemia, the less efficient circulation, and the less well oxygenated blood, the respiratory centre is called upon to perform very great exertions. The respiratory movements are not only rapid but forcible; and the bronchial tubes have to be emptied by coughing. It is of vital importance to the patient that these two centres should be kept alive to do what is demanded of them. The means at our disposal are those which improve the circulation, oxygenate the blood, and stimulate the centres. The stimulating action of cold has already been mentioned, and of drugs atropine and strychnine are the best. Atropine has the great advantage that it helps to dry up the bronchial secretions and so to keep the tubes clear. It is especially indicated when cough is deficient and the secretions accumulating. Ammonium carbonate might be useful as a respiratory stimulant if it were not also an expectorant and emetic.

Expectorants are never required unless pneumonia has supervened on bronchitis; in this case ammonium carbonate may be used cautiously, so as neither to upset the stomach nor to make the bronchial secretion too abundant. When bronchitis has supervened on pneumonia expectorants are dangerous. Such patients are always in danger of suffocation; and to give expectorants is only to help to drown the patient in his own secretions. A timely emetic may be of value; but it must be given early, and before the vomiting centre is too depressed to respond. Not infrequently the emetic is given too late, when even large doses fail to excite vomiting, and the patient's condition is then uncomfortable to himself and embarrassing to the physician.

Sleeplessness is always a difficult symptom to deal with successfully. In mild cases with a high temperature, tepid sponging or a bath may relieve the patient's restlessness and give him some hours of refreshing sleep. In others sleeplessness is due chiefly to the pleuritic pain, which may be treated by local applications or even by opium. But in severe cases the sleeplessness is of complex origin, and when long continued becomes a serious feature which must be dealt with. In some cases it seems to be associated with cardiac failure; and we find that venesection or a prolonged administration of oxygen together with cardiac stimulants may induce sleep. In other cases the mental excitement is such that sleep is impossible without the use of some hypnotic drug. Alcohol is an excellent hypnotic in some patients; it reduces their mental excitement and therefore the pulse-rate. Sometimes, however, it has an exactly opposite effect; the excitement is increased and the pulse-rate goes up. Of other hypnotic drugs, veronal combines efficiency with safety more nearly than any other; paraldehyde and chloralamide are both safe, but the former is unpleasant, and the latter uncertain. Chloral is efficient, but it must be given with caution when the heart is failing. In some cases, however, the general distress and discomfort are so great that no drug but opium will produce sleep. Though opium and its alkaloids are not excreted by the kidneys in appreciable quantities, they are not necessarily dangerous either in albuminuria or nephritis; but they may

be very dangerous when the exertions of the respiratory pump are an essential part of the circulation. The cases of pneumonia which call for opium as a hypnotic are nearly always accompanied by cardiac failure; and the greater the circulatory failure, the more questionable is the use of opium. Nevertheless we are occasionally forced to use it as the lesser evil; and provided that the risk is appreciated, the danger is slight. In a doubtful case opium or morphine should be combined with atropine; and the nurse should be instructed to watch the patient at frequent intervals, and to report at once any increase of lividity or slowing of the respirations.

Delirium.—If a patient is alcoholic, it is wise to begin the administration of alcohol from the first, and to increase the dose should he shew signs of becoming delirious. An injection of apomorphine, gr. $\frac{1}{30}$, has been strongly recommended for the treatment of delirium in an alcoholic patient; but we have not had any experience of its use. In other patients delirium is best treated by cold baths or packs, together with alcohol and cardiac stimulants.

In the treatment of *convalescence* from pneumonia there is fortunately little to discuss. Like typhus, and in striking contrast to enteric and scarlet fever, pneumonia is a disease which either kills the patient or leaves him much as he was before. As soon as the temperature falls, alcohol and other medicines should be omitted or greatly reduced. Sleep should be encouraged, and food given in accordance with the patient's returning appetite. The state of the heart is the only condition which at all frequently makes us forbid the patient to get up as soon as he feels strong enough to do so.

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CHRONIC INTERSTITIAL PNEUMONIA

SYNONYMS.—*Chronic Pneumonia; Pulmonary Cirrhosis; Fibroid Lung.*

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THIS name is given to a clinical group of cases of long duration and of different causation in which the place of the lung tissue is taken to a greater or lesser extent by fibrous tissue, and in which the changes are sufficiently extensive to give rise to a definite set of physical signs and symptoms.

It is true, as Dr. S. West points out, that "chronic pneumonia" and "interstitial pneumonia" are not convertible terms, the one being descriptive of a clinical condition and the other of a pathological state. "Pulmonary cirrhosis" is not more defensible, and of all the various synonyms "fibroid lung" is perhaps the least objectionable in many ways. Nevertheless, the combined title of "chronic interstitial pneu-

monia" is in common use, and its clinical significance is generally understood; it is on these grounds alone that the name can be defended, and on which it is retained here. The name "fibroid phthisis," also employed as an equivalent title by some writers, is ambiguous, and indeed many of the earlier cases recorded by Andral, Corrigan, Addison, and Sir Andrew Clark were undoubtedly tuberculous. Inasmuch as the designation pulmonary phthisis at the present time implies a tuberculous affection of the lung, in whatever form it may appear, it should only be used to describe a disease which is due to infection by the tubercle bacillus.

The cases included in the category of chronic interstitial pneumonia are those following bronchopneumonia, pleurisy, very rarely lobar pneumonia, pneumoconiosis, and syphilis, among other causes.

Nothing more clearly indicates that this disease is only a clinical group than that two of the conditions referred to, namely, syphilis of the lung and pneumoconiosis, are described in separate articles; it is probable that in process of time this group will be still further depleted as its various etiological factors become differentiated. Again, the varieties of the disease cannot be any more strictly limited or defined than can its title. From the pathological standpoint there may be a local or a more diffuse change; it is, however, only the diffuse change which concerns us here, and which is rendered easier of recognition during life owing to the unilateral distribution of the lesion in the majority of cases.

Since this condition is chiefly a clinical one, the boundaries of which are as yet somewhat imperfectly defined both in its origin and in its pathological connexions, the most practical method of classifying the various groups appears to be to arrange them according to their cause; this plan is therefore adopted in this article.

Etiology.—(1) *Acute Lobar Pneumonia*, and (2) *Primary Chronic Interstitial Pneumonia.*—Most modern writers agree that although chronic pneumonia may supervene on an acute lobar pneumonia, this is a very rare sequence of events. When a patient recovers from an acute pneumonia the process is, as a rule, complete; though occasionally, in debilitated or alcoholic subjects, resolution may be long delayed. Although circumstances which interfere with convalescence, such as a relapse or serious disease of other organs, may give the disease a chronic character, yet, as Wilson Fox says, cases in which a tardy, but progressive, improvement takes place cannot properly be spoken of as chronic pneumonia.

Addison described as results of acute pneumonia conditions which he named "uniform albuminous induration" and "grey induration." Charcot, in his monograph on pneumonia, gives an account of a patient who died four months after the onset of an acute attack, in whom the symptoms and physical signs persisted, and at whose autopsy the affected lung was the seat of grey fibroid induration throughout, whilst the other lung, although enlarged, was free from disease. This case he regarded as one following an acute pneumonia. In the Guy's Hospital series of cases, referred to later, there is no case which can be classed as undoubtedly

belonging to this group. Wilks and Moxon, in discussing the origin of chronic lobar pneumonia, refer to the cases in which, after an illness of a few weeks, the patient dies and the lung is found uniformly albuminised, as Addison termed it. They admit that, although rare, there is a true chronic pneumonia, as described by Charcot, due to inflammation of, and exudation into, the alveoli; but it is rather significant that, with their wide experience of work in the post-mortem room, they do not refer to any individual case. Thus, although we must admit that a chronic lobar pneumonia may follow the acute form, the rarity of this sequence of events is extreme, and indeed in Charcot's case it is almost impossible to deny the pre-existence of chronic disease, upon which a more or less acute inflammatory process had supervened. The same remarks apply to cases, such as those reported by Dr. Coupland and by Dr. Auld, in which the onset, the course, and the symptoms differed materially from those of the classical acute pneumonia and so give considerable support to the opinion that this group of cases of chronic pneumonia is really a special form of pneumonia distinct from the acute form, and due to a slowly progressive subacute fibrosis of the lung. Dr. P. Kidd in writing on "subacute indurative pneumonia" supports this conclusion by two cases, and refers to Heitler as one of those who deserves most credit for differentiating this disease from acute lobar pneumonia. An excellent case belonging to this group was in Guy's Hospital, under the care of Sir Cooper Perry, to whom and to Mr. O. V. Payne we are much indebted.

Case 1.—Male, aet. forty-five years, was seized with a sudden pain in the left side twelve weeks before admission into hospital, followed by a cough and increasing dyspnoea. There was no history or evidence of syphilis past or present. The man was a compositor, and stated that his work was neither dusty nor did it necessitate working in a badly ventilated room. He did not smoke, and drank very little beer and no spirits. On admission his countenance was dusky, the lips and ears were cyanosed, and the respiration-rate was 44 per minute. The patient was very definite with regard to the onset of his illness, and the doctor in charge of him said that at no time, in the three months previous to the patient's admission, had there been any symptoms of an acute illness, such as lobar pneumonia. There was some impairment of the percussion note at both bases and tactile vocal fremitus was deficient; the respiratory murmur and voice-sounds were deficient at the bases and no adventitious sounds were audible. There was no organic disease elsewhere, and frequent examinations shewed that tubercle bacilli were absent from the sputum. At the end of the first month in hospital the percussion note at the right base had become resonant, but that over the left side was still impaired. The percussion note beneath the left clavicle was also impaired. During the second month cough became more prominent and the sputum more abundant in quantity. In the course of the third month the percussion note became still more impaired, but at no time was there characteristic bronchial breathing, the inspiratory murmur being harsh, as was also the expiratory murmur, which was in addition unduly prolonged. The temperature frequently rose two or three degrees above normal at night, and the respiration-rate gradually increased to 40-50 per minute. Death occurred six months from the onset of the illness, being

preceded by an attack of acute bronchitis and pleurisy. The autopsy shewed recent pleurisy with some old adhesions on both sides. The upper lobe of the left lung and the upper part of the lower lobe were slate-grey in colour, firm and tough, cutting with difficulty on account of the fibrous tissue; the lower half of the lower lobe was dark in colour, heavy, and friable. In the right lung the appearance was similar, but the change was not so far advanced. Some of the tubes in the upper lobes were slightly dilated. There were no thick septa, no cavities, and no evidence of tuberculosis. On histological examination a great increase in the fibrous tissue of the lung was found affecting the walls of the alveoli; the alveoli contained exudation products which were undergoing conversion into fibrous tissue; in some of the alveoli blood-vessels were seen springing from the walls, whilst in others the vessels were obliterated by the newly-formed fibrous tissue.

This is a good example of what one of us (J. F.) believes to be a primary chronic interstitial pneumonia; the patient had never suffered from acute pneumonia, the onset of the illness being gradual; but, as Mr. Payne points out, had there been an attack of acute lobar pneumonia, the case would have been described as a characteristic example of a chronic pneumonia following an acute attack.

Case 2.—Another case, that of a man, aet. fifty, who was in Guy's Hospital in 1900 with haemoptysis, probably belongs to this category. He had had an attack of bronchitis and pleurisy five years previously, followed by a persistent cough. Haemoptysis occurred first in 1898 and occasionally in small quantities since that year. The patient was well nourished, but somewhat cyanosed, and presented clubbing of the fingers. The temperature varied between 101° and 103° F. for five days and gradually fell to the normal; the haemoptysis, which was profuse at first, ceased in about a week. Neither tubercle bacilli nor fragments of lung tissue were found in the sputum. He was discharged after being an in-patient for a month. Two years later he was again admitted with haemoptysis. In the interval he had suffered from some cough and shortness of breath on exertion, yet on the whole his progress had been satisfactory. He was discharged a second time and attended as an out-patient until October 1906, when he was again admitted into hospital, this time with carcinoma of the pylorus which proved fatal. The physical signs in 1900 were those of bronchitis and emphysema, with probably some dilatation of bronchial tubes at the right base. In 1902, in addition to the previous signs, there was an impaired note over the upper half of the lower right lobe with rather indefinite bronchial breathing, bronchophony, and pectoriloquy, and below this the note was impaired and the respiratory murmur deficient. At the autopsy in 1906, that is, six-and-a-half years after he first came under observation, the right lung was found to be attached to the chest wall, the diaphragm, and the pericardium by old fibrous adhesions of no great thickness. The lower lobe was contracted, fibroid, and shewed some dilatation of the tubes. The left lung, with the exception of some recent hypostatic pneumonia, was free from change.

The features of this form of chronic pneumonia are throughout different from those of acute lobar pneumonia. The progress of the disease is more gradual, although it may be acute, or subacute. The symptoms

are those of irregular fever associated with dyspnoea, cough, and sometimes with rigors. There is not the sudden critical fall in temperature seen in acute pneumonia, and the physical signs are slower in appearing, less definite, and do not entirely disappear. There may be more or less blood in the sputum. The constitutional effect is less marked in the earlier stages of the disease. The duration of Heitler's cases varied from five weeks to nine months, but it is probable that, as in Case 2, the disease may become partially arrested and persist as a chronic pulmonary lesion.

In further consideration of the causation of chronic pneumonia reference will be made to the post-mortem records of Guy's Hospital for the fifty years 1857-1906. In this period 21,317 necropsies were performed, among which there are 46 cases of well-marked pulmonary fibrosis. In agreement with the limitation accorded, at the commencement of this article, to the disease in question, we have only selected well-marked cases, omitting those in which a small area of lung tissue was affected and choosing only those cases to which the name of chronic pneumonia in its clinical form could be applied. We have carefully excluded all cases of possible tuberculous or syphilitic origin; it may, however, be noted that in the period of fifty years there were eleven cases in which the condition of the lung, and the presence of associated specific lesions in other organs, pointed to syphilis as the possible cause of the pulmonary fibrosis. For much assistance in obtaining these statistics our best thanks are due to Dr. C. H. Rippmann, Medical Registrar to Guy's Hospital.

The remaining causes will be dealt with under the following heads:—(3) Cases possibly of pleuritic origin; (4) Cases originating in broncho-pneumonia; (5) Cases due to obstruction of a bronchus; (6) Cases of doubtful origin.

(3) *Pleurogenous pneumonia* connotes a pulmonary fibrosis due to invasion from the pleura. Wilson Fox was doubtful whether such a process, unaccompanied by pneumonia, could extensively invade the lung. On the other hand, Sir A. Clark, Dr. Bastian, Prof. Osler, and others hold that a primary dry pleurisy may, partly by compressing the lung, gradually lead to an interstitial fibrosis; this view is corroborated by the cases in the Guy's Hospital series, which contains in this category 12 cases with one lung and 2 cases with both lungs affected.

In these cases the condition of the pleura is very striking and quite different from that seen in any other group. The pleura is described as "obliterated and half an inch thick," as "an eighth of an inch thick with trabeculae passing into the lung," as "an eighth of an inch thick and continuous with septa of fibrous tissue traversing the lung." The extension into and invasion of the lung from the pleura are so well defined that it is hardly possible to doubt the relation between the two, though it may be impossible to prove it. In two of the cases the condition was apparently preceded by a pleural exudation, an old empyema being found in one case, whilst in the second a serous effusion had been aspirated four years before death and a

year later a rib was resected and 2½ pints of pus set free. It is noteworthy that Clark, Hadley, and Chaplin state that they could not recall a single instance of fibroid disease with a previous history of pleural effusion, and that it rarely follows on empyema. Still, rare as this sequence is, pleural effusion, when very chronic and causing collapse of the lung, must be regarded as an occasional cause. All the Guy's Hospital cases, except two, aged respectively sixteen and eighteen years, were in adults, and in most of them there was no history of any definite acute illness. When we consider how insidious the origin and course of pleurisy sometimes is, it seems possible, in view of the morbid changes present in this group of cases, that the pathology may be akin to the cases of primary chronic pneumonia mentioned on p. 255, except that the process in this case begins in the pleura instead of in the lung.

The lung is reduced in size to a greater degree in this group of cases than in any other, and from it many of the classical descriptions of chronic pneumonia have been drawn. For example, among the 14 cases above mentioned, the lung is in one described as "much reduced in size and occupied by chronic pneumonic deposit," and in another as "shrunken to a third the size of the right: consisted of cartilage-like fibrous tissue."

Sutton's conception of a general tendency to "fibroid degeneration" as an etiological factor in chronic pneumonia does not receive any support from this group of cases, inasmuch as there were no examples of fibroid changes in other viscera. Moreover, according to the Guy's series of cases, such changes are not more common in this disease than in many other chronic diseases of the heart and lungs, in which induration of the liver and kidneys, associated with some overgrowth of their interstitial tissue, frequently supervenes.

(4) *Cases following Bronchopneumonia and Bronchitis.*—In all long-standing and recurrent cases of bronchopneumonia and bronchitis, the peribronchial connective tissue becomes invaded by the inflammatory exudation, and the intra-alveolar exudation products, as well as those around the bronchioles, may become organised and converted into fibrous tissue to such an extent as to produce a chronic interstitial pneumonia. Further, in these cases bronchial dilatation is common, and the pneumonic changes may be secondary to the bronchiectasis. Inasmuch as pulmonary fibrosis also may give rise to dilatation of the bronchi, the two conditions, bronchiectasis and pulmonary fibrosis, may co-operate and mutually act as cause or effect. Clark, Hadley, and Chaplin confirm the views of other observers that bronchopneumonia is a frequent antecedent of pulmonary fibrosis, especially in early life, and they state that the great preponderance of this cause over all others is only met with in cases which have begun in early life. The importance of this disease as a cause of chronic pneumonia in early life is well shewn by the cases in the Guy's Hospital series; out of the total 46 cases there were 10 cases of unilateral fibrosis following bronchopneumonia, and 4 cases in which both lungs were implicated. Measles and whooping-cough are the diseases which preceded

the bronchopneumonia in most of the cases, and on referring to the ages of the patients it is seen that, with one exception, they occurred in early life; 8 of the cases being under five years of age, and the others six, seven, ten, twelve, seventeen, and twenty-seven years respectively.

In this group, although the pleura is involved, it is much less so than in the previous group, being either "a little thickened" or "presenting old adhesions." The lung, on the other hand, is described as firm, tough, and shrunken, and usually there was a more or less widespread infiltration which, in the cases examined microscopically, was found to be both interstitial and alveolar in distribution. This group of cases is well illustrated by the case of a boy aged ten years whose case was reported by one of us (J. F.) in 1900 (13). Six years before admission into Guy's Hospital he had suffered from measles and whooping-cough. During his last year of life he had four acute attacks of bronchopneumonia, in each of which he was an in-patient in the hospital, the last one leading to his death. The autopsy shewed a diffuse peribronchial and perivascular fibrous change in the lungs, and also alveolar fibrosis and some thickening of the pleura.

As a cause in adults bronchopneumonia is practically non-existent, for relapsing bronchopneumonia, apart from the forms due to a specific cause, such as the tubercle bacillus or to the irritation due to the inhalation of particles of dust, as in the cases of pneumoconiosis, does not occur.

In cases due to affections of the bronchi occurring in later life, a prolonged chronic bronchitis is the chief cause, and these cases come mostly under the group of the pneumoconioses.

(5) *Cases due to Compression or Occlusion of a Bronchus.*—The 7 cases in the Guy's Hospital series due to this cause were all unilateral, and resulted from either an aneurysm of the aorta or a malignant growth. Most writers do not lay much stress upon obstruction of a bronchus as an important cause in the etiology of chronic pneumonia, but that it is so, is proved by its presence in 7 out of the 46 cases from the Guy's Hospital records, or in 15 per cent. This cause must, therefore, be borne in mind as one of practical importance, if only for the reason that the origin of the physical signs in the affected lung in this group of cases is so often overlooked. Even with skiagraphy as an aid to diagnosis, it is possible that a small saccular aneurysm of the descending thoracic aorta invading a bronchus may still remain undiscovered until it ruptures or until it is discovered at the autopsy.

The pleura is mentioned as being thickened or presenting adhesions in 5 of the cases. The fibrosis in the lung was situated below the site of the obstructed bronchus, and in all the cases the lower lobe was the seat of disease. The fibroid change in the collapsed portion of the lung was well developed, and the lung is variously described in the reports as being "densely fibroid" or as being "infiltrated with fibrous tissue."

(6) *Cases of Doubtful Origin.*—In the Guy's Hospital series of cases there were 11 cases in which the cause of the pulmonary fibrosis was doubtful, one lung being affected in 5, and both lungs in 6 cases.

Although, as already seen, the active etiological factor can be determined in a considerable proportion of the cases, the difficulty of deciding this in every instance is quite comprehensible when it is remembered how chronic the disease may be and how imperfect is the previous history of many of the patients. It is possible that some of these so-called doubtful cases should be included in the group of primary chronic interstitial pneumonia, and the post-mortem appearances lend some support to this view, but it is impossible to decide from pathological examination alone.

The pleura was affected in all the cases in which one lung was affected, but not to any great extent; the lung, on the other hand, is described as being contracted and fibroid, and in the cases in which both lungs were implicated the appearances were for the most part very similar.

Morbid Anatomy and Histology.—The disease is commonly confined to one lung; out of the 46 cases from Guy's Hospital there were 34 cases in which one lung was involved, and 12 in which both were affected, a somewhat greater proportion than usual of the group of bilateral cases.

The morbid process may start in the pleura, in the interlobular connective-tissue, around the blood-vessels or the bronchi, or in the alveoli, or in two or more of these situations simultaneously; thus, the process is by no means limited to the interstitial tissue of the lung, and therefore, even from a pathological point of view, the term "interstitial pneumonia" does not correctly describe this disease.

In some cases, especially those of the pleurogenous group, the pleura is very dense and thick, often half an inch or more in thickness, and so firmly adherent to the lung and chest wall that the lung can only be removed by cutting it out of the thorax. Septa from the thickened pleura may be seen extending into, and branching in, the subjacent lung tissue. In the other groups of cases the pleura is also affected and may be thickened to some extent, or may present old fibrous adhesions.

The lung is, in most cases, much reduced in size, sometimes lying, a mere fibrous relic, at the back of the thorax against the spinal column. When part only of the lung is involved, such as the base or the lower lobe, the upper lobe may shew compensatory hypertrophy. In cases in which the chronic pneumonia is consecutive to bronchopneumonia or is a primary chronic interstitial pneumonia, the reduction in size is generally not so great; for example, from the Guy's series such a lung is described as "firmer and smaller than normal, fibroid," but not as "much contracted" and "permeated with fibrous tissue" as is the description in one of the pleurogenous cases. The lung is extremely firm, tough, and more or less airless. The new fibrous tissue is white and dense, cutting like gristle; in some cases it is distributed in broad septa with narrower bands branching out from the main ones; in others the lung tissue is permeated by a fine fibrous network which gives it a marbled appearance. The pulmonary tissue itself is darker than in the healthy parts of the lung, and varies from a slate-colour to an almost black tint.

The bronchi are frequently dilated and their walls thickened: so common is this result that it is mentioned as present in 31 out of the 46

cases in the Guy's Hospital series; ulceration of the lining membrane of the bronchi occasionally occurs; in some the bronchi are dilated so as to form cavities, whilst in other cases the cavity formation is the result of a gangrenous process. The branches of the pulmonary artery within the lung may be thickened and dilated.

The structures of the mediastinum, in cases of unilateral fibrosis, are often drawn over towards the affected side, and the corresponding side of the thorax may be deformed and sunken and the shoulder depressed. The healthy lung is generally enlarged and emphysematous.

Dr. P. Kidd describes the histological appearances somewhat as follows:—There is a growth of the connective tissue of the lung which takes the place of the normal vesicular structure. Groups of small round cells may be found in the neighbourhood of the fibrous areas. The alveoli may be collapsed and present thickenings of their walls, and branches of dilated capillaries are often seen in large numbers, especially in the walls of the smaller bronchi. In the earlier stages of the disease the fibro-cellular thickening of the alveolar walls may cause compression of the pulmonary vesicles; a similar fibrous hyperplasia is commonly seen in the interlobular and peribronchial tissue. In the alveoli collections of large epithelial cells and leucocytes may exist, or an intra-alveolar fibrosis is present as the result of organisation of the inflammatory exudation and an ingrowth of granulation tissue.

In the cases originating in a bronchopneumonia the same peribronchial, perivascular, and alveolar fibrosis is often found, whilst in other cases the fibrosis implicates chiefly the interalveolar and interlobular tissue, or the pleura and its interlobular processes. Marchand believes that the thickening of the pleura disposes to the fibrosis. He points out that the pleural adhesions give greater rest to the lung, whilst the air entry is lessened and the blood supply is increased, owing to the freer communication between the pulmonary and systemic circuits. The framework of the pleura and of the lungs being continuous, the nutrition of each is readily influenced by any poison which, perhaps acting upon one part only in the first place, ultimately spreads and produces fibrotic change in other parts.

Age and Sex.—To some extent the *age* at which the disease is found depends upon the cause. In the Guy's Hospital series of 46 cases the ages at death were as follows:—

Ages at Death.	No. of Cases.
0 to 10 years	12
11 „ 20 „	4
21 „ 30 „	5
31 „ 40 „	8
41 „ 50 „	6
51 „ 60 „	5
61 „ 70 „	6
	46 cases.

Thus, out of these 46 patients, 35, or 76 per cent, died before reaching the age of fifty years, and 29 patients, or 63 per cent, before forty years. Although comparatively small, these figures confirm the statements of previous observers, such as Wilson Fox, to the effect that chronic pneumonia materially shortens life, even though some patients may live till sixty to seventy years of age. On investigating the causes of death in those who succumbed between sixty to seventy years, it is found that two of them were cases of pulmonary fibrosis secondary to a malignant growth occluding the bronchus, and that in a third, the patient, aged seventy years, died as the result of an accident. Thus the percentage of deaths directly due to the disease at the earlier ages is probably even higher than is stated above. Again, the fatality of the disease in children is evidenced by a fatal issue in 12 cases, or 25 per cent, within the first ten years. Clark, Hadley, and Chaplin give the average duration of their 45 cases as 11·87 years, but point out that if all these cases were followed to their termination the average would be far longer. Wilson Fox, in his series of cases, found that nearly two-thirds died before attaining forty years of age.

Sex.—The disease is more often seen in men than in women: in the Guy's Hospital series there were 39 males and 7 females.

Symptoms and Physical Signs.—The three prominent *symptoms* are cough, dyspnoea, and expectoration. These symptoms vary considerably according to the extent of the lesion, which, if extreme, may be associated with great dyspnoea and cyanosis. In most cases the patient readily becomes short of breath on exertion. The cough is frequently paroxysmal, especially if bronchiectasis is present, when expectoration may be abundant, and the sputum may become foul as the result of a bacterial infection of the secretion retained in the tubes. Haemoptysis sometimes occurs, either in considerable quantity or merely as streaks of blood in the sputum. Dr. Bastian found that there had been haemoptysis in more than half the cases in his series.

Epistaxis takes place occasionally after severe bouts of coughing. There is often no pyrexia, and in any case the temperature is never high except in the presence of some complication, such as septicaemia from ulceration of bronchial tubes, or in some cases belonging to the pneumonic group.

The physical signs vary according to the form and extent of the disease. In well-marked unilateral cases there may be retraction and deficient movement of the affected side, the shoulder is depressed, and the spine may be curved laterally. On percussion the note is more or less impaired, and in cases with great thickening of the pleura and shrinking of the lung the note may be quite dull. On auscultation variations in the character of the vesicular murmur are observed; the murmur is deficient or absent over some areas, or it is high-pitched or bronchial in character, with perhaps hollow or cavernous breathing in other places. Variation, again, is the characteristic feature of any adventitious sounds which may be present; for example, medium or large rales are heard, or, where

cavities or considerable bronchiectases exist, the rales have a more consonating character. Vocal fremitus differs according to the form of the disease, being in some cases increased, in others diminished; but it is seldom entirely absent, as in cases of pleurisy with effusion. The transmission of the voice-sounds, as well as the character of the vesicular murmur, may be very different in cases with great dilatation of the tubes, being diminished or increased according as the tubes are obstructed or not. The heart is displaced towards the affected side in all cases in which the lung is much contracted.

Clubbing of the fingers is occasionally met with, although, without doubt, it is mainly the consequence of the associated bronchiectasis rather than of the chronic pneumonia. In Case 2 (p. 257), clubbing of the fingers existed, and there was some dilatation of the bronchi; in another case belonging to the "pleurogenous" group there was clubbing, but no bronchiectasis. As regards the osteo-arthropathy, sometimes present in cases in which the fingers are clubbed, and most commonly seen in cases of chronic pulmonary disease, there is little doubt that sooner or later chronic pneumonia will be included in the list. But Marie's osteo-arthropathy group is a rare condition, and since his original description in 1890, there is no record, among the Guy's series, of any of the cases having been associated with changes in the bones and joints as well as clubbing of the fingers (*vide* also Vol. III. p. 64).

Duration.—In a considerable number of cases chronic interstitial pneumonia proves to be a disease of long duration. It may last for twenty years or even more, but this is exceptional. When it appears in early life the duration is much less, and also in those patients in whom the disease is extensive, especially when it is combined with bronchiectasis. In cases of the pneumonic type, whether possibly subsequent to an acute pneumonia or belonging to the primary subacute pneumonic group, the duration of life, according to most observers, is considerably less than that given above. This opinion is confirmed by the cases given in this article, and by Heitler's cases, quoted by Dr. P. Kidd, in which death occurred at periods varying from five weeks to nine months.

Complications and Results.—The Guy's Hospital series of cases presented the following complications, which fairly represent those usually met with. They may be grouped into three classes, as follows:—

(1) *Those of the Cardiovascular System.*—The most common was dilatation and hypertrophy of the right side of the heart, which in many cases led to death from cardiac failure, with dropsy and other signs of a disturbed circulation, such as tricuspid regurgitation, pulsation in the veins of the neck, and cyanosis. In one case the thickened tricuspid valve had led to tricuspid stenosis; in others there was dilatation with thickening and atheroma of the pulmonary arteries, or again ante-mortem intracardiac thrombosis.

(2) *Acute Affections of the Lung.*—A recurrent subacute, or acute, bronchitis, or bronchopneumonia, were common causes of death. Where

bronchiectasis was present with ulceration of the bronchi, a septic bronchopneumonia, or gangrene, resulted in some cases.

(3) *Other Complications.*—A cerebral abscess was present in one case of bronchiectasis. Pericarditis, simple or suppurative, was also seen. In one of the recurrent bronchopneumonic cases a suppurative pneumococcal meningitis proved fatal. Infection of the pleural cavity, causing a simple or purulent effusion, and lardaceous disease also occurred in some of the cases. Complications mentioned by other observers, in addition to the above, are various forms of septic or pyaemic infection, and acute articular lesions.

Diagnosis.—In some cases the diagnosis is easy; in others it is exceedingly difficult. One of the most important points to be borne in mind is that, as in so many other diseases, a right decision does not depend upon one or more pathognomonic signs and symptoms, but upon a wide survey of probabilities, amongst which the past history of the case and its physical signs and symptoms must be carefully considered together. The conditions which are most likely to be confounded with chronic interstitial pneumonia are :—

(1) *Chronic Pulmonary Tuberculosis.*—This disease almost always affects both lungs, the apices in particular, and other organs are likely to be invaded by the tubercle bacillus. Accordingly the presence of laryngitis and aphonia, diarrhoea, signs of tuberculosis of the testes, of the lymphatic glands, and of other organs, indicate that the disease, however chronic, is tuberculous. Chronic pneumonia, on the other hand, is frequently a unilateral and local affection. The diagnosis may be decided by the discovery of tubercle bacilli in the sputum, although in some of the very chronic tuberculous cases the specific organisms are so few in number as to require many examinations before they are found. Calmette's tuberculin ophthalmo-reaction may prove to be of value in these cases (*vide* p. 360).

(2) *Pleurisy with Effusion and Empyema.*—Next to chronic pulmonary tuberculosis an empyema is perhaps the affection which is most likely to be confounded with chronic pneumonia. The course of fibroid disease of the lung is prolonged, whereas that of pleurisy with effusion is usually acute. In most cases of pleural effusion the heart is displaced away from the affected side, but this sign cannot be invariably relied upon, as in cases of long standing some contraction of the affected side, with consequent displacement of the heart towards that side, is present. Again, considerable difficulty may arise in cases of a localised effusion; for example, a collection situated between the lobes, in which there is little displacement of the heart, some impairment of the percussion note posteriorly and bronchial breathing, or in which the note on percussion is completely dull only in the axilla or as far back as the scapula. The physical signs may then be so alike that the only means of diagnosis is by exploratory puncture; this must often be made in several places before a decision can be reached.

(3) *Compression or Occlusion of a Bronchus.* — Inasmuch as this cause

may give rise to extensive pulmonary fibrosis, and as some mediastinal tumours, in particular an aneurysm, may be so small as not to give any signs of their presence by pressure upon other organs or structures, the actual cause of the physical signs is very likely to be overlooked. The most frequent source of error in such cases is a small aneurysm of the termination of the arch or of the commencement of the descending thoracic aorta, and this possibility must therefore be remembered in any case of doubtful origin, as one which may perhaps be discoverable by *x*-ray examination of the thorax.

Again, in cases due to malignant tumours the cancerous cachexia is often very little marked, and hence, if there are no signs due to pressure upon other structures, the diagnosis is rendered very difficult.

(4) *Thickened Pleura.*—In these cases the patient's constitutional condition is good, and although the chest wall may be retracted, yet there are no signs of dilatation of the bronchi or of excavation of the lungs, and the voice-sounds are always diminished.

(5) From malignant disease of the lung (*vide* p. 509).

Prognosis.—Pulmonary cirrhosis is always a grave but rarely a hopeless condition. The forecast varies with the age of the patient and the amount of lung involved, with the duration of the disease, and, most of all, with the degree of general disturbance, as well as the presence or absence of complications such as bronchiectasis or a cardiac lesion; loss of appetite, anaemia, wasting, sweating, vomiting, or diarrhoea are unfavourable circumstances. When the patient's weight is maintained, and he eats and sleeps well, we may hope that even extensive cirrhosis of the lung may gradually lead to contraction and obliteration of cavities, and final cicatrisation of the affected parts with hypertrophy of the opposite lung. Such a complete cure is no doubt exceptional; more often the disease passes into a permanently chronic condition, and the patient dies at last from bronchitis affecting the sound lung, or from some other intercurrent affection.

Treatment.—From the nature of the case, the treatment must be tentative and expectant, following the indications of the patient rather than of the local disease. We endeavour to keep the expectoration from becoming fetid, and to check its amount, to relieve cough, particularly at night, by paregoric and other anodynes, and to hasten the process of cicatrisation by occasional counter-irritants, or by strapping the affected side with plaster. Inhalations of turpentine, thymol, terebene, or creosote are often useful in lessening the secretion and correcting fetor. At the same time, by help of mineral acids and bitters, particularly quinine and nux vomica, we try to improve the patient's appetite; with the same object we give him varied and abundant food, consulting rather his own caprice than ordinary rules of diet; if stimulants are thought desirable, by far the most useful, if the patient can bear it, is malt liquor, particularly porter.

Fibrolysin is a drug which, from its reputed success in the treatment of other forms of slowly progressive fibrosis, deserves a trial. There are

cases on record of delayed resolution of the lung after pneumonia in which injections of fibrolysin have been followed by disappearance of signs thought to be due to the development of a pulmonary fibrosis. The sources of possible fallacy in this latter type of case are obvious; and although in some cases of Dupuytren's contraction, of scars after burns, and of cicatricial stenosis of the oesophagus most favourable results have been reported, yet it should be borne in mind that against these are to be put in the scale unreported cases in which improvement has not been so apparent, and impartial consideration has left some doubt in the mind of the observer as to the benefit of the treatment.

Whenever the weather permits it, the patient should be taken out of doors. When this is impracticable, he may sit before a widely open window, warmly wrapped up, and breathing through the nostrils with the mouth persistently closed. Fresh air often proves the most powerful promoter of appetite and of sleep.

Cases of cirrhosis of the lung are greatly benefited by climatic treatment; removal from dust-laden workshops and from foggy towns to pure air is the first step to improvement, and may often cut short the disease in its early stage. A mild and equable climate, such as that afforded by the south-west coast of England and many parts of Ireland, is the best for these patients.

There is no doubt that these cases are among those that derive most benefit by spending successive winters and springs on the Riviera, at Palermo, Corfu, Cairo; or in islands like Madeira, the Canaries, or those of the Southern Pacific. If the patient's means are ample, this arrangement is the best than can be made for his advantage.

P. H. PYE-SMITH, 1898.
J. FAWCETT, 1909.

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ABSCESS

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THE definition of an abscess as a circumscribed collection of pus must be taken with some limitations in the case of the lung, as certain collections which conform to this definition are by common consent excluded from the category of abscess of the lung. These exceptions are suppuration inside dilated bronchi or in a hydatid cyst, and, though bounded by the parenchyma of the lung, the cavities arising in the ordinary course of pulmonary tuberculosis. There is not, however, any hard and fast rule, and clinically suppuration in a large dilatation of a single bronchus or as the result of rapid softening of a large tuberculous focus is spoken of as an abscess. Indeed the difficulties of fixing the boundaries or even determining the exact position of a collection of pus are sometimes so great, even during an operation, that it is probable from their situation about the line of the interlobar septa that many of the reported cases of abscess of the lung have in reality been encysted or interlobar empyemas.

Etiology.—Though the list is not exhaustive, the chief conditions which give rise to abscess of the lung are as follows:—Acute lobar pneumonia, bronchopneumonia, aspiration pneumonia; infective embolism; impaction of a foreign body in a bronchus; bronchial stenosis (pressure from without by aneurysm or growth), or narrowing of the lumen by stricture (syphilitic or malignant); bronchiectasis; tuberculosis; suppuration of a hydatid cyst; extension from suppuration outside the lung; perforation of the oesophagus from malignant disease; injury. Chronic (non-tuberculous) abscess of unknown origin is also recognised.

Injury is a rare cause, and gives rise to abscess formation chiefly or only in the case of penetrating wounds, for example by a bullet, which enable infective material to enter the lung. The abscess resulting from perforation of the oesophagus—a not uncommon accident in malignant disease—and those due to bronchial stenosis or to the presence of a foreign body should perhaps be included in the group of cases caused by aspiration. In the two latter conditions the partial closure of the bronchus is followed by dilatation of the subsidiary bronchi in the

affected area, and subsequently consolidation and abscess supervene. In *bronchiectasis* the abscess may be local as a result of ulceration of the bronchial wall, or aspiration may lead to infection of the lung at a distance. A careful search of the literature shews that *tuberculosis* rarely causes pulmonary abscess; one of the few recorded cases is Sir W. Macewen's, in which the whole left lung was converted into a vast abscess cavity, and on incision gave exit to 160 oz. of pus containing tubercle bacilli and pyogenetic organisms. Under *abscess arising from extension from without* come rupture of an empyema into the lung or of an abdominal abscess through the diaphragm. Gastric ulcer has been recorded as the cause of such an abscess, but in the great majority of these cases an abscess of liver, usually tropical, erodes the diaphragm and invades the already adherent lung. It is interesting to note that in this condition the pus, as a rule, does not contain either bile or amoebae, the dense wall of the hepatic abscess completely shutting off the liver.

The source of the *infective embolus* which leads to infarction and abscess of the lung is frequently, especially in childhood, infective thrombosis caused by chronic otitis media; a similar thrombosis, however, may occur in any part of the body and lead to a like result; and as a matter of fact a considerable proportion of the cases reported under this heading have arisen in connexion with disease of the pelvic viscera in women. Infective endocarditis is another fertile source of such emboli. In these conditions multiple abscesses of the lung are apt to form, and may be but a part of a general pyaemia. From the point of view of treatment, however, it is important to remember that multiple abscesses of the lung may occur apart from general pyaemia.

The preceding may be regarded as the rarer causes of abscess of the lung. In the majority of cases some form of pneumonia is responsible; out of Tuffier's list of 49 cases submitted to operation, 23 were metapneumonic. Although abscess is a rare event in acute lobar pneumonia (three abscesses in 253 fatal cases collected by Aufrecht), if all forms of pneumonia are included the preponderance would be still more striking than appears from Tuffier's figures, which mainly refer to true lobar pneumonia. Bronchopneumonia, and especially influenzal pneumonia (Leichtenstern), may also lead to abscess. Apart from its occurrence as a late complication of some recognised form of pneumonia, recorded cases shew that abscess often supervenes early in the course of anomalous acute lung disorders, which cannot be given an exact name, but present fever, cough, and obscure signs in the chest. Possibly these cases may go on to the chronic (non-tuberculous) abscess of obscure origin recognised by some writers, but it should be remembered that a quiet necrosis of the lung, terminating in abscess, also occurs without obvious cause, especially in the aged.

Aspiration.—Increasing attention has been paid in recent years to aspiration, in other words the inhalation of infective material from or through the mouth, as a cause of pneumonia. Under this heading are included the pneumonia supervening in the course of paralysis or

insanity, that following ether-anaesthesia or submersion, and that which complicates disease or operations in the mouth. These forms of pneumonia may all terminate in abscess of the lung. Especial interest attaches to the occurrence of aspiration-abscess in early life, and even in the new-born, to which Orth and Silbermann first drew attention. To explain the recorded cases of pulmonary abscess in the first few days of life, it has been suggested that infective material is inhaled from the vaginal secretions during birth; and, as bearing on this, Silbermann found that out of his 12 cases the mothers were septic in 10 instances. The influence of aspiration in the production of abscess of lung in perforating malignant growths of the oesophagus, and possibly in bronchial stenosis, has already been mentioned.

Bacteriology.—In the aspiration cases *Bacillus coli* and *Micrococcus tetragenus* have been found, and in one case (after submersion) *Bacillus subtilis* in pure culture (Aufrecht). In the pneumonic cases, Friedländer's pneumo-bacillus (Cohn), the pneumococcus (Zacker), and the influenza bacillus (Hitzig) respectively have been the active agents, though more often the ordinary pyogenetic organisms, streptococci and staphylococci, have been associated with them. In one case in the course of enteric fever *Diplococcus pneumoniae* was present (S. Phillips). Four cases, and four only, of primary amoebic abscess of lung unconnected with abscess of liver have been reported after dysentery (Tuffier). In the cases of extension of a tropical abscess of the liver to the lung amoebae have usually been absent.

Morbid Anatomy.—*Site.*—The abscess is in the lower lobe in 80 per cent of the cases (Tuffier).

Not infrequently there is not any single and definite abscess, but a considerable area of disintegrating lung is infiltrated with pus and presents an appearance like a sponge. A lining membrane is rarely found, the wall of the abscess being formed in recent cases by friable hepatised lung, and in the chronic cases by fibroid tissue, which may be so tough as to need incision with a knife before it can be opened.

Symptoms and Physical Signs.—The general *symptoms* are to a large extent those of the original condition on which the abscess has supervened. In the pneumonic cases cough, fever, and pain in the chest are already present, but the suspicion of an abscess may be aroused by persistence of the fever and sweating, or by a febrile recrudescence after a decline. In the non-pneumonic group there may be symptoms pointing to the lungs; but in both groups there is often no distinctive evidence of an abscess until a sudden eruption of purulent sputa occurs; and in the closed cases, namely those in which the abscess does not communicate with a bronchus, even this sign fails us. The diagnosis of an abscess must, as a rule, rest on the profuse expectoration of pus and the presence in the pus of elastic fibres.

Physical Signs.—The signs of a cavity might naturally be anticipated; but in many of the recorded cases in which the abscess has been a considerable distance from the surface, cavernous signs have been absent,

and there has only been dulness with bronchial or weak breathing and crepitations. Inflammatory oedema over the site of the abscess has been noted occasionally. The position of an abscess may be determined by skiagraphy.

The *expectoration* is copious and purulent; sweet or offensive, more usually the latter, and often blood-stained, though there is not the same tendency in abscess as in gangrene to profuse haemorrhage. It is important to note that sputa with the characteristic appearance of the so-called "liver pus" have been observed in cases of pure acute abscess of the lung, uncomplicated by liver abscess. Microscopically fat-crystals and haematoidin can be seen, but the one distinctive feature of the sputa from an abscess of lung is the presence of elastic tissue. Considering the importance of this point in the diagnosis of an abscess, especially from an empyema which has burst into the lung, no fragment should be regarded as elastic tissue unless its fibres to some degree recall the structure of an alveolar wall.

Complications.—When the abscess is at all superficial, pleurisy is very common, and may lead to a serous or to a purulent effusion. Pyopneumothorax may result from rupture, and in very rare instances general subcutaneous emphysema has resulted (Senator, Dix). Haemoptysis may occur; serious haemorrhage is infrequent, but it has been known to prove fatal (Dix). As in all suppurative conditions of the lung, especially if fetid, cerebral abscess may arise.

Course and Treatment.—Spontaneous evacuation of the abscess has in a considerable number of instances led to its cure (H. R. Beevor, Newbolt); but more commonly the evacuation is incomplete, so that profuse expectoration continues, and the general symptoms, including the fever, persist.

In a few instances inhalation of creosote or similar substances has accompanied, it should perhaps be said rather than promoted, recovery; more benefit may be expected from their intratracheal injection. In an abscess of any size such means will usually prove ineffectual, and recourse must be had to drainage. But since success may result from spontaneous evacuation, a fair trial may be given to expectant treatment.

Operation.—Tuffier's statistics based on 43 cases, shew that a cure followed incision and drainage in 33; death occurred in spite of operation in 10, but in 7 of these the abscess was not opened. In the successful cases the cure is often complete, the cavity being so entirely obliterated that not even a fistula remains; the more recent the abscess and the softer its wall, the more likely is a perfect result to follow.

The difficulties of the operation consist chiefly in the exact localisation of the abscess and the condition of the pleura. To avoid infection of the pleural cavity its two surfaces must be adherent. Fortunately in 87 per cent of the cases adhesions are present (Tuffier), though they are not always sufficiently extensive and firm. Though the mobility or otherwise of the lower border of the lung in respiration may aid in deciding whether or not adhesions are present, this question can only be

settled by careful inspection of the pleura (Tuffier). When there is pleural friction or an effusion the surface must obviously be free. In the presence of a well-marked vomica the localisation of the abscess presents little difficulty, but in the absence of such signs its position must be determined by exploratory puncture. This, however, should be postponed till the pleura is exposed, for the reason just mentioned.

The incision is made over the most likely spot, a rib is freely resected, and the pleura is exposed and inspected or even palpated through a small opening (Tilton), the danger of pneumothorax with retraction and collapse of the lung being borne in mind. When there are no adhesions the two pleural surfaces are sutured together round a small area, the conclusion of the operation being postponed for forty-eight hours to secure adhesion. This delay, however, as shewn by recorded cases, is not absolutely necessary, and the operation may be completed at one sitting. The pleural surface being adherent, the lung is aspirated until the cavity is struck. With the needle as a guide, the lung is then opened up, dressing-forceps being employed so to avoid haemorrhage, and a tube is inserted. In many instances, however, the lung has been incised with a knife without serious bleeding. Should the abscess cavity not be struck, a track should still be made in the lung and a tube inserted, as experience shews that the abscess often ruptures later into the channel thus made.

In the after-treatment of the case, flushing the cavity is by common consent to be avoided, on account of the danger of washing infective material up a bronchus into the lung beyond.

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GANGRENE

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BY gangrene of the lung is understood not merely necrosis but also putrefaction of the necrotic areas. In dealing with the causation of the disease it will be seen how important it is to insist on this point. Necrosis alone is not necessarily accompanied by the fetor so characteristic of gangrene. It is true that in a few instances which are still classed under gangrene, notably the gangrene of diabetes, this offensive odour is wanting. These cases, whatever may be thought of them, are exceptions, and in the vast majority of instances the association holds good and gangrene means mortification plus putrefaction.

Morbid Anatomy.—The condition was first recognised as a separate entity by Laennec, and his masterly description of its macroscopic appearances left but little to be added. He divided cases of pulmonary

gangrene into two forms, the circumscribed and the diffuse, the latter being so rare that he had seen but two instances in eighteen years. In the *circumscribed* form the necrotic gangrenous areas are small and are not prone to invade the neighbouring tissue of the lung, each being limited and surrounded by a zone of hepatisation, which is not part of the disease but due to reactive inflammation in the healthy tissue. This is a point of importance for, as will be seen later, some have argued that this area of consolidation is the remains of an antecedent pneumonia which paved the way for the gangrene. Three stages can be distinguished in the process: (*a*) recent mortification (gangrenous eschar), the affected area being moist but firmer than normal and usually blackish-green, though sometimes dirty grey in colour; (*b*) liquefaction, the necrotic tissue breaking down into a fetid pulp; and (*c*) excavation.

The *diffuse* form involves a large part of a lobe or even of a whole lung, and is distinguished from the circumscribed by the absence of the limiting zone of hepatisation, the diseased part merging into and tending to invade the sound tissue of the lung.

Bacteriology. — Organisms in gangrene were first discovered by Virchow (1846) in the shape of sarcinae; Kannenberg later noted the presence of two infusoria, *Monas* and *Cercomonas*, and since then numerous saprophytic organisms have been recognised, namely, *Spirillum buccale*, *Proteus vulgaris*, *Micrococcus tetragenus*, *Leptothrix buccalis*, and fungi (Rajat and Péju). In association with these are usually pathogenetic bacteria (streptococci and staphylococci); and the exact part to be assigned to these on the one hand and the saprophytic organisms on the other has been the subject of much discussion which cannot be regarded as settled even now. Some hold that the saprophytes produce putrefaction in tissues previously prepared by pathogenetic organisms, others that they can unaided cause gangrene; Rajat and Péju, for example, state that they have produced gangrene by the injection of cultures of blastomycetes, and according to Netter injection of saliva into the lungs of animals gives rise to gangrene (on account of the flora of the mouth) as surely as does faecal matter. Bonome found *Staphylococcus pyogenes aureus* or *albus* in all his 8 cases; and as the injection of these organisms in pure culture into the lungs of rabbits gave rise to gangrene, he concludes that they are the special cause of the necrosis. Hirschler and Terray, though finding *Staphylococcus pyogenes aureus*, *albus*, and *cereus* together with *Bacillus pyocyaneus* and *Micrococcus tetragenus*, assign the gangrene to a special micrococcus also present, which gave off the characteristic odour in cultures and formed indole and skatole. Babes will not allow that the ordinary organisms of the air can act on healthy lung so as to cause gangrene, and insists that their activity is confined to the production of putrefactive changes when they have been enabled to multiply in tissues already necrosed by associated pathogenetic organisms. He admits, however, that the bacteria of the mouth may in rare cases acquire special virulence, and may then unaided cause gangrene. In 24 cases he found that associated with saprophytes there were in 2 cases staphylococci, in

12 streptococci, in 3 pneumococci, in 10 bacilli akin to the diphtheria bacillus, and in 3 cases bacilli resembling the bacillus of malignant oedema. The streptococci and the pneumococci were noted to be very virulent. He also points out that many bacteria are able to produce gangrene and to decompose the tissues if present in exceptional numbers or exceptionally virulent. In a case of cystitis with decomposing urine a special bacillus was isolated from the softening lung, which on culture gave off an ammoniacal odour; from another case (gangrenous pneumonia) a member of the proteus group, which was pathogenetic to mice and rabbits, was obtained.

Acid-fast Bacilli.—In 5 cases Ophüls found mixed cultures of acid-fast bacilli in all, the other organisms being streptococci, staphylococci, or pneumococci; Rabinowitsch also has isolated from pulmonary gangrene a bacillus akin to the butter bacillus. Mayer, quoted by Ophüls, isolated acid-fast bacilli from the tissues in 10 out of 58 cases; inoculation experiments, however, were negative, possibly because the bacilli were not injected direct into the lung, a common source of error. It is interesting to note in the light of these observations that Tuffier found bacilli resembling tubercle bacilli in the sputa and wound discharges of cases of gangrene, which recovered completely and subsequently were entirely free from all signs of tuberculosis and from tubercle bacilli. Ophüls places these bacilli among the streptotricheae, and believes that they act in conjunction with the pathogenetic organisms; the constant presence of the latter is strong evidence that they play an active part, and it is probable that by injuring the tissues the cocci favour the growth of the acid-fast bacilli which produce necrosis and liquefaction or gangrene of the lung. (Compare art. "Streptothrix Infections," Vol. II. Part I. p. 317.)

Anaerobes.—Recent French work (Guillemot; Veillon and Zuber) has brought to light the important part played by anaerobes in fetid processes generally. In sections of gangrenous lungs they are found in great numbers in the zone of active necrosis where other organisms are scanty or absent. These anaerobes include a number of bacilli, cocci, and spirilla, especially the *Bacillus ramosus* which is almost constantly present in gangrene of lung and is often associated with *Bacillus fragilis* and *Micrococcus fetidus*. Guillemot produced embolic foci of gangrene in the lungs of rabbits and guinea-pigs by the intravenous injection of *Bacillus ramosus* together with other anaerobes. He admits the presence of aerobes (*B. coli*, *Proteus vulgaris*, a non-pathogenetic streptococcus, and staphylococci) in gangrenous foci, but these are few, and the overwhelming preponderance of the anaerobes shews that they are the causal agents. Fortineau has described a facultative anaerobe, an encapsuled diplo-bacillus staining with Gram, which was pathogenetic to animals and caused putrefaction in cultures. On the other hand, Péhu and Horand, in a case of otogenic gangrene of the lung, isolated *Bacillus coli* from the blood and the lung, but failed to find any anaerobic organisms.

A review of the whole subject brings out the multiplicity of the

bacteria concerned in gangrene, and shews that no one micro-organism can be regarded as the specific agent.

Etiology.—These organisms may reach the lung by the bronchi, by the vessels when carried in infective emboli, or in rare instances by direct extension (trauma). The chief conditions which give rise to gangrene may be classified as follows :—

I. Lung conditions (invasion by bronchi).

Pneumonia :—

Acute croupous.

Bronchopneumonia.

Aspiration-pneumonia ; foreign body ; stenosis of bronchus ; perforation of oesophagus ; conditions of disease in the mouth ; insanity ; paralysis.

Fetid bronchitis.

Bronchiectasis.

Tuberculosis.

II. Embolism.

III. Injury (contusion or penetrating wound, especially gunshot).

The *predisposing conditions* are age, debility and malnutrition, alcoholism, certain diseases, such as diabetes mellitus, and infectious fevers, especially measles and influenza.

Gangrene may occur as an *epidemic* (Mosing, quoted in Nothnagel ; Bard and Charmeil), and then appears as Laennec's diffuse form, implicating large areas of the lung.

The relative frequency of the disease and of the various conditions which favour its occurrence is best seen from a table, such as the following from Hensel. In 5072 autopsies there were 83 cases of gangrene of the lungs due to the following conditions :—pneumonia 14 (croupous 8) ; phthisis 11 ; embolic 26 (including endocarditis 3, phlebitis 3, pyaemia 9, 2 of which were gonococcal and 2 from otitis) ; carcinoma 10 (7 of which were oesophageal) ; bronchiectasis 5 ; cachexia 5 ; injury 3 ; and aspiration 9 (3 carcinoma). The chief point calling for comment in this list is the high proportion of cases of phthisis ; for it is generally agreed that gangrene is rare in tuberculosis, so much so indeed that some have supposed that there is an antagonism between the two.

Pneumonia.—Great discrepancy of opinion prevails as to the part played by pneumonia in the production of gangrene, one school (Leyden, etc.) considering that pneumonia is almost a necessary antecedent condition, the opposite school (Laennec, Trousseau) pointing to the extreme rarity of gangrene as a complication of that disease (Aufrecht did not find a single case in 1500 cases of pneumonia). The truth is that the consolidation associated with gangrene is not due to a primary pneumonia, but is induced by the organisms responsible for the gangrene ; the consolidation is therefore consecutive to the gangrene and not its precursor. Babes, from his observations, concludes that consolidation is often entirely absent, gangrene, even in the diffuse form, supervening directly on a haemorrhagic oedema without any alveolar exudation.

Croupous pneumonia, then, is rarely the cause of gangrene, which moreover is seldom lobar but usually bronchopneumonic in its distribution, and this only because of the invasion by the bronchi. True bronchopneumonia, however, may precede gangrene, as is seen in the infectious fevers (measles). Influenzal pneumonia (Leichtenstern) is especially prone to end in gangrene.

Aspiration-pneumonia causes the gangrene occurring in paralysis of the larynx, in the insane, in perforation of the œsophagus, and in the course of various diseases of the mouth.

Age.—Gangrene is rarer in children than in adults, but it is more frequent than abscess, and occurs even in the early months of life. The infectious fevers, especially measles, and the otogenous and aspiration groups account for most of the cases. A special feature of gangrene in childhood is the frequent absence of fetor from the breath (Holt, W. L. Carr; in two-thirds of the cases, Renault), and as there is no sputum the disease remains latent. Barthez and Rilliet stand alone in recognising a special connexion with tuberculosis (in 10 out of 26 cases).

Symptoms.—Fever is rarely absent, the temperature often being high and irregular with wide oscillations; prostration is marked, and there may be diarrhoea. The cough is severe. The expectoration is usually copious and extremely offensive, the fetor defying description and being peculiar to the disease. On standing the sputa tend to separate into three layers: the lowest purulent and containing whitish plugs made up of fatty acids, the middle fluid, and the upper frothy. Elastic tissue would naturally be expected and may be found in the sputa, but, as the result of some destructive process, is not so constantly present as in abscess. Severe recurrent haemorrhages, which have often been fatal, are a prominent feature (one quarter of the cases, Barthez and Rilliet) in gangrene, and are far more frequent than in abscess of the lung; they depend on necrosis and ulceration of a vessel and may occur at any time in the course of the disease, even after operation and drainage.

Latent Gangrene.—In some instances the fetor described as characteristic of the sputa is absent, and this even in the diffuse form of the disease (MacFarland). Since not only fetor of the breath but even expectoration may be entirely wanting, diagnosis may be impossible. Latency is not uncommon in young children (Holt, W. L. Carr), in whom diagnosis is always hampered by the absence of expectoration, and in the gangrene of diabetes (v. Noorden). It has been suggested that in some of these cases the gangrenous focus is not in communication with a bronchus, but in others the lung itself has been found sweet at a necropsy.

Diabetic Gangrene.—The symptoms and course of the gangrene which complicates diabetes vary according to the amount of sugar in the urine (v. Noorden); in severe cases (more than 5 per cent sugar) it takes an acute pneumonic form with high fever, whilst in the slighter cases (less than 5 per cent sugar) it runs a subacute or chronic course with catarrhal signs and little fever. In the acute form the sputa and lungs

are rarely fetid, but the chronic cases may shew fetor. In both forms severe haemorrhages are common.

The **physical signs** in gangrene will necessarily vary according to the form and stage; the diffuse form may present dulness on percussion, rales, and the signs of consolidation over a wide area; in the circumscribed form the signs are less extensive. In the stage of excavation the signs of a vomica, if superficial, may be found, but they are often absent. In one instance (Steven) pulsation over a gangrenous lung, analogous to the pulsation of an empyema, was observed.

In the **diagnosis** of gangrene the peculiar fetor and signs of pulmonary disease are necessary to prove that the lung is the source of the fetid expectoration. An almost similar condition may arise from bronchiectasis or the rupture of a putrid empyema into the lung, but in neither of these conditions is elastic tissue present in the sputa (*vide* p. 147).

Complications.—Pleurisy leading to a serous or purulent effusion is common. The pleura itself may become gangrenous and a pneumothorax may result. Cerebral abscess or meningitis may occur.

Treatment.—In a few cases spontaneous evacuation has resulted in a cure (Wilson Fox).

Of medical means the subcutaneous injection of guaiacol (Lop) has been successful, but the intratracheal injection of creosote is more likely to be effective, and may be given a trial. Unless improvement occurs no long delay, on account of the danger of extension, should be allowed before having recourse to operation.

It must be premised, however, that only cases of circumscribed gangrene are amenable to surgery. The operation follows the lines described in the section on abscess of lung and the same precautions with regard to the pleura are to be observed (*vide* p. 271). Fortunately adhesions are the rule; they were absent in 6 only of the 74 operation cases collected by Tuffier; in 14, though absent at the site of operation they existed in the neighbourhood. Haemorrhage is a grave danger peculiar to gangrene both during and after the operation. Secondary haemorrhage occurred in 9 cases and was fatal in 4 (Tuffier). This complication should be met by plugging the cavity (Tuffier), and by carefully adapting the length of the tube so that its end lies within the cavity and does not press on any part of its wall. Lavage of the cavity is inadvisable on account of the risk of thus spreading infection into the healthy lung.

The first benefits of drainage are seen in the relief of cough, expectoration, and fetor, the temperature falling later. If the fever persist or return, either the drainage is insufficient or there is an untouched focus left in the lung and the wound must be opened up again. It is interesting to note that Tuffier finds an accession of fever and fetor, due to anaerobes, not uncommon even when the patient is doing well. Improved ventilation of the cavity by widening the track is all that is needed to relieve this.

Cure is usually slow, and as a rule the tube should not be omitted for six weeks. Tuffier, dealing with 72 cases, finds that recovery takes place in 40 per cent after operation; Herczel, on the basis of 91 cases, estimates that recovery occurs in 61 per cent of the cases, the percentage of recoveries being greater and the results better when operation is undertaken early in acute cases. Among the causes of death were multiplicity of lesions in one or both lungs, the main focus being sometimes missed, cerebral abscess, and haemorrhage.

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PULMONARY TUBERCULOSIS

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Etiology.—The causation of pulmonary tuberculosis, or phthisis pulmonalis, is a matter of far-reaching importance to the human race, inasmuch as statistics shew that one-thirteenth of the total death-rate of the world is attributable to this disease. The infective nature of tuberculosis first definitely raised by Villemin in 1865 was finally established by Robert Koch's classical experiments in 1882. At the same time a survey of the facts shews that infection does not cover the whole ground of the etiology of tuberculosis, and inquiries by Drs. Bulstrode and Miers have demonstrated that in Great Britain the mortality from pulmonary tuberculosis had begun to decline before the infective character of the

disease was recognised. In other words, the reduction in the death-rate cannot be explained by precautions taken against infection, but must be attributed to the improvement in general hygiene, which has been such a conspicuous feature of the last half-century.

The disease was known to Hippocrates (460-377 B.C.); and in all probability it has existed from the earliest times.

Geography. — Laborious and careful research has shewn that the geographical distribution of pulmonary tuberculosis is coextensive with the habitable regions of the globe, and in Hirsch's words it is "a disease of all times and countries."

But although it cannot be admitted that any part of the world manifests a complete immunity from this disease, Lombard's maps shew that it is all but absent in certain Arctic regions, deserts, and places situated at great altitudes; in other words, as pointed out by Dr. Ransome, just where the population is most scanty. If we survey the statistics of various countries, a special incidence on certain districts and towns comes out in the clearest manner. It is perhaps doubtful, as Hirsch remarks, whether a comparison of the statistics of different countries possesses the same value as a study of the returns of individual towns or districts, which ensure a greater degree of accuracy.

Climate.—The influence of climate has been much discussed. Some writers hold that phthisis is commoner in hot than in cold countries; others again consider that it is of more frequent occurrence in temperate climates. But a review of the information at present available leads to the conclusion adopted by Hirsch, that "the mean level of the temperature has no significance for the frequency or rarity of phthisis in any locality." A few examples will illustrate this point. The mortality from this cause in Iceland is very low, whereas in North Greenland phthisis is one of the commonest causes of death. On the north coast of Africa, Morocco and Algiers are distinguished by a remarkable freedom from consumption; but at Tunis, and at Alexandria and Damietta on the sea-coast of Egypt, the disease is very prevalent: in the interior of Upper and Lower Egypt, on the other hand, phthisis is decidedly uncommon. Other discrepancies equally striking might be quoted to prove that places sharing a similar climate may widely differ in their phthisis death-rate.

Consumption seems to follow in the wake of advancing civilisation, especially where men congregate together in large numbers. All accounts agree as to its extraordinary prevalence in New Caledonia, Hawaii, Tahiti, and other South Pacific Islands. There is a strong consensus of opinion that phthisis became far more rife in these parts, and also among the Maoris of New Zealand, since the date of the European immigration; when, as Hirsch says, "the natives began to adopt the manners and habits of the Europeans." Until recent times the mortality from this disease among the troops of the British Army in the most widely separated parts of the world was deplorably high, more particularly in times of peace; and often considerably exceeded the mortality of the resident population. Improved hygienic arrangements in the barracks, especially

as regards overcrowding and ventilation, have reduced the death-rate from phthisis in the most remarkable manner.

Such facts cannot be reconciled with the belief that climate is an important etiological factor. But whilst the evidence negatives the opinion that hot climates favour phthisis, all authors are agreed that the disease in tropical countries assumes a most acute and virulent type.

Moisture.—A maleficent influence has been ascribed to moisture of the atmosphere and soil. In America, Bowditch was led to believe, by an inquiry into the incidence of phthisis on the inhabitants of certain places, that the disease is most prevalent in areas where the soil is impregnated with moisture. He found in certain localities that efficient drainage was followed by a diminution of phthisis. Milroy's investigations in Scotland gave similar results. Working out the same idea in England, a few years later, Sir George Buchanan made the discovery that in several towns the phthisis death-rate had undergone a notable decrease since the introduction of an improved system of sewerage—a result which he attributed to draining of the subsoil water. He accordingly expressed the opinion that the mortality from consumption is directly related to the degree of dampness of the soil. But there are certain considerations which make it difficult to regard this conclusion as one of general application. For example, in one of the towns investigated by Buchanan the mortality from phthisis rose remarkably after carrying out the drainage work; moreover, in Berlin, and some other towns in Germany and in England, improvement in drainage has not been followed by the good results anticipated by Buchanan. Lastly, in some of the districts quoted by Buchanan in support of his hypothesis, Kelly's subsequent investigation shewed that the diminution in the phthisis rate noted at first was not sustained in subsequent years. It is indeed significant that in so wet a country as Holland the death-rate from phthisis is rather low. From these considerations we are driven to admit with Hirsch that other etiological factors beside the influence of soil are probably concerned—factors that "serve to neutralise the benefits even of the most favourable conditions of soil."

Altitude.—Observations made in divers parts of the world have left no doubt of the infrequency of phthisis at higher altitudes, though instances of the disease are not wanting even at the very highest points. The sparseness of the population at such levels may account to some extent for their relative immunity, but not entirely; for in some large commercial and not very sanitary towns in Mexico, and on the Andes, situated at an elevation of from 7000 to 13,000 feet, the extreme rarity of phthisis is generally admitted; a proof, as Hirsch writes, "that the influences which go with very considerable altitudes have the power to overcome those detrimental things that arise from a bad kind of hygiene and social life, in so far as they tend to produce consumption."

Statistics from Switzerland strongly confirm the opinion that a great elevation affords some protection, though they supply no proof of anything like complete immunity. The explanation of the beneficial

action of altitude is by no means clear. The extreme freedom of the air from impurities of all kinds and the dryness of the atmosphere have been alleged as the principal causes. But in the case of the unsanitary towns on the Andes above referred to, the absence of organic atmospheric impurities cannot be assumed; and that dryness of the air does not in itself confer any protection is clearly shewn by the returns from the towns on the sea-coast of Egypt to which attention has already been directed. Hirsch makes the suggestion that people living at great elevations and breathing rarefied air are obliged to make deeper inspirations, and acquire in consequence a more vigorous development of the respiratory organs, which are thus enabled to offer a more powerful resistance to external influences. The bearing of this view on the bacillary origin of the disease will be discussed farther on.

No *race* is exempt from the ravages of consumption. Hirsch states that among the Kanakas—the natives of New Caledonia—two-fifths of the total mortality is due to phthisis. And Prof. Osler states, on the authority of Surgeon Kennedy, that the mortality from this cause in a tribe of Red Indians of the Rocky Mountains living in a splendid climate amounts to 23 per cent of the total death-rate. The Negro appears to be extremely vulnerable, especially when removed from his own country; and in this race phthisis runs a very acute course.

The evidence with regard to the Jews is somewhat ambiguous. There is a general impression that Jews are less afflicted with tuberculosis than Christians. This has been accounted for by the more careful selection of carcases in Jewish slaughter-houses, and by the more frequent house-cleanings practised by the Hebrews. There is some reason to believe that this favourable estimate applies only to the well-to-do members of the community. Further investigation must decide whether the current opinion is correct or not.

Sociological.—We have now to consider another class of etiological factors; the density of population, and certain injurious influences connected with trades and occupations, particularly those which involve an indoor life.

As the general result of statistical inquiry in different countries, it is clearly proved that the mortality from phthisis is lower in the country than in the towns; and that in the case of towns the mortality on the whole increases with the population. The proneness to phthisis manifested by dwellers in towns seems to be largely connected with overcrowding in rooms badly ventilated and lighted. Numerous investigations have attested the high death-rate from phthisis in convents, sisterhoods, military barracks, and above all in prisons. These institutions have been notorious for overcrowding and defective ventilation. In jails and convents insufficient food and indoor confinement have no doubt militated also against the health of the inmates; but these factors cannot be said to have been operative in the case of military barracks. Happily the hygienic reforms of recent times have effected an enormous reduction in the mortality from phthisis in such institutions.

Sedentary occupations, whether in town or country, appear to dispose to the disease. Certain trades, particularly those which are associated with much dust, enjoy an evil distinction on account of the prevalence of consumption among their workers. Attention was chiefly directed to this point by Greenhow's excellent reports, in which he traced the influence of dusty occupations in originating diseases of the lungs. It is generally believed that the sharper particles of dust are most injurious. Flint-workers, needle-polishers, file-cutters, grinders, and potters supply the largest contingent of pulmonary diseases. It is still undecided whether most cases of this sort attributable to dust are of a tuberculous nature or not. (*Vide* art. "Pneumoconiosis," p. 448.)

No *age* is exempt from pulmonary tuberculosis, though it is less common at the two extremes of life.

The view, which prevailed until recent times, that infants and children under two years of age are scarcely ever attacked, has been proved to be incorrect. Landouzy found that in several fatal cases of bronchopneumonia in children under two years, some of which during life were ascribed to measles or cold, tubercle bacilli were present in the bronchopneumonic patches, although the naked-eye appearances of tuberculosis were not recognisable. These observations were made at an infant asylum in Paris, in which institution one-third of the deaths among the children proved to be the result of some form of tuberculosis.

The statistical results with regard to age and sex for the period 1851-1880 obtained by Dr. W. Ogle, formerly superintendent of statistics, General Register Office, quoted in the first edition of this work, must be revised in the light of Dr. Tatham's investigations of more recent times. According to Dr. Tatham, Dr. Ogle's successor, to whom I am much indebted for ready help, the greatest mortality occurs between the ages of fifteen and seventy-five. In children the greatest liability coincides with the approach of puberty, the liability beginning rather earlier with girls. Females are somewhat less liable than males under five years, considerably more liable from five to twenty years, and less liable at subsequent ages. The relation of phthisis mortality to sex has been reversed in the last half-century. The female rate was higher in the period 1851-60 than the male by 8 per cent. The male rate for 1901-5 is higher than the female by 42 per cent. Again, the age of maximum phthisis mortality since 1896 has been for males from forty-five to fifty-five years, for females from thirty-five to forty-five years, as compared with previous periods in which the maximum male rate was from thirty-five to forty-five years, the female from twenty-five to thirty-five years. Dr. Tatham finds that there has been a great diminution in the mortality from phthisis in recent years. In proportion to the living at all ages, phthisis now destroys in each year less than half the number that succumbed to it annually half a century ago. Among persons of both sexes below the age of twenty-five years phthisis mortality has fallen on the average by more than 60 per cent. From the age of twenty-five onwards to the close of life the fall has been considerably

less marked, its incidence has been exceptionally favourable to the female sex.

It is not easy to account for the excess of the male rate in the first five years of life. But as regards the decided excess of the female mortality over the male between the ages of ten and twenty, Dr. J. F. Payne points out that it is at this period of life that the difference between the outdoor life of boys and the indoor life of girls begins; and he suggests that the excessive female mortality at this age is connected with the existence of unfavourable conditions in the house. But, as he further remarks, "the greater liability of the male sex to phthisis after thirty-five years of age seems to be quite unexplained by such considerations."

Dr. Tatham's like Dr. Ogle's Tables shew that the excess of the female death-rate is not related specially to the child-bearing period, as the male rate begins to exceed the female after the age of twenty.

In connexion with differences of sex we may now briefly consider the influence of menstruation, pregnancy, parturition, and lactation.

Menstruation.—There is no clear evidence that this function, whether at its commencement or subsequently, exerts any definite causative influence. Irregularity or arrest of the catamenia seems at times to be connected with the onset of haemoptysis; but the nature of this association is probably less intimate than at first sight it appears to be. For it may be safely concluded that a considerable pulmonary haemorrhage at the outset of the phthisical symptoms is a sure sign that the disease is already of long standing, although perhaps hitherto quite latent. Arrest or disorder of the menstrual flow may occasion reflex vascular disturbance, and so give rise to haemorrhage from lungs already diseased; but the occurrence is not by any means common.

Pregnancy.—The influence of pregnancy has been much debated. The disease not infrequently appears to extend during this period; but the impossibility of fixing the date at which the disease begins renders the question a difficult one. Wilson Fox considered that the rapid increase of phthisis in women between the ages of twenty and thirty-five points somewhat strongly to the influence of pregnancy in the development of the disease. The force of this argument is weakened by the fact that the increase in the male rate in the same period is even more pronounced. Dr. R. E. Thompson, as the result of a statistical inquiry into the subject of phthisis in women, concludes "that the susceptibility of single women is rapidly diminished after thirty years of age, whilst that of married women maintains its intensity between twenty-five and forty years of age (that is, during the child-bearing period)."

Parturition.—It is not common to find that symptoms of phthisis set in directly after parturition, though this event has generally an accelerating effect upon pre-existing disease.

Lactation, by its debilitating influence on weakly women, may no doubt act as an indirect cause. Dr. Pollock states that the periods of puberty, of gestation, of parturition, and of lactation are fraught with danger to persons disposed to phthisis.

The influence of these conditions on the established disease will be considered in a subsequent section.

General Depressing Influences.—Among the remoter causes of phthisis may be reckoned all conditions that tend to lower the standard of health; such as insufficient food, anxiety, grief, excessive mental work, want of exercise, fresh air, and sunlight. Among diseases that have the same general effect diabetes mellitus must especially be named—a point on which all authorities are now agreed. It is interesting to note the liability of diabetics to another disease of microbic origin, namely, carbuncle.

Concerning the etiological importance of chronic alcoholism, malignant disease, and syphilis, agreement is less general. Both clinical and post-mortem experience alike support the view that topers are prone to tuberculous affections. The frequent association of peritoneal tuberculosis with cirrhosis of the liver is generally recognised by pathologists. It has been urged that alcohol has a preventive action; and that it tends to promote fibroid changes if tuberculosis should be contracted; both statements are at variance with my own experience.

The association of pulmonary tuberculosis and malignant disease of various organs is by no means rare, though it is very uncommon to find evidence of simultaneous activity of the two diseases. Mr. Roger Williams's statistical investigations appear to him to justify the conclusion that the proclivity to cancer is closely allied to the tuberculous diathesis.

A history of syphilis is not rarely obtained from phthisical patients; but if the former disease be possessed of any etiological influence, it can only be of an indirect character.

Rheumatism, gout, chlorosis, dyspepsia have also been regarded as etiological factors; but their connexion with phthisis is not intimate. The prevalence of tuberculosis in asylums for the insane is generally admitted, but the relation between the two complaints is still a matter of dispute. According to one view infection takes place in the asylum owing to defective hygienic conditions. On the other hand, Dr. Mott, from recent post-mortem experience at Colney Hatch Asylum, is of opinion that the number of cases in which the disease may have been acquired during the patient's residence in the asylum is very small.

The frequency with which pulmonary tuberculosis appears after measles, influenza, and, to a less degree, after whooping-cough is well known. Although these diseases cannot be regarded as immediate causes, it must be admitted, more particularly in the case of influenza and measles, that they are apt to precipitate an eruption of tuberculosis; whether it be in consequence of the attendant pyrexia, or of some other action of their specific virus. There is more to be said in favour of the view that a latent tuberculous focus is lighted up, than that tuberculosis is initiated by the presence of another disease. On the other hand, it is possible that influenza and measles may cause certain changes in the bronchial and pulmonary epithelium which result in a lowering of their power of resistance, and thus lay them open to the invasion of tubercle.

Pneumonia.—It is an old belief that croupous pneumonia may terminate in phthisis; but it is now quite certain that this sequence of events is infinitely rare. Two principal fallacies have been concerned in the origination of this erroneous opinion; in the first place, certain rare cases of pulmonary tuberculosis begin with severe constitutional symptoms, and with signs of extensive infiltration of the lung, simulating acute pneumonia; secondly, delayed resolution, or the exceptional supervention of chronic pneumonia, may give the impression that croupous pneumonia has terminated in phthisis. Patients suffering from the latter disease often declare that their illness began with "inflammation of the lungs"; but such statements will seldom stand the test of a critical examination.

Bronchitis not uncommonly appears to have been the starting-point of phthisis, and there is nothing improbable in such a belief; but, more often, careful inquiry will elicit the fact that symptoms of phthisis preceded the attack of bronchitis. In many instances in which the tuberculosis appeared to have supervened on chronic bronchitis, an autopsy has demonstrated that the bronchitis was itself symptomatic of chronic pulmonary tuberculosis. The fact that many phthisical persons attribute their illness to a simple catarrh possesses little scientific value; for what ailment do patients not put down to catching cold?

Pleurisy.—The oft-repeated observation that an attack of pleurisy is frequently followed by phthisis, led to the belief that the latter disease is the result of pleurisy. But there is no doubt that, in such circumstances, the original pleurisy has itself been of a tuberculous nature; and secondary, as a rule, to tuberculosis of the lung. There is no reason to think that pleurisy in itself disposes to pulmonary tuberculosis. In metapneumonic pleurisy, whether sero-fibrinous or purulent, in which the effusion is directly due to the pneumonic process, recovery is generally complete and permanent. It is believed by Koch and others that pleuritic adhesions, by impeding the movement of the chest walls and lung, may dispose to phthisis. But patients suffering from deformity of the chest—as the result of kyphoskoliosis, rickets, or caries of the spine—wherein the thoracic movements are greatly restricted—so rarely acquire pulmonary tuberculosis that Rokitansky came to the conclusion that the two affections are antagonistic.

Trauma has been supposed to play an important part in the causation of pulmonary tuberculosis. Mendelssohn has published nine cases of his own, with a reference to seventeen other recorded cases, in which injuries to the chest, of various kinds, were followed by pulmonary tuberculosis. In some instances haemoptysis occurred at the time of the injury or soon afterwards; in others cough and symptoms of pleurisy ensued within a few days or weeks. In one or two cases an interval of a few months, and, in one case, of two years, separated the accident from the appearance of definite symptoms. Mendelssohn ascribes the occurrence of phthisis in such circumstances to laceration or contusion of the lung, and infiltration of its tissues with blood or inflammatory products, favouring

the entrance and germination of the tubercle bacilli, which he assumes to be more or less ubiquitous. From the rapidity with which pulmonary symptoms appeared in most of these instances, it seems more reasonable to suppose that injury to the chest wall may rouse into activity some latent tuberculous focus, possibly by laceration or loosening of its fibrous capsule. As the result of direct questions put to many hundred patients suffering from phthisis, I have met with but a comparatively small number who referred their complaints to an injury of any kind. In one or two instances, when the patient gave a history of injury to one side of the chest, physical signs of disease were confined to the opposite side.

Antagonism of other Diseases.—Malaria has been said to confer a protection against pulmonary tuberculosis, but investigations in malarious localities in various quarters of the world have proved that no such antagonism exists.

An attack of erysipelas has been followed by arrest of the pulmonary disease in a few recorded instances.

Disease of the Heart.—Rokitansky taught that all conditions which induce a state of venosity of the blood impart an immunity from tuberculosis. Among the affections included in this category he placed cardiac dilatation and hypertrophy, whether primary or the result of valvular disease, congenital malformation of the heart and great vessels, aneurysms, deformity of the chest depending on rickets, lateral curvature or caries of the spine, pleural effusions, chronic bronchitis, emphysema, bronchial dilatation, pregnancy, or any other condition tending to obstruct the passage of venous blood through the right side of the heart. The relation of some of these affections to phthisis has been already mentioned; but the influence of cardiac disease must now be considered. It is undoubtedly uncommon to find phthisis and disease of the heart in the same patient, but this association is by no means so rare as Rokitansky's statement would imply. Most writers agree in saying that mitral stenosis is scarcely ever met with in this association; this combination is rare, but I have seen at least a dozen clinical examples; and in five other cases the two conditions were found on post-mortem examination to be associated. (*Vide* also art. "Mitral Obstruction," Vol. VI.)

Rokitansky's view that the antagonism of the two affections depends on the venosity of the blood has been objected to by Lebert and others, on the ground that the subjects of congenital stenosis of the pulmonary artery are exceedingly prone to contract tuberculosis. But in such persons, as Lebert himself admits, the lungs are often small and undeveloped, and their nutrition must be below the average. And, although the bronchial arteries are abnormally developed, in order to supplement the pulmonary circulation, the lungs are still very inadequately supplied with blood, and are less capable than normal lungs of resisting the action of the tuberculous virus. It appears then that, in the case of pulmonary stenosis, increased venosity of the blood is not the sole or perhaps the chief influence at work; and Lebert's objection is possibly

not so fundamental as it has been held to be. Dr. Pollock considers that hypertrophy and dilatation of the heart retard the progress of tuberculosis, and that under such conditions a prolonged duration may safely be anticipated. This observation is a very true one, and affords support to the theory of antagonism.

It seems, then, that Rokitansky's doctrine is true, though true in a more limited sense than that in which he intended it to be taken. All diseases of the heart which bring about a passive congestion of the lungs confer a certain degree of protection against pulmonary tuberculosis; but, in the words of Peacock, "this opposition certainly in no degree amounts to an incompatibility."

Gout.—In the rare instances in which gouty persons acquire tuberculosis the disease runs a very chronic course.

P. K.

Infection.—Investigators, such as Ullersperger, Waldenburg, Uffelmann, and Predöhl, who have made a special study of the history of tuberculosis, are unanimous that until the beginning of the nineteenth century consumption was widely regarded as a contagious disease. Thus, Galen (Neuburger, p. 388) affirms that the putrid discharges from the lungs of consumptives are dangerous, and that those who occupy the same rooms, wear the clothes of consumptives, or even eat and drink with them, contract the disease, unless the infection of the discharges is first destroyed. After the revival of learning, there are frequent references in medical writings to the infectivity of consumption, and in the eighteenth century Morgagni stated that it was dangerous to make necropsies on tuberculous patients. In Italy especially, stringent laws were passed with regard to the destruction of the effects of consumptives and the cleansing of their dwellings. At the beginning of the nineteenth century, and largely as the result of the teaching of Bayle and Laennec, the contagion view was doubted, and its place was largely taken by the belief that phthisis depends essentially on a special diathesis, persons with this constitution being peculiarly liable to contract the disease. So completely indeed did the diathetic doctrine come to dominate the views on tuberculosis that in 1848 Sir Thomas Watson stated that he did not consider phthisis communicable from person to person. "Neither," he says, "can the disease be easily (if at all) generated in a sound constitution. Nor is it ever imparted, in my opinion, even by one scrofulous individual to another. The disorder, I am convinced, does not spread by contagion." But in 1867 William Budd, of North Tawton, as the result of pathological and epidemiological considerations, came to the conclusion that tuberculosis is a true zymotic disease of specific nature in the same sense as enteric fever. It never originates spontaneously, but is perpetuated solely by the law of continuous succession. "The tuberculous matter itself," he says, "is (or includes) the specific morbid matter of the disease, and constitutes the material by which phthisis is propagated from one person to another and disseminated throughout society. The

destruction of this matter on its issue from the body by means of proper chemicals or otherwise, seconded by good sanitary conditions, will lead to its disappearance." These views were destined to be accepted universally as the results of the work of Villemin in 1868, and especially of Koch fifteen years later. The data which led Budd to these conclusions were various pathological conditions which suggested the evolution and multiplication of a morbific matter within the body, and its tendency to be eliminated or cast out. He also noted the importance of the geographical distribution of consumption in past and present times, and especially its great fatality now in countries which, when first discovered by Europeans, were known to be entirely free from it. The original immunity and present fatality from tuberculosis was strikingly borne out in the case of the South Sea Islands. When America was first discovered phthisis was unknown among the Indians, although now very fatal among them (Rush). Budd also drew attention to the prevalence of tuberculosis in convents, harems, barracks, and penitentiaries, where the inmates live in relatively close contact with each other. With the discovery of the tubercle bacillus, and the proof of its causal connexion with the disease, it could no longer be doubted that infection plays a part in the propagation of phthisis. To demonstrate the exact degree of danger from infection, inquiries on a large scale were set in motion among the medical men of America, England, Germany, Austria, and France. The results, however, were not very satisfactory, as a very large number appeared to be unable to answer the question whether phthisis was infective or not. This difficulty is largely to be attributed to the long latent period of the disease, and the difficulty of recognising it in its early stages. The endemic character of the disease in all civilised countries at the present time renders the tracing of any individual case to an infective origin a matter of difficulty, and lastly it is difficult or impossible to delimit the exact part played by disposition or diathesis.

In recent years numerous observations have accumulated upon the infection in families, in houses, trades, and especially the degree of conjugal infection. With regard to the latter, many isolated reports go to shew that women may be infected from their husbands, or husbands from their wives. Sir Hermann Weber published a case in which a consumptive man apparently infected each of his four wives, all of whom died from the disease. Recently Pope, Karl Pearson, and Miss Elderton, have published an exhaustive analysis by modern statistical methods of over 35,000 married couples in their relation to tuberculosis. Whilst pointing out the defects in the statistical material and the influence of assortative mating, they ultimately concluded (1) that there is a sensible but slight liability to infection between married couples; (2) that this is largely obscured or forestalled by the occurrence of infection from outside sources; (3) that the liability to the infection depends on the presence of the necessary diathesis; (4) that assortative mating probably accounts for at least two-thirds and infective action for not more than one-third of the whole correlation observed in these cases.

Like other intensely parasitic diseases of chronic character, there can be little doubt that prolonged exposure is necessary to successful infection, and that even then many escape. The careful investigations of Schlenker, Naegeli, and Burkhardt have shewn that the immense majority of adult cadavera present tuberculous changes in a latent, quiescent, or arrested form; from this it must be inferred that man possesses or acquires a considerable degree of immunity to tuberculosis, and it must be admitted as possible that repeated re-infections with small doses may increase the immunity, granting the absence of a disposition to the disease. Dr. Payne, and more recently Theobald Smith, have drawn attention to the tendency of microbes, in their evolution towards an exclusively parasitic existence, to offer considerable resistance while sojourning in the body. In virtue of this resistance they may remain for long periods in the body, in circumscribed lesions which ultimately break down and discharge their contents outwards.

W. BULLOCH.

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W. B.

House-Infection.—A considerable number of observations has now been recorded in support of the view that the tuberculous virus clings to certain dwellings.

Dr. Ransome's investigations in Manchester and Salford have shewn that tuberculosis is especially apt to haunt houses situated in close courts, narrow streets, and, above all, houses built back to back, where ventilation is necessarily defective. Similar observations have been made in America and Germany. In some of the cases published the evidence is very strong, as, for instance, in the following by Engelmann. A newly-built flat, in a fairly sanitary condition, but badly lighted and ventilated, had been occupied for eight years by three families in succession; all of them had presented a clean bill of health until the family X took up its residence in the same quarters. In this family the mother was consumptive when she came, and died in the flat. Shortly afterwards the family left, having lived there for one year only. The flat was next occupied by the family Y, of seven persons, all healthy; after a year's stay they left, and some years later the father, mother, and one son died of phthisis, and a boy of chronic peritonitis. A third family, Z, all healthy to begin with, next took the rooms; one child died of meningitis, another of marasmus, and a third contracted hip disease; subsequently the father died of phthisis, another child of meningitis, the mother acquired consumption, and a child became scrofulous. A fourth healthy family, W, next came into residence; after a time the mother became phthisical, and two children died of meningitis. In reference to these facts, Dr. Payne remarks: "Summing up the history it appears that for eight years the dwelling was free from tuberculous diseases. Then came one year's tenancy by a person already tuberculous. After this, in a period of twelve years, at least twelve cases of tuberculous disease were traced to this source. It is noted that the dwelling was never vacant, the new tenants entering while it was, so to speak, still warm from the last; and during the whole period it was never painted or cleaned." In other parts of the same house, where cleaning was not neglected, but the conditions were otherwise the same, no cases of tuberculosis could be traced. The facts point strongly to infection in the case of the third and fourth families (Z and W); but in respect to the second family (Y) the evidence is not so convincing, as according to Engelmann's statement some years elapsed between the tenancy of the infected house and the deaths of some of the members from tuberculosis. Dr. John Macdonald has reported a similar instance of house-infection in the case of a crofter's family on the West Coast of Scotland. The family of 14 persons, free from hereditary predisposition, occupied a dwelling consisting of two rooms with stone walls, thatched roof, clay floor, and very damp, which they kept in excellent condition. One daughter, who had been in service, came home with a suppurating finger, developed phthisis, and died of tuberculous meningitis in less than two months after her return. Subsequently the father, mother, four sisters, and one brother developed tuberculosis, and five out of the seven died. The hypothesis that the virus is air-borne, and intimately connected with dust, helps us to understand how house-infection may come about. In most of the instances recorded the victims lived in small, ill-ventilated rooms, so that the chances of infection were thereby much

increased. The smaller the room the less the likelihood of adequate ventilation, and the greater the opportunity for the accumulation of dust.

An important side-light is thrown on this part of the subject by the returns of the mortality from phthisis, at ages ten to twenty, in the male and female sex among certain agricultural populations in England and Germany, which shew a marked excess of the female over the male death-rate. In other words, the males at these ages, who lead an outdoor life, suffer much less from consumption than the females, who spend most of their time indoors. Although, as Dr. Payne points out, this disparity in the phthisis death-rate may be explained on the ground that the open-air life of the men is healthier, it is quite as logical to say that the indoor life of the women exposes them to some injurious influence derived from the dwellings. We know that the tubercle bacillus is apt to cling to ill-ventilated and insufficiently cleaned rooms inhabited by phthisical persons, conditions only too well fulfilled in the houses of the poor. It is hard to resist the conviction that these facts are most readily to be explained by the more prolonged exposure of the women to the risk of house-infection. In towns the male death-rate from phthisis exceeds the female. The difference here, no doubt, depends to a large extent on the unfavourable conditions under which men commonly work in rooms badly ventilated and dusty, and also, perhaps, as Dr. Ransome maintains, on the more general use of common lodging-houses by males, and the constant resort of the working man to the public-house, and his long-continued inhaling of the sputum-laden air.

The great preponderance of the phthisis rate on the female side between the ages of ten and twenty, as shewn by Ogle's and Tatham's tables, corresponding, as it does, with the period in which the outdoor life of boys and the indoor life of girls differ most widely, points in no uncertain manner to the dwellings as the source of the mischief.

Heredity.—Phthisis has always been accounted one of the most hereditary of all diseases. Numerous statistics, dealing with this point, are at hand; but, seeing that some refer to parental inheritance only, while others include collateral influence also, and in view of the fact that information concerning collaterals is less likely to be precise, we may confine our attention more particularly to parental inheritance.

The extent to which parental heredity is manifested in the subjects of phthisis has been very variously stated, Portal rating it as high as 66 per cent, Louis as low as 10 per cent. We may, perhaps, regard 30 per cent as about the proportion in which, according to most investigators, a history of parental heredity can be obtained. It has been maintained that fathers transmit to sons more frequently than to daughters, mothers to daughters more frequently than to sons. But the statistics of Walshe, R. E. Thompson, and Wilson Fox do not support this assertion. Heredity is generally but not universally regarded as playing a more important part in females than in males. It is stated that more female than male patients give a history of phthisis in the parent; and that among all hereditary cases maternal is in excess of paternal inheritance. In some

cases inheritance seems to have been derived from grandparents or great-grandparents, the parents having played the part of silent carriers of the disease. According to several observers, phthisis is manifested at an earlier age in those that evince an hereditary taint. After the age of twenty-five the acquired cases equal the inherited, and ultimately outnumber them. According to Dr. R. E. Thompson, a greater severity of form and a shorter duration of life characterise the hereditary cases; but the experience of Dr. C. T. Williams does not confirm this conclusion.

Enough has now been said to shew that, after all the labour expended on this subject, no general agreement has yet been reached.

It is evident that the investigation of this question is exposed to many fallacies, a few of which may be mentioned. In the first place, many deaths of parents and grandparents may have been wrongly attributed to bronchitis, pleurisy, or pneumonia, when the affection was really tuberculous. Against this, of course, in other cases death may have been erroneously ascribed to tuberculous disease. In dealing with a large number of cases these opposing fallacies will to some extent neutralise each other. A more important source of error depends on the undoubted fact that many ancestors reputed healthy have been the subjects of arrested tuberculosis. Again, parents may not manifest signs of phthisis till after the death of some of their offspring from this cause.

In the case of heredity among collaterals—brothers and sisters, uncles and aunts, cousins—the same fallacies must arise, but with an important addition. In all families, but especially among the poor, the mortality of infants and young children is very high; and there can be no doubt that the existence of tuberculosis at this age is very largely overlooked, death being ascribed to marasmus, diarrhoea, bronchitis, or broncho-pneumonia. On the whole, it seems that the tendency of the fallacies referred to would be to underestimate rather than to exaggerate the influence of heredity. The heredity of phthisis has received two widely different explanations. According to the prevailing opinion, it is not the disease itself that is inherited, but a disposition or tendency to acquire the disease when exposed to the necessary influences; the other view is, that the germ of the disease is directly communicated from the parent to the embryo.

The doctrine of hereditary predisposition has been assailed on more than one ground. In the first place, the existence of a peculiar bodily confirmation in the children of phthisical families, the tuberculous and scrofulous diatheses so much insisted upon by some writers, has been called in question. It is admitted that some of the features described are often seen in persons suffering from phthisis, though it is believed that to a considerable extent they are attributable to wasting of the muscles and adipose tissue, or to enlargement of external lymphatic glands, and are, therefore, manifestations of existing disease. These objections seem to be justified; but the hypothesis of hereditary proclivity does not necessitate the assumption of a special bodily habit, and the abandonment of this postulate does not materially weaken the

position of those who hold to the doctrine of predisposition. It has been objected that the percentage of family inheritance reckoned up from phthisical patients does not truly represent the influence of heredity, and that the percentage should be compared with the incidence of the disease in healthy families. Moreover, it is suggested that what is inherited is not a special disposition to tuberculosis only, but a general delicacy or vulnerability to adverse conditions of all kinds. According to Beneke this vulnerability is connected with the relatively small size of the heart in such persons. Others again would explain the prevalence of the disease in certain families by the greater opportunities of infection that exist in the dwellings of such persons. The first objection may be admitted as valid; but in order to arrive at accurate conclusions on this basis the subject would require investigation on a much larger scale than has been hitherto attempted. As Dr. Kingston Fowler points out, it is obviously misleading to work back from the consumptive member of a family to the parents, and to deduce the influence of heredity from a comparison of the percentage incidence of phthisis in the children of the phthisical and non-phthisical—a method adopted by some investigators in this field. For this practically assumes that there is a consumptive in every family, and takes no account of the families in which, in many unselected series, no member is phthisical.

Professor Karl Pearson has recently made an exhaustive statistical study of a limited number of cases of pulmonary tuberculosis, based on records furnished by Dr. W. C. Rivers from Crossley Sanatorium. These records include the total number of brothers and sisters, with particulars about them, the position of the patient in the family, and the age at which the disease developed, also an account of the parents, grandparents, uncles, and aunts. The conclusion is drawn that the diathesis of pulmonary tuberculosis is undoubtedly inherited. A larger number of investigations on these lines may be expected to throw further light on the question of heredity.

With regard to the explanation of heredity on the hypothesis of family infection, it seems that although this may account for many cases it will not explain all. Instances are not wanting where several members of a family, widely separated from one another, have manifested the disease in succession. If, however, the extreme latency of the tubercle bacillus postulated by some writers could be substantiated, the question of heredity would at once assume a new aspect altogether. Before proceeding to discuss the doctrine based upon this hypothesis, it may be pointed out that the existence of a family susceptibility to other infectious diseases—as to enteric fever, scarlatina, and diphtheria—has long been recognised by epidemiologists.

To Cohnheim we owe the suggestion that heredity depends upon the direct transmission of the tuberculous virus to the embryo—a view which has been further developed by Baumgarten. This author holds that infection of the respiratory and digestive tracts will only account for a small proportion of the cases of tuberculosis; and by a process of exclusion

he is led to the belief that heredity is the most potent factor in the continued existence of the disease. After rejecting the notion of hereditary predisposition mainly on the strength of arguments derived from the results of the experimental inoculation of animals, Baumgarten embraces the doctrine of the direct inheritance of the tubercle bacillus or its spores. According to his view the microbe may either be introduced through the placenta and thence infect the fetus through the umbilical vein ("placental infection"), or it may find access to the ovum itself either in the ovary or after its passage into the Fallopian tube ("germinative or conceptional infection"). In the latter case the microbe would mostly be conveyed by means of spermatozoa, though an observation of Jani's suggests that the bacilli may enter the Fallopian tube from the peritoneal cavity. The possibility of germinative infection from paternal sources cannot be denied in view of the discovery, by Jani and Weigert, of tubercle bacilli in the healthy testes and prostate glands of phthisical men. Virchow objected to the view that germinative infection plays an important part in heredity, on the ground that the presence of the bacillus must interfere with or arrest the development of the ovum; but Baumgarten urges that this argument is negatived by the history of congenital syphilis, and by the analogy of the pébrine disease of silkworms. In the case of syphilis, although miscarriages may occur, it commonly happens that the child is apparently healthy at birth, and signs of the disease do not appear for some weeks; a period of latency, therefore, undoubtedly ensues between infection of the ovum or fetus and the first few weeks of extra-uterine life. In the pébrine disease, which is caused by a psorospermial organism, Pasteur has shewn that the ova of the silkworm become infected with the spores of the parasite; but in spite of this the eggs are hatched normally, though the caterpillars ultimately succumb to the growth of the parasite in their bodies.

Baumgarten would explain the latency of the pébrine disease, congenital syphilis, and inherited tuberculosis by the supposition that the actively growing embryonic cells inhibit the development of the respective microbes.

Some interesting researches by Maffucci have an important bearing on this question. Tubercle bacilli from a tuberculous fowl were introduced into fertilised hen's eggs and incubation was allowed to proceed. Maffucci found that the bacilli did not multiply, but underwent a regressive change into granules exhibiting the staining reactions characteristic of the normal bacilli. The chick was hatched out in the usual way, but after about the twentieth day the bacilli began to develop, and a typical tuberculous infection ensued, the liver being conspicuously involved. If the dose of the bacilli introduced be small no visible tubercles form, but the chicken nevertheless dies of extreme marasmus, and bacilli are found in the organs in small numbers. The analogy suggested with congenital syphilis, the pébrine disease, and congenital tuberculosis of fowls is both interesting and instructive.

Placental or germinative infection may explain the rare cases in which

tuberculosis is found in the fetus or new-born infants; and also perhaps the less uncommon instances in which the disease arises during the first few months of life. But there seems to be no sufficient reason for the belief that the tubercle bacillus or its spores may remain dormant from the time of conception of the ovum to adult or middle life. Baumgarten would go even farther, for he applies his hypothesis to explain atavism occurring in tuberculous families; and would trace the inheritance of the microbe to a grandparent or even more remote ancestor, when the parents have remained healthy. The evidence in favour of Baumgarten's hypothesis is not strong, and is mainly drawn from observations on animals. Fetal tuberculosis has now been demonstrated in several cases in calves, but in man such an occurrence is extremely rare. Landouzy and Martin have published a case in which the apparently healthy fetus of a phthisical mother proved capable of infecting animals with tuberculosis, to shew that tubercle bacilli may be present in the tissues without exciting any manifest lesion. The hypothesis of direct inheritance does not appear to be reconcilable with the facts disclosed by Ogle's statistics. A reference to his table shews that the mortality from phthisis declines greatly after the completion of the second year until the tenth year, when it begins to rise again, attaining its maximum at a much later age. Moreover, the marked difference in the incidence of the disease on the two sexes at various ages is quite inexplicable on Baumgarten's hypothesis.

The only conclusion at present warranted is that direct inheritance is of decidedly subordinate importance to extra-uterine infection, however acquired.

P. K.

The Paths of Infection in Pulmonary Tuberculosis.—Investigators are unanimous in their belief that the tubercle bacillus may enter the human body through various portals. Great diversity of opinion, however, prevails as to which is the main route along which the bacillus passes to invade the lung and to give rise to that most common and formidable type of the disease, pulmonary tuberculosis. As the determination of the paths of infection is of fundamental importance in connexion with the vast machinery which has been set in motion in all civilised countries, during recent years, for the prophylaxis of pulmonary tuberculosis, it is necessary to consider, first, the accepted channels along which the bacillus may be borne, and secondly, to determine, if possible, which is the path of election.

(1) *Inhalation-Tuberculosis.*—According to this view, tubercle bacilli either pass into the bronchi and alveoli to produce a primary tuberculosis there, or, having traversed the walls of the respiratory surface, they lodge in the tracheo-bronchial glands. Multiplying in this site, they ultimately gain access to lymph- and blood-channels, along which they are borne to the lung, where they settle and undergo further development.

(2) The bacilli invade the mucous membrane of the nose, mouth, and pharynx either in inspired air or with food or other infected object.

From the primary portal of invasion the bacilli pass to the regional lymphatic glands in the neck, and ultimately enter the blood-stream, and are thus carried to the lungs.

(3) *Ingestion- or Deglutition-Tuberculosis.*—Bacilli are swallowed with food, mucus, saliva, etc., from the upper air- and food-passages, and, after escaping from the stomach through the pylorus, they either produce a primary intestinal tuberculosis, or, and this is more frequent, they traverse the intestinal epithelial barrier to become lodged in the mesenteric glands, whence they are carried by the thoracic duct and blood-channels to the lung.

(4) *Inoculation-Tuberculosis.*—Bacilli pass through the skin or urogenital mucous membrane and gain the lymphatic glands, being ultimately lymph- and blood-borne to the lung.

(5) *Congenital Tuberculosis.*—Bacilli penetrate the ovum from tuberculous sperm, or, and this is more probable, infection of the developing fetus takes place from bacilli which have successfully traversed the placental vessels from a tuberculous mother.

Clinical and pathological observations shew that the two last methods may be discounted as frequent causes of pulmonic invasion, and the discussion has centred round the other methods. It may be stated at once that the problem is not so much one of aerogenic as opposed to ingestion tuberculosis, but rather of aerogenic *versus* lymphatic and haemic invasion; for it must be remembered that in their upper parts the respiratory and alimentary tracts are fused, becoming separated from the pharynx downwards. From a practical standpoint the question at issue is whether the lung lesion is primary and due to direct aerogenic infection, or whether it is secondary in so far that the bacilli have been carried to the lung by lymph- and blood-channels. Daily observations at the bedside and in the post-mortem room would seem to teach that the respiratory path is the one by which the tubercle bacillus passes to the lungs; and it was long ago suggested that the disease was really induced by the inhalation of material containing the tubercle virus (Villemin, 1868). Many experiments, in which animals were caused to inhale pulverised and atomised phthisical sputum, led Tappeiner, Schottelius, Bertheau, Veraguth, Wargunin, Weichselbaum, and others to infer that this was proved by the results obtained. Gebhardt and Preyss were also able to demonstrate that enormous dilutions of tuberculous sputum can lead to inhalation-tuberculosis. The question was considered as settled by the series of 217 inhalation experiments performed by Koch with pure cultures of the bacillus which he had isolated. Without exception every animal developed pulmonary tuberculosis, and Koch formulated in a precise manner the doctrine that infection takes place by the inhalation of dried and pulverised phthisical sputum.

By the classical experiments of Hans Buchner (1888), it was shewn that after being inhaled, bacteria may actually be found in the blood; and in recent times Nenninger, Paul, Ficker, Beitzke, and others have also shewn that microbes may be aspirated from the mouth into the lung.

Thus, Beitzke dropped emulsions of *Bacterium prodigiosum* slowly and carefully into the mouths of rabbits, and on killing them thirty minutes later, was able to demonstrate the existence of the microbe in the trachea, bronchi, and alveoli. Experimenting in a similar manner, Paul succeeded in six out of ten instances in finding the microbes used in the lungs. With regard to the ultimate fate of microbes which have been inhaled, Klipstein, Nenninger, Snel, Paul, Quensel, and Wyssokowicz are of opinion that, in so far as they produce no pulmonic lesion, they are destroyed in the lung itself or escape to the bronchial glands. The inhalation hypothesis of pulmonary tuberculosis also received support from the numerous experiments in which animals were made to inhale soot, emery, and other particles (Zenker, Knauff, Ruppert, von Ins, and especially Julius Arnold). Direct intratracheal inoculation of atomised sputum or cultures of the tubercle bacilli succeeded in the hands of Villemin, Lippl, Watanabe, and Herxheimer. Nevertheless, a small number of investigators, either in consequence of preconceived physical deductions (Sänger), or in consequence of negative results from inhalation (Hildebrandt, Buttersack, Sirena and Pernice, de Toma, Cadéac and Malet), maintained that infection through the air-channels is unlikely or impossible. In spite of their objections, however, the inhalation doctrine was widely accepted and taught, and further researches were carried out to determine in what physical form the sputum is inhaled. As a result of numerous experiments, Cornet concluded that the chief danger exists when sputum becomes dried and diffused in the atmosphere; whereas Flügge and his co-workers M. Neisser, Sticher, Beninde, Nenninger, Köhlisch, from a long series of ingenious experiments, have concluded that it is only in very exceptional circumstances that phthisical sputum becomes dry enough to pass into the condition of dust. Flügge, mainly relying on the work of Laschtschenko, Heymann, and Beninde, is of opinion that the main danger is the inhalation of sputum in the moist state, and especially in the form of minute droplets or spray which is expelled from the mouths of consumptives during the acts of coughing, sneezing, and even speaking. Both by microscopic examination and by animal experiment Heymann demonstrated the existence of droplets, a result confirmed by Moeller, Königer, Kirstein, Hillier, and Ziesche. Moeller exposed slides near phthisical patients, and in 16 out of 30 cases found tubercle bacilli by the microscope alone; he also found tubercle bacilli three times in the mucus of his own nose, and in the nasal secretions of seventeen attendants and eighteen ward-maids in a sanatorium. Straus had previously had similar experiences. In the Faroe Islands, where the conditions of life are peculiar, Boeg, from observations prolonged over a series of years, considered that 77 per cent of his cases had contracted phthisis from sprayed sputum. The great dissemination of tuberculosis in Asiatic Turkey was explained by Christ on a like assumption. As a result of all these experiments and observations, it was asserted by the end of the nineteenth century that pulmonary tuberculosis is an inhalation disease, an assertion in harmony

with the opinion expressed by Koch in his well-known London address in 1901, that the main, if not the only, source of human tuberculosis is the human consumptive. From this time onwards researches were vigorously prosecuted on the point raised by Koch that human and bovine tubercle bacilli differ. At the same time a number of pathologists —Aufrecht, von Baumgarten, Ribbert, Grober—were also drawing attention to the possibility that infection of the lung might occur through channels other than the respiratory tubes. The whole question of the manner of infection of the lungs was reopened for discussion as the result of von Behring's address at the Naturforscher Versammlung in Kassel (September 1903). Dealing with the post-genital origin of tuberculosis, he affirmed that the *milk* taken by the suckling is the main source of tuberculosis. Based on the observations of Roemer that genuine proteins pass unchanged through the intestinal mucous membranes of foals, calves, and small laboratory animals, von Behring asserted that the same may occur in the case of bacteria, the mucous membrane of the bowel behaving like a large-pore filter. In support of this statement he cites experiments in which anthrax bacilli introduced directly into the stomach of very young guinea-pigs, produced fatal anthrax infection, whereas in the case of adult animals, they escaped from the bowel. He also found it possible to infect very young guinea-pigs with tubercle bacilli in this way. To account for the fact that consumption preponderates after the period of childhood is passed, von Behring presupposes the existence of a very lengthy latent period amounting to months, years, or even decades, tubercle bacilli taken into the alimentary canal in infancy remaining dormant, so to speak, all the time, and ultimately bursting out to give rise to manifest tuberculosis in adult life.

Coming from such a distinguished observer as von Behring, although on a seemingly slender experimental basis, these views have created widespread interest, and have been the starting-point for the development of doctrines calculated to upset beliefs supposed to rest upon sound clinical, anatomical, and experimental data. For, whereas inhalation was regarded as the main method of infection, there are now those who deny this altogether, and refer the pulmonary lesion to tubercle bacilli passing from the intestine into the lymphatic glands, to be ultimately lymph- and blood-borne to the lungs. It will therefore be necessary to consider the most recent anatomical and experimental data bearing on this question under two heads: (*a*) Is infection by inhalation possible? (*b*) Is inhalation the commonest mode of infection, or do the tubercle bacilli invade the body mainly by the alimentary tract?

(*a*) In addition to the negative results mentioned above, Cadéac and Malet have pointed out that animals may inhale with impunity air charged with tubercle bacilli; for in the case of 38 guinea-pigs and 11 rabbits, they were successful in inducing inhalation-tuberculosis in five instances only, and even in two of these there were lesions which indicated that the bacilli had passed to the lung by the alimentary tract. Schlossmann and Weleminsky have also had negative results. Vallée inoculated large

doses of tubercle bacilli directly into the trachea of two calves, and six months later was unable to find any disease of the lung or bronchial glands. In a more extensive research, in which several milligrams of living bacilli were introduced into the naso-pharynx of twelve cattle, pulmonary tuberculosis was not induced, although tuberculosis of the retro-pharyngeal, cervical, and tracheal glands was noted in four instances. Calmette and Guerin are also opposed to the inhalation view, and consider that tubercle bacilli can gain access to the alveoli only after being introduced beyond the bifurcation of the trachea.

On the other hand, Hartl and Hermann, Bartel and Neumann, Findel, Heymann, Ballin, Pfeiffer and Friedberger have obtained results entirely opposed to these. Hartl and Hermann, using suspensions of *Bacillus prodigiosus*, shewed that penetration into the alveoli was possible, although the majority of the microbes were retained in the upper respiratory passages; and Bartel and Neumann confirmed these observations in the case of tubercle bacilli. The most convincing experiments are those carried out by Findel (1907), with a very perfect technique, especial interest attaching to the comparison he was able to make between the quantities necessary to produce inhalation- and deglutition-tuberculosis respectively. In dogs, 0·141 mgrm. of a living culture (4,900,000 T.B.) produced extensive pulmonary tuberculosis when inhaled, whereas 172·0 mgrm. (6020 million T.B.) administered through a stomach tube into the alimentary canal produced no effect. In other words, a dose 1220 times as large as that required to produce tuberculosis of the lungs produced no effect when tubercle bacilli were administered by way of the digestive system. In an extensive series of experiments on 83 guinea-pigs, quantities ranging from 20 to 290,000 tubercle bacilli were inhaled, and down to doses of 62 tubercle bacilli all animals not dying from intercurrent disease shewed extensive tuberculosis, almost confined to the lungs and bronchial glands. Of 6 animals receiving still smaller doses (3 with 40 T.B. and 3 with 20 T.B.), there was manifest tuberculosis in 2 (namely, 2 with 20 T.B.). In feeding experiments, on the other hand, quantities ranging from 19,100 to 382,000 did not produce any lesion whatsoever. Similar results have been obtained by Reichenbach in the case of young goats, Alexander in the case of rabbits, and Kuss and Lobstein and Pfeiffer and Friedberger in the case of guinea-pigs. In the experiments of the latter 1000 times the dose required to produce tuberculosis as a result of inhalation had no effect when introduced into the stomach. A large number of experiments done with soot particles may also be brought into line here. As was mentioned above, it was generally accepted as settled that anthracosis is due to the inhalation of soot. Vansteenberghe and Grysez (1905), however, affirmed that pulmonary anthracosis in guinea-pigs really arises by ingestion of carbon particles—a revival of an old view of Villaret's. They considered that the particles pass from the intestine by the lymphatics into blood, whence they are deposited in the lungs. This view is in opposition to the classical researches of Ponfick and of Hoffmann and Langerhans, who found that particles gaining access to the blood are

deposited in the spleen, liver, bone-marrow, and lymphatic glands. According to Vansteenberghe and Grysez, when animals are made to inhale air laden with soot, the latter does not appear in the lungs when the oesophagus is occluded. If a bronchus is plugged, the oesophagus being patent, both lungs become equally anthracotic. These views, extended by Calmette, Vansteenberghe, and Grysez, have met with almost universal contradiction at the hands of Aschoff, Schultze, Mironescu, Beitzke, Remlinger, Basset, Kuss and Lobstein, Nieuwenhuyse, Heller and Wolkenstein, Ruata, and others; and the inhalation hypothesis of anthracosis may be definitely looked upon as standing unshaken.

Inasmuch as experimental pulmonary tuberculosis rarely exhibits the localisation and changes so characteristically met with in man, there have not been wanting morbid anatomists who consider that the problem of the origin of pulmonary consumption in man is to be solved by a study of the early apical lesions. Prominent among investigations on these lines are the observations of Birch-Hirschfeld, who from the extensive autopsy material in Leipzig was able to obtain 34 cases so early that they could be utilised for inferences as to the origin of apical tuberculosis. He came to the conclusion that the disease originates in the walls of bronchi of the third to the fifth order, especially in the bronchus apicis posterior, and that the disease must be the result of inhaling tubercle bacilli; he attributed the frequency of the affection of the apex to the direction of the bronchi in this site, and to the fact that in corrosion preparations demonstrable abnormalities may interfere with the degree of respiratory movements; in other words, that there may be disposing factors rendering the apex peculiarly liable to invasion. Schmorl was able in the main to confirm these results in 25 cases (out of a post-mortem material of 4000 cases), in some of which the lesion was limited to the wall of bronchi of the fifth to the seventh order. Abrikossow, from a study of very minute lesions, 1·5-5 mm. in diameter, also believed that the disease began in the bronchi, although invasion of the alveoli rapidly takes place. According to him the primary lesion is a tuberculous peribronchitis, which spreads centrifugally and centripetally. After the onset of caseation, particles become aspirated into the alveoli and set up tuberculosis in this site. Ribbert, on the other hand, considers that whereas the infection is aerogenic, the lung lesion is not primary, as the tubercle bacilli pass through the alveoli by lymph-vessels to the tracheo-bronchial glands, where they collect in considerable numbers and give rise to manifest tuberculosis. Ultimately they get into the blood, and, passing through the pulmonic vessels, are arrested mainly in the apex. In criticising Ribbert's views Schmorl has pointed out that in bronchial-gland tuberculosis the number of tubercle bacilli is usually small, and that at a relatively early period there is a tendency to obliterative inflammation of the vessels which would render a blood invasion unlikely. In fifteen cases of primary extra-pulmonic tuberculosis Schmorl found the lungs normal thirteen times. It will thus be seen that even in the matter of the earliest lesions in man opinion is divided, and many doubt whether the problem can be solved by the anatomical mode of investigation.

(*b*) In recent years attention has been directed to the possibility that infection of the lungs may be due to bacilli passing from the naso-pharynx to the cervical glands, or even through the lower division of the alimentary tract; and here again the problem has been attacked from two aspects, namely, experimental deglutition-tuberculosis and pathological-anatomical studies in man. Since the classical researches of Chauveau (1868-1872) it has been known that animals may be infected by bacilli passing through the intestinal wall. At first this view was denied, but afterwards was put on a broad experimental basis by the researches of Gerlach, Günther and Harms, Bollinger, Parrot, St. Cyr, Toussaint, Orth, Wesener, Sidney Martin, and others. As far as this doctrine applies to man opinions were very divided, although in general it was assumed that the danger of infection by tuberculous matter in food was not comparable to that of inhalation. In recent years Calmette, Guérin, and Breton have emphasised the great importance of the alimentary system as a portal of invasion for tubercle bacilli, and in this respect have asserted themselves as adherents of von Behring's views mentioned above (p. 302). It has also been believed for some time that even though bacilli may enter the body by way of the intestines they may produce no primary disease in the wall, but, escaping through, are first arrested in the mesenteric lymphatic glands, or even pass into the blood. This view is founded on the experiments of Cornet, Wesener, Dobroklonski, Bisanti and Panisset, Kovács, Nicolas and Descos, Ravenel, Porcher and Desoubry. Bisanti and Panisset, for example, fed dogs on soup containing tubercle bacilli, and within four to five hours demonstrated the presence of bacilli in the heart's blood. Three and three and a half hours after ingestion in milk, Nicolas and Descos found tubercle bacilli in the chyle. Four hours after introducing bacilli suspended in melted butter into the stomach, Ravenel found them in the mesenteric glands. Even in normal conditions Porcher and Desoubry found that considerable numbers of bacilli pass into the chyle during digestion. There are also a good many data to shew that after ingestion of bacilli pulmonary tuberculosis may occur, although there may be no tuberculosis of the alimentary canal or its regional lymphatic system (Bollinger, Aufrecht, Orth, Weleminsky, Ravenel, Malm, Jensen, Kovács, von Behring, Schlossmann and Engel, Schroeder and Cotton). Indeed Weleminsky considers that transport of tubercle bacilli from the intestine to the bronchial glands is the common mode of infection, and he holds that these lymphatic glands occupy a remarkable position in the animal economy, inasmuch as they are not, as has generally been believed, the regional lymphatic glands of the thoracic viscera, but are terminal reservoirs receiving the lymph of the whole body and pouring it by a special efferent duct, the truncus broncho-mediastinus, into the left subclavian vein. This revolutionary view has been entirely denied by Hart, Kitamura, Beitzke, and Oehlecker as a result of their observations in animals. To what extent ingestion of infective material plays a part

in tuberculosis in man cannot be settled by experimental inquiries in animals. When we come to consider the evidence of alimentary tuberculosis in man as derived from pathological-anatomical observations, the state of affairs is even more confused; indeed the diversity of opinion is so great that the whole question would appear to be in urgent need of complete re-investigation. Taking into consideration the published data it is important to consider separately the upper and lower divisions of the alimentary tract with reference to the question of deglutition- and ingestion-tuberculosis in man; for the upper end being aero-digestive it is conceivable that tubercle bacilli may be swallowed directly with food containing them or in the secretions of the naso-pharynx. Tuberculosis of the tongue, mouth, palate, and gums is admittedly rare, but since tuberculosis of the cervical lymphatic glands is excessively common, it is assumed that tubercle bacilli must frequently pass through the mucous membranes which these glands drain. In the great lymphatic pharyngeal ring including the lingual and faucial tonsils the anatomical structure is such that microbes must frequently enter either with inspired air or food. Primary tuberculosis of the tonsil occurs in 5 per cent of all enlarged tonsils (Fränkel); in 1671 cases quoted by Wood the percentage worked out at 5·2. The tuberculosis of cervical glands must, however, come from invasion of the mouth region, and the bacilli apparently escape to the glands at a very early date without involvement of the mucous membrane. With reference to the question of intestinal tuberculosis as indicating the primary seat of invasion opinion is much divided, not only among workers in different countries, but even in the same country or town. These differences of opinion are mainly explicable in the interpretation of the observations, and the manner in which those affected are placed in different categories as regards age. To this it may be added that in their statistics some authors speak of alimentary tuberculosis as including lesions of the tonsils and cervical glands as well as the genuine intestinal and mesenteric cases. Dealing with the latter class as indicating undoubted ingestion- or deglutition-infection it is impossible to refer to all the works which have appeared on this subject. At one time primary intestinal tuberculosis was regarded as extremely rare, but as the experimental production of tuberculosis by feeding became well established it was considered that the consumption of tuberculous milk was associated with a considerable incidence of tuberculosis, especially in early life. In England in particular this doctrine acquired considerable notoriety through the observations of Woodhead, Still, Shennan, Symes and Fisher, Guthrie, Carr, Batten, Kingsford, Price-Jones, and others. From their work it would appear that in 1560 autopsies in children primary tuberculosis was found in the intestine or lymphatic glands pertaining thereto in 290 cases = 18·6 per cent. In the United States Northrupp, Emmet Holt, and Bovaird in New York report 319 autopsies with 3 cases of primary intestinal tuberculosis or ·94 per cent. In 115 autopsies in the Children's Hospital in Philadelphia, Hand found the percentage to be 8·7. In 220 children

dying from diphtheria Councilman, Mallory, and Pearce found latent tuberculosis 35 times = 16 per cent; among these 13 = 5·9 per cent of the total mortality, or 37·1 per cent of latent tuberculous cases were of intestinal origin. From Germany the results are very divergent; thus Baginsky in 933 cases found no primary intestinal tuberculosis, and in a second series of 806 necropsies in children only 6 out of 144 cases of tuberculosis = 4·1 per cent. In 203 autopsies made by Orth only 2 cases occurred of primary intestinal tubercle among a total of 47 tuberculous cases. In 1903 Ganghofner published a series of 973 necropsies, of which only 5 = 0·5 per cent were of primary intestinal tuberculosis. Biedert saw only 16 cases in 3104 necropsies in children. Next to the English statistics in point of frequence come the reports from Heller's Institut in Kiel; between 1873 and 1894 there were 714 post-mortem examinations on children dead from diphtheria. In 140 of these (19·6 per cent) tuberculosis was accidentally discovered, and 53 (37·8 per cent) of these latent cases were referred to a primary intestinal infection. Analysing the 15,000 necropsies made in Kiel in thirty years, Hof referred 25·1 per cent to primary intestinal tuberculosis. From the study of necropsy material comprising 1820 cases Lubarsch noted tuberculosis in 60·6 per cent; in 297 necropsies in children he found tuberculosis 63 times, and of these 14 (= 21·2 per cent) were referable to intestinal infection. In children over one year the percentage of alimentary tuberculosis was actually 23·8 per cent. In 26 necropsies made by Nebelthau in tuberculous children intestinal lesions were found in 5 (19·2 per cent). With these may be compared the careful observations of Francis Harbitz who, on taking the total fatal cases and adding the latent cases, found the primary lesion in the respiratory tract in 41 per cent, and in the digestive tract in 22 per cent. The combined infection of the respiratory and alimentary tracts shewed 20·5 per cent, general lymph-gland tuberculosis 9·4 per cent, and cases of doubtful origin 6·8 per cent. Fibiger and C. O. Jensen, from the Friedrich's Hospital in Copenhagen, examined 213 bodies of all ages, and found tuberculosis beginning in the intestine 13 times (6 per cent). Ipsen, continuing these observations on 600 cases, noted primary tuberculosis of the digestive system in 32; 102 of the cases were children between 0-15 years and dead from diseases other than tuberculosis. The variations which may take place in one and the same town are strikingly seen in the reports from Berlin. In the Bethanien Hospital (1904-5) Edens in 31 tuberculous necropsies considered that 35·5 per cent were of primary intestinal origin; whereas in the pathological department of the Charité, Orth in 77 necropsies found only 8 of digestive origin. Hamburger, in Vienna, recently found tuberculosis in 335 out of 848 necropsies, but in no single case was the primary source of the disease certainly in the intestine. The causes of these differences are not easy to determine; one factor, however, is the inclusion of different age-limits in the statistics. In the following compilation

this is strikingly borne out when the amount of ingestion-tuberculosis between 0-15 years is compared with that between 1-15 years :—

	Councilman, Mallory, and Pearce, 1901.	Heller, 1902.	Ganghofner, 1903.	Lubarsch, 1904.	Orth, 1904.	Edens, 1905.	Total.
Number of necropsies in children from 0-15 years . . .	220	714	973	297	203	123	2530
Cases of Primary Intestinal Tuberculosis	13	53	5	14	2	11	98
Percentage	5·9	7·4	0·5	4·7	0·98	8·9	3·8

	Wagener, 1903.	Wagener, 1905.	Lubarsch, 1904.	Edens, 1905.	Edens, 1907.	Orth, 1904.	Orth, 1904.	Total.
Number of necropsies in children from 1-15 years.	76	67	52	91	74	131	73	564
Cases of Primary Intestinal Tuberculosis . .	16	11	12	11	10	2	9	71
Percentage. . . .	21·1	16·4	23·0	12·0	13·5	1·5	12·3	12·5

From the table it is evident that very great differences will appear in statistics according to the limits of age which are arbitrarily taken. Further, great differences may no doubt be expected in the interpretation of the same anatomical condition by different pathologists. Indeed, it is desirable that the whole subject should be revised, especially in the light of recent experiments, which shew that the case under discussion may be much more complicated than is generally believed. We have seen above that there are good grounds for the belief that tubercle bacilli may fail to produce any recognisable change at the point of inoculation, the first evidence of infection being an invasion of the regional lymphatic glands. It has, however, been asserted recently that even the first lymphatic glands corresponding to the portal of invasion may be passed, the disease appearing in glands higher up in the lymphatic system, and nearer the blood paths. If this is true, it becomes a matter of very serious difficulty,

if not an impossibility, to determine by anatomical investigations the exact region in which the bacilli have penetrated the body. The experimental grounds which have led to this new belief are given by J. Bartel, who fed guinea-pigs with a single tuberculous repast containing bacilli of human origin. Like other observers he obtained negative results as far as concerned manifest tuberculosis, but on inoculating emulsions of the apparently healthy mesenteric glands into the abdomens of other guinea-pigs he arrived at a different conclusion in so far that he was able to produce tuberculosis by the inoculation. He found that the tubercle bacilli might remain for as long as 104 days in this latent condition, namely, without shewing any appearance of giving rise to manifest tuberculosis. Bartel and Spieler have emphasised the importance of this pre-tuberculous or "lymphoid stage," which is characterised by a slight lymphoid hyperplasia with swelling of the gland; microscopically there is no histological evidence of tuberculosis, tubercle bacilli are scanty or cannot be found, but inoculation into healthy guinea-pigs proves that the glands contain living tubercle bacilli. The importance of this lymphoid stage is seen in the following table, in which a comparison is made between the relative frequency of manifest tuberculosis and tuberculosis which can be induced by inoculation:—

	Tuberculosis produced by Inoculation.	Macroscopic Tuberculosis.
Tonsil and neighbourhood .	11·7 per cent.	0 per cent.
Cervical glands . . .	58 ,,	45 ,,
Bronchial glands . . .	52·9 ,,	64 ,,
Mesenteric glands . . .	100 ,,	45 ,,

In conjunction with Neumann, Bartel has also drawn attention to the manner in which different glands behave towards tubercle bacilli, for the lymphoid stage is the more common in the case of the cervical and mesenteric glands, whereas tuberculosis becomes manifest in a more severe degree and at an earlier date in the case of the bronchial glands. If these results are correct the attempt to locate the portal of invasion of tubercle bacilli in man becomes extremely difficult and complicated, as in the absence of extensive inoculations in animals latent tuberculosis may be completely overlooked. We may therefore inquire whether there is any evidence from human pathology to support Bartel's contention, and whether it is necessary to confine the term "latency" to the occurrence of tubercle bacilli without macroscopic or microscopic evidence of tuberculosis. A considerable literature exists on this subject as shewn by the work of Loomis, Pizzini, Kaelble, Harbitz, Macfadyen and MacConkey, Rosenberger, Weichselbaum and Bartel, Calmette, Guérin and Déléarde, Goodale, Rabinowitsch, Weber and Baginsky, and Joest. Pizzini inoculated guinea-pigs with emulsions of the peribronchial, cervical, and mesenteric glands of thirty non-tuberculous individuals, and in twelve instances proved the existence of tubercle bacilli. In 91 children without any evidence of tuberculosis Harbitz found 18 were infective

(10 being under one year of age). Thirteen times the infection followed inoculation of the cervical glands. Macfadyen and MacConkey inoculated the mesenteric glands of 20 children free from tuberculosis, and in five instances produced tuberculosis. Their inoculations with emulsions of thirty-four tonsils and forty-four adenoids, however, were negative. In 21 non-tuberculous cases, including 10 children, Rosenberger induced tuberculosis six times by inoculation. Goodale inoculated emulsions of eleven tonsils and adenoids, and on one occasion obtained a positive result, the bacillus isolated being of the bovine type. In Rabinowitsch's case of a child dead from bronchopneumonia, the mesenteric and cervical glands, although apparently free of tubercle, were proved to contain tubercle bacilli of the human type. Weber and Baginsky had only one positive result in the case of the glands of 26 non-tuberculous children, and most recently Joest was altogether unable to prove the existence of latency in the absence of definite tuberculous structure.

Even if it be admitted that tuberculosis of the lymphatic glands is common, great difference of opinion exists as to the manner of transport of the bacillus to the lung. Thus, although many hold that pulmonary consumption is preceded by cervical-gland tuberculosis, the path by which this takes place is stated very variously by authors. Thus Dieulafoy, Volland, and Chiari state that tubercle bacilli pass in the lymph stream through the trunci lymphatici into the venous system, and thence to the lungs. Others again hold that the bacilli pass from the cervical to the supraclavicular glands, and thence to the apex of the lung (Grober, Klebs). Others again consider that tubercle bacilli pass from the cervical glands to the bronchial glands, whence they get into the blood and are carried to the lungs (Aufrecht, Gördeler, Grawitz, Weleminsky, Harbitz). Whilst the descriptions of anatomists differ very considerably with reference to the normal distribution of lymphatic glands and vessels, the recent careful injections made by Most and by Beitzke with the aid of Gerota's method go to shew that there are not any vessels passing from the cervical to the bronchial glands, and that if infection take place from the cervical glands it must be by way of the trunci lymphatici and superior vena cava. The assertion by Weleminsky that the bronchial glands receive the lymph of the mesenteric glands is not confirmed by the work of Hart, Oehlecker, and Kitamura, who have vindicated the position of the bronchial glands as appertaining to the lungs.

Since it has been shewn that tuberculosis of the lung may follow inoculation of tubercle bacilli apart altogether from infection by way of the lungs or alimentary system, some authors have formulated the hypothesis that there are disposing factors which render the lung peculiarly vulnerable. Askanazy, for example, saw typical pulmonary tuberculosis follow the intravenous inoculation of a very minute quantity of bovine bacilli into the rabbit, Morpurgo observing the same result in the rabbit and guinea-pig after intra-arterial inoculation. Von. Behring and Neufeld produced pulmonary tuberculosis by inoculating with bovine bacilli goats that had previously been immunised with bacilli of the

human type. In the case of rats inoculated subcutaneously or intraperitoneally with bovine bacilli Bongert observed pulmonary tuberculosis. The direct introduction of tubercle bacilli into the stomachs of very young guinea-pigs was followed by pulmonary tuberculosis (Schlossmann Ravenel), whereas a repetition of this result by Strassner was negative. Bartel treated rabbits first with attenuated *Perlsucht* and subsequently with virulent *Perlsucht* bacilli, and saw isolated pulmonary tubercles after intraperitoneal inoculation. Orth also succeeded in inducing cavernous phthisis in rabbits that had been inoculated with tubercle bacilli obtained from cold-blooded animals. These experiments prove that the lung is very apt to become the seat of disease irrespective of the site of the inoculation of the bacilli, though we do not know the exact nature of this vulnerability or disposition. The craving of the human mind for concrete explanations has, however, led several investigators to formulate an anatomical basis of the lung disposition and especially of the apical disposition. Thus, in 1859, Freund emphasised the importance of symmetrical or asymmetrical stenosis of the upper thoracic aperture due to shortening of cartilage of the first rib in causing abnormal ventilation of the lung and rendering it prone to infection. Birch-Hirschfeld also drew attention to abnormalities in the course of the bronchus apicis posterior as shewn by corrosion preparations, this, along with the ascending direction of the bronchus, probably acting as a disposing factor. Schmorl has emphasised the importance of a furrow on the lung caused by the first rib. Hart has made an elaborate investigation on 400 adults and 100 children in order to solve this problem; from puberty onwards he finds that the superior thoracic aperture alters in shape, and during the process the apex rises and comes to occupy the bend which has taken place in the head and neck of the first cervical rib near the vertebral column. This alteration may, however, fail to occur, the upper aperture of the thorax remaining of the infantile type and in consequence a stenosis, which may be symmetrical or asymmetrical, ensues. In his 400 adult necropsies Hart found this 114 times, and this comprised only 11 (9·6 per cent) healthy apices. Twenty-five (22 per cent) had tuberculous change with a tendency to heal, whereas 78 (68·4 per cent) were the subjects of progressive apical tuberculosis. In a table he shews the relationship between the normal and stenosed apertures thus :—

	Normal Aperture.	Stenosed Aperture.
Lungs healthy . . .	47·2 per cent.	9·6 per cent.
Tuberculosis wholly or partially healed	36·4 „	22·0 „
Progressive tuberculosis . .	16·4 „	68·4 „

Hart considers that the stenosis of the upper thoracic aperture is of great importance, especially in connexion with tuberculosis between puberty and the thirtieth to fortieth year. Of 72 consumptives who had not yet attained their fortieth year 58 (= 80·6 per cent) had stenosis, whereas out of 53 consumptives over forty there were 14 only or 26·4 per cent

with this anomaly. Rothschild has attempted to shew that a potent disposing element in the production of apical tuberculosis is an exostosis which takes place between the manubrium and gladiolus sterni at the angulus Ludovici. This view has, however, been strenuously denied by Hart, v. Hansemann, and Lissauer on the ground of anatomical observation. Others, however, have laid less weight on gross anatomical lesions, and have considered that the explanation of the disposition of the lung is a much more subtle problem which at the present time cannot be solved. In recent years there has been a general tendency to regard tuberculosis as essentially a disease of lymphatic tissue. In this lymphatic tissue the bacillus multiplies, produces its characteristic lesions, and in a large number of cases becomes transported by the blood stream into the lung. As we have seen the lung is prone to become infected irrespective of the manner of inoculation. From the lung the bacillus makes its way into the outer world, the lung being "the appointed channel for the elimination of the tubercle bacillus and consequent preservation of the parasitic race" (Payne). The nature of the extraordinary predisposition of the lung remains in darkness at the present time. It will probably be long before the disposition factor can be practically dealt with in the individual case. In the meantime the object of medicine is to carry the prevention of phthisis to the highest practical possibilities by placing, as Guinard has happily put it, "sentinelles à toutes les portes." In deciding whether all the portals are worthy of equal consideration we must look back on the data given above, and here it seems to me that the older view that the inhalation of human tuberculous sputum constitutes the gravest source of danger still retains its importance in comparison with the more modern view which attributes to deglutition the principal part in the incidence of tuberculosis. The possibility that the ingestion of tubercle bacilli in children gives rise to tuberculosis more frequently than was formerly supposed must be admitted, but it would appear to be still true that in the adult pulmonary consumption is essentially an inhalation disease. Even when it is admitted that deglutition-tuberculosis in children is common, it does not follow that this is necessarily due to the ingestion of bacilli of bovine origin, as there are multitudinous chances for the introduction of human tubercle bacilli into the lymphatic apparatus of the throat and even into the lower parts of the alimentary canal. It is impossible at the present time to make any categorical statement as to the exact relations between human and bovine tubercle bacilli, but that tuberculous sputum is the chief element of danger to man cannot be doubted, and the main arguments in favour of a primary localisation in the lung as a result of aerogenic infection are, (1) the great dissemination of tuberculous sputum from multitudes of consumptives; (2) the early anatomical lesions in the lungs; (3) that very minute doses induce tuberculosis when inhaled, the lung being apparently the most easily infected of all organs. To this it may be added that the importance of infection with bovine bacilli sinks into the background in countries such as Japan (Kitasato), Turkey

(Rieder), Greenland (Nansen, Kjier, Rördam), Egypt (v. Becker), Rumania (Babes), Asiatic Turkey (Christ), and the Gold Coast (Fisch), where apical tubercle is very frequent, but where cow's milk is drunk sparingly or not at all.

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Morbid Anatomy.—Tuberculosis is in its origin a local disease depending on the lodgment and growth of the tubercle bacillus; but in virtue of its infective character it not only extends by continuity from the primary lesion, but it tends also to invade other parts of the body.

Fever and other constitutional effects of tuberculosis are often out of all proportion to the extent of the local disease, and must be ascribed to the circulation in the blood of some as yet unrecognised chemical poison produced by the bacillus.

We have now to consider the changes in the lungs that result from the *invasion* of the tubercle bacillus. The initial lesions exhibit certain differences according to the manner in which the microbe is introduced into the organ. Excluding the comparatively few cases in which the pulmonary disease is due to direct extension from neighbouring lymphatic glands, or from the osseous parietes of the thorax, it may be said that the bacillus gains entrance in one of two ways, through the blood-vessels or through the bronchial tubes. In the former case the entry of a large number of bacilli into the circulating blood gives rise to an eruption of miliary nodules disseminated through the whole lung, and through many organs of the body. In such cases, as was first pointed out by Buhl, a caseous focus will almost invariably be found in some lymphatic gland; or, possibly, in the lung itself. It is probable that the introduction of a small dose of the bacilli may have as its result a circumscribed lesion of the lung. In either case infection is brought about by an embolic process, the microbe being arrested in the alveolar capillaries. The presence of the bacilli in the first instance provokes a specific cellular growth in the capillary wall, but the process soon extends into the cavity

of the air-sacs, where a similar cell growth develops. If the microbes enter the lung through the air-passages they appear to become arrested in the terminal bronchioles or alveoli, in which parts the epithelium is not ciliated. From the bronchiole the cell growth invades the peribronchial sheath and alveolar cavities, the result being an islet of peribronchitis and bronchopneumonia. Tuberculous growths, wherever situated, are devoid of blood-vessels. In generalised miliary tuberculosis the pulmonary changes are but a part of the general infection of the body, though the lung may suffer most. As death results in a few weeks at the latest the tubercles in the lungs have not time to go through the usual cycle of changes manifested in the cases which run a more chronic course.

Inasmuch as the lesions of chronic tuberculosis differ in degree rather than in kind it will be convenient to study the process in the chronic form. Since the time of Louis the preference of tuberculosis for the apex of the lung has been universally recognised; the earliest lesions are found about one to two inches below the extreme apex. In rare instances the disease begins in other parts of the lung, as at the base of the lower lobe; but in adults, a primary basic origin is exceedingly rare, and is probably not found in more than one in 400 or 500 cases: in children it is relatively less infrequent, but this is due to the fact that in them primary tuberculosis of the bronchial glands is more common and attains to greater proportions than in adults. Many cases of tuberculosis in children, apparently basic in origin, are really due to direct extension from caseous bronchial glands. In rare cases of irregular localisation, whether in children or adults, the disease has originated in the vertebrae. At an early stage of the disease the lesion will be found to consist of one or more small greyish nodules, the centre of which corresponds to a bronchiole; as these nodules increase in size they tend to acquire a racemose shape owing to the growth of miliary granulations at the periphery. In man it is not easy, as a rule, to trace the earliest steps of the process in the primary nodule, as before the patient's death regressive changes have already set in; but from a study of the secondary nodules developed in similar cases we may conclude, as Rindfleisch long ago taught, that the process begins in a terminal bronchus and thence spreads to the corresponding lobule—that is to say, the lesion is essentially bronchopneumonic. In the early stages we find the mucous membrane of the bronchiole swollen and infiltrated with cells, and the surface more or less denuded of epithelium. The cavity of the tube contains mucous secretion mixed with pus cells. Tubercle bacilli may sometimes be recognised in the secretion as well as in the cellular infiltration. A similar cell growth, with a varying number of bacilli, is found in the peribronchial sheath and in the corresponding alveoli. At the periphery of the tuberculous area the cells are entangled in a scanty meshwork of delicate fibres; but in no cases, save the most chronic, is fibrillation visible at the centre of the tubercle. By degrees the cellular growth extends to the neighbouring lobules, where the same process is enacted; and thus the original nodule may become more or less lost in a diffuse infiltration or tuberculous

pneumonia. The direct propagation of the disease is brought about by the spread of the tubercle bacilli along the lymph spaces and vessels in the interstitial tissue of the lung. In the course of the tuberculous

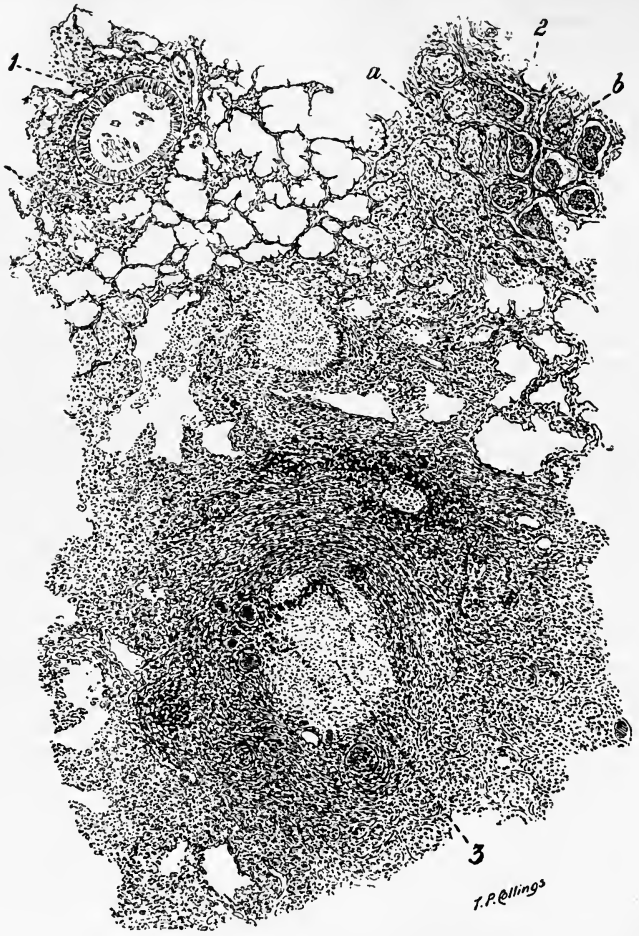

Fig. 18.—Composite photograph taken from three different sections, illustrating the development of the tuberculous process. (Low power.) 1. Islet of tuberculous peribronchitis, a bronchiole with surrounding tuberculous infiltration. 2. Patch of tuberculous "pneumonia": *a*, Early stage—alveoli stuffed with large pale epithelioid cells (not recognisable with so low a power); *b*, Later stage—alveoli contain granular necrotic masses, the outlines of the cells having disappeared. 3. Fibro-caseous tuberculous nodule, shewing a pale amorphous caseous centre embedded in concentrically arranged fibro-cellular connective tissue, which contains a few giant-cells in its inner zone. Coarse black carbon particles in places.

process the walls of the alveoli and, in a lesser degree, the coats of the small arteries and veins become involved in the cell growth. Perforation of the wall of a pulmonary vein and entrance of the bacilli into the

blood is, as was first shewn by Weigert, one of the commonest modes of general infection of the body in cases of pulmonary tuberculosis. A small artery may be affected in like manner, and a localised eruption of miliary tubercles take place in the lung in the area of distribution of the affected vessel; but in most cases extra-alveolar lesions are of quite subordinate importance to the changes occurring within the air-sacs. In the most chronic varieties of tuberculosis the *development of fibrous tissue* is the predominant feature; and this leads to a thickening of the inter-alveolar, peribronchial, interlobular and subpleural connective-tissue. *Tubercle bacilli* are found in and among the various cells but not in the fibrous tissue itself.

The destiny of the tuberculous growth is twofold. In the first place, the cells undergo *necrosis*; their outline becomes indistinct, the nucleus disappears, and the cell is converted into a finely granular or hyaline mass, which then becomes fused with neighbouring cells in a similar state of degeneration. As a result of this change large areas of the affected organ become transformed into opaque, yellowish-white material, resembling cheese—a result known as caseous degeneration or necrosis. The cause of this change is uncertain, but it may depend, as Sir Watson Cheyne suggests, on some chemical poison elaborated by the bacilli. Caseation is regarded by Weigert as an instance of coagulative necrosis. Cheesy foci may remain unaltered for a considerable time; but they are very liable to undergo liquefaction, and when a communication is established with a bronchus the softened material is evacuated and a cavity or vomica is formed. In some cases the process of softening and excavation originates in a small bronchus. Tubercle bacilli are found in immense numbers in the cavities, but in caseous material they are generally very scanty. Cavities also contain various pyogenetic cocci; but, according to some observers, suppuration may be excited, not only by such cocci, but also by the tubercle bacillus. A caseous or necrotic change is probably never altogether absent at some period in the development of any tuberculous formation, and, as a rule, this is the prevailing feature; but, at the same time, in most cases of pulmonary tuberculosis in man, and in all chronic forms without exception, another process of a conservative or reparative character is recognisable in the shape of a *growth of connective tissue*. This change begins at the margin of the tuberculous area, where it constitutes a species of fibrous capsule. It is doubtful whether this be a direct result of the tuberculous process, or whether it be attributable to reactive inflammation around the tubercle. In some cases the central caseous mass becomes thus shut off from the surrounding parts, and complete arrest of the disease is effected. The cheesy matter may subsequently become calcified, or it may be gradually permeated by connective tissue and converted into a solid fibrous knot. Fibrosis and encapsulation are the natural mode of healing. The well-attested frequency with which old fibrous tubercles or calcareous nodules are found in the lungs at post-mortem examinations of patients dying of other diseases, shews that recovery from tuberculosis is by no means so

rare as was formerly supposed. In the great majority of cases, however, the fibrous change is more limited, indications of a capsule can scarcely be recognised, and fresh islets of tuberculous disease spring up on the confines of the original patch. These secondary foci, which depend on the spread of the bacilli along the lymphatic spaces, go through similar stages of cell growth, necrosis, and connective-tissue development. According as the necrotic or fibrous change preponderates, the case assumes an acute or chronic complexion; but the combinations of the two processes are subject to infinite variety. Thus a case originally of a marked fibroid type may be complicated by the occurrence of acute destructive disease in other parts of the lung; or, again, though this is far less common, rapidly progressing tuberculosis may undergo partial arrest and pass into a chronic fibroid stage. In ordinary cases we find some indications of healing at the apex, while in the more recent lesions necrosis is the predominant factor.

For simplicity's sake the development of the disease has been sketched as it affects individual sections of the lung; but, as a matter of fact, the process is far more complicated. While separate foci of tubercle go through the stages just described, various *secondary changes* of a congestive, inflammatory, and oedematous nature commonly ensue in the intervening portions of lung. These conditions are partly the result of compensatory hyperaemia; but in the main they depend on obstruction of the smaller bronchi, and on the lobular collapse that follows.

Collapse soon passes into *bronchopneumonia*, which, if not from the first actually tuberculous, soon becomes so. In such cases scattered caseous spots are seen embedded in reddish, solidified lung. The pneumonic condition, at first, is usually patchy or lobular in distribution; though from the coalition of numerous individual foci the consolidation may ultimately involve the greater part of one lobe. On section the surface is moist, flat, and glazed; seldom dry and granular, as in croupous pneumonia: this difference depends on the fact that the exudation is mainly composed of cells and oedematous fluid, and contains little fibrin.

In some instances the consolidation has a pale pinkish-grey gelatinous appearance, the "gelatiniform infiltration" of Laennec. This condition seems to be due to the existence of marked anaemia and oedema in addition to the alveolar catarrh and collapse. In such infiltrations it is not uncommon to discover small specks of caseous necrosis, which stamp the process as essentially tuberculous. Sometimes a large area or even a whole lobe presents a more or less uniform greyish or yellowish consolidation, known as caseous pneumonia. In such cases, as a rule, old caseous foci, or a cavity, will be found at the apex, suggesting the secondary nature of the diffuse infiltration.

Acute croupous or lobar pneumonia is stated by many authors to be a common termination of pulmonary tuberculosis. I am convinced that this is an error. An experience of some thousand necropsies of cases of this disease has not furnished more than a few isolated instances in which progressive tuberculosis of the lung was complicated by acute fibrinous

pneumonia. During the first influenza epidemic, two or three cases, in patients who succumbed to an acute pneumonia of more or less lobar dimensions, revealed an oedematous, ill-defined consolidation, consisting microscopically of cells and oedematous fluid without any fibrin; these may have been modified instances of acute lobar pneumonia, but with these and a few other exceptions the above statement holds good.

Phthisical patients are, indeed, often cut off by acute intercurrent disease of the lower lobes; but this is essentially bronchopneumonic, and probably depends on the inhalation of septic microbes from ulcerative cavities in the lung.

In the more chronic cases a localised *emphysema* is not uncommon, especially where contracting lesions are separated by tracts of unaltered lung. This condition, which is most pronounced towards the apex, and anterior margin of the upper lobe, may be so extensive as almost to mask the original disease. The affected lung may present the appearance of large superficial bullae, or the form of emphysema may be more diffuse. The surface of such portions is often puckered from the contraction of subjacent fibrous patches or cavities. Emphysema in these circumstances is compensatory, and results from obliteration of adjacent alveoli. It is necessary to distinguish clearly between true emphysema, which is a degenerative atrophy of the alveolar walls and capillaries, and what may best be described as pulmonary distension. When one lung is contracted, the opposite lung undergoes vicarious enlargement, the alveoli becoming uniformly enlarged without being otherwise altered; the expanding lung passes across the middle line of the sternum and encroaches upon the space formerly occupied by its fellow. The effect of this enlargement is an increase of alveolar surface, and consequently an improved aeration of the blood. This condition has been named "hypertrophy of the lung," a description which implies increased function, and is therefore strictly correct. It is probable, however, that this condition may, in time, pass into true emphysema.

Cylindrical *dilatation of the smaller bronchi* is not uncommon, and may be found in any part of the lung, whether its texture be spongy or indurated. Bronchiectasis is to be attributed mainly to the positive expiratory pressure of cough acting on the bronchial walls, softened by inflammatory or other changes.

In all chronic cases *pigmentation* is a more or less marked feature; it depends mainly on the deposit of particles of carbon derived from the atmosphere. Old fibroid lesions have a blackish or slaty colour, which contrasts sharply with the red, yellow, or greyish tint of other parts of the lung.

The process of softening of the caseous material and the formation of cavities have been already briefly alluded to. The liquefaction which occurs has been likened by Duclaux to the ripening of cheese, and is probably due to autolytic enzymes liberated from the cells. The shape of *pulmonary cavities* varies greatly. They may be rounded or oval; but more often they are sinuous or anfractuous, in consequence of the

coalescence of separate vomicae, and of the irregular extension of the excavating process. Cavities are often traversed by tough septa and bridles, and are then described as trabeculated. The trabeculae were formerly said to consist of persistent bronchi and blood-vessels, but they have been shewn by Dr. William Ewart to be chiefly composed of condensed airless lung, representing the remains of collapsed alveolar tissue originally separating discrete cavities. The ridges and stumps often observed on the walls of vomicae, are relics of trabeculae destroyed by ulceration.

In acutely developed and extending cavities the wall is ragged, and formed by soft caseating or necrotic material. Such cavities are commonly filled with thick pus, their walls softened and in a state of purulent infiltration. Chronic and quiescent vomicae are lined with a definite pyogenetic membrane, like that of a chronic abscess. The lung-tissue around may be indurated or simply collapsed; less frequently spongy or emphysematous. Extension usually takes place by slow ulceration of individual cavities, which tend ultimately to coalesce; but in some cases acute suppuration and sloughing cause rapid destruction of the lung. Excavation sometimes begins as a tuberculous bronchiolitis, ulceration subsequently extending through the thin bronchiolar wall to the surrounding alveoli. In other cases a dilated bronchus may undergo secondary ulceration and become sacculated. It may be very difficult to decide whether such cavities were originally bronchiectatic or pulmonary. True bronchiectatic cavities are seldom very large, whereas those of pulmonary origin may involve the greater part of a lobe, or even the whole of one lung. Excavations of this magnitude are always the result of fusion of several cavities. In the great majority of cases excavation originates in the lung, and is not bronchiectatic. A fuller treatment of this subject is to be found in the article on "Bronchiectasis" in the present volume (pp. 129 and 144).

In the course of excavation the bronchi become ulcerated and eaten away, so that ultimately their wall passes insensibly into the lining membrane of the vomica. Cicatrisation may cause narrowing or virtual obliteration of the bronchial orifices. Chronic cavities not uncommonly undergo a considerable reduction in size, as the result of contraction of their capsule or of the neighbouring lung. It has even been asserted that they may close completely, but there is no proof of this except in the case of quite small cavities, and such an event, in view of the imperfect removal of the secretions effected through the bronchi, must be regarded as highly improbable. A vomica resembles a chronic abscess discharging externally through a narrow sinus; unless the abscess can be freely opened it will not granulate up thoroughly, and will continue to secrete for years. Contraction of a cavity is, however, promoted by a spongy yielding condition of the adjacent lung.

Fibrosis is an essential feature in all chronic excavation, and, as we have seen, the same change is always present in chronic tuberculous consolidation. In the most pronounced examples of this condition fibroid

induration is associated with excavation. In either case fibrosis causes shrinking of the lung, the upper lobe as a rule being most affected ; but at times the whole lung becomes uniformly contracted. In extreme cases the lung may be reduced to the size of a man's fist. Contraction of the lung is followed by elevation of the diaphragm and of the abdominal viscera, displacement of the heart and mediastinum to the affected side, and a varying amount of depression of the chest wall. When the lung is not too firmly adherent to the ribs, a contracting cavity at the apex may shift slightly outwards and backwards towards the fixed point, the root of the lung, as shewn by Dr. C. T. Williams.

The primary cavity is situated at the apex of the upper lobe. *Secondary cavities* may be formed in any part of the lung, but Dr. William Ewart pointed out that excavation is especially prone to attack a definite region, the apex of the lower lobe, and at a date anterior to the implication of the lower part of the upper lobe. The base and anterior border of the lower lobe are least prone to excavation, just as these parts are the last to be involved by the disease.

It remains now to consider *the mode in which the tuberculous process extends through the lungs.* In generalised miliary tuberculosis, where infection, for the most part, is derived from a caseous lymphatic gland—that is, from a source external to the lungs—the pulmonary blood-vessels are flooded with bacilli, and the lungs become stuffed with miliary granulations from apex to base. In chronic pulmonary tuberculosis the lungs become gradually but progressively invaded by a process of auto-infection, the primary focus being situated at the apex of one upper lobe. In a moderately advanced case we find one lung more diseased than its fellow, and towards the apex of the former a cavity or cavities with tough walls, the tissue around being pigmented and fibroid, and often containing some caseous nodules. In the lower part of the same lung we see scattered tuberculous nodules and masses, some softening to form small cavities. The other lung presents lesions of a similar appearance and localisation, but in a less advanced stage. It sometimes happens that the disease becomes partially arrested in the lung first attacked, while in the lung secondarily involved it extends progressively from apex to base.

It cannot fail to strike the observer that the secondary lesions in the lung are not the result of direct extension by continuity from the apex, for the individual foci are separated by tracts of healthy lung-tissue. Nor is it possible to believe that tuberculosis spreads exclusively or mainly by lymphatic or vascular channels ; for, in cases in which the disease is not too advanced, the lesions often consist solely of a cavity at the apex of the upper lobe surrounded by a zone of tuberculous infiltration, and some racemose masses of tubercle at the apex of the lower lobe ; the rest of the lung being unaffected. Extension to the lower lobe is evidently effected through the bronchial tubes, infective secretion being inhaled from the apical cavity into the bronchi of the lower lobe. This view is in harmony with the results of the "inhalation tuberculosis," artificially produced by exposing animals to a spray of tuberculous sputum. It also accords with

the fact that the prevailing lesions in man are bronchopneumonic in character. Dr. Ewart explains the marked proclivity of the apex of the lower lobe to secondary excavation, by the fact that the bronchus supplying this part is a wide, straight tube coming off horizontally from the main bronchus, a condition which appears to favour the inhalation of infective secretion from cavities in the upper lobe. Dr. J. K. Fowler also has pointed out that the distribution of tuberculous disease follows a very definite path. From the initial lesion at the apex the process spreads downwards in the upper lobe. Excavation of this region is followed by secondary disease of the apex of the lower lobe on the same side, and of the apex of the upper lobe of the opposite lung. Dr. Fowler states that the former district is involved before the latter; but the apex of the opposite upper lobe seems often to be the first point to be affected with secondary disease, though the apex of the lower lobe of the lung primarily attacked, is almost always implicated at an early date. The lower part of the upper lobe is then gradually infiltrated, and simultaneously the disease extends from the apex of the lower lobe forward and downward along the interlobar septum. The base and anterior border of the lower lobe are the last parts to be affected.

In the process of destruction *blood-vessels* for the most part become obliterated as the result of thrombosis; but when rapid excavation is taking place, ulceration may extend into large vessels and cause severe haemorrhage. In cases of a more chronic nature it is not uncommon to find aneurysmal dilatation of branches of the pulmonary artery lying in the walls of a vomica. In my post-mortem examinations aneurysms were found in 15 per cent of all cases of pulmonary tuberculosis; these aneurysms consist of a lateral expansion of the vessel on its exposed side. In rare instances an artery crossing a cavity becomes uniformly dilated to form a fusiform aneurysm. In either case the dilatation is to be attributed to two causes: (i.) to arteritis and softening of the arterial coats, the result of extension of inflammation from the cavity; (ii.) to withdrawal of support from the wall of the exposed vessel. Pulmonary aneurysms vary in size from that of a pin's head to that of a plum, but they are seldom larger than a cherry. It is usual to find only one aneurysm; though, at times, several may be discovered in the same cavity or in different parts of the lung. In one extraordinary case I found twenty-two aneurysms in one lung. Rupture of the sac is a common event, and is by far the most frequent cause of profuse haemorrhage. In a series of 80 cases of fatal haemoptysis, examined by myself, a ruptured aneurysm was found in 70. When rupture does not occur, thrombosis is apt to ensue. Thrombosed aneurysms are often met with in cases in which haemorrhage has not taken place. Observation shews that aneurysms, after leaking for some time, may become ultimately cured by coagulation of their contents. When the cavity containing the aneurysm is small, the pressure of the effused blood may be sufficient to prevent further haemorrhage. If the patient live long enough, the healed aneurysm in time undergoes necrosis and may entirely disappear.

Localised *gangrene* occasionally takes place in connexion with rapidly spreading excavation. It is, however, remarkable that, in spite of the existence of numerous profusely secreting cavities, putrid changes are very rarely met with as a result of tuberculous disease (*vide* also p. 277).

Pleurisy is a well-nigh constant accompaniment of the pulmonary disease, and is mostly due to extension. Pleurisy may also be consecutive to peritonitis, the virus being transmitted from one serous cavity to the other through the lymph spaces of the diaphragm. Primary tuberculosis of the pleura is said to occur, but of this there is some doubt. In cases of apparently primary pleural origin the disease may have started in a small caseous bronchial gland which has escaped detection.

Fibrinous exudation is the commonest form, but sero-fibrinous effusion often ensues. Empyema is uncommon in adults, though less rare in children. Haemorrhagic exudation is occasionally met with, and may be attributed to rupture of the newly-formed capillaries of the inflamed pleura. In many cases tuberculous granulations and, less frequently, caseous nodules can be recognised in the serous membrane. But it is not infrequently impossible to discover any naked-eye signs of tubercle, whether in cases of fibrinous, sero-fibrinous, or suppurative pleurisy. In some instances of this description the microscope may reveal the presence of isolated miliary tubercles in the thickened pleura. There can be little doubt that the granulations in the pleura, as in the peritoneum, may undergo complete fibrous transformation. It is not improbable that in some instances pleurisy may have a non-tuberculous origin. In any case the ultimate result of pleurisy is to cause more or less thickening and adhesion of the pleura. The former may attain to considerable dimensions in chronic cases, especially at the apex of the lung, where the pleural investment may measure as much as an inch in thickness.

Rapid softening and excavation of the peripheral parts of the lungs are apt to cause perforation of the pleura and entrance of air into the serous cavity, if the pleural space at the affected spot have not previously been obliterated by adhesions.

Pneumothorax causes collapse of the lung, and is followed in most cases by effusion of serous or, more often, of purulent fluid in consequence of the entrance of tubercle bacilli and pyogenetic cocci from the lung.

It is not unusual to discover more than one perforation of the pleura. The opening may be situated at any point where the pleural surfaces are not adherent. The middle third of the lung corresponding to the lower part of the upper lobe and upper part of the lower lobe is the most frequent site of perforation. Occasionally the air escapes into the subcutaneous tissue of the chest wall or into the mediastinum, and surgical emphysema is produced. At times a cavity in the lung may extend outwards through the pleural adhesions and give rise to emphysema, or to an abscess in the chest wall communicating with the lung. Pneumothorax was found in 11 per cent of the cases of phthisis which I examined after death.

The bronchial, mediastinal, and tracheal *glands* are very often the seat

of secondary tuberculous deposit. They may also be primarily affected, and, as already mentioned, the disease may extend thence to the lung or pleura. The extreme frequency with which arrested tuberculous lesions, in the shape of calcareous nodules, are found in these glands is well known to all who are in the habit of making necropsies.

Stenosis of a main bronchus is occasionally caused by enlarged glands in children; but this very seldom occurs in adults, as their bronchial tubes are much firmer. The smaller bronchi may be compressed in adults as in children. Marked obstruction entails some degree of collapse of the lung, and sometimes gives rise to bronchial dilatation beyond the seat of pressure. In one case I found that a large calcareous bronchial gland had perforated the bronchus and set up ulceration, which had extended at another point into a larger branch of the pulmonary artery.

Suppurating caseous bronchial glands may perforate the trachea, bronchi, lung, oesophagus, or pericardium. Sudden death has more than once resulted from the entrance of a caseous gland into the trachea. In cases in which a fistulous communication is established between the oesophagus and the air-passages a septic bronchopneumonia ensues, and pulmonary gangrene has been a relatively frequent complication.

From the foregoing sketch it will be seen how manifold are the lesions of phthisis pulmonalis. The unity of phthisis, that is to say, the essentially tuberculous nature of the disease first advocated by Laennec, was long and vehemently disputed; but the truth of this doctrine was at length removed from the sphere of controversy by Koch's discovery of the tubercle bacillus. The presence of the specific microbe in miliary granulations, caseous nodules, caseous pneumonia, and pulmonary cavities supplies a positive demonstration of the pathological identity of these apparently different manifestations. Hence such distinctions as tuberculous, pneumonic, tuberculo-pneumonic, catarrhal, and scrofulous phthisis, always artificial and unworkable, are now entirely superfluous.

P. K.

Histology and Histogenesis.—A general account of the lesions produced by the tubercle bacillus has been given in Vol. II. Part I. p. 262. As far as the lung is specially concerned, the following may be added. The chaos which prevailed as to the nature of tubercle in the first half of last century was largely swept away by Virchow, who shewed that caseation is not, as had been supposed, pathognomonic of the tuberculous process. It is one termination of tuberculosis which is essentially characterised by its initial cellular structure. Virchow mentioned the existence of giant cells, as had Rokitansky previously, but laid no special stress on their presence. The diagnostic importance of these striking cells was emphasised by Langhans, and especially by Schüppel, who was the first to describe in detail the architecture of the acute miliary tubercle. He distinguished (1) small lymphoid round cells; (2) epithelial-like cells of considerable size; and (3) giant cells, which he regarded as almost diagnostic of tuberculosis. Since Virchow's researches, all investigators have

been interested in the histogenesis of these cellular elements—a problem still under discussion. Virchow regarded the cells of the tubercle as descendants of the fixed tissues, a view widely upheld by Rindfleisch, Arnold, Ziegler, v. Baumgarten, and by most recent workers, such as Kockel, Schieck, Broden, Wechsberg, Herxheimer, Kostenitsch and Wolkow, Watanabe, and Miller.

On the other hand Cohnheim, and before him Addison, were inclined to attribute a preponderating part in the new growth of cells to the wandering corpuscles of the blood, a view revived in more recent years by Metchnikoff; and supported by many of his pupils (Yersin, Stschastny, Tchistovitch, Borrel, Morel and Dalous). Others, again (Koch, Pawlowsky, Leredde), have taken a middle standpoint, and consider that both wandering and fixed cells participate in the building up of the tubercle. Human tuberculous lesions are generally unsuitable for the study of the histogenesis of the process, the finer structure and development having been worked out as a result of experimental inoculations made with tuberculous material or living cultures of tubercle bacilli. In the majority of cases rabbits and guinea-pigs have been the animals used. When visible to the naked eye the tubercle is found histologically to be a conglomerate of cells, mainly of epithelioid character. Whether these cells are supported on a reticulum of fibres, as maintained by Wagner, is doubted by Friedländer; and Kockel, v. Baumgarten, and Kostenitsch and Wolkow regard the apparent reticulum as the remnant of the pre-existing ground substance which has been opened out by the developing cells. Another question, which has been the subject of discussion, is to what extent exudative accompany the formative phenomena. Orth in particular has sharply separated the two processes, whereas v. Baumgarten considers that all tuberculous tissue-products are combinations of proliferative and exudative processes, the relative proportions of these to each other depending upon the quantity and the quality of the virus employed for the inoculation. With regard to the initial change following the introduction of tuberculous material into the animal body, v. Baumgarten in his classical publication came to the conclusion that the virus of tuberculosis exerts a direct formative irritation on the fixed tissue-cells, causing these to multiply by a process of karyokinesis. All subsequent workers have confirmed the existence of mitosis in the early stage of tuberculosis, although some doubt whether this is an initial process. The most recent experimental work carried out on rabbits by Borrel, Kostenitsch and Wolkow, Wechsberg, Watanabe, and Herxheimer, have added many new facts, especially as concerns the very earliest phenomena in the evolution of the tubercle. In studying these early changes it is essential that the emulsions of bacilli, used for the inoculation, should be as homogeneous as possible. The bacillus employed is not a matter of indifference, bovine bacilli being much more effective in rabbits than those of the human type. As a rule, definite changes can be made out within a few hours of the inoculation. When fine suspensions of bacilli are introduced directly into the veins of rabbits the first change is a phagocytosis by

polynuclear leucocytes in the capillaries of the lungs. From their very careful and extensive studies Kostenitsch and Wolkow distinguish the following phases: (1) primary signs of reaction (exudation); (2) primary polynuclear leucocytosis; (3) reaction of the local cell-elements and formation of epithelioid cells; (4) mononuclear leucocytosis; (5) degeneration of the tubercle with secondary polynuclear leucocytosis. Wechsberg considers that the first act of the tubercle bacilli is to damage the cells of the vessels, as well as the connective-tissue (collagen and elastic) fibres, and that this primary tissue lesion, following the hypothesis of Weigert, is the cause of the neoplasia which follows. Even the newly-formed cells are damaged, in so far that the process shews little tendency to organisation and to the formation of new vessels. The protoplasm undergoes partial necrosis, the whole new formation ultimately dying and caseating. These views have been confirmed by Herxheimer, who introduced suspensions of bacilli directly into the trachea; within half an hour after the inoculation he saw the bacilli taken up by large cells which, with Watanabe, he regarded as alveolar epithelium. Within a short time polynuclear leucocytes arrive on the scene, and there is demonstrable disappearance of elastic tissue from the walls of the alveoli. By the end of the first day mitoses are visible, and the formation of epithelioid cells proceeds, according to Herxheimer, from the epithelium of the alveoli as well as from fixed connective-tissue corpuscles. These soon undergo a partial breaking down, and at the periphery there is a great influx of small round cells of lymphoid habitus. Where these latter come from is not certain. Watanabe also observed at a very early stage a swelling and desquamation of the alveolar epithelium with serous exudation and emigration of leucocytes into the alveoli. Apparently, therefore, the bacilli first produce damage and destruction of pre-existing structures, this leading to a secondary new formation, which, in turn, is destroyed by the toxic action of the virus. With regard to the exact mode and site of origin of the epithelioid cells opinions differ. Most admit a production from connective-tissue and lymphatic endothelium (Wechsberg, Watanabe, v. Baumgarten, Kockel, Schieck, Kostenitsch and Wolkow). Miller regards the blood-vessel endothelium as also playing an important part, whilst Weigert, Cornil, Straus, and others also think that parenchymatous cells (epithelium) may also contribute to the structure. By the French school leucocytes are considered to be the forerunners of the epithelioid cells. Similar obscurity surrounds the origin of the giant cells which are variously stated to be formed by confluence of fixed cells (Kockel, Kostenitsch and Wolkow), blood-corpuscles (Metchnikoff, Borrel), or multiplication of nuclei of epithelioid cells without corresponding division of protoplasm (v. Baumgarten, Weigert, Langhans).

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W. B.

SYMPTOMS.—The manner of invasion of pulmonary tuberculosis varies somewhat in different cases. From the slowness of growth manifested by the tubercle bacillus we might expect the invasion of the disease to be gradual. In the great majority of cases this is so, and certain general or constitutional symptoms often precede those of local disorder of the respiratory organs. But as in a considerable number

of cases the disease begins more or less abruptly, we must distinguish (A) acute, and (B) chronic tuberculosis.

A. Acute Pulmonary Tuberculosis.—Three forms of the acute disease may be recognised.

I. *Lobar-pneumonic Form.*—In this form—the rarest of the three—the whole of one lobe, nearly always the upper lobe, or the greater part of one lung becomes converted into a solid gelatinous or caseous substance. The consolidation, though massive, usually presents some scattered foci of older date, suggesting that the diffuse pneumonia is secondary to an originally localised form of tuberculosis.

This sequence of events is well illustrated by cases in which a cavity exists in the apex or other part of the lung, in which circumstances the diffused infiltration may be attributed to the inhalation of infective secretions from the cavity. But in a few recorded instances the caseous infiltration has been perfectly uniform, which observations support the belief that the affection was, from the first, lobar and acute, all parts having been simultaneously and equally attacked. In some of these cases there was a cavity in the lung which may have been the starting-point of the pneumonia. Miliary tubercles may sometimes be discovered in the lower lobe or in the opposite lung; caseous nodules are more common. Tuberculous pleurisy, mostly of the dry variety, is a constant accompaniment.

The disease may begin sharply with a rigor, high fever, dyspnoea, pleuritic pain, and a short cough with mucoid, tenacious sputum, which may be rusty or may contain florid blood. Occasionally the attack begins with haemoptysis. Herpes labialis is not uncommon. The patient often attributes his illness to a chill.

The foregoing mode of invasion closely simulates acute pneumonia. In other cases the onset may be less abrupt, the patient experiencing a malaise, aching in the back and limbs, and slight cough and expectoration, before the onset of marked pyrexia and other pneumonic symptoms. Physical examination discovers signs of consolidation, dulness, tubular breathing, crepitant or sub-crepitant rales, bronchophony and increased tactile vocal fremitus. The breath-sounds may be merely weakened, and no tubular breathing may be heard for some time. Pleuritic friction is frequently met with; signs of effusion are somewhat rare. The whole picture is that of acute pneumonia, for which the disease is almost invariably mistaken at first. But no crisis appears, and the fever persists for weeks. In a few instances the temperature becomes lower, and after a few days the symptoms abate somewhat; but the improvement is only short-lived and the patient relapses into his former condition. The fever for the first two or three weeks manifests a remittent character, the evening temperature being one or two degrees higher than the morning, and ranging from 103° to 104° F. Later the temperature falls somewhat and assumes a hectic character. From the first the patient wastes rapidly and exhibits extreme prostration, sometimes passing into a typhoid state with dry tongue, subsultus, and mild delirium. In the less rapidly fatal

cases signs of excavation of the lung gradually come on. The sputum becomes muco-purulent, and is found to contain tubercle bacilli, and perhaps elastic tissue. A fatal termination may be reached in less than a fortnight; more often life is prolonged for six weeks or two months. Now and then the disease gradually loses its acute character and assumes the form of chronic pulmonary tuberculosis.

The diagnosis during the first week or ten days presents great difficulties. In some instances the invasion is less sudden, and the severity of the symptoms less pronounced than in cases of acute lobar pneumonia. But these distinctions are often wanting. In the tuberculous form the fever is less continuous and is generally marked by irregular remissions. The pulse-respiration ratio, again, is less deranged than in acute pneumonia; for the pulse-rate is greatly increased, often reaching 130 to 140, with respirations of 30 or 40.

It has been said that in tuberculous cases the breath-sounds over the affected lobe are more often weak and suppressed than tubular, but this sign is by no means constant; moreover, this sign is not very rare in croupous pneumonia. From acute pneumonia with delayed resolution the disease may be discriminated by the progressive wasting and prostration, as well as by the fluctuating high temperature which accompanies it; for in the former complaint, in spite of the persistent pulmonary consolidation, the general condition mends and the temperature falls. In doubtful cases the appearance of signs of excavation, and, above all, the detection of tubercle bacilli in the sputum, are the only facts on which a positive diagnosis can be based. The complications of this form of tuberculosis do not differ materially from those attending the chronic variety, under which head they will be discussed; but it may be said that complications are much less frequent in acute cases, owing to the rapid termination entailed by the severity of the pulmonary lesions.

II. *Bronchopneumonic Form.*—This form, which is much less uncommon than the last, represents what has been called galloping consumption or phthisis florida. The special anatomical features consist of disseminated tuberculous foci, of various sizes, which may be soft, yellowish-white, and cheesy; or greyish, slightly pigmented, of racemose shape, and somewhat indurated. Miliary tubercles are seldom to be seen. In most cases rapid softening and excavation of the nodules is a very prominent feature. Small suppurating cavities with soft ragged walls are scattered through both lungs. In the apices of the upper lobes the cavities are generally larger, and in some cases the apex is the seat of old fibrosis and excavation. The lung-tissue separating the nodules is often hyperinflated, especially towards the anterior borders; in other parts the nodules are embedded in tracts of greyish-red consolidation, more particularly towards the back. This fusion of the individual foci may ultimately result in a diffuse infiltration of lobar dimensions. The bronchi are always deeply injected, and contain abundant purulent secretion. The localisation of the lesions is essentially bronchopneumonic and lobular, and depends on the inhalation of tubercle bacilli from a cavity in the

lung or from external sources. Pleurisy in some form, whether dry, sero-fibrinous, or sanguineous, is always present. The larynx and large air-passages are more prone to tuberculous ulceration than in the lobar-pneumonic form, in consequence of the more profuse secretion discharged from the cavities and bronchi in the present variety.

The mode of onset is subject to considerable variations. Occasionally without any early period of ill-health the patient is suddenly seized with rigors and other symptoms of acute pneumonia: more often the disease begins insidiously with a cough, which, after the lapse of a few weeks, is succeeded by fever, malaise, and other constitutional symptoms. Haemoptysis is occasionally the first symptom. In some instances the disease begins with symptoms of gastric disturbance, loss of appetite, furred tongue, and vomiting; and the real nature of the malady is not recognised until the chest is examined.

In recent years this form of tuberculosis has not uncommonly followed an attack of influenza. Whatever the mode of invasion, marked wasting and loss of strength soon appear. Haemoptysis is not very common, and is seldom profuse. The sputum at first is muco-purulent, but it soon becomes more puriform, and sometimes acquires a greenish-yellow colour; in some cases it has a reddish brick-dust colour for weeks. Tubercle bacilli and elastic tissue are generally recognised before long. Night sweats are frequent, and often are very profuse. The temperature ranges high, reaching 104° F. at times; the fever is fluctuating, being marked by morning remissions of one or two degrees: as the disease proceeds, the temperature becomes more hectic. Anorexia, vomiting, aphthous stomatitis, a dry red tongue, and diarrhoea are very common, and the patient is apt to pass into a typhoid state. In the worst cases death ensues in three or four weeks, but the end is more often deferred for three or four months. Very occasionally the acute progress of the disease is stayed, and the patient lingers on for eight or nine months.

Physical examination at first reveals nothing more than signs of general bronchitis; but subsequently pleuritic friction and patches of dulness on percussion, more particularly at the apices, make their appearance, and signs of excavation may ultimately be discovered. In some instances the signs may predominate at the base of the lower lobe. In the most acute cases no cavernous signs can, as a rule, be recognised, as death takes place before the cavities have reached sufficient size to permit of their detection. Moreover, the patches of distended lung-tissue which separate individual foci, tend to obscure the existence of extensive disease. The diagnosis at first rests on the discovery of physical signs of broncho-pneumonia accompanied by great prostration and loss of flesh. But the detection of tubercle bacilli in the sputum may alone enable us to decide whether the disease be tuberculous or not. In the case of young children the difficulties are greatly enhanced, for no sputum is obtainable, and death commonly takes place before softening and excavation can be recognised.

III. *Acute Miliary Tuberculosis.*—In this form the pulmonary condition

is frequently dwarfed by the symptoms of general infection. This condition, from its resemblance to typhoid fever, is sometimes described as the typhoid form of acute tuberculosis. In other instances the disease manifests a special incidence on certain organs, and types have been distinguished varying with the parts of the body principally affected; for instance, the cerebral, the abdominal, and the pulmonary (*vide* Vol. II. Part I. p. 298).

It has been the custom to draw a sharp distinction between acute miliary tuberculosis and phthisis on account of the marked difference in the clinical symptoms of the two affections; but an eruption of miliary granulations in the other organs is a fairly common complication of chronic pulmonary tuberculosis, and is to be attributed to the entrance of a large number of tubercle bacilli into the pulmonary veins. Moreover, many cases, clinically indistinguishable from the typhoid or disseminated type of acute tuberculosis, are found after death to present old circumscribed tuberculous lesions of the lung, which had escaped recognition during life. In fact, the acute miliary form differs from chronic tuberculosis of the lung, only in the acuteness of its course, and in the more widespread infection of the body. In the pulmonary type, which alone will be considered here, the disease may advance in an acute or subacute manner, without any premonitory symptoms. In a large proportion of cases a period of ill-health, of variable duration, precedes the onset of the disease. The symptoms first noticed are cough, expectoration, dyspnoea, and occasionally pleuritic pain. Dyspnoea, as a rule, soon becomes the predominant feature, and is often accompanied by marked cyanosis. Haemoptysis is uncommon; but now and then it is the earliest symptom. The temperature is generally high, reaching 103° F. to 104° F., and the morning remissions are less pronounced than in the bronchopneumonic form.

Some cases have been known to run their course without any definite elevation of temperature. The pulse, from the first, becomes rapid and weak. Examination of the chest reveals signs of general bronchitis, fine bubbling rales, and rhonchi on both sides. At first no dulness on percussion can be elicited, but the anterior parts of the lungs are found to be rather hyper-resonant, the change depending on compensatory distension of the alveoli—the so-called "acute emphysema." As the disease progresses, pleuritic friction-sounds are often heard, and patches of dulness pointing to secondary bronchopneumonia may sometimes be recognised. In these parts the breath-sounds may be tubular, but more often become muffled. This difference does not depend on the preponderance of consolidation or pleural effusion; for, in the absence of pleuritic exudation, the vesicular breathing may be greatly diminished by the concomitant bronchitis and lobular collapse. Lobar pneumonia is an occasional complication. The patient rapidly loses flesh and strength, dyspnoea and cyanosis increase, the cough grows more troublesome, and the sputum—which at first was mucoid—now becomes muco-purulent. It is rare to find tubercle bacilli in the expectoration, and when this

happens, a cavity, often a very small one, will generally be found in some part of the lung. The spleen is more or less enlarged, and may sometimes be recognised by palpation.

The diagnosis is occasionally easy, but more often difficult. In the presence of general bronchitis, associated with marked dyspnoea, cyanosis, pyrexia, and rapid emaciation, the diagnosis presents little difficulty. But in cases in which the evidence of bronchitis is slight or absent, the disproportionate amount of dyspnoea is a diagnostic point of considerable value.

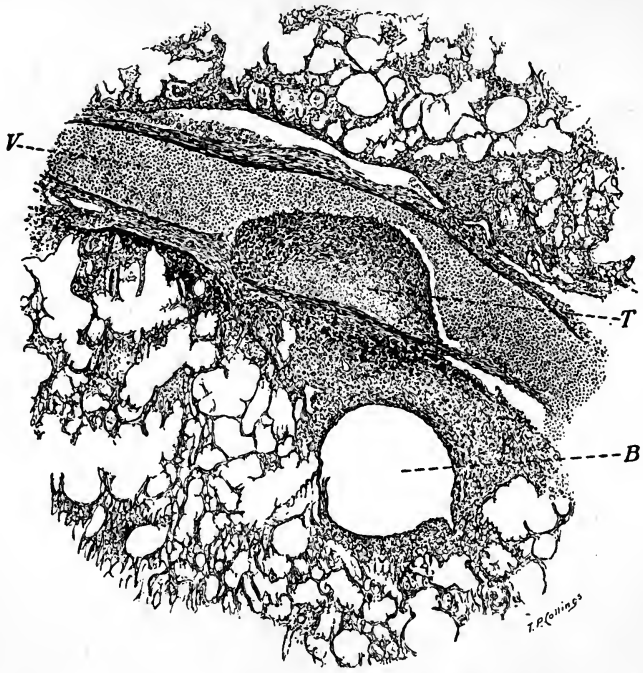

FIG. 19.—Photomicrograph of a section of the lung from a case of acute miliary tuberculosis, shewing the mode in which general infection occurs through branches of the pulmonary veins. (Low power.) V, Small pulmonary vein; T, tuberculous growth from intima, projecting into the lumen of the vein; B, small bronchus shewing tuberculous infiltration of its walls.

Tubercles may occasionally be recognised in the choroid by means of the ophthalmoscope, and tubercle bacilli have, in a few instances, been found in the blood; but unfortunately such evidence is rarely to be obtained.

B. CHRONIC PULMONARY TUBERCULOSIS.—The following modes of invasion may be recognised in their order of frequency:—

(i.) *Insidious.*—The commonest prodromal symptoms are loss of flesh and strength, accompanied, in some cases, by a slight evening rise of temperature. Less frequently the disease is ushered in under the guise of anaemia, or of a functional derangement of the digestive system.

(ii.) *Bronchitic.*—After frequent attacks of bronchial catarrh, or without any previous tendency to bronchitis, the disease begins with cough and expectoration, which are attributed at first to a common catarrh ; but after a few weeks or months pyrexia and other constitutional symptoms make their appearance. In some instances careful inquiry will establish the fact that a period of ill-health existed before the appearance of the cough. Many cases with such a story have originated in influenza.

(iii.) *Pleuritic.*—The first definite symptom is pain of pleuritic type, increased by cough or deep inspiration. The pleurisy is generally of the dry form, but effusion may take place. Pyrexia and other symptoms of phthisis may follow hard on the pleuritic seizure, or the pleurisy may gradually disappear, and the patient make a temporary recovery, only to fall ill again later with pronounced symptoms and signs of pulmonary tuberculosis.

(iv.) *Haemoptoic.*—In this class, the "phthisis ab haemoptoe" of the old authors, the first symptom to attract attention is haemoptysis. When the haemorrhage is profuse, it almost certainly indicates rupture of an aneurysm in a vomica, that is, old-standing disease, even when no other evidence of a pulmonary lesion is forthcoming.

(v.) *Laryngeal.*—Phthisis occasionally begins with laryngeal symptoms ; hoarseness, loss of voice, hyperaesthesia, or paraesthesia of the throat being the most common (*vide* art. Vol. IV. Part II. p. 195).

Symptoms.—A constant, and perhaps the most important symptom from the diagnostic point of view is *cough*. At first dry, short, and infrequent, it is accompanied, sooner or later, by expectoration, and may become so incessant as to prevent sleep and to set up vomiting, whereby the patient's strength becomes reduced in the most serious manner. There is no direct relation, however, between the gravity of the disease and the severity of the cough. Some patients, with extensive pulmonary lesions, have little or no cough ; whilst in others, with comparatively slight disease, cough may be the predominant symptom. Cough is generally most troublesome in cases of progressive disease, and where the larynx, trachea, and large bronchi are actively engaged ; but it depends to a considerable extent on the excitability of the nervous centres. When the larynx is extensively affected the cough is peculiarly muffled and hoarse. In some cases, especially when large cavities form in the base of the lung, it assumes a paroxysmal character. Coughing fits occur most frequently in the early morning, owing to the accumulation of secretion in the larger air-passages during the night. In some cases an irritable cough is excited by the ingestion of food, and the fit may end in vomiting. This occurrence is partly to be explained by the mechanical compression of the stomach and abdominal viscera against the diaphragm ; but vomiting so often follows slight fits of coughing that it seems necessary to assume the existence of a neurosis of the vagus in these patients.

Expectoration.—In the early stages expectoration is scanty and mucoid ; but it soon becomes muco-purulent, and is commonly very viscid. At

times it is thin and watery, from admixture with saliva. As the disease progresses, the sputum collects into small thick lumps of a dirty white or yellowish colour; this "nummular sputum" is more common where cavities have formed in the lung, but it may be met with in cases of simple bronchitis and of bronchiectasis. It is not uncommon in the same specimen to find small yellowish spots or streaks mixed with frothy mucous secretion —the mixture representing bronchial secretion and pus from cavities in the lung. At times, especially in advanced cases, the sputum becomes uniformly opaque and thick, and may assume a greenish colour. Expectoration is sometimes markedly paroxysmal, especially where cavities exist in the lower part of the lungs. Blood is often discharged with the sputum. The blood-stained sputa may be bright red, or, when blood-clots have been retained in cavities or bronchi for some time, the colour may be dark purple or blackish. In certain instances the sputum presents a brownish or chocolate colour from decomposition of blood in the cavities or bronchi. In other instances it may be of a brick-red tint, especially when active ulceration of the lung is going on; but it seldom has the rusty, tenacious character of acute pneumonia. Fetor is practically unknown in the absence of such complications as bronchiectasis or gangrene. In the more chronic forms of phthisis small particles of calcareous matter, consisting mainly of phosphate of calcium, are coughed up from time to time. These pulmonary calculi represent caseous material that has undergone calcification, and has become loosened in the process of excavation. Sometimes they shew a tendency to branch, so that some think that they may come from the small bronchi. I have found them on many occasions in the recesses of old cavities in the lung. Calcareous bronchial glands occasionally perforate the air-passages and are expectorated. The discharge of pulmonary calculi implies ulceration of the lung or air-passages, and is a sign of chronic disease; but no further diagnostic value can be assigned to it.

As regards the importance of the sputum of phthisis, it must be allowed that the naked-eye appearances alone possess no certain and pathognomonic significance, if we except the presence of blood and calcareous matter. The former will be considered under the head of haemoptysis. It is doubtful whether chalky masses are expectorated in any disease other than tuberculosis of the lungs or bronchial glands; consequently this event has a certain diagnostic significance. For the methods of examining the sputum see p. 354. The detection of tubercle bacilli in the sputum is a certain sign of tuberculosis of some part of the respiratory tract.

Instances of primary tuberculous ulceration of the larynx or pharynx are infinitely rare, but the number of bacilli shed from the surface of such ulcers is insignificant when compared with the enormous masses discharged from cavities in the lung. When the sputum contains a large number of bacilli we may reckon on the existence of a vomica, whether large or small.

Haemoptysis is one of the most striking symptoms of the disease.

Streaks of blood may be seen in the expectoration of many other affections, and are the result of capillary haemorrhage from the lungs or air-passages: such streaks are seldom of much importance; nevertheless they occasionally herald the approach of a more profuse haemorrhage. When the amount of blood brought up is considerable, the significance is far greater.

Haemorrhage from the lungs may occur as the result of hyperaemia and rupture of capillaries, or of gross pulmonary lesions involving perforation of vessels of considerable size. Slight attacks of haemoptysis are mainly due to capillary haemorrhage from the lungs, less frequently from the large air-passages, and are indicative of inflammatory or congestive states. When, however, the blood expectorated can be measured by ounces, the bleeding must be attributed to rupture of an artery or vein of some size. Perforation of vessels, generally of an artery, may be effected in three ways:—(α) The walls of the small pulmonary arteries and veins may become infiltrated with a tuberculous growth. The usual consequence of this change is thrombosis of the affected vessel; but in the case of the arteries, softening of the vascular wall may lead to rupture, and some of the small haemorrhages of phthisis are probably thus produced. (β) The ulcerative process, associated with excavation of the lung, may perforate an artery of considerable size, and occasion alarming haemorrhage. It seems strange, at first sight, that this does not happen more often; but the tendency in all but the more rapid forms of tuberculous destruction is towards thrombosis of vessels. This is a more important cause of haemoptysis than the preceding, but it is very much less common than the next (γ), namely, rupture of an aneurysm in a cavity in the lung: this is by far the most common cause of profuse haemorrhage.

Haemoptysis may prove directly fatal from cerebral anaemia, though a termination by syncope is uncommon. The usual cause of death is asphyxia, which results from flooding of the bronchi with the effused blood. Ruptured aneurysms may become closed by thrombosis and the patient recover. There is every reason to believe that most cases of profuse haemoptysis which end in recovery, are due to the rupture of an aneurysm, and that ulceration of large vessels is a much less frequent cause.

The old view that the extravasation of blood can set up inflammatory and destructive changes in the lung—"phthisis ab haemoptoe"—is no longer entertained.

One of the points adduced by Niemeyer in support of this notion, namely, that pyrexia often appears a few days after the haemorrhage, is more easily explained by the aspiration of infective cavity secretions, mixed with blood, into other parts of the lung, leading to tuberculous bronchopneumonia. An attack of haemoptysis is occasionally determined by some obvious cause of vascular excitement, such as mental agitation, muscular exertion, straining at stool, or menstruation; but more often the patient suddenly begins to cough up blood without any warning,

often while in bed. Haemoptysis is generally repeated frequently, and may last for hours or days with intermissions. The blood expectorated is generally bright and frothy; but when it has gathered slowly in cavities or in the bronchial tubes it may be dark and clotted. The quantity lost varies considerably; as much as two or three pints may be brought up in a short time. When the flow is not excessive the blood is often mixed with sputum, a point of considerable diagnostic importance; and in most cases expectoration of blood-stained secretion continues for a day or two after all active haemorrhage has ceased. The bleeding may manifest a marked tendency to recur at intervals for some time; in such cases the rent in the walls of the aneurysm has undergone only partial repair, and leaking goes on from time to time. The patient is almost always greatly alarmed by the supervention of haemorrhage. The face is pale and bedewed with sweat, the extremities cold, and the pulse is feeble; the bodily temperature sinks below the normal. Blood is brought up with a frequent short cough, and is often swallowed. When the haemorrhage is arrested the temperature returns to the normal range, and on the third or fourth day may rise three or four degrees. After the attack, patients are much exhausted and depressed; partly in consequence of the loss of blood, but still more as the result of nervous shock.

Some patients shew no serious deterioration of health after the immediate debilitating effects of the haemorrhage have passed away; but in not a few instances, under the influence of repeated attacks of haemoptysis, chronic disease assumes a subacute, progressive character, a result attributable to the violent inspiratory efforts provoked by the presence of blood in the bronchi, and the consequent insufflation of infective secretion into healthy lungs.

Some writers have described a special variety of phthisis under the name "haemorrhagic," but there does not appear to be any sufficient reason for the subdivision. Cases beginning with a sudden haemoptysis repeated, perhaps, at intervals for a considerable time, may subsequently run the ordinary course of chronic phthisis without any further haemorrhage. Other patients presenting the usual form of disease may succumb after a succession of attacks; or their first haemorrhage may prove fatal. Haemorrhage is an accident which may complicate any case of the disease, and is not a satisfactory basis for classification.

Dyspnoea.—A subjective sense of dyspnoea is seldom complained of, save in the later stages of the disease; though most patients with progressive phthisis exhibit increased frequency of respiration, especially on slight exertion. The rate of respiration rises slightly in the evening. The absence of dyspnoea is explained by the tolerance acquired during the slow, insidious progress of the pulmonary affection, and also, as has been suggested, by the low standard of respiratory requirement due to the reduced volume of blood.

When chronic lesions are complicated by acute tuberculosis, especially in its miliary form, and when pneumothorax occurs, urgent dyspnoea may arise.

Pain in the Chest.—Many patients have pain in the chest, mostly in the axillary or mammary regions, varying in degree from a slight aching sensation to the agonising stitch of pleurisy. Severe pain is nearly always referable to the implication of the pleura, in which case tenderness to percussion is often met with. Vague rheumatoid pains in the chest have been regarded as very significant; but in the absence of other symptoms more directly pointing to the lungs, little importance can be attached to them. They are, not infrequently, of muscular origin, and may be attributed to the violence of the cough. Dragging pain over chronic cavities, associated with retraction of the chest wall, is sometimes a persistent symptom depending on stretching of the adjacent pleura and intercostal nerves. The muscles of the chest wall in some cachectic patients are extremely tender to percussion, and the slightest tap may promote muscular contraction; but this increased excitability of the muscles is not peculiar to the disease.

General Symptoms.—Pyrexia is a symptom hardly less significant, from the point of view of diagnosis, than cough; and of infinitely more value as a measure of the activity of the disease. The cause of the elevation of temperature must be ascribed to the presence in the blood of some soluble poison produced by the bacillus. It is generally agreed that the pyrexia of tuberculosis attains its maximum, and may often be exclusively present in the post-meridian hours of the day. A slight evening rise of temperature may be one of the earliest symptoms. Some observers have noted a persistently subnormal temperature as the first definite indication of the disease. Accordingly careful thermometric observations, night and morning, should be made in all cases of obscure ill-health, especially in young persons.

The onset of fever is sometimes accompanied by slight shivering, but a marked rigor is seldom observed except in acute cases. The maximum temperature is generally found from 4 to 8 P.M., and the minimum from 2 to 8 A.M. In exceptional cases the order is reversed, the morning temperature being higher than the evening—the "inverse type." This may be only temporary, or the same relation may be preserved throughout the whole course of the case.

Two main forms of pyrexia may be distinguished, the intermittent and the remittent. One or other form may predominate or prevail exclusively for weeks or months, but various combinations are apt to arise; in fact, one of the characteristics of tuberculous fever is its fluctuating and irregular course.

In the first or intermittent type the temperature is normal or slightly subnormal in the morning, and reaches 100° to 103° F. in the evening. In the higher grades of this form the fall is still more pronounced, and may amount to 7° or 8° F., the thermometer sometimes registering a temperature as low as 94° or 95° F. The second or remittent type shews a maximum temperature of 103° to 104° F., the minimum temperature being 2° to 3° lower, but not reaching the normal level. A slight degree of intermittent fever, where the maximum, for the most

part, does not exceed 101° to 102° F., is often found in the early phases of the complaint; but a similar temperature curve may be recorded at any stage. When the range of temperature is greater, and more particularly when the morning reading is below normal, profuse sweating is very common, and the resemblance to the hectic fever of pyaemia is very close. The remittent form of fever commonly betokens active tuberculous infiltration, and is more often met with in the acute varieties of tuberculosis, but may also appear temporarily in chronic phthisis as the result of acute exacerbations or of intercurrent disease. In acute miliary tuberculosis, uncomplicated by suppuration in the lung or elsewhere, the type of fever is generally remittent, a fact which would point to this being the form of pyrexia peculiar to tuberculosis.

Pulmonary phthisis never runs its whole course without fever, but in many chronic cases there may be no appreciable rise of temperature for long periods of time. Observations by Dr. C. T. Williams have shewn that pyrexia may be absent even when the disease is making rapid progress. But this is a very unusual course, and it may be stated as a general principle that activity of the disease is indicated more surely by pyrexia than by any other symptom or sign.

A high evening temperature with a markedly subnormal morning temperature (95° to 97°) is a common feature of advanced and progressive disease, though in such cases the fever may assume the remittent type at any time. Towards the close of life the temperature generally tends to fall. The very low temperature registered in pneumothorax, in some cases of excessive pulmonary haemorrhage, and in the comparatively rare instances in which perforation of the intestine occurs, must be attributed to the effects of shock. When we consider the various processes of infiltration, necrosis, and suppuration occurring in the lungs, as well as the numerous complications that may arise, we cannot be surprised at the great variations exhibited by the temperature chart.

It is necessary to mention the assertion of Peter, that the temperature of the skin differs on the two sides of the thorax, the higher reading being found on the side corresponding to the lung more affected. Most observers have failed to verify this statement, and a similar want of symmetry in the temperature of the two armpits has occasionally been observed in other conditions.

Sweats.—Profuse perspiration is a common symptom in pyrexial cases, though it has no constant relation to the fever. Sweating is most pronounced in the early hours of the morning, when the temperature of the body is at its lowest; but it also occurs sometimes while the fever is continuously high. Night sweats may occasionally occur in apyrexial periods, in which case they seem to be due to fits of coughing.

Sir Lauder Brunton has suggested that sweating is the result of exhaustion of the respiratory centre in the medulla, and consequent accumulation of carbonic acid in the blood; the effect of this being to stimulate the sweat centres. This symptom is certainly more prevalent in advanced cases, associated with excavation and suppuration of the

lung; but it is not uncommon in early and circumscribed disease, in which case Brunton's hypothesis seems less applicable.

Emaciation is one of the most frequent and important symptoms, and may proceed to an extreme scarcely reached in any other disease; hence the name phthisis and consumption.

The greatest loss of weight is witnessed in chronic cases, but although sometimes at first comparatively slight in the acute type which terminates in a few months, it is never absent altogether. Wasting affects all the soft parts, but especially the fatty and muscular tissues. It has been said that the liver does not share in the general wasting, but this statement is probably to be explained by the great liability of the liver to congestion and to fatty and amyloid changes, conditions which involve enlargement of the organ. The loss of flesh is mainly, though not exclusively, due to the increased metabolism inseparable from the febrile process. Patients with a high temperature lose weight as long as the fever continues; and, as a rule, when the heat of the body becomes normal, wasting ceases. Moreover, a certain correspondence between the degree of the fever and the loss of weight can often be recognised. At the same time a considerable degree of fever is not incompatible with an actual increase in weight, if an adequate supply of food can be taken, and if digestion and absorption be unimpaired. In apyrexial cases the weight of the body may remain stationary for months, or even years; but when pyrexia appears, loss of flesh soon follows.

The early emaciation, which not uncommonly precedes any appreciable rise of temperature or other signs of disease, cannot be thus explained. In the absence of any definite knowledge on this point we may adopt the provisional hypothesis that the toxins of tuberculosis may cause a general failure of nutrition apart from any febrile movement. Functional derangements of the stomach and diarrhoea, by their interference with digestion and assimilation, are potent causes of wasting.

Debility.—A sense of weakness and loss of energy, both of mind and body, are commonly felt at a very early date, and not infrequently appear to be out of all proportion to the extent of the disease.

Anaemia.—In certain patients the complexion acquires a peculiar faded yellowish tint, which has been well likened to that of a dead leaf. In other cases the appearance is that of chlorosis. But examination of the blood generally shews no definite change, or, at the most, there is slight secondary anaemia, still more rarely true chlorosis (Lloyd Jones). In active pyrexial disease a moderate degree of leucocytosis is common.

The pulse in all progressive cases is rapid and of low pressure; sometimes it is full, but more often small. The frequency of the heart's action is not invariably determined by the degree of fever, but seems rather to stand in direct relation to the extent and activity of the disease, and to the strength of the patient; consequently the pulse is a most valuable index of the gravity of the case. The pulse is generally somewhat more frequent in the evening, but exceptions to this rule are met with. Some authors have regarded a persistent rapidity or ready excite-

ment of the heart as important premonitory symptoms; and there is no doubt that cardiac erethism is often present at a very early stage of the disease.

Cyanosis is seldom a marked symptom, except as the result of serious pulmonary or cardiac complications, though the fingers, toes, lips, ears, and nose often present a slightly dusky or livid hue, in marked contrast to the general pallor. Coldness of the extremities and extreme sensitiveness to trifling depressions of temperature are a common complaint, and further testify to the feebleness of the circulation.

Skin and Hair.—In connexion with the subject of nutrition reference must be made to the state of the skin and hair. The skin of tuberculous patients is generally very oily, and the sweat has a peculiarly pungent garlicky odour. In some emaciated subjects, on the contrary, a dry branny condition, "pityriasis tabescentium," may be observed. The texture of the skin in one type of patients is delicate and thin, and the complexion transparent; whilst in another class the skin is coarse and the complexion dull and muddy,—distinctions which are included in Sir William Jenner's classical description of the tuberculous and scrofulous diatheses respectively. But in the majority of phthisical persons no such peculiarity can be recognised, though in all cases of long-standing some degree of pallor is wont to appear. Pigmentation of the skin may become so marked in certain chronic cases that Addison's disease may be simulated. It has been regarded as due to suprarenal insufficiency and has been designated Addisonism by Boinet, who found that of 37 cases of this condition in pulmonary tuberculosis with excavation 30 shewed fibrosis of the adrenals, 3 the presence of small tubercles, and 4 caseous tubercles. Tinea versicolor is observed rather frequently on the chest and back, but no special significance can be assigned to this parasitic complaint. Lupus is only occasionally found in phthisical patients.

Clubbing of the fingers and toes is not uncommon in the more chronic cases. Under this heading two conditions are included—a bulbous enlargement of the terminal phalanges, the drumstick form; and the parrot's beak form, in which the nails are incurved and sometimes striated and thickened. The former, which is less common, is seldom so pronounced as in bronchiectasis. Combinations of the two forms are often met with. The swelling in the first has not been satisfactorily explained. Skiagrams shew that it is not the result of bony enlargement.

Pulmonary osteo-arthropathy is occasionally seen, but much more rarely than in bronchiectasis or empyema. When osteo-arthropathy exists clubbing of the fingers seems always to be associated. (*Vide* also art. "Osteo-arthropathy," Vol. III. p. 64.)

The hair, participating in the general malnutrition, may become thin and straight; but this change is by no means constant, as in some persons the hair of the head and beard remains very thick, and the trunk may be unusually hirsute. In children and young persons the body is sometimes covered with a growth of fine downy hair.

Physical Diagnosis.—Certain abnormal forms of chest are met with

in many phthisical subjects. Two special varieties may be mentioned on account of the frequency with which they occur. In the first, named alar or pterygoid by Galen and Aretaeus and in our own day by Dr. Gee, the angles of the scapulae project like wings, the ribs are unduly oblique, the shoulders fall, and the length of the thorax from above downwards is increased, but the antero-posterior diameter is small. In the second or flat type the chest in front is flat instead of being rounded, and the sternum may even be depressed below the level of the costal cartilages, which lose their curve and become straight. These peculiarities are certainly common in tuberculous persons, but they are frequently met with also in persons who remain free from the disease. Moreover, many phthisical persons have large and well-formed chests. It cannot be said, in other words, that there is any type of thorax peculiar to phthisis, although the chest, in common with the muscles and bones, is often ill-developed. Much more importance is to be attributed to partial deformities of the chest and walls, the result of pulmonary disease.

Before discussing the physical diagnosis of the disease in its early stages, it may be well to recall briefly a few anatomical facts. The initial lesion consists of a small nodule or group of nodules situated somewhat below the extreme apex of the lung. The nodule is broncho-pneumonic; that is, it consists of a localised bronchitis with surrounding lobular consolidation. The neighbouring parts of the lung at first remain spongy and practically unaltered, so that the nodule is enclosed in a shell of healthy pulmonary tissue.

Physical examination of the lungs at this period may yield a completely negative result, especially when the focus of disease is small, and the layer of spongy lung around is fairly thick. As long as the surrounding lung is crepitant, percussion gives no dulness. The earliest signs are almost exclusively discovered by auscultation, though at times, on inspection and palpation, a slight diminution of respiratory movement may be recognised in the subclavian region. Owing to the persistency of the apical catarrh, and to the consequent lobular collapse, the entry of air into the corresponding section of lung is diminished, and the breath-sounds become weakened. Jerky, interrupted, or wavy breathing—the "respiration saccadée" of the French—is not very uncommon, but is not pathognomonic, and may often be heard in neurotic or hysterical, or even in healthy persons. Weakness of breathing at the affected apex is often associated with increased loudness of the vesicular murmur on the opposite side—a condition known as compensatory or puerile breathing, which is sometimes erroneously regarded as an indication of disease.

Another important and early sign is furnished by harshness of the breath-sounds affecting the expiratory sound to a greater degree, and at an earlier date than the inspiratory. The expiratory murmur at the same time acquires a higher pitch, and becomes so prolonged as to equal or exceed the length of the inspiratory sound. This change is an early indication of consolidation, the character of the breath-sounds being modified, without having actually attained to the bronchial or tubular

type. It is necessary to distinguish this condition from mere prolongation of the normal expiratory murmur, which may be the result of bronchial obstruction, as in bronchitis, emphysema, and asthma, and is then generally associated with a weak vesicular inspiration. At this period the vocal resonance and tactile fremitus may be slightly increased, or there may be no recognisable alteration.

It will be convenient at this point to make a passing reference to what may be called the physiological dissimilarity of the right and left

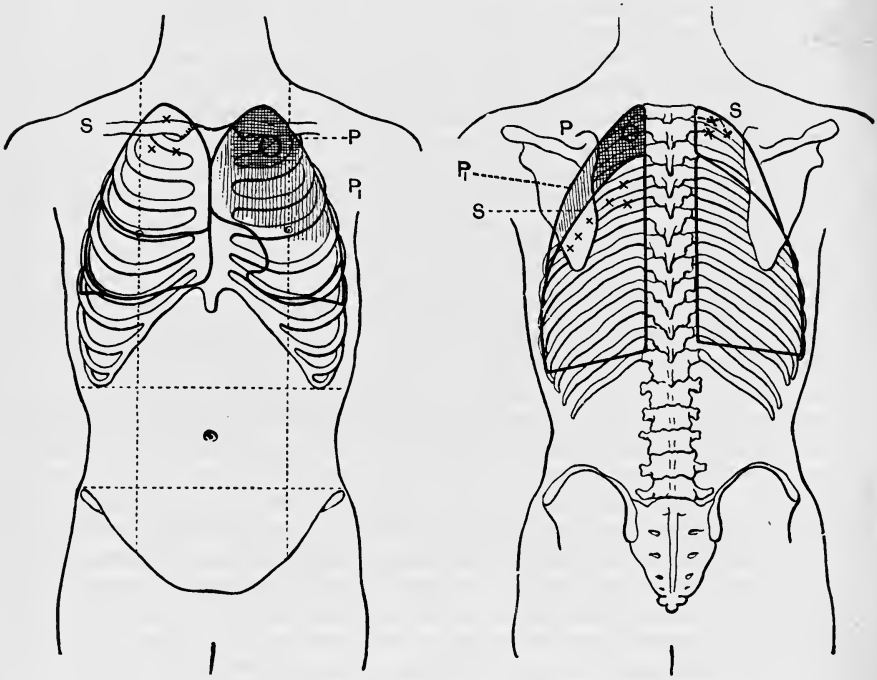

FIG. 20.—Diagram illustrating the localisation of tuberculous lesions in the lungs. P, Primary lesion (double shading); P_I, local extension from primary lesion (single shading); S, secondary lesions.

apices. In the large majority of healthy persons, especially in thin subjects, the breath-sounds are louder, the expiratory murmur more audible and prolonged, and the vocal resonance and fremitus more pronounced at the right than at the left apex. Occasionally the breathing may even be tubular at the extreme right apex. This difference probably depends upon the following facts: the right main bronchus is slightly wider and more vertical in direction than the left; the bronchus to the upper lobe is given off higher up, that is, nearer to the trachea; and the apex of the lung lies slightly closer to the trachea on the right side. The general effect of these conditions is to favour the conduction of the glottic sounds to the right apex. Accordingly we must bear this in

mind in estimating the importance of any slight want of symmetry of the auscultatory signs at the apices.

In some instances a slight impairment of the inspiratory expansion of the affected apex or some flattening below the clavicle may be the only physical indications of disease. The want of mobility may be recognised by inspection, but is more easily detected by palpation; the hands of the observer being placed on the subclavian region on each side, and the patient directed to breathe deeply while standing in the erect position. At this time also fine crackling or subcrepitant rales may be heard over the affected area. These rales, which are less fine than the true crepitant rale of Laennec, are mostly heard during inspiration, and are probably caused by the separation of the moist surfaces of the small bronchi. In some cases in which the bronchial obstruction is more pronounced no adventitious sounds are audible during ordinary respiration, but when the patient coughs, a shower of crackling rales is produced by the explosive separation of the swollen bronchial walls. At times subcrepitant rales can only be elicited during the deep inspiration that follows cough.

Persistent rhonchi at one apex may sometimes be the only adventitious sounds. A systolic murmur, heard beneath the clavicle, was thought to indicate consolidation of the apex of the lung, and was attributed to the effects of pressure of the infiltrated lung on the subclavian artery; or, with greater probability, to contraction of the thickened pleura at the apex. Similar murmurs may be heard in anaemic and other persons, and are not any certain guide to disease of the lungs. Thus far physical signs gave evidence of bronchitis confined to the apex of the lung, the character of the breath-sounds possibly suggesting the existence of a small patch of consolidation surrounded by spongy lung. As the infiltration is often massed at several centres, islets of spongy tissue separate the individual nodules, and for a time mask to a great extent the signs of consolidation. Thus when the lobules around the tuberculous patches are hyper-inflated the percussion may be slightly higher pitched than normal, tympanitic, or even hyper-resonant.

As the disease extends, the lung becomes more airless, and adhesive pleurisy is set up. The inspiratory expansion becomes decidedly restricted, vocal fremitus is increased, and the percussion resonance undergoes progressive impairment. The breath-sounds assume a more definitely tubular or cavernous quality; bronchophony or pectoriloquy appears, and the rales become larger and more ringing or metallic. This complete assemblage of signs is by no means generally, or indeed often presented, except in fairly advanced cases. Tubular breathing may appear at a comparatively early period, but this is unusual; and with marked dulness, bronchophony, and coarse crackling rales, the respiratory murmur may remain simply weakened with slight prolongation of expiration.

The comparatively late appearance of tubular breathing is mainly due to the obstruction of the bronchi, which is so generally present, and to the irregular composite nature of tuberculous consolidation.

Dulness appears first at the supraclavicular and supraspinous fossae, and thence extends downwards over the front of the chest. For the recognition of slight degrees of dulness light percussion and careful attention to the sense of resistance are required. Direct percussion of the inner third of the clavicle is very useful in some cases. Increased conduction of the heart's sounds to the corresponding apex generally accompanies and sometimes precedes loss of resonance to percussion. Increasing size of the rales, with a sharply conducted or ringing character, is generally described as marking the presence of softening; but the same signs may be furnished by profusely secreting bronchi of considerable size situated in solid lung.

Rhonchi of a croaking or metallic quality are not uncommon at this period, this peculiarity being imparted to them by the adjacent solid lung or cavities. Dulness gradually extends over a considerable portion of the upper lobe, and rales become audible at the apex of the opposite lung, and at the infraspinous fossa on the same side; that is, at the apex of the lower lobe.

The date at which signs of excavation can be recognised varies greatly. In some cases a cavity may be detected almost as soon as consolidation can be diagnosed, whereas in others it may be months or even years before this is possible.

Signs of Excavation.—Over a cavity of considerable size the percussion is generally more or less impaired, and it may be markedly dull in consequence of the surrounding infiltration and of the pleuritic thickening which so often coexist. As excavation proceeds, the dulness may diminish. The resonance is often of tympanitic, tubular, or amphoric quality, as well as slightly dull, resembling the note produced by percussion of the trachea in the neck. Percussion may elicit the cracked-pot sound when a cavity communicates freely with the bronchus, and its walls are sufficiently elastic. This sign is not pathognomonic of a cavity, as it may often be obtained by percussing the chest of a healthy infant while crying, and is sometimes found in cases of pneumonia and pleural effusion. The bell sound—"bruit d'airain"—is occasionally heard over large cavities.

According to Wintrich, the pitch of the tympanitic percussion-sound over a cavity becomes raised when the patient opens his mouth. An alteration of pitch may sometimes be recognised when the patient changes from the sitting to the lying position, or conversely (Gerhardt); but these changes are seldom pronounced, and give little practical assistance. It is, however, to auscultation that we must mainly trust for the diagnosis of pulmonary excavation. In well-marked cases the breath-sounds are tubular or cavernous—the term "tubular" is used here as synonymous with "bronchial."

Some writers maintain that there is no difference between tubular and cavernous breathing, unless it be in the greater intensity and hollowness of the latter. Flint makes the relative pitch of the inspiratory and expiratory sounds the basis of distinction. According to this author, cavernous breathing is generally of lower pitch than tubular, and the

expiratory sound is of lower pitch than the inspiratory; whereas the pitch of tubular breathing is generally higher than that of cavernous respiration, and expiration is higher pitched than inspiration.

The breath-sounds over a cavity may be very weak, or even absent when the bronchial opening is small or obstructed in any way, as by profuse secretion or by cicatricial contraction. If the vomica be separated from the chest wall by a zone of spongy lung the respiration may be simply blowing, with prolonged expiration.

The "metamorphosing" breathing of Seitz consists of an inspiratory sound, harsh or rough at its commencement, becoming hollow or tubular towards the end of the act of inspiration. This sound is supposed to be due to the removal of a partial obstruction of a bronchus as inspiration proceeds. It is not a common sign, and it is not certain that it is exclusively a cavernous sign. Amphoric breathing is pathognomonic of a large air-containing cavity with smooth walls. Large gurgling rales are often heard where cavities contain abundant secretion, and this may be the only auscultatory evidence available at times. When such sounds are audible in regions like the apex, which contains no bronchi of large size, they are very significant of cavities. Auscultation of the cough gives valuable, perhaps the most valuable, evidence of excavation. In a cavity containing fluid and air the agitation produced by cough often gives rise to rales of a splashing character, resembling on a small scale the succussion sound of pneumothorax. Rales of this description are very suggestive of a cavernous origin. A metallic or amphoric echo of the cough is less common but is quite characteristic.

Post-tussic suction is another highly significant sign; it consists of a high-pitched, sucking, inspiratory sound, immediately following the forced expiration of cough, and is due to the elastic recoil of the cavity walls. This has been well named the "indiarubber-ball sound" by Dr. Mitchell Bruce.

Metallic tinkling is occasionally heard over large smooth-walled cavities. The vocal resonance is generally increased, bronchophony or pectoriloquy being very common; but the latter is not so decisive a test of excavation as is generally believed. In rare cases an amphoric quality is imparted to the voice when other metallic phenomena are present. In some cavities, where the breath-sounds are feeble, the resonance of the voice may be diminished, especially if the bronchus be obstructed. Cardio-pulmonary systolic murmurs are sometimes heard over large thin-walled superficial cavities lying close to the heart, mostly in the left upper lobe. These murmurs have been attributed to expulsion of air from the cavity through a bronchus by the impact of the heart on the lung.

Similar cardio-pulmonary murmurs may be occasioned towards the anterior margins of the upper lobes, especially the left, in the absence of any cavity in the lung, if the heart's action be much excited. In cases of contractile disease of the left upper lobe, a systolic murmur is not uncommonly audible in the second left interspace close to the sternum,

the bruit being due to traction of the lung on the pulmonary artery. In one case of this sort there was also a marked systolic thrill in this region, which suggested the possibility of stenosis of the pulmonary artery; but an autopsy shewed that it was due simply to contracting lung. Functional murmurs were present in 81, or 6 per cent, of 1289 patients at the Adirondack Cottage Hospital (L. Brown).

A few instances have been recorded in which a systolic murmur was produced by an unsupported and dilated branch of the pulmonary artery crossing a cavity. It should be mentioned that the chest wall may be markedly retracted over the site of a chronic contracting cavity.

Some writers, following Sir Andrew Clark, recognise "fibroid phthisis" as a peculiar variety. Most of these cases are but pulmonary tuberculosis in a very chronic form. There is little in the physical signs to distinguish them from non-tuberculous chronic pneumonia, except that in the former the disease is nearly always most pronounced in the upper lobe, and the apex of the other lung is often involved. In the fibroid or contractile form of pulmonary tuberculosis, signs of excavation are generally to be recognised at one apex, associated with much dulness over the upper lobe or over the whole lung, together with displacement of neighbouring organs. When the left lung is affected the heart is drawn outwards and upwards, and pulsation may be felt as high as the second rib or clavicle; or the apex beat may be discovered in the axilla. In such cases the shock of the second sound may often be recognised in the upper intercostal spaces by palpation. In two of the most extreme instances of displacement of the heart in this disease I found the heart beating under the angle of the left scapula.

When the right lung is contracted the heart is drawn over and may lie wholly to the right of the middle line, the pulsation sometimes reaching as far out as the right axilla. The diaphragm and abdominal viscera are raised by the contracting lung, especially when the upper lobe is principally involved. On the left side the tympanitic resonance of the stomach may extend as high as the fourth or fifth rib. In extreme contractile cases the opposite lung is always considerably enlarged, and may pass beyond the middle line of the sternum into the opposite half of the thoracic cavity. It is often extremely difficult to detect any signs of disease in a lung thus distended, though a post-mortem examination in these circumstances will nearly always reveal the existence of deeply-seated tuberculous lesions. The fact cannot be too strongly insisted upon, that in the presence of distension or emphysema of the lung extensive foci of disease may escape recognition altogether.

Irregular Forms.—It seems advisable, at this point, to make a few remarks concerning the physical diagnosis of certain irregular forms of the disease.

Emphysematous Form.—In this variety the history as well as the physical signs are those of bronchitis and emphysema. In addition to hyper-resonance on percussion, together with weak inspiratory and prolonged expiratory murmurs, careful percussion will sometimes elicit slight

comparative dulness at one supraspinous fossa, and perhaps above the clavicle. There may be no further deviation from the normal type of emphysema. In other cases, on coughing, a few muffled rales may be audible at one apex. If, as often happens, diffused rhonchi are also present, the difficulties of diagnosis are much increased. The shape of the chest is often flat instead of being rounded, a matter of some importance. In emphysematous people with such a formation of thorax, especially if there be much wasting or if haemoptysis have occurred at any time, the possibility of tuberculosis should be carefully considered, and the sputum should be repeatedly examined for tubercle bacilli.

Pleuritic Form.—Reference has already been made to the onset of pulmonary tuberculosis with symptoms of pleurisy. Signs of fluid effusion, thickened pleura, or dry pleurisy in one axilla or at the base, may be the only recognisable signs. It is of the utmost importance in all cases of pleurisy to keep in mind the close relation of this affection to tuberculosis. Double pleurisy, whether there be effusion of fluid or not, is nearly always tuberculous—the principal affections that have to be excluded being renal disease, acute rheumatism, and intrathoracic growths. Where a large effusion occupies the whole of one pleural cavity, no evidence of tuberculosis can be obtained from physical examination of the affected side.

At times rales or other morbid signs may be detected at the apex of the other lung, but too much importance must not be attributed to such a discovery, as in cases of this description the unaffected lung is often the seat of compensatory hyperaemia and oedema. Similar evidence of apical disease in cases of basic dry pleurisy, on the contrary, has a very definite and positive value. But the sputum may be the only trustworthy evidence of the tuberculous nature of the complaint. Cytodiagnosis may be employed where fluid can be removed from the pleura. If the cells obtained by centrifugalisation shew a marked preponderance of lymphocytes, tuberculosis should be suspected (*vide* p. 545).

It is commonly said that an insidious onset characterises tuberculous pleurisy, whereas an acute invasion is more suggestive of the simple idiopathic variety. No reliance can be placed on such statements. Tuberculous pleurisy may commence in the most acute manner; and a chronic insidious onset is not rarely witnessed in cases running a favourable course. In any case of pleurisy, marked wasting, or a history of haemoptysis, should arouse suspicion.

Anomalous Distribution of Physical Signs.—When signs of infiltration or excavation are confined to one base, or predominate there, an accurate diagnosis may be very difficult, in view of the extreme rarity of primary tuberculosis of this part. The fact that physical signs of disease are confined to or predominate at the base, by no means proves that there is not, at the same time, older disease of the apex of the upper lobe, a point which I have several times established on post-mortem examination. This depends on the fact that when the lesions are covered by a shell of healthy lung considerable masses of tuberculous disease, or even cavities,

may exist towards the central part of the upper lobe without giving any evidence of their presence.

Disease confined to the base of one lung in most cases is not tuberculous, and we have, in such instances, to exclude various affections, the most important of which I may here enumerate:—chronic pneumonia with or without bronchial dilatation, localised pleurisy, abscess of the liver, new growths, hydatid cysts of the lung or liver, and subphrenic abscess. Examination of the sputum is of the utmost value in such circumstances. It is well, at the same time, to remember that these diseases may be complicated by a secondary tuberculosis, and the discovery of tubercle bacilli may divert attention from the primary affection. Chronic contracting lesions of the apex of the upper lobe, particularly on the right side, may so uncover the great vessels at the base of the heart as to cause pulsation to be felt in the upper intercostal spaces, and thus aneurysm may be simulated. This is more likely to occur on the right side, where, on more than one occasion, I have known the association of dulness, pulsation, systolic murmur, and accentuated second sound to give rise to considerable suspicion of aortic aneurysm in middle-aged men.

Laryngeal Form.—Where laryngeal obstruction exists, the entry of air into the lung may be so greatly diminished that auscultation may give no trustworthy indications of the actual condition of the lungs. The amount of pulmonary disease, without any corresponding auscultatory signs, which may exist under such circumstances is surprising, and can only be appreciated by those who have been able to compare the post-mortem appearances with the results of physical examination during the patient's life. Percussion sometimes gives more valuable assistance than auscultation; but the most certain information is often afforded by the sputum test.

Diagnosis.—The diagnosis rests, in the first place, on the presence of chronic disease of the lung, affecting mainly or exclusively the apex of the upper lobe. Signs of persistent catarrh, consolidation, or excavation of this part are, for practical purposes, conclusive evidence of tuberculous disease.

The existence of tubercle bacilli in the sputum is an absolute proof of tuberculosis of some part of the respiratory tract. In the absence of tuberculous ulceration of the larynx, pharynx, or oral cavity, the lung may be regarded as the source of the bacilli, even if auscultation and percussion give no indication of any pulmonary lesion, or if physical signs of disease be found in aberrant situations.

Most writers consider the subject of physical diagnosis under three stages—the first, second, and third stages of phthisis. Such a division of the subject implies that physical examination may be trusted to decide at which of these stages the disease has arrived—an assumption by no means warranted by the facts. As a description of the history of individual tuberculous foci, there is not much fault to be found with the time-honoured division into three stages of consolidation, softening, and excavation; but these distinctions are, to some extent, misleading. In

the first place, as soon as the stage of softening is reached excavation has begun; in other words, the two processes are more or less concomitant; moreover, the rule is to find in the same lung—often in close proximity—solid nodules, softening caseous masses and fully-formed cavities: in other words, all three stages are run simultaneously.

On the clinical side of the question auscultation and percussion enable us to recognise consolidation with no little accuracy, and in many cases the existence of a cavity is revealed by certain physical signs; but there is no distinctive sign of softening whatever. In the majority of cases, where, as the result of physical examination, the patient is said to be suffering from phthisis in the first stage, cavities already exist. This is frequently proved to demonstration by the detection of elastic tissue and numerous bacilli in the sputum of cases in which auscultation and percussion point only to catarrh, or to slight consolidation of one apex. It is a matter of everyday experience that cavities in the lung may escape detection during life; and I have known the most experienced physicians diagnose excavation where post-mortem examination shewed that none existed. The effects of this artificial classification on the patient's mind have, in many instances, been most pernicious. For, knowing that there are three stages, and hearing that he has a cavity in his lung, he concludes that, as he is in the last stage, his days are numbered. As a matter of fact, many persons in whom a cavity can be diagnosed are in a better condition, and have far more favourable prospects, than others in whom there are only signs of the first stage. It is time that the three stages were consigned to a well-merited oblivion.

Skiagraphy.—Opinions differ as to the value of skiagraphy in the diagnosis of pulmonary tuberculosis. Areas of consolidation, cavities, and pleural effusions undoubtedly give indications which may afford useful information to an experienced radiographer. Limitation of the movement of the diaphragm on the affected side, as seen with the fluorescent screen, is believed to be an early sign of tuberculosis. But it is still a matter of dispute whether skiagrams or screen observations give as early and as trustworthy indications as the older methods of physical examination (*vide* art. "*X*-Rays in Medicine," Vol. I. p. 493). P. K.

Specific and Microscopical Diagnosis.—Apart from the physical methods of chest examination, there are others whereby the presence of tuberculosis may be proved or inferred. Some of these methods are specific in so far that they demonstrate the existence of tubercle bacilli or of anti-bodies produced as a result of the invasion of the bacilli. These anti-bodies are of the nature of agglutinins or opsonins, and may be tested *in vitro*, or the experiment may be carried out in the patient's body by the inoculation of tuberculin subcutaneously (Koch), cutaneously (Pirquet), or into the conjunctiva (Wolff-Eisner, Calmette). The presence of tuberculosis may also be suspected from the examination of the cells present in the expectoration (cytodiagnosis), or from the presence of elastic tissue.

Sputum.—The most certain method of diagnosis is the direct demonstration of tubercle bacilli in the sputum. When the bacilli are present in any quantity this is easy. A fresh sample of the morning sputum should be poured into a flat glass dish and examined against a dark ground, the small opaque yellowish specks being transferred by means of a sterile platinum wire or forceps to a slide or cover-glass. It used to be considered a heresy to use a slide instead of a cover-glass, but where the question is one of the diagnosis of tuberculosis a slide is preferable, as a much larger area can be prepared for examination, the slide is not easily broken, it is easily manipulated, and is cheap. By means of a platinum wire a large part of the slide may be covered with a thin layer of the sputum. The film is then dried in the air, fixed in the flame, and stained. The method universally used depends on the fact that the bacillus is acid- and alcohol-fast. (Vol. II. Part I. p. 269.) The ordinary method is to pour some carbol-fuchsin into a test-tube, heat to the boiling-point, and pour the hot stain on the film to be stained. After one or two minutes wash in water, and decolorise with 25 per cent sulphuric or 33 per cent nitric acid or other acid. Wash well in water, treat the film with spirit or alcohol, and finally counterstain with a slightly alkaline solution of methylene blue. The tubercle bacillus retains the fuchsin stain, other bacteria and cells are stained blue. This Ziehl-Neelsen method requires no great skill, occupies a few minutes only, and ought to be carried out in all cases in which cough and expectoration have existed for some time. In spite of the vast numbers of sputum preparations which are examined all over the world, no essential alteration in the technique of sputum staining has occurred for years. Recently, however, Carl Spengler of Davos has described methods by which he states that he can diagnose by the microscope bovine (*Perlsucht*) bacilli from human tubercle bacilli. He asserts that the *Perlsucht* bacilli differ from those of the human type, in that they are larger and shew sporoid bodies (German "splitter") in their interior. The *Perlsucht* bacillus is also said to be less acid-fast, and therefore to require less rigorous decolorisation with acid for its demonstration. The technique proposed by Spengler is to mix a particle of sputum with a minute drop of 1 per cent solution of potash on a slide. A film is made and fixed, care being taken not to overheat; stain with Loeffler's blue, then wash in water; stain in slightly warmed carbol-fuchsin, wash again, then treat with methylene-blue solution with the addition of one or two drops of 15 per cent nitric acid for a few seconds. Wash, dry, and mount. In an examination of 112 cases of pulmonary tuberculosis Spengler found in 61 per cent a mixed infection of *Perlsucht* and human bacilli; in 20 per cent human bacilli alone; in 14 per cent "splitter," and small rods, and in 5 per cent *Perlsucht* bacilli alone. From these results Spengler regards the majority of cases of consumption as mixed infections of human and *Perlsucht* bacilli, and bases his inoculation therapy thereon (cf. p. 390). Every one with experience in examining tuberculous sputum must have been struck with the extraordinary variation in size and thickness and even shape of the tubercle bacilli in

different cases; but that any accurate conclusions can be drawn from these seems very doubtful. At any rate, it does not appear to me that Spengler has proved that it is possible to diagnose bacilli of bovine and human origin under the microscope. This really touches most debatable ground upon which it is quite impossible to make any definite statements at the present time.

It is admitted that early diagnosis of tuberculosis is most important from a therapeutic and prognostic standpoint, and it often happens that in these cases the bacilli may be present in very small numbers only. For dealing with cases of this kind, a large number of methods have been devised by Biedert, Mühlhäuser, Czaplewski, Jochmann, Beitzke, Dilg, Nebel, van Ketel, Spengler, and others. These depend mainly on the homogenisation of the sputum by alkalis, carbolic acid, etc., with subsequent sedimentation or centrifuging to collect the bacilli as a deposit for microscopic examination. The best method is that of Mühlhäuser and Czaplewski, as modified by Beitzke, and consists in shaking one part of sputum with four parts of a 0·2 per cent solution of soda in a bottle closed by a rubber stopper. If homogenisation does not take place, more soda solution may be added, and even heat applied. When the sputum is uniformly liquid, one to two drops of phenol-phthalein solution are added, and then drop by drop a 5 per cent solution of acetic acid, until the red colour of the phenol-phthalein is just decolorised. During the addition of the acid, the sputum should be thoroughly stirred with a glass rod. It is then allowed to settle for twelve to twenty-four hours, or still better centrifugised, the deposit being spread on a slide and stained as above. Where these methods fail, and the sputum is not grossly infected with other bacteria, resort may be had to the inoculation of a guinea-pig—an extraordinarily sensitive test. The time which has to elapse is, however, a drawback, as it may take four weeks or more before the guinea-pig shews coarse evidence of tuberculosis, and this is especially the case when the number of bacilli is very small.

The number of bacilli in sputum varies enormously, and no accurate conclusion as to the extent of the disease can be drawn from sputum examination. Ambulant cases of phthisis in relatively good health may expectorate immense numbers of tubercle bacilli. On the other hand, it may be difficult to find them in cases progressing fairly rapidly. With the onset of ulceration bacilli are usually easily found. For handy comparison of the number of bacilli at different times in the same individual various methods are used. Ritter expresses it as a fraction in which the numerator represents the number of bacilli, and the denominator the number of microscopic fields containing the bacilli; thus $\frac{10}{1}$ represent 10 tubercle bacilli in each field. A less exact but more extensively used scale is that of Gaffky:—

No. 1 = 1 – 4 T.B. in the whole preparation.
„ 2 = 1 T.B. in several fields.
„ 3 = 1 T.B. in each field.
„ 4 = 2 – 3 T.B. in each field.

No. 5 = 4 – 6 T.B. in each field.
„ 6 = 7 – 12 „ „
„ 7 = fairly numerous T.B. in each field.
„ 8 = numerous „ „
„ 9 = very numerous „ „
„ 10 = enormous numbers „ „

Evidence of Tuberculosis from the Demonstration of Anti-bodies in Vitro and in Vivo.—The demonstration of *agglutinins*, which has proved so valuable in the diagnosis of enteric fever, cholera, Malta fever, and other infections, can only rarely be applied with success to the diagnosis of tuberculosis, as the reaction is very inconstant and the concentration of serum required is relatively high. Another technical difficulty consists in obtaining a homogeneous emulsion of the bacillus for examination.

Variations in the Tuberculo-opsonic Index of the Serum.—Determinations of fluctuations in the tuberculo-opsonic index may be utilised in the diagnosis of tuberculosis; although in the absence of regional symptoms or signs, it is impossible to locate the disease to the chest by this test alone. The basis of the belief that variations occur in the tuberculo-opsonic index in tuberculosis is, that when the serums of normal individuals are compared amongst each other the range of variation lies between ·8 and 1·2. This has been determined on a large number of healthy people by Bulloch, Urwick, Fraser, Flemming, Lawson and Stewart, Turban and Baer, and v. Szabóky, and others. In the most recent series of 44 individuals comprising 635 examinations, Dr. Flemming, indeed, considered that 76 per cent had opsonic indices lying between ·95 and 1·05, and that only ·8 per cent were under ·9, and that 1·7 per cent had an index above 1·10. Opsonic indices above 1·2 and below ·8 are repeatedly found in cases of pulmonary tuberculosis. Sir A. Wright's original conception that in tuberculosis the opsonic index is persistently lowered, was soon dispelled by the observations carried out in his laboratory by Dr. Urwick; of 33 cases of consumption taken at random from different hospitals and comprising all stages of the disease, Dr. Urwick found 25 with an index over the normal limit. Seven had an index below normal, and in one case the index was normal. He was also able to shew that, contrary to the condition in normal people, the opsonic indices of consumptives are subject to fluctuations; this was interpreted by Sir A. Wright as being due to constant auto-inoculations, poisons passing from the infected foci and giving rise to an increased production of opsonic substances in the serum. Most workers have confirmed these observations, although it is right to state that some hold that the errors in opsonic determinations are so considerable that it is impossible correctly to interpret the results. In recent times Dr. Inman has laid great stress on the importance of auto-inoculations in the course of pulmonary tuberculosis. In cases of rapidly advancing disease the tuberculo-opsonic index may vary within very wide limits, and within very short periods. In more chronic cases the index may be high or low over a considerable number of days. Even where the index is normal, while the patient is at rest in

bed, it may rise or fall with increased respiratory movements or bodily exercise, as has been shewn by the extensive observations of Dr. Inman on the patients undergoing work and exercise under Dr. Paterson's system at the Frimley sanatorium. Even in early cases, at a stage when no sputum can be obtained for examination, the instability of the tuberculo-opsonic index, in association with symptoms or signs pointing to pulmonary disease, may be of great diagnostic value.

Subcutaneous Injection of Tuberculin.—Whereas the determination of agglutinins or opsonins is carried out *in vitro*, specific anti-bodies may be recognised *in vivo* by the use of tuberculin, a method of diagnosis which has gained an increased number of adherents in recent years. The basis of the use of tuberculin as a diagnostic agent was Koch's observation that an organism already tuberculous is extremely sensitive to tuberculin. In his first publication on the subject in 1890 he pointed out that it was possible by its use to produce specific reactions in persons suffering from tuberculous disease. The great hopes that were raised in the early 'nineties that tuberculin would cure phthisis were, as is well known, rapidly dispelled, and indeed it was asserted mainly on the authority of Virchow that its use was fraught with grave danger, and as a result tuberculin in man was almost entirely discarded. Its use as a diagnostic agent for tuberculosis in cattle demonstrated on a very extensive scale its great value and its comparative harmlessness, and by degrees its administration in man has come to be better understood; and at the present day it may be stated with certainty, on the basis of many thousands of observations, that it is of the greatest service in the certain recognition of pulmonary tuberculosis, especially in doubtful cases. It is impossible for considerations of space to deal with the literature on which this statement is based, and it must suffice to refer to the writings of a few workers only, namely, R. Koch, Beck, Petruschky, Moeller, Götsch, Spengler, Bandelier, and Roepke, Löwenstein, and Pickert.

The essential improvement in the method of administration of tuberculin in recent years consists in the recognition that the *reaction* should be minimised as far as is possible for the diagnosis. It is best to use the so-called "old tuberculin" (Tuberculinum Kochii), manufactured by Meister Lucius and Brüning at Höchst ("Höchst Tuberculin"), as it is more or less constant in strength and is accurately tested. Tuberculin is a syrupy brownish liquid which, in the undiluted state, will keep indefinitely. To make the necessary dilutions for diagnostic purposes the operator should provide himself with 1 c.c. and 10 c.c. graduated pipettes, two sterile test-tubes, and some 0·5 per cent carbolic acid solution. The pipettes should be sterilised. By means of the 10 c.c. pipette, introduce 9·9 c.c. carbolic solution into test-tube I., and then by means of the 1 c.c. pipette add ·1 c.c. of tuberculin, and mix by shaking. In each c.c. of the mixture there is ·01 c.c. of tuberculin. To test-tube II. add 9 c.c. of carbolic solution and 1 c.c. of mixture from test-tube I., and mix by shaking. One c.c. of the mixture in tube II. contains ·001 c.c. of tuberculin. 10 c.c. of this 1 per mille solution contain $\frac{1}{100}$ c.c. It is customary to describe this

$\frac{1}{100}$ c.c. as 1 centigram or 10 mgr., and to say that 1 c.c. = 1 mgr. This is, chemically speaking, incorrect, as the specific gravity of tuberculin is higher than that of water, and 1 c.c. contains more than 1 mgr. by weight. For subcutaneous inoculation a glass syringe of 1 c.c. capacity, and calibrated to tenths, is desirable. The skin is disinfected and the tuberculin inoculated preferably below the shoulder-blades, about the level of the last rib. The time of the inoculation is of some importance, both to the patient and the doctor. By inoculating between 8 and 10 A.M. the reaction can usually be observed towards evening, without the patient being disturbed during the night. The temperature should be taken every three or four hours for two or three days before inoculation; for example, at 8, 11, 2, 5, and 8 o'clock, and the temperature should not exceed 99° F. (37°·2 C.) at the highest, as the changes induced by the modern dosage of tuberculin are so slight that an error may easily be made, a positive reaction being masked by a febrile temperature at the time of the inoculation. In women an inter-menstrual period should be chosen.

Dose.—The question of dosage is one of the greatest importance. Koch originally recommended beginning with 1 mgr. If there is no rise of temperature at all, 2 mgrs. may be injected two days later. If there is even a slight rise of temperature, only a quarter of a degree for instance, the dose is not raised but repeated as soon as the temperature is normal again, as it often happens that the same dose may produce a definite reaction on its second application. According to Koch this is an infallible sign of tuberculosis. If the first small doses produce no reaction whatever, 5, and finally 10, mgrs. may be inoculated, and for certainty's sake Koch gave the last dose twice. Bandelier and Roepke consider that it is advisable in all cases to start with not more than $\frac{2}{10}$ mgr., rising according to the temperature indications to 1 mgr., 5 mgr., and 10 mgr., the latter being used once only. Löwenstein considers that in the majority of cases it is not necessary to increase the dose beyond $\frac{2}{10}$ mgr., this quantity being inoculated on three or four occasions. The majority consider that a dose of 10 mgr., which can be borne without reaction, is evidence that the patient is free from tuberculosis. It is important to note that early cases often react with the smaller doses, old-standing cases requiring the larger doses before a positive reaction is obtained. In the case of children the dose should be suitably lowered, beginning with $\frac{1}{10}$ mgr. and passing to $\frac{5}{10}$ mgr., 2·5 mgr., and 5 mgr. The *reaction* following the introduction of tuberculin in a tuberculous subject is twofold, viz. general febrile, and local. The latter is specific and, in tuberculous lesions visible to the eye, as in lupus, is of an inflammatory character. Under the microscope there is considerable leucocytic exudation, necrosis of the tuberculous tissue, and great transudation of plasma into the tissues. In the case of the lung, in which the local reaction is, of course, invisible, it may be surmised by increase in the cough and expectoration, and tubercle bacilli may make their appearance. The febrile reaction is usually regarded as partly specific and partly the general effect produced by bacterial proteins, as pyrogenic

properties have been proved to follow the inoculation of proteins other than those of tuberculin (Hueppe and Scholl, Buchner, and many others). Still the non-specific protein reaction necessitates the administration of doses greatly in excess of those used in diagnosing tuberculosis by tuberculin, so that the febrile reaction following the use of tuberculin in quantities of about one milligram may be regarded as specific. To what extent healthy non-tuberculous persons are influenced by tuberculin is doubtful; Koch placed the boundary at 25 mgrs., stating that even normal individuals may react with this quantity. On the other hand, Hamburger has recently shewn that quantities of 10-100 mgr. may be borne, without any visible effect whatsoever, by children of ages ranging between 0-14 years. In one of his cases, a girl, 500 mgr. produced no rise of temperature or other symptom. Bertarelli surpassed even this by inoculating himself with 1·25 c.c. (1250 mgr.), which was tolerated without the slightest symptom except a slight local redness. It has generally been stated that children are more tolerant to tuberculin than adults, but it would seem that the real explanation of this is that many children are entirely free from tuberculosis, whereas a very large number of adults have been infected, and at post-mortem examination shew unequivocal signs of tuberculosis. Koch himself had severe symptoms from a dose of 250 mgr.

The rise of temperature in a positive reaction is of the greatest importance, as it can be objectively measured. In general a rise of at least 0·5° C. is regarded as a positive effect. With temperatures of 100-100·2° F. the reaction is said to be slight, medium when the temperature ranges from 100·2-102° F., and severe when it is above 102° F. The reaction is very variable in different subjects, but in a large number it has begun in about six to eight hours, and reached its height within twelve hours, to decline and disappear in perhaps thirty hours; in some cases, however, the reaction may be delayed for twenty-four hours. Besides the fever, there are other symptoms of illness, such as shivering in varying degree, followed by feeling of heat, headache, often severe, pain in the back, vomiting, acceleration of cardiac action, and tightness in the chest. A tendency to cough with expectoration is no doubt referable to the specific local changes in the tuberculous foci. There are various contra-indications to the use of tuberculin; of these the most important are febrile temperatures, recent haemorrhages, cardiac or renal disease of organic character, and epilepsy; and Moeller and Kayserling add hysteria.

Tuberculin is indicated in doubtful and early cases, but it should be resorted to only in the absence of other specific evidence of tubercle. In the manner described above its administration may be looked upon as safe, and as offering the most accurate evidence next to the actual bacterioscopic proof of tubercle bacilli.

Cutaneous (Pirquet) and Conjunctival (Wolff-Eisner, Calmette) Reactions.—Apart from the specific reaction following the subcutaneous inoculation of tuberculin, it has been shewn by Pirquet that characteristic

changes develop locally where tuberculin is applied to the abraded epidermis. In communicating his extensive results by this method at the Berlin Medical Society on May 8 and 15, 1907, Wolff-Eisner, in the subsequent discussion, pointed out that the instillation of a drop of 10 per cent tuberculin into the conjunctival sac produced a local reaction, consisting of redness and swelling of the conjunctiva. Some weeks later (June 17) Calmette published results on the conjunctivae of 16 tuberculous and 9 normal people with a 1 per cent solution of a precipitate obtained by the action of alcohol on tuberculin. This has been followed by numerous papers in medical journals in all parts of the world on this subject, so that already a large body of evidence exists on the value of these methods, especially the so-called conjunctival reaction.

Pirquet's Method of obtaining the Cutaneous Reaction.—The inner side of the forearm is washed with ether. From a drop-bottle 2 drops of old tuberculin are placed on the skin at a distance of 10 cm. from each other. With an instrument resembling a burr a slight lesion is made in the skin between the two drops of tuberculin, and subsequently through the middle of each of the two drops themselves. After this superficial scarification a few fibres of cotton wool are laid on for a few minutes, and then removed. The first lesion is to act as a control and demonstrate the amount of traumatic reaction, which usually consists of a small raised-up papule surrounded by a faint rose-coloured halo, disappearing in a few hours. The same phenomena are seen at first in the area of the scarified tuberculin drops, but if a positive reaction takes place a renewed growth of the red halo ensues after a latent period of a few hours, the reaction being, as a rule, fully developed by the end of forty-eight hours. In the centre there is a raised lesion measuring 10-30 mm. in diameter, its colour varying in different shades of red. Its boundaries may be circular or irregular; after the acme has been passed the exudation begins to diminish, the bright red colour becomes paler, passing through colours like those of a bruise, and generally shewing pigmentation for some time. Slight scaling of the epidermis is the rule. In the great majority of cases there are no general symptoms, and complications are very rare. The histological changes, which have been studied by Bandler and Kreibich, are found to consist of inflammatory foci in the cutis and subcutis and reaching down to the fat. The foci, which are found especially around hair-follicles or sweat glands, consist mainly of mononuclear cells, but epithelioid cells and atypical giant cells have also been met with.

Conjunctival or Ophthalmo-reaction.—Wolff-Eisner originally recommended the use of a 10 per cent solution of old tuberculin, but the reaction is much more specific with smaller concentrations, such as 1 per cent to 2 per cent. Calmette uses a 0·5 per cent solution of the precipitate obtained by the action of alcohol on tuberculin; this solution corresponds roughly to a 5 per cent solution of old tuberculin, and is sold in commerce under the name "tuberculin test," but it does not possess any advantages over the ordinary dilutions of tuberculin. One or two drops

are instilled into the inner angle of the eye, the eyelids being held together for a moment afterwards. The other eye serves as a control. The traumatic reaction in healthy people is at the most a faint redness, which disappears in a few hours. In cases in which it is positive the reaction is very different, and three degrees of severity can be differentiated: (1) redness of the caruncle and the conjunctiva palpebralis; (2) marked redness with involvement of the conjunctiva sclerae, and with swelling and increased secretion; and (3) intensive redness of the whole conjunctiva, chemosis with marked fibrinous or purulent secretion and small ecchymoses.

The onset of the reaction usually occurs in three to six hours, and increases up to the tenth to twelfth hour, after which it begins to recede, and usually disappears in thirty-six hours. With the very severe degrees of reaction the process may last for two or three weeks. The existence of any eye trouble contra-indicates the use of this method. It must also be remembered that "scrofulous" persons, especially children, often shew a high degree of hypersensitivity to even minute quantities of tuberculin. In general, too, the same eye should not be used for more than one experiment. Citron recommends in doubtful cases one drop of a 2 per cent solution of tuberculin in the left eye. If the reaction is positive the right eye may receive 1 drop of a 1 per cent solution to make doubly certain. When the reaction in the left eye with 2 per cent solution is negative, a drop of a 4 per cent solution should be placed in the right eye. The cheapest and best method is to dilute down the tuberculin as required.

Specificity of Reaction and Comparative Value of the Subcutaneous, Cutaneous, and Conjunctival Modes of Application of Tuberculin.—The striking result obtained by Pirquet shewed that very characteristic lesions are produced in the skin on the application of tuberculin. To determine how far these lesions are specific these results may be tested by comparison with those of post-mortem examinations, or of clinical observations only. In Pirquet's series of 124 autopsies in children it was found that in 64 which were free from tuberculosis, all had given a negative reaction; of 14 in whom tuberculosis was found accidentally at the autopsy, 10 had given a positive reaction and 4 negative; whereas of 45 cases dying of tuberculosis, 31 had shewn positive and 14 negative reaction, all the negative cases in the latter group being tested for the first time within twelve hours of death. According to Pirquet, a positive result does not occur without pathological anatomical evidence of tubercle. Negative reactions in general indicate freedom from tuberculosis; the reaction, however, may fail in the last stages of tuberculosis. The reaction is also found to be in close agreement with clinical experience, especially in regard to children. By the cutaneous method carried out on 757 children, Pirquet found that out of 130 patients clinically tuberculous, 113 gave a positive reaction; out of 512 patients clinically free from tuberculosis, 104 gave a positive reaction; and that out of 115 doubtful cases a positive reaction was obtained in 56; that is

to say, 87 per cent of children with clinical evidence of tuberculosis shew the reaction as well as 20 per cent of those who clinically have no tuberculosis. The negative cases in which tuberculosis was manifestly present were in the majority of instances cachectic and in the last stages of the disease. The conjunctival reaction comes even nearer to clinical estimations. In Petit's series of 2974 collected cases, of 740 clinically tuberculous patients 698 gave a positive reaction; of 938 clinically non-tuberculous patients 173 gave a positive reaction; and of 185 clinically doubtful patients 114 gave a positive reaction; in other words, 94·3 per cent of clinically tuberculous cases gave a positive reaction, and only 18·4 per cent of clinically non-tuberculous. Pirquet has pointed out that the cutaneous reaction may be positive in a large number of adults; this agrees with the frequence of tuberculous infections as shewn by post-mortem examinations. Indeed, like the agglutination test for enteric fever, the reaction should be judged not so much from a qualitative as from a quantitative point of view. With reference to the exact comparative value of the subcutaneous, cutaneous, and conjunctival methods there are not many publications. To gain accurate information the three should obviously be tested simultaneously, as the application of tuberculin by one method may lead to hypersensitive action when one or both of the other methods are subsequently employed. Ferrand and Lemaire compared the results of inoculating 32 children with 0·2 mgr. of tuberculin with those of the cutaneous and conjunctival reactions on the same children at the same time, and 20 times the three reactions agreed; in 11 cases the cutaneous agreed with the subcutaneous result, whereas the conjunctival effect was different. It is impossible at the present time to say which is the better method, although it would seem that the application of the tuberculin to the conjunctiva harmonises slightly better with clinical experience. In general, it would seem that in clinically certain but not very far advanced cases of tuberculosis, the reaction is almost without exception positive both by cutaneous and conjunctival methods. With late cases of tuberculosis, however, the reaction may be negative, or if present, of slight degree.

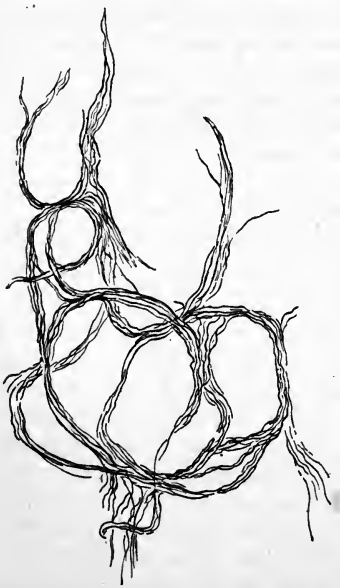

FIG. 21.—Elastic tissue from the lung, with well-marked alveolar arrangement. Prepared from sputum by Fenwick's method. (Low power.)

In addition to the methods described above, tubercle may be suspected from the presence of *elastic tissue in the sputum*. To demonstrate this, the

sputum is mixed with an equal quantity of caustic soda of the strength of 20 grains to the ounce, and the mixture is then boiled and allowed to settle for some hours in a conical glass, or a deposit may be obtained by means of a centrifuge. The elastic fibres may be recognised by examining the deposit fresh or by some specific staining reaction, such as Weigert's resorcin-fuchsin method. Van Voornveld compared the results obtained by examining 3143 samples of sputum for bacilli and for elastic tissue, and found that the amount of the latter stood in relation to the number of tubercle bacilli. With sputa containing bacilli in "Gaffky 5" scale and onwards, elastic fibres were constantly found. Besides elastic tissue, the presence of large numbers of mononuclear round cells in the sputum is in favour of tuberculosis. Löwenstein has recently drawn attention to the occurrence of phagocytosis of tubercle bacilli in stained films, and he considers that this is met with in cases with marked tendency to chronicity or in recent cases in which the prognosis is good.

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The complications of phthisis are mostly referable to the transmission of the tubercle bacilli to other parts of the body. In the case of the pharynx, larynx, and trachea, tuberculous changes are mainly produced by the direct inoculation of these parts with the sputum which is constantly passing over them. But in secondary tuberculosis of the genito-urinary, nervous, and osseous systems, infection is conveyed by the blood—the microbes, for the most part, effecting an entrance into the circulation through branches of the pulmonary veins.

Laryngeal tuberculosis is almost always secondary to the same disease of the lungs, though in a few well-authenticated cases the lungs have been found on post-mortem examination to be unaffected. The larynx is very frequently implicated; according to my post-mortem statistics this happened in 50 per cent of all cases of pulmonary tuberculosis. In many cases the lesions were recent, and were evidently due to late infection of the larynx. If we exclude all patients in the last stages, it may be said that laryngeal tuberculosis is clinically recognisable in from 20 to 25 per cent. The lesions consist of infiltration or swelling and ulceration. The localisation is a matter of great diagnostic importance.

Tuberculous affections shew a marked preference for the posterior part of the larynx, the hinder extremities of the vocal cords, the inter-arytaenoid fold, and the laryngeal surface of the arytaenoid cartilages. The epiglottis is less frequently implicated, and the ventricular bands are seldom involved, except in widespread disease of the larynx. The progress of tuberculosis is slow, contrasting strongly with the relatively rapid course of tertiary syphilitic ulceration. The early symptoms are those of chronic laryngitis; hoarseness, tickling, a sense of fatigue on using the voice, and various other paraesthesias referred to the throat. Pain on swallowing is a far more important symptom, and is generally associated with swelling or ulceration of the epiglottis or arytaenoid regions. Inspiratory stridor and dyspnoea depend for the most part on massive swelling of the epiglottis and aryepiglottic folds; but in certain cases extreme stenosis occurs from mechanical fixation of the cords in the median position, in consequence of infiltration around the crico-arytaenoid joints.

In the obstructive form of laryngeal tuberculosis difficulties in physical examination of the chest frequently arise; for when the entry of air into the lungs is much curtailed auscultation may discover nothing more than weakness of the breath-sounds. Hence the importance of an accurate laryngoscopic diagnosis, and repeated examination of the sputum cannot be too strongly insisted upon. It should not be forgotten that aphonia in phthisical persons is not uncommonly the result of functional

paresis of the adductor muscles of the vocal cords. The trachea is rarely affected except in advanced cases of pulmonary tuberculosis, and the larynx nearly always shews similar and more extensive disease. (For a detailed account *vide* art. "Laryngeal Tuberculosis," p. 195; and for laryngoscopic appearances, Plate VIII. in Vol. IV. Part II.)

Bronchial Glands.—The bronchial, mediastinal, and tracheal glands are very prone to tuberculous disease. In adult cases this adenopathy, as the French style it, scarcely ever gives rise to definite symptoms or physical signs. The glands most affected are the anterior or pretracheal, and the subtracheal which lie beneath the fork of the trachea. In children the enlargement of the glands may be so pronounced as to cause obstruction of the large bronchial tubes, or even of the trachea. Bronchial obstruction, if pronounced, leads to pulmonary collapse; in which case dulness on percussion and weakness of the breath-sounds, or tubular breathing, will be found over the affected area. When the upper lobe is concerned the similarity to phthisis may be very close. In some cases the continued absence of adventitious sounds may suggest the glandular origin of the lesion, as in some cases under my care which ended in recovery. Dulness and tracheal breathing over the manubrium may occasionally be found when the pretracheal glands are greatly enlarged. It is said that dulness may be recognised in the upper interscapular region; but I have never met with this myself; and it seems unlikely that enlarged glands in the fork of the trachea and, therefore, lying in front of the spine, should occasion dulness in the situation indicated. A venous hum heard over the manubrium when the head is strongly retracted is said by Dr. Eustace Smith to be an early and reliable sign of enlarged subtracheal glands in children. The subjects of this complaint sometimes suffer from a spasmodic cough like whooping-cough, and from attacks of dyspnoea, attributable to pressure on the vagus trunks (*vide* p. 617).

Compression of the recurrent laryngeal nerve, more particularly on the left side, may cause paralysis of the corresponding vocal cord. Perforation of the oesophagus by a suppurating caseous gland, when the abscess opens into a bronchus, is apt to give rise to septic bronchopneumonia, and gangrene of the lung may follow. Rupture of a glandular abscess into the trachea may cause fatal asphyxia. In many instances caseous glands undergo calcification, and the disease is thus arrested.

Pneumothorax is one of the most serious and fatal complications, statistics proving that the patient rarely survives this accident by more than one month at most; though exceptions to this rule are to be met with. It is at first sight remarkable that pneumothorax does not occur more frequently, considering the tendency of pulmonary cavities to extend outwards towards the pleura. Dr. Samuel West's experiments enable us to understand why perforation of the visceral pleura is not necessarily followed by pneumothorax, even when there are no adhesions. For, as he shews, before the elastic recoil of the lung can assert itself, the normal cohesion of the two layers of the pleura must be overcome, and

this requires considerable force; in other words, the force of cohesion considerably exceeds the elasticity of the lungs. He concludes that "pneumothorax, in its initial stage, must be an active process. Some force will be required to overcome the normal cohesion between the two layers of the pleura, and to separate them. This must be obtained by expiration, and pneumothorax, therefore, in its initial stage, is an expiratory process, and not essentially different in its production from surgical emphysema. As soon, however, as separation has been effected, the elasticity of the lungs will come into play, and air will enter the pleura until its retractility is completely satisfied" (*vide* p. 519).

Inasmuch as perforation of the pleura is always succeeded by inflammation the force of cohesion may soon be supplemented by adhesive pleurisy, and the entry of air into the pleural sac may be thus prevented. In cases in which the opposite lung is extensively diseased the dyspnoea at first is very great, and death may occur in a few minutes; but the immediate consequences of the perforation are almost invariably recovered from. Physical examination of the affected side shews absence of movement, increased fulness of the intercostal spaces, diminished tactile fremitus, and hyper-resonance or tympanitic percussion-note. On auscultation the breath-sounds are absent or feeble—at times amphoric, and the vocal resonance is diminished; occasionally amphoric echo of the voice may be obtained. Percussion by means of coins, or with a plexímeter and percussion hammer, while the stethoscope or naked ear is applied to the chest, yields a clear metallic sound, the bell sound, or *bruit d'airain*. Metallic tinkling and amphoric echo of the cough may also be heard. The Hippocratic succussion-splash can often be detected when fluid effusion has occurred, if the ear be placed on the chest and the patient be shaken sharply. The heart is displaced to the opposite side, except in the rare instances in which it is fixed to the sternum by adhesions, or in which the opposite lung is solidified or completely adherent.

This displacement is not due to the pressure of the pneumothorax as is commonly assumed; for in such cases, as shewn by Sir R. Douglas Powell, manometric measurements may indicate no positive pressure in the pleural cavity; and his experiments have demonstrated that the dislocation of the heart is due to the unopposed elastic traction of the sound lung. The diaphragm and the abdominal viscera on the corresponding side, being no longer held up by the elasticity of the lung, sink downwards. In some cases depression of the liver or spleen may be detected by palpation. Although effusion nearly always ensues, it may be difficult to obtain clear evidence of its presence. Sometimes there is a small area of dulness at the base, shifting to an unusual degree with the position of the patient. In other cases there may be no signs of fluid except the succussion-splash, which, however, is quite decisive. The absence of dulness is to be explained by collection of the fluid in the cup-shaped space formed by the depressed diaphragm. In more chronic pneumothorax a copious exudation may occur, and the air gradually become absorbed. In these circumstances there will be marked dulness

and other signs of simple pleural effusion, from which the case can only be distinguished by the history. The effused fluid is generally purulent, but may be sero-fibrinous.

Instances of complete recovery after pneumothorax have been recorded by many observers. In most of these the perforation of the pleura occurred without any previous evidence of pulmonary disease; and, although it is probable that many of them were tuberculous, this cannot be stated with certainty. In a much smaller number of cases, where pneumothorax appeared in the course of manifest pulmonary disease, life has been prolonged for months or years. The occurrence of pneumothorax seems, in some instances, to exercise an inhibitory effect on the disease in the affected lung—a result probably to be attributed to the altered blood-supply consequent on the pulmonary collapse.

Pleurisy.—A certain degree of pleurisy occurs in every case, although it may be unaccompanied by any symptoms. Signs of dry pleurisy, without any evidence of effusion, are often met with. When a dry rub is heard over a considerable area—usually the lower part of the chest—it not uncommonly indicates progressive disease; but there are many exceptions to this rule. Pleural effusion occurring in the course of pronounced phthisis is seldom very profuse, perhaps because the pleural cavity has been already partly obliterated by adhesions. The fluid is generally sero-fibrinous, sometimes purulent, and occasionally sanguineous. Cases have been recorded in which rapid absorption of an effusion was followed by acute generalised tuberculosis. This, however, is a very rare sequence of events, and the relation may be accidental. Some cases of tuberculous empyema have originated in pneumothorax, in which the opening has been closed by inflammation, and the air has been gradually absorbed. Empyema is much more unfavourable than sero-fibrinous effusion, as absorption cannot be expected, and treatment by incision is rarely successful, except where the pulmonary disease is strictly limited. Small empyemas very occasionally undergo inspissation and arrest. Sanguineous effusion is less common than the statements of writers would lead one to suppose. Pleural effusion, like pneumothorax, may exercise a retarding influence on the pulmonary disease in virtue of the collapse of the lung which ensues.

Pneumonia.—As already stated on p. 322, croupous pneumonia occasionally attacks patients with pulmonary tuberculosis; but this is very uncommon. Most of the authors who mention this subject consider that the course of the disease is not materially influenced by intercurrent pneumonia. In the only instance of this accident that I have met with, the pneumonia ended favourably with a well-defined crisis, and the old apex lesion was left in the same condition as before the acute attack.

Tuberculous persons are apt to acquire more or less acute broncho-pneumonia from time to time; but most of these attacks represent acute exacerbations of the tuberculous process. Influenza, attacking the subjects

of phthisis, may set up pneumonia of the bronchopneumonic kind, less frequently the lobar.

Circulatory System.—The heart of phthisical persons is small, and shews atrophic changes, occasionally slight fatty change in the muscular fibres, and very rarely solitary tuberculous masses in its muscular walls. It is rarely that such lesions give rise to any functional disturbance. In some of the most chronic cases dilatation of the right ventricle may occur.

Endocarditis is not very uncommon, and is sometimes attributable to previous attacks of acute rheumatism, but by no means always. In a few cases tubercle bacilli have been discovered in the valvular vegetations; but the relation of endocarditis to tuberculosis is still in need of investigation. Dilatation of the heart, whether due to valvular defects or myocardial disease, exercises a retarding effect on the progress of pulmonary tuberculosis. Attacks resembling pseudo-angina pectoris may be encountered; and it is said that they occur more often where the left upper lobe is contracted and the heart much exposed. It is doubtful whether this association amounts to anything more than a coincidence.

Pericarditis is generally due to extension of tuberculosis from the pleura or anterior mediastinal glands, or occasionally from the peritoneum. In a few recorded cases a pulmonary cavity has perforated the pericardium, and produced pyopneumopericardium. Tuberculous granulations or caseous nodules may be seen in the serous membrane; or the tuberculous nature of the affection may only be demonstrable by the microscope. The effusion, as a rule, is scanty and sero-fibrinous in character; occasionally purulent or haemorrhagic. There is always much fibrinous exudation, and usually more or less adhesion of the two layers. Tuberculous pericarditis generally escapes recognition during the patient's life; though, from its weakening effect on the muscular wall of the heart, it must be regarded as an important complication.

Pulmonary embolism, from detachment of thrombi formed in the right ventricle or auricle, is an occasional occurrence. When haemorrhagic infarction of the lungs ensues the condition may generally be diagnosed. But if no infarction be produced embolism may pass unrecognised, especially in moribund patients. Thrombosis of branches of the pulmonary artery may take place in the last stages, but this is not a common event. In some advanced cases we find great œdema of one leg from thrombosis of the large veins. Tenderness and induration can generally be discovered in the course of the affected vessel. Purpuric spots may appear on the lower extremities in conditions of cardiac debility.

Alimentary Canal.—Tuberculous ulceration of the lip is extremely rare, but the tongue and other parts of the oral cavity are more often affected. Ulceration of the tongue appears most commonly on the dorsum, but it may attack the sides, and occasionally the fraenum. In cases of extensive tuberculosis of the soft palate and pharynx ulceration some-

times invades the buccal mucous membrane and the gums, and in rare instances the latter may be primarily affected. The soft palate, uvula, and the pillars of the fauces are more often attacked; the prevailing lesion consisting of diffuse submucous infiltration and swelling, with shallow serpiginous ulceration. Miliary nodules may be seen in the base of the ulcer at times. Tuberculosis attacks the posterior wall of the pharynx less frequently than the palate. The usual lesions are circular ulcers with raised edges and granulations in the base, and superficial ulceration extending from the posterior pillars of the fauces. In some instances the larynx also is extensively affected, and the tuberculous disease appears to have originated there. But ulceration of the pharynx or tongue may occur without any laryngeal complication, and is generally due to infection from the sputum; but it may be part of a generalised tuberculosis.

Tuberculous ulceration of the oral cavity may be occasionally mistaken for syphilis, or for malignant disease. Herpes of the pharynx simulated miliary tuberculosis of the soft palate for a time in two tuberculous patients who came under my notice. For the diagnosis of such cases reference should be made to Vol. IV. Part II. p. 134. In tuberculous affections of these parts pain is always a prominent symptom, and interferes greatly with the act of deglutition; in consequence of which the nutrition of the patient suffers seriously. Aphthous stomatitis is a fairly common complication in the terminal stages, and may occasion great discomfort.

The tongue presents no special features in phthisical patients, and its condition varies with the state of the oral cavity and alimentary canal. In cases of intestinal ulceration it is sometimes red, glazed, and raw-looking; but similar appearances may be observed where no ulceration of the stomach or intestine exists. The red line on the gums, to which much attention was paid formerly, is by no means characteristic, and, moreover, is not very frequent.

Isolated instances of oesophageal tuberculosis have been recorded, but the gullet rarely shews any morbid change. Tuberculous ulceration of the stomach is extremely rare. A mammillated condition, pointing to chronic gastritis, is not uncommon. Chronic interstitial gastritis, atrophy of the glandular cells, and dilatation of the stomach have been found in some cases, but, as a rule, no morbid appearances are presented; the gastric symptoms are mostly dependent on functional derangements. Symptoms of dyspepsia, such as loss of appetite, cardialgia, flatulence, and constipation, are very common. Vomiting is often a very troublesome symptom: sometimes it is associated with a red irritable state of the tongue and epigastric pain, and is attributable to gastric catarrh; but more frequently it is unrelated to any affection of the stomach, and is excited by fits of coughing, which are apt to arise after meals and are possibly a result of hyperaesthesia of the vagus. Attention to the state of the stomach and digestion is of great importance in the treatment of all cases.

The *intestine* is more often the seat of secondary tuberculosis than any other organ. In my post-mortem examinations the intestine was involved in 70 per cent of all cases of phthisis. The lesions are mostly situated close to the ileo-caecal valve; the last few feet of the ileum and the caecum being most frequently attacked: but tuberculosis may shew itself in any part of the alimentary canal from the duodenum to the anus. The fact that the process begins in Peyer's patches and the solitary follicles, where the lymphatic system is most highly developed, suggests that the virus is absorbed from the intestine; and it is probable that the bacilli are conveyed by sputum, which has been swallowed.

In the small intestine the ulcers are at first more or less rounded, and extend laterally, the edges and base being thickened, and the latter often studded with granulations or small caseous foci. On the peritoneal surface groups of miliary tubercles are often seen, with localised peritonitis; and on this surface whitish beaded cords, representing lymphatics filled with tuberculous material, may be traced from the ulcer towards the mesentery. In the colon the ulcers are more elongated in a transverse direction, and often partially or wholly encircle the gut. Thickening is less conspicuous than in ulceration of the small intestine, and subserous tubercles and localised peritonitis are seldom seen. Partial cicatrisation of tuberculous ulcers is not uncommon, and at times stenosis may result. Owing to the thickening of the base of the ulcers, and the marked tendency to the formation of adhesions between neighbouring coils of intestine, perforation is generally prevented; but this accident is less rare than is generally supposed: the peritonitis which ensues will be restricted or general according to the presence or absence of adhesions. Circumscribed purulent peritonitis is by no means rare; and, when occurring in the caecal region, is very liable to be mistaken for simple perityphlitis. The symptoms of intestinal tuberculosis are few and uncertain; they may be indicated as diarrhoea, localised pain and tenderness in the abdomen; but, unfortunately, none of these can be depended upon. Cases of the most severe ulceration of the small intestine or colon may run their course without any definite pain or tenderness, and may be accompanied by obstinate constipation from paralysis of the muscular fibres of the gut. Diarrhoea may be due to other causes, especially enteric catarrh and lardaceous disease. In the case of ulceration the stools may have a pale yellow or drab colour, but they commonly present no characteristic features. Local tenderness is more common with the diarrhoea of ulceration. In some instances the discovery of tubercle bacilli in the motions will put the diagnosis beyond all doubt. The presence of pus in the stools cannot often be detected, and is generally symptomatic of ulceration, in which case bacilli are likely to be found; but an abscess communicating with the intestine will have to be excluded: a large amount of pus would be in favour of an abscess. Small quantities of blood may be discharged with the motions, but copious haemorrhage is very rare: however, in two patients under my care death resulted from profuse bleeding. In one case only could a post-mortem examination be

obtained, and here a tuberculous ulcer of the colon was found to be the cause of the haemorrhage. In severe ulceration the activity of the process in the lungs seems, at times, to become arrested. (*Vide* also Vol. III. p. 569.)

Fistula in ano can sometimes be traced to a burrowing tuberculous ulcer of the rectum; but it is not uncommon, in cases of this description, to find the lower part of the bowel free from ulceration or obvious disease.

It is by no means certain that ischio-rectal abscess is always or indeed generally of tuberculous origin.

In two female patients who came under my observation, with advanced tuberculous ulceration of the intestine and rectum, the muco-cutaneous margin of the anus and the neighbouring skin were affected with a superficial serpiginous ulceration of similar nature.

The diagnosis of lardaceous disease of the intestine can only be arrived at when there are signs of similar disease of the liver, spleen, or kidney. Enlargement of the spleen or liver, with albuminuria, casts in the urine and polyuria, coexisting with diarrhoea, would strongly suggest lardaceous disease; but it must be remembered that lardaceous degeneration and tuberculous ulceration may exist in the same patient and in the same intestine. A marked degree of anaemia is very general in cases of lardaceous degeneration. Transient diarrhoea is mostly attributable to simple catarrh, the diarrhoea of ulceration and amyloid disease being very persistent.

The liver may contain miliary tubercles, large caseous nodules, or occasionally tuberculous abscesses; but, as a rule, these affections are clinically unrecognisable. In one case that I examined a hypophrenic abscess was caused by a perforating tuberculous abscess of the left lobe of the liver. Enlargement of the organ is most frequently caused by fatty and amyloid degeneration. The presence of a large spleen, albuminuria, and diarrhoea would be in favour of lardaceous disease, especially if the edge of the liver be thick and very firm. Cirrhotic enlargement is relatively of frequent occurrence in cases of chronic tuberculous peritonitis. It is possible that cirrhosis may be causally related to peritoneal tuberculosis. Miliary tubercles and extensive fatty change are commonly associated with the cirrhosis of tuberculous subjects.

Enlargement of the spleen is a frequent symptom of lardaceous disease, and is only likely to be confounded with the secondary splenic tumour of hepatic cirrhosis. In both cases the spleen is very firm. In acute generalised tuberculosis, as in other specific fevers, the spleen may be enlarged, whether it contain miliary tubercles or not; but its consistency is soft. Caseous nodules may be found in the spleen, especially in children, but they possess no clinical importance.

Tuberculous peritonitis may be part of a general tuberculosis, or it may be due to extension from the abdominal organs—intestine, lymphatic glands, and female generative organs; or it may be the result of infection from the pleura or pericardium, the bacilli being transmitted through the lymph spaces of the diaphragm.

The statistics of the Brompton Hospital shew that whereas tuberculous ulceration of the intestines occurs in over 75 per cent of the fatal cases of pulmonary tuberculosis, tuberculous peritonitis, which is regarded as due to bovine tubercle bacilli, occurred in 4 per cent only.

Miliary tuberculosis of the peritoneum is often unaccompanied by any symptom whatever; but it may give rise to ascites, in which case some degree of chronic peritonitis will be found. In another form the tuberculous lesions consist of large nodules or masses, which are generally more or less caseous, but may at times be mainly or entirely fibroid. Caseous and fibro-caseous nodules may coexist in the same case. Ulcerative softening of the caseous masses sometimes leads to fistulous communications between neighbouring coils of intestine and to the formation of multiple abscesses. When the individual nodules coalesce large masses are formed which may be recognised by palpation during life. The great omentum is frequently much thickened, shortened and rolled up, forming a thick transverse band just above the umbilicus; but omental growths may be situated in the lower part of the abdomen also. The omentum may also undergo a general tuberculous infiltration, giving it the appearance of a thick apron hanging down in front of the intestine. (For a detailed account see art. "Tuberculosis of the Peritoneum," Vol. III. p. 957.)

Urogenital System.—Miliary tubercles and small tuberculous foci in the kidney may be accompanied by slight albuminuria, or may cause no symptoms. The important caseous form of tuberculosis of the kidney is fully dealt with in the article in Vol. IV. Part I. pp. 685-691.

In addition to the foregoing affection phthisical patients may acquire acute or chronic nephritis, lardaceous disease, and granular kidney. The commonest of these lesions is lardaceous disease. Slight degrees of this degeneration may need the application of iodine for their recognition, and in such cases no clinical symptoms would be presented. The higher grades of this disease are always combined with a varying amount of chronic nephritis, the kidneys in such cases being large, pale, and translucent, with yellowish opaque patches in the cortex. The surface is generally uneven, and the capsule adherent.

The amyloid disease affects principally the glomerular capillaries, but also the small arteries, the vasa afferentia and vasa recta. Degenerative changes in the convoluted tubes are due partly to the obstructive effects of the lardaceous disease of the vessels supplying these structures; and partly to the blood state, in which the lardaceous degeneration itself originated. In association with these changes a varying amount of scattered cell-infiltration and fibrosis is nearly always found; these represent reactive inflammation secondary to parenchymatous degeneration. The urine in such cases is abundant, of low density, and contains albumin in considerable quantities, and hyaline casts. Dropsy is uncommon. The other forms of renal disease mentioned above present no features to distinguish them from similar affections in non-tuberculous subjects. Acute nephritis is uncommon, and is probably of haemato-

genous origin and attributable to absorption from ulcerative cavities in the lungs. Granular kidney is not uncommonly met with in elderly and middle-aged persons, and is sometimes accompanied by slight degrees of lardaceous degeneration. It is very doubtful whether there be any causal relation between granular kidney and pulmonary tuberculosis. In cases in which albuminuria supervenes, a fall of temperature and a diminution of the activity of the pulmonary disease are not uncommonly observed.

Phosphaturia is said by Sir R. Douglas Powell to be an early indication of phthisis. Ehrlich's diazo-reaction is found in febrile progressive forms of tuberculosis, but no diagnostic significance can be attached to it. Tuberculous ulceration of the bladder is not very common, and is mostly associated with similar disease of other parts of the genito-urinary system. The symptoms are those of cystitis. Tubercle bacilli may be found in the urine. Tuberculous disease of the epididymis is much less uncommon, but this affection and tuberculosis of the prostate and vesiculae seminales come rather within the sphere of the surgeon.

Tuberculosis of the uterus is decidedly rare. The disease, which attacks the lining membrane of the fundus, consists of tuberculous infiltration, which is soon succeeded by caseous necrosis and ulceration. The uterine cavity commonly contains thick cheesy pus, and is apt to be somewhat dilated. There is rarely much enlargement of the organ. The Fallopian tubes are much more frequently attacked, and are seldom spared where the uterus is affected. In tuberculous salpingitis similar lesions are found in the mucous membrane; but the thickening and dilatation of the tubes attain to much greater proportions.

Tuberculosis of the ovary is one of the rarest occurrences: the only case I have seen is recorded by Dr. Habershon. In this case both ovaries contained tuberculous abscesses which communicated with the Fallopian tubes and intestine.

Tuberculous peritonitis is not uncommonly attributable to extension from the Fallopian tubes or uterus. It is probable that genital tuberculosis may also be caused by infection from the peritoneum; but more often the disease is communicated through the blood. The possibility of direct sexual infection cannot be denied.

The exhausting influence of lactation is notorious. Menstruation is nearly always much deranged, apart from any definite lesion of the generative organs. Amenorrhoea or scanty, infrequent menstruation, is the rule in this disease, and may be one of the earliest symptoms of it. Very occasionally menorrhagia occurs, but is seldom persistent.

The *suprarenal bodies* occasionally contain isolated caseous nodules, which cause no symptoms. Still more rarely both adrenals are converted into firm caseous or caseo-calcareous masses, in which case symptoms of Addison's disease may supervene (*vide* Vol. IV. Part I. pp. 398, 426).

Osseous System.—Secondary tuberculosis of the osseous system and joints is not very common, and may shew itself, among other places, in the vertebrae, sternum, and ribs, giving rise to chronic abscess in

connexion with the chest walls. This subject possesses more surgical than medical interest.

Nervous System.—The mental attitude of many phthisical patients is one of irrepressible hope, especially in the less chronic forms. Such persons often asseverate that if they could but get rid of some particular symptom, such as cough or shortness of breath, they would be perfectly well; and they go on making plans for the future within a few hours of their death. But in most cases presenting definite symptoms of mental derangement depression is the prevailing feature. Melancholia, stupor, delusions of suspicion or persecution, religious foreboding, insomnia, hallucinations, a suicidal tendency, and refusal of food are among the commonest symptoms. Maniacal excitement is much less frequent. For further information the reader is referred to the section on Insanity in Vol. VIII. of this work.

Tuberculosis is much less liable to affect the nervous system in the course of chronic phthisis than in acute tuberculosis. It is also of much more frequent occurrence in children than in adults. In most cases the tubercle bacilli are conveyed through the blood. The cerebrospinal meninges are the parts most commonly attacked, the tuberculous process being grouped especially along the small vessels. The growth of tubercles is soon followed by fibrinous exudation, in consequence of which the pia mater becomes much thickened.

Meningitis nearly always predominates or is exclusively localised at the base of the brain, and extends thence to the Sylvian fissures, the ventricles, the surface of the cerebellum, the pons Varolii, and the medulla. The ventricles are often much dilated and filled with turbid fluid—"acute hydrocephalus" of the old writers, the convolutions becoming flattened by pressure. The cortex of the brain and the walls of the ventricles are often much softened, from extension of the inflammation of the pia mater, so that the process is more correctly described as a meningo-encephalitis. Tuberculous nodules or masses may grow in the brain tissue, and sometimes attain to a considerable size. These solitary tubercles or tuberculous tumours are found most frequently in the cerebellum and cerebral hemispheres, but they may arise in any part of the brain and are often multiple. Small tuberculous nodules are not infrequently found in the cortex, extending inwards from areas of chronic tuberculous meningitis.

Lastly, meningitis, encephalitis, or myelitis may be due to extension from neighbouring bones of the cranium or spine.

The symptoms of meningitis are many, and can only be briefly enumerated:—headache, irritability of temper, fretfulness, coma, convulsions, marked retardation, acceleration, or irregularity of the pulse, Cheyne-Stokes respiration, vomiting, retraction of the head and abdomen, rigidity and weakness of limbs, Kernig's sign, paralysis of cranial nerves, optic neuritis. Retention of urine is very common towards the close, and pyrexia is nearly always present. Headache is perhaps the most common symptom in the more chronic form. Tuberculous tumours of the brain

give rise to symptoms not differing from those of other cerebral tumours. For a full account of this subject reference must be made to the appropriate articles.

Alcoholic neuritis not uncommonly ends fatally from pulmonary tuberculosis, but peripheral neuritis with extensor paralysis of the extremities may occur in pulmonary tuberculosis apart from the influence of alcoholism, and may possibly be due to toxins absorbed from the lungs. Some of the pains and tenderness affecting the limbs in phthisical patients may possibly be of neuritic origin. Beau grouped these together under the name "melalgia." It is difficult at present to discriminate the pains which many patients in advanced phthisis complain of. Some are probably neuritic, others myalgic; whilst, in some instances in which pains fly about from one part to another and affect the joints, the resemblance to rheumatism is very close. In these last the rheumatoid pains are possibly a septicaemic symptom, depending on absorption from pus-secreting cavities in the lung. Suppurative otitis media is not very uncommon, but it is seldom that tubercle bacilli can be discovered in the pus. (For "Tuberculous Otitis Media" see art. Vol. IV. Part II. p. 453.)

P. K.

Mixed and Secondary Infections.—The occurrence of microbes other than tubercle bacilli in the sputum of consumptives led at a relatively early period to the belief that many of the peculiarities in the course, duration, and termination of pulmonary tuberculosis might be due to their influence rather than to that of the tubercle bacillus itself. Koch indeed in his classical paper on the etiology of tuberculosis had drawn attention to the occurrence of micrococci in the capillaries in a case of miliary tuberculosis of the lung, and he had pointed out that such "mixed infections," to use the name given by Brieger and Ehrlich, are by no means uncommon. During the next few years a large number of observations were made by Cornet, Babes, Petruschky, Kitasato, and especially by Spengler and by Ortner, the conclusion ultimately being arrived at that pulmonary tuberculosis in its later stages, at any rate, is essentially a mixed infection. Before considering the actual data obtained with reference to the different microbes complicating pulmonary tuberculosis, it is necessary to emphasise the distinction between mixed and secondary infections. The term mixed infection is generally applied to the condition in which more than one kind of microbe invades the body at the same time, whereas in "secondary infections" one microbe precedes the other in point of time. In pulmonary tuberculosis the latter is without doubt the most important, the passage of the secondary invaders being facilitated by the lowering of the protective mechanism of the body resulting from the primary infection by the tubercle bacillus. A further point of great importance is that the ulcerative processes associated with necrosis and caseation must dispose in a high degree to the possibility of secondary microbic invasions. It is generally impossible by the ordinary routine bacteriological examination of stained films of sputum to determine

what part the associated bacteria play in the pulmonary lesion, for, as Menge has pointed out, tubercle bacilli may be associated in the secretions with living saprophytes, which do not play any part in the pathological condition. Such "secretion-symbioses" must be distinguished from "infectious or tissue-symbioses," in which the various microbes are all participating in the disease. In the case of pulmonary tuberculosis a combination of secretion- and tissue-symbiosis is the one usually present; certain saprophytic microbes vegetate in the secretions only, whereas others appear to play an important part in invading the tissues and aiding the tubercle bacillus in the work of destruction. Writers differ considerably on the question whether an accurate estimate of the process in the lung can be determined by examination of the sputum during life —a point manifestly of the greatest importance in connexion with prognosis and treatment. Schröder and Mennes, Lannelongue and Achard, Schabad, and Sata are inclined to the belief that no great significance can be placed on the examination of sputum as evidence of lung infection, whereas Koch, Cornet, Petruschky, Spengler, Brieger and Neufeld, Ophüls, Foulerton, Ehrhardt, and others think that with certain precautions in the examination the sputum is a reflection of the morbid process in the lung. These precautions have been emphasised by Koch and Kitasato. According to the latter the sputum must be thoroughly washed, so that the associated adventitious bacteria are mechanically removed from those occupying the centre of the tuberculous masses. For this purpose the mouth should first of all be carefully washed out with sterile water, the sputum, especially that expectorated in the morning, being collected in a sterile vessel containing sterile saline solution. With sterile forceps a typical mass is selected and separated, the central part being transferred to several changes of sterile saline solution. The examination is then made by means of the ordinary methods of bacterial investigation. Working with this technique a large number of investigators have found that cocci occupy the central area of sputum masses in association with tubercle bacilli. When a comparison is made between the sputum examined in this way and the condition of the lung after death, it is found that in a large number of cases streptococci appear to play a very important part. Indeed, Petruschky, Spengler, and others consider that streptococci are largely responsible for the hectic fever so frequently met with in pulmonary tuberculosis. Next in frequency to streptococci, staphylococci, pneumococci, *Micrococcus tetragenus*, *Bacterium influenzae* have been met with, and more rarely Friedländer's bacillus, diphtheria-like bacilli, and *Bacillus pyocyaneus*. In the very careful and extended observations of Spengler there appeared to be a close connexion between the conditions found in the sputum and lung respectively. A considerable amount of discussion has taken place with reference to the pneumonic processes complicating pulmonary consumption. Thus, Ortner holds that these are almost invariably coccal in origin, whereas Fränkel and Troje, Ophüls and others consider that the tubercle bacillus, when in pure culture, can set up typical caseating bronchopneumonia by

aspiration. Fränkel and Troje also consider that in some cases the products of tubercle bacilli or of broken-down tissue are the initial starters of the pneumonic process. The flora of phthisical cavities is very varied, and includes streptococci, staphylococci, pneumococci, *Bacillus pyocyaneus*, *Bacillus coli communis*, *Bacillus lactis aerogenes*, pseudo-diphtheria bacilli (Ehret, Schutz, Ravenel and Irwin), sarcinae, yeasts, spirilla. Flick has drawn attention to the frequence of pseudo-diphtheria bacilli, pneumococci, and streptococci in haemorrhagic cases of tuberculosis.

With reference to the localisation of the tubercle bacillus and its associates there are various possibilities; in general it may be said that both remain more or less localised to the lung. In some cases, however, the tubercle bacillus may remain local, while the associated microbes generalise by entering the blood stream. According to the older observations of Jakowski, and of Michaelis and Meyer, microbes may be found in the blood during life. Hirschlaff examined 35 cases of progressive phthisis, and found *Staphylococcus albus* in the blood in 4. Teissier in 63 cases found staphylococci 6 times, and streptococci 3 times in blood. On the other hand, with more perfect technique, the results of blood cultures made during life were almost all negative (A. Fränkel, Lasker, and Jochmann). In examinations made after death the percentage of positive results has been much increased, and is to be attributed to post-mortem emigration of microbes. It is difficult to estimate the exact part played by the associated bacteria in tuberculosis at the present time. But from the frequence with which they are found in the central parts of the sputum and in the lung tissue, acting independently or in conjunction with tubercle bacilli, there can be no doubt that they play a part. How important this part is must be left for future investigation, and in this respect a co-operation of bacteriologists, morbid anatomists, and clinicians would be of the greatest importance.

W. Bulloch.

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W. B.

Course.—The course of pulmonary tuberculosis is essentially variable and fluctuating, intervals of quiescence or apparent arrest alternating with prolonged periods of fever and other constitutional symptoms. In a large percentage of cases the disease is for the most part slowly progressive, and death ensues in a few years at the latest. The average duration of phthisis has been variously estimated. Louis found that in more than half the cases observed death occurred in less than nine months. The mean duration has thus been stated:—twenty-three months (Louis and Bayle); two years (Laennec and Andral); four years (C. J. B. Williams and Sir J. Clark): Dr. C. T. Williams, from analysis of a thousand cases among private patients, put it at seven years and three-quarters. On account of the great difficulty so frequently met with in attempting to fix the date of onset of the disease such calculations are fraught with uncertainty. Those physicians who have had much experience of the disease at special as well as general hospitals, will probably agree that statistics derived from the latter source exclusively would give a very

erroneous impression of the duration of phthisis. Patients admitted into general hospitals are either exceptionally ill, or are suffering from some serious complication. The mortality among such patients is naturally very high, and the duration of the disease may often be measured rather by months. Most valuable are the statistics collected by Dr. J. E. Pollock from 3500 cases of phthisis attending the out-patient department of the Brompton Hospital.

"Here (among the out-patients)," as he truly says, "are seen individuals of all classes, excepting the highest, and of all ages and occupations. The necessities of home cares and of continuing the daily work are but little interfered with by a visit once a fortnight to their physician; but these urgent claims of domestic life shut out large numbers from the possibility of availing themselves of indoor treatment in a hospital. The large class affected with chronic slow phthisis are, therefore, found chiefly among the out-patients.

"The average duration, while under observation, of all the cases taken together was two years six months and three-fifths nearly, but this represents only a part of the period of the affection, and in it are included cases of the most acute and rapid form as well as those which have become chronic."

The actual duration of the cases must have been considerably longer, and the whole average duration of the disease, as Dr. Pollock says, must be raised beyond four years. An experience of twelve years' out-patient work at the Brompton Hospital has convinced me that Dr. Pollock is far nearer the mark than those who would limit the average duration to two years.

The complexion of the malady, while running a chronic or slowly advancing course, is liable at any time to undergo a complete change, depending on acute exacerbation of the pulmonary disease. Fever and other constitutional symptoms often herald renewed activity of the tuberculous process before physical examination gives any decided indication of extension. In other instances we find the signs of disease slowly extending for some time without any corresponding aggravation of the patient's symptoms.

The lines along which the disease spreads in the lungs have been described in the section on the pathology. It is very important not to be satisfied with exploration of the front of the chest only, but to examine with care the back also, more especially the supraspinous fossa—that is, the posterior aspect of the upper lobe—and the interscapular region just below the spine of the scapula, which corresponds to the apex of the lower lobe, a part specially prone to secondary tuberculosis. And, as Dr. J. K. Fowler quite rightly insists, search should be made for signs of disease extending from behind forwards from the apex of the lower lobe along the upper border of the same lobe, the position of the septum dividing the upper and lower lobes being roughly indicated by the "vertebral border of the scapula, when, with the hand upon the spine of the opposite scapula, the elbow is raised above the level of the shoulder."

The upper part of the axilla is another region that must be carefully investigated, as it is in this space alone that the outer aspect of the upper lobe is accessible to examination; and signs of excavation may sometimes be found at the apex of the axilla only.

Towards the close of life bubbling rales are generally heard over the whole of the chest, and are an indication of pulmonary oedema, the result of cardiac failure. It is usual to find resonance to percussion over the lower part of one or both lower lobes up to the very end; a fact which is to be explained by the persistence of patches of spongy lung between the tuberculous masses.

Where the fatal termination is not directly or indirectly dependent on complications, but is the result of slowly extending disease, death most frequently occurs from exhaustion. Asphyxia is seldom the cause of death except in acute forms of tuberculosis. In most chronic cases death is preceded by profound emaciation and debility, which steadily increase in spite of the considerable quantity of nourishment the patients often continue to take. Bed-sores may form if the nursing be not vigilant, and oedema of the legs is not uncommon. The pulse becomes more rapid and feeble, the temperature gradually falling often becomes subnormal, tracheal rales appear, and the end comes quite peacefully.

In the comparatively few cases in which complete arrest of the declared disease takes place, the constitutional and local symptoms gradually subside, and the patient regains his health. The physical signs at the same time undergo certain modifications, or occasionally disappear entirely. In most cases, although rales and other adventitious sounds cease to be heard, signs of consolidation and contraction of the apex persist, or some degree of localised emphysema is developed.

Prognosis.—Of the many complicated problems presented to the physician the prognosis of pulmonary tuberculosis is one of the most difficult. An accurate prognosis would involve full knowledge of the parasite and its host, as well as of their environment. At present little is known concerning variations in the virulence of the tubercle bacillus as it occurs in the body of man.

Still less information is forthcoming as to the bio-chemical conditions of the human organism which retard or favour the development and activity of the parasite. For practical purposes we have to estimate the prognosis, in the first instance, by a careful consideration of the effects of the disease, immediate and remote, in each patient. By these means we are able to gauge, approximately, the severity of the malady and the resisting power of the individual. Furthermore, an acquaintance with the natural history of tuberculosis, including the influence of heredity, of previous or concurrent diseases, and of various conditions of life, and lastly, the knowledge of the effects of treatment, will be required if we would forecast the probable course of pulmonary consumption. The symptoms of the patient, representing the result of disordered function, are of the first importance. Of all the general symptoms fever is the most important. A markedly intermittent or remittent pyrexia, in the absence of acute

intercurrent affections, is very significant of progressive disease, and is, therefore, of bad augury. At the same time it must be remembered that a considerable degree of fever is not incompatible with gain of weight and other signs of improvement. Moreover, after periods of severe pyrexia the temperature may fall, and the disease enter upon a chronic phase. Nevertheless, it may be accepted as a general principle that the existence of marked pyrexia always necessitates a very guarded, though not necessarily an entirely unfavourable, prognosis.

A slight evening rise of temperature, with a fall to normal or slightly below normal in the morning, is not uncommonly present in comparatively favourable cases. The supervention of fever in the course of a mild chronic case is often one of the first indications of renewed activity of the tuberculous process, which may prove intractable. The absence of fever does not in itself justify the expression of a hopeful opinion, for, as we have seen, an apyrexial temperature may accompany advanced and active disease. Subnormal or collapse temperatures have a very ominous import. Emaciation signifies deficient alimentation (whether due to insufficient feeding, digestion, or assimilation), or profound constitutional intoxication. In the first case the cause is more amenable to treatment, and the outlook is consequently less unfavourable. A persistently rapid or easily excited pulse is indicative of debility, or of a state of general nervous erethism, both of which are very undesirable features. The unfavourable significance of a persistently low blood-pressure has been insisted on by Marfan. Anaemia and debility are also an evidence of profound constitutional impression, and must therefore darken the prognosis.

Among the more important symptoms of local disorder we must reckon dyspnoea depending on diffuse or acutely extending pulmonary changes. When these changes consist in disseminated miliary tubercles, or in lesions of the bronchopneumonic or pneumonic type, the gravity of the symptom can hardly be exaggerated. Expectoration, profuse, purulent, and containing numerous elastic fibres, implies progressive destruction of lung. Absence or scantiness of expectoration is, at times, a marked feature in severe cases: this is mostly, but not exclusively, seen in children and women, who often swallow their sputum. But while too much importance must not be assigned to the quantity of the sputum, scanty or moderate expectoration is on the whole a good sign.

The expectoration of pulmonary calculi is never met with except in very chronic cases.

The significance of fetor varies with its cause. When the odour has a sickly or slightly fishy character, due to the retention of secretion in cavities, it is of less moment than when it possesses the penetrating odour of bronchiectasis: in the latter case the dangers of septic bronchopneumonia and other accidents are added to those already existing. The supervention of gangrene renders the prognosis quite hopeless.

The number of tubercle bacilli in the sputum is no accurate measure of the extent or severity of the disease, and is largely a question of dis-

charge. In some acute cases the bacilli may be very scanty, whereas in other cases, quiescent and circumscribed, the sputum may teem with them; complete and permanent disappearance of the microbes is a most hopeful sign; but their continued presence in the sputum does not preclude a protracted and favourable course (*vide* p. 355).

An incessant and intractable cough, especially when it interferes with sleep and causes vomiting, adds greatly to the exhaustion of the patient. Some of the most irritable coughs depend on catarrhal affections of the upper air-passages, and can often be relieved; but cough associated with signs of persistent diffuse bronchitis is often indicative of widely disseminated tuberculous lesions.

The state of the digestion is of the greatest importance. Where the symptoms of gastric disorder, or of faulty absorption or assimilation, prove rebellious to treatment the prospects of improvement are small indeed.

In attempting to weigh the indications of physical examination of the lungs, the two chief points requiring attention are the character and the extent of the disease. An acute onset is commonly followed by progressive invasion of both lungs, and has the gravest significance. An insidious bronchitic or haemoptoic onset is more favourable. Rapidly extending disease is always of ominous significance. Rales and other morbid signs scattered widely over a large part of both lungs, especially in pyrexial cases, point to disseminated lesions, a most unfavourable type of disease; but similar physical signs, without much fever, may sometimes persist for months or years in cases where the disease takes the form of discrete fibro-caseous or fibroid processes. Cases with severe symptoms and relatively slight physical signs are to be regarded with suspicion, for the true extent of the pulmonary disease is generally masked by other conditions; on the other hand, the presence of marked signs of consolidation or excavation of one upper lobe is not inconsistent with a chronic and favourable course so long as the lower lobe and the opposite lung remain comparatively free.

Signs of contraction are a sure index of chronicity. Localised and stationary disease is a good element in prognosis. The disappearance of rales is, in general, a favourable feature.

After what has been said in a previous section about the stages of phthisis, it is futile to base the prognosis on considerations which are so apt to be fallacious. If, in a chronic case, we could be sure, which we cannot be, of the absence of softening and excavation, the prospects of arrest would be better than if cavities had already formed, for the existence of a cavity carries with it the risk of extension by means of inhalation of infective secretions into distant bronchi. Moreover, there is no evidence that a vomica of any size can become obliterated by cicatrisation; whereas we know that tuberculous nodules often undergo healing by encapsulation, calcification, or fibrous transformation.

Among the most ominous complications are meningitis and pneumothorax. Pleurisy with effusion sometimes appears to exert a retarding influence on the pulmonary affection. Empyema is unfavourable. Dry

pleurisy is regarded by some authors as a very unfavourable sign; but this is by no means generally true. The appearance of the diffuse infiltrating form of laryngeal tuberculosis, with its tendency to produce dysphagia and stenosis, betokens a speedy termination. Oft repeated haemoptysis depresses the patient morally as well as physically; and under such circumstances the possibility of a sudden and fatal issue has always to be reckoned with.

Tuberculous peritonitis and intestinal ulceration cause great wasting and prostration, and generally hasten the patient's end. Tuberculosis of the abdominal lymphatic glands and generative organs tends to aggravate the general condition, and is commonly a sign of generalised disease.

Pronounced lardaceous disease of the viscera is a most serious complication of chronic cases, pointing, as it does, to profound derangement of nutrition. A combination of diabetes and phthisis is also a most grave condition.

The presence of cardiac hypertrophy and dilatation, or of marked emphysema, justifies the opinion that the duration of the disease will be long.

The environment is a matter of much importance. A patient living in a healthy country place, under suitable climatic conditions, has better prospects than one who is compelled to dwell in a large town, especially if his life be spent in dusty or smoky rooms. Again, pecuniary means have a direct bearing on the prognosis: those who can procure, not only the necessaries, but also the luxuries of life, and can afford to rest, are in a better position to battle with the disease than those who must work hard for a living. Nevertheless, among poor hospital patients we see, not very infrequently, persons who have been suffering from phthisis for ten years or more, and who still go on working under the most adverse circumstances. A history of previous good health is a hopeful feature, as a greater capacity of resistance may be expected where the general health has not been already undermined. The influence of age has been much disputed. As a general rule, pulmonary tuberculosis runs a more rapid course in children and young adults than in older persons, among whom the chronic form is rather the rule. Cornil and Hérard suggest that tuberculosis is more chronic in old people, because heredity has already weeded out those of least resistance. Nevertheless, acute disease may occur in elderly patients, and, conversely, the phthisis of children may be chronic. Each case must be estimated on all the data; and the influence of age can only be credited with a very subordinate importance.

It has been said that the duration of the disease is shorter in women than men. If we exclude the cases associated with pregnancy and parturition, it is doubtful whether this statement be true.

The influence of heredity is undoubtedly an important one. It is a common belief that this factor determines the earlier manifestation of the disease. A strong predisposition is an unfavourable element, as in

such cases there often appears to be a general lack of vitality and resistance. But, although this is generally true, hereditary influence cannot be ranked on a level with considerations derived from a careful estimation of the effects of the disease in the individual patient. The best results may be expected in cases presenting the following features: apyrexia, or a subfebrile temperature; weight stationary or increasing; signs of disease confined to one lung or to limited portions of both lungs (especially if associated with contraction or emphysema); a quiet pulse and nervous system; a good digestion; absence of serious complications; a good family and personal history, and favourable hygienic surroundings.

TREATMENT.—**Preventive.**—If, as our present knowledge appears to shew, the sputum of tuberculous persons be one of the main sources of the disease, it is obvious that the complete destruction or disinfection of this secretion should be our first duty. In many hospitals this is effected by means of special destructors, or furnaces, in which the sputum is burnt. In private houses, where this method is difficult of application, the expectoration, after previous disinfection, may be discharged into the drains. For general purposes saponified cresol in a strength of 10 per cent is the best disinfectant. When mixed with an equal quantity of the sputum, this solution destroys the infectiveness of the bacilli in twenty-four hours. Sputum should not be thrown on the dust-bin, where the contents may dry and become a further source of danger. In all cases, whether in hospitals or private houses, patients should be directed to use spittoons containing a suitable disinfectant. If, in spite of advice to the contrary, patients use handkerchiefs for receiving the sputum, these should be burnt; or at any rate should be scalded before being sent to the wash.

Persons suffering from phthisis should be warned not to spit about the streets, or the house, or into any vessel which does not contain some disinfectant. Underclothing, linen, sheets, and pillow-cases should also be scalded before being washed, especially in the case of bed-ridden patients, with whom the chances of contamination are greater. Phthisical persons should occupy separate beds. Bedrooms and sitting-rooms so occupied must be carefully cleaned with a damp cloth, so as to avoid raising a dust; and should be well aired and exposed to light every day. Rooms that have been inhabited by such patients should be thoroughly cleaned, and, if possible, white-washed, painted, and re-papered before being used by other persons.

It is desirable that patients should be provided with separate sets of knives, and forks, and spoons; but, in default of this precaution, all table utensils, as well as plates, cups, glasses, should be scrupulously cleaned.

Milk is undoubtedly a vehicle of disease, and should be carefully boiled or sterilised; particularly when intended for children. For the principles on which slaughter-houses and dairies should be regulated, and for further information on the general question of prophylaxis, the article "Tuberculosis" (Vol. II. Part I. p. 258) should be consulted.

In persons threatened with tuberculosis, and in others with a strong family predisposition, more especially in the case of children, the importance of a good general hygiene can hardly be overestimated.

Abundance of fresh air in the dwelling—especially in bedrooms—secured by suitable methods of ventilation, a large amount of outdoor life in pure country air, a generous diet, including a large proportion of fatty constituents, daily cold sponging of the body, and the use of flannel or similar underclothing, are amongst the most necessary conditions. In the case of children the throat needs special attention; enlarged tonsils should be removed, and catarrhal affections must not be neglected. The opinion is now warranted that the tonsils are frequently the portals by which tubercle bacilli enter the body; at any rate, in primary tuberculosis of the cervical lymph glands. The question of the removal of caseous glands, and the surgical treatment of tuberculous disease of bones and joints, are matters of great importance, but cannot be discussed here. Tuberculous mothers ought not to suckle their infants.

The choice of a profession or trade is a matter of no small consequence. Occupations in which life is mainly or largely spent in the open air are the most favourable; but, in the case of the poor, outdoor work generally implies more or less heavy labour, which is often prohibitive under the circumstances. Many people, in whom tuberculous affections of bones, joints, or lymphatic glands have been cured or partially arrested, manage to carry on successfully various sedentary trades or professions. Dusty occupations, as in the case of millers, bakers, knife-grinders, stone-masons, and the like, are fraught with special dangers to vulnerable persons. Free ventilation of dusty workshops is all-important, and serves to minimise, to a large extent, the dangers of the aforesaid trades.

There can be no doubt whatever that persons suffering from progressive disease ought not to marry. In cases of quiescent or apparently arrested tuberculosis there is room for difference of opinion. When all symptoms of disease have disappeared, the sputum no longer contains bacilli, and the general health remains good, marriage, in the case of men, may be undertaken after the lapse of two or three years without any great risk. Women incur far greater danger in connexion with pregnancy, parturition, and lactation; for it is well known that, under the influence of such conditions, quiescent tuberculous lesions are apt to prove the starting-point of active disease. If, however, the tuberculous process can only be regarded as quiescent, and bacilli continue to be expectorated, marriage ought to be forbidden in either sex. Most writers agree on this point as regards women; but some have urged that men, under these circumstances, may be allowed to marry on the ground that their lives are thereby made happier; and that, if children should be begotten, they tend to die off early, and the race does not appreciably suffer. The morality of such advice need not be discussed here; but the possibility of a phthisical husband directly or indirectly infecting a healthy wife cannot be disregarded; and the risk of adding to the

already high tuberculous death-rate is one that no medical man should willingly countenance. However, as all writers point out, the question of marriage is seldom decided, solely or even mainly, on medical grounds (*vide* p. 292).

P. K.

Specific Treatment.—The discovery by Koch of the tubercle bacillus had the immediate effect of stimulating the study of the therapeutics of tuberculosis. At first many believed that the microbe could be attacked *in vivo* by agents known to have an inhibitory or bactericidal effect upon it *in vitro*, and at this time antiseptic agents, such as creosote, guaiacol, formol, menthol, and ichthyol, were introduced and given an extended trial, but it was soon found that such therapeutic agents are powerless to kill the bacillus in the body. The striking results which had followed Pasteur's work on the prophylaxis induced by attenuated cultures led Koch to the conception that a specific alteration of the body might be produced by inoculation of the tubercle bacillus or its products. Pasteur had attempted prevention only of disease. To Koch belongs the credit of having been the first to attempt therapeutic inoculation. While he was working on this subject the momentous discovery of antitoxin was made by Behring and Kitasato, and after the first disastrous era of tuberculin therapy there were many who believed that a cure for consumption would be found in the passive immunisation by means of anti-tuberculous serums rather than the active method suggested by Koch. The bacterio-therapeutic remedies which have been advocated for tuberculosis are thus divisible into two groups: (1) Active immunising agents—tuberculins and other bacillary products. (2) Passive immunising agents—serums of animals actively immunised (Maragliano's and Marmorek's serums especially).

1. *Active Immunising Agents. Tuberculin of Koch.*—The experimental basis for the use of tuberculin as a therapeutic agent was Koch's observation that considerable quantities of killed cultures of tubercle bacilli can be borne by normal animals with at most local symptoms, such as abscesses; whereas in the case of tuberculous animals similar doses produce death, and even very minute quantities may cause severe local and general reaction, ending in a partial amelioration of the animal's condition. It was apparent in Koch's experiments that the bacillus is absorbed only with great difficulty, as it may be found after long intervals at the point of its inoculation, where it may induce late abscesses. Any amelioration that may take place in the tuberculous process must, as Koch argued, be due to substances which had passed out of the bodies of the bacilli. After numerous attempts to extract such substances *in vitro*, Koch finally recommended glycerin; the extract of the bacilli in which was called tuberculin, or old tuberculin (T.O.). As is now well known, this is prepared by growing the bacilli in 4 per cent glycerinised bouillon. After abundant surface growth has taken place the cultures are poured into a vessel, and the temperature being

slowly raised from 60° to 90° C., evaporation ensues, whereby the liquid is concentrated. When the fluid has in this way been reduced to one-tenth of its bulk the thick brown liquid is passed through a filter; the filtrate is tuberculin. As was mentioned above, this substance injected into tuberculous subjects gives rise to pyrogenic and phlogogenic phenomena, the latter including hyperaemia, emigration of leucocytes, and necrosis of the tuberculous foci. In recommending tuberculin for the treatment of tuberculosis Koch emphasised this necrotic process as fundamental, and in carrying out his immunisation experiments in man and animals he concluded that the dose of tuberculin should be successively raised until no more fever or local reaction ensued. The failures and even disastrous results witnessed in the early tuberculin era, when the immunisation process was carried out in this way, led to considerable modifications, both with regard to tuberculin itself, and especially the manner of its use. In his attempts to improve the vaccin, Koch extracted the cultures of bacilli by means of a decinormal solution of caustic soda, obtaining in this way an alkaline tuberculin, styled T.A. This, however, proved no better, as it was prone to be followed by abscesses, and in order to overcome the difficulty of absorption, Koch was ultimately (1897) led to recommend the mechanical comminution of the bacillary bodies in a mortar. To this end highly virulent tubercle bacilli are dried *in vacuo*, and are then thoroughly crushed by machinery. The dust is shaken well with distilled water, and the mass is then centrifuged. By this means a separation takes place into an upper opalescent fluid (T.O.) and a deposit (T.R.). The latter constitutes the so-called Koch's new tuberculin T.R., which is finally prepared by suspending the deposit in water. In commerce it is sold in bottles containing 2 mgr. (·002 gram) of solid substance per c.c. (Ruppel). Still more recently Koch has advised the "New Tuberculin Koch Bacillen Emulsion," in which no attempt to separate T.O. and T.R. is made, the comminuted bacilli being simply suspended in equal quantities of water and glycerin. One cubic centimetre of this preparation contains 5 milligrams of powdered tubercle bacilli. The various Koch's tuberculins are manufactured by Messrs. Meister Lucius and Brüning.

Other tuberculins—Denys' tuberculin.—Since the application of heat necessarily produces deterioration of the vaccin as prepared by Koch's method, Denys merely filters the bouillon cultures of bacilli, using the filtrate without any subsequent concentration by evaporation or other means. Landmann attempts to make a complete extract of tubercle bacilli by evaporating the cultures *in vacuo* at 37° C. to one-tenth of their bulk. This is mixed with the extracts obtained in saline solution, water, and glycerin, when the bacilli are treated at temperatures ranging from 40° C. to 100° C. The final product is called *Tuberkulol*. Beraneck also mixes the extracellular and intracellular toxins, and his tuberculin prepared in this way has been extensively used and recommended. Klebs extracted the cultures by means of alcohol, obtaining in this way "*tuber-*

culocidin," a purified product resulting from precipitation by sodium bismuth iodide being his "*antiphthisin*."

Believing that human and bovine tubercle bacilli are fundamentally different, and that a large percentage of cases of consumption are really of bovine origin, Spengler has recommended tuberculins made of bovine cultures. These are of two classes: one, P.T.O. (Perlsucht Tuberculin original), is analogous to the ordinary T.O.; the other, P.B.E. (Perlsucht Bacillen Emulsion), is analogous to Koch's new tuberculin, and, according to Spengler, possesses bactericidal properties. A great many other workers have prepared extracts, mostly in water. Maragliano distinguishes three poisons, namely, a tuberculous toxalbumin, a watery toxic extract, and the poison of the defatted bacilli. Behring, Römer, and Ruppel have made the most complete study of this subject, and have shewn that from tubercle bacilli may be obtained 8·5 per cent of tuberculinic acid, 24·5 per cent nucleoprotamine, 23 per cent nucleoprotein, 26·5 per cent fat and wax, 9·2 per cent mineral substances, and 8·3 per cent proteinoids. When tested on animals, Behring and Kitaschima found that tuberculinic acid possesses in a high degree the properties of Koch's tuberculin. Von Behring's tulase is a preparation of tubercle bacilli which have been extracted with chloride of sodium. It is supposed that it contains all the active substances of the bacillus, but from the dearth of essential particulars as to its mode of preparation and action little is known about it. Von Behring recommended it chiefly as a prophylactic.

Inoculation of Living Cultures of Tubercle Bacilli—Jennerisation.—In the last few years experiments have been carried out on a very extensive scale with reference to the protection of cattle against tuberculosis. It has been demonstrated by von Behring, Koch, and Baumgarten that bacilli of human origin may induce a certain degree of immunity against perlsucht bacilli. Conversely, Klemperer has attempted to cure tuberculous human beings by inoculations of living cultures of bovine bacilli. Five consumptives received altogether fifty-three inoculations without untoward accident and with some measure of success. Spengler has also shewn on himself that living perlsucht bacilli are non-virulent.

Although many different bacillary products have been recommended in the treatment of tuberculosis the great bulk of the published work deals with Koch's tuberculins, and it will be necessary to consider them in greater detail. Tuberculin and allied substances are bacillary products, and of course are entirely different from antitoxic serums. In attempting to treat a human being with a bacillary product the medical man is assuming the *rôle* of an immunisator, and is in the position of him who inoculates horses for the production of antitoxic serums. From the very extensive experience which has been gained from the immunisation of animals certain general principles have been deduced. At the same time it cannot be too clearly understood that in the active immunisation of an animal, and much more of a man, it is impossible to map out any course of dosage which is to be rigorously followed. If this is attempted

it will not be long before the immunisator finds himself in difficulties. Nothing has more clearly shewn the fundamental differences in susceptibility of different human beings so much as the bacterial inoculations which have been carried out in the last few years. Apart from not injuring the patient, the process of active immunisation is a difficult one, and requires much experience in order that the best results may be obtained as the process is essentially to determine in a particular case the production of anti-bodies to a maximal extent and of optimal qualities. Further, it may be necessary in focal diseases, such as tuberculosis, to combine the pure immunisation treatment with other methods which will determine a flux of blood with its specific protective properties to the nidus of infection.

As we have seen above, Koch considered that the phlogogenic properties of tuberculin were of cardinal importance in inducing a disappearance of the tuberculous focus in so far that it led to demarcation, sequestration, and extrusion of the affected tissue. Besides this inflammatory reaction tuberculin acts as an antigen, giving rise to anti-bodies usually spoken of as anti-tuberculins. In the first tuberculin era Koch, by gradually increasing the dose of tuberculin, strove to reach a point at which a maximal dose of the poison could be tolerated without reaction, as he considered that this shewed an absence of tuberculous tissue. In trying to achieve this end, however, the patients often suffered severely, and in not a few cases there was pathological-anatomical evidence that the tuberculous foci had been lighted into activity with consequent "mobilisation" of the bacilli. These results made such an impression on the medical world that within a few months of its introduction tuberculin was almost entirely discarded as a therapeutic agent. Its total disappearance would in fact have been certain had it not been that some observers were so convinced of its value that in spite of a certain number of failures they persisted in studying the best conditions for its administration. In particular, Goetsch drew attention to the mistake in forcing the inoculations, with consequent reactions, and he adopted a much milder course, emphasising the importance of proceeding slowly with very minute doses, and avoiding reactions as far as possible. This principle has been accepted by all subsequent workers, among whom may be mentioned Petruschky, Spengler, Moeller, Bandelier, Löwenstein, Hammer, Roepke, Heron, M'Call Anderson. In following out Goetsch's method it must be clearly understood that amelioration or arrest of the tuberculous condition may be attained without any subjective or objective clinical changes on the part of the patient. This has been determined in cases of lupus and tuberculosis of the pharynx and larynx. Indeed, it is the special object of the immunisator to avoid all reactions. Many patients, however, are apt to develop hypersensitiveness to tuberculin in spite of all precautions. This hypersensitiveness or anaphylaxis manifests itself in this way, that a dose previously borne without any indication of symptoms induces a reaction if repeated, and this may occur very early in the treatment, and even with minute doses. The

exact nature of anaphylaxis is not yet understood, but its recognition is of the greatest importance, and its onset must be met by stopping the treatment, or by the return to very minute doses. With Goetsch's mild method it can often be prevented, and this principle of treatment has extended the scope of tuberculin treatment in so far that the risk to the patient is reduced practically to a vanishing point. All stages of the disease may be treated, and inoculation may also be combined with sanatorium treatment.

Opinions differ with regard to the manner in which the immunisation is best carried out. In Germany, following the Koch tradition, and on the basis of experience gained in the immunisation of animals, it is considered advisable to increase the dose progressively until a maximum is reached. It must, however, be remembered that tuberculin in its various forms is not altogether analogous to diphtheria or tetanus toxins, but belongs to the group of endotoxins. The experience gained hitherto shews that the inoculation of endotoxins does not give rise to a degree of immunity comparable to that induced by the inoculation of exotoxins. Indeed, a very common result of the attempt to produce an endotoxin immunity is the establishment of a condition of anaphylaxis, which may be so intense that the process has to be stopped. This has been specially studied in the case of tuberculin by Löwenstein and Rappoport. Still, most observers have advised the gradual increase of the dose as far as possible. Sir A. E. Wright, on the other hand, considers that this is unnecessary as long as the same minute dose causes an increase in the anti-body content of the serum, and it cannot be doubted that many cases of localised tuberculosis have been cured by his method. But up to the present the number of consumptive cases treated on this principle is small in comparison with the numbers treated by the German method. Whereas the majority recommend the subcutaneous method for introducing the tuberculin, others have advised intravenous, pulmonic, cutaneous, and oral administration. With regard to the latter it has generally been held to be ineffective, as apparently the tuberculin passes with difficulty through the alimentary mucous membrane, or is destroyed by the digestive juices. Recently, however, Dr. A. Latham, Moeller, and others have revived this method, and they administer the tuberculin either in saline solution or in normal horse serum or in capsules. Dr. Latham states that he has obtained fluctuations in the opsonic index with quantities of tuberculin as small as $\frac{1}{20,000}$ mgr. Krause also recommends the oral method, the tuberculin (T.R.), suspended in a fatty menstruum, being put up in small keratin capsules. This is sold in commerce under the name "phthysoremid." As was pointed out, there are great individual differences in the tolerance towards tuberculin, so that it is impossible to lay down any hard-and-fast rules as regards dosage. On the lines of the German method, the following are approximately the quantities of old tuberculin (T.O.) to be used. The initial dose is usually $\frac{1}{100}$ mgr., rising to $\frac{3}{100}$, $\frac{6}{100}$, $\frac{1}{10}$, $\frac{2}{10}$, $\frac{3}{10}$, $\frac{5}{10}$, $\frac{7}{10}$,

1, 1·5, 2, 3, 5, 7, and 10 mgr. If at any time the symptoms of anaphylaxis make their appearance the dose should be materially decreased, with a pause in the inoculation. If 10 mgr. are tolerated without reaction the dose may then be cautiously increased to 15, 20, 30, 50, 70, 100, 150, 200, 300 mgr., and even up to 1000 mgr. With tuberculin T.R. the successive doses recommended are $\frac{1}{500}$ mgr., $\frac{2}{500}$, $\frac{3}{500}$, $\frac{5}{500}$, $\frac{2}{100}$, $\frac{3}{100}$, $\frac{4}{100}$, $\frac{5}{100}$, $\frac{6}{100}$, $\frac{1}{10}$, $\frac{2}{10}$, $\frac{3}{10}$, $\frac{4}{10}$, $\frac{5}{10}$, $\frac{6}{10}$, 1, 2, 3, 4, 5, 6, etc., up to 10 mgr. For the new tuberculin (bacillary emulsion), begin with $\frac{1}{1000}$ mgr., passing through $\frac{2}{1000}$, $\frac{3}{1000}$, $\frac{4}{1000}$, $\frac{5}{1000}$, $\frac{7}{1000}$, $\frac{10}{1000}$, $\frac{15}{1000}$, to $\frac{2}{100}$, $\frac{3}{100}$, and gradually progressing to quantities like 1, 2, $2\frac{1}{2}$, 3, 4, 5, and 10 mgr.

Following Sir A. E. Wright, others have considered that such doses are unnecessary and even inadvisable, as the same dose may produce fluctuations in the opsonic index over prolonged periods. The comparative value of the two methods cannot be satisfactorily estimated at the present time in the case of consumption. Petruschky has laid special stress on the carrying out of the immunisation in a series of stages, several weeks or months of inoculation alternating with periods of rest. The tuberculins introduced by Carl Spengler are administered on the same bases as tuberculins of human origin.

Criteria for Estimating the Results of the Inoculations.—To gain an insight into the changes occurring in the course of the immunisation, most observers have relied on the accurate study of clinical symptoms, such as the onset and duration of fever, subjective or objective phenomena referable to the thorax, changes in weight and the feeling of well-being or the reverse on the part of the patient. Others have sought to gain more accurate information by quantitatively measuring the content of the blood serum in tuberculous anti-bodies. Of these the agglutinins have been extensively studied, but have been found unsatisfactory as measures of the degree of improvement. In England and America a large amount of evidence has been collected in favour of the estimation of opsonic anti-bodies as a guide to correct dosage and the interspacing of the doses. Arneth has drawn attention to the importance of careful blood-counts during the course of the immunisation. He considers that the so-called polynuclear neutrophil leucocytes can be referred to several groups according to the indentations or number of the individual nuclei; thus in healthy people he found (1) mononuclear forms with a round or indented nucleus, 5 per cent; (2) forms with two nuclei, 35 per cent; (3) with three nuclei, 41 per cent; (4) with four nuclei, 17 per cent; (5) with five nuclei, 2 per cent. In tuberculosis he noted a predominance of the forms with one or two nuclei. Thus, in a case of fatal pulmonary tuberculosis he found 46 per cent of group 1, 49 per cent of group 2, 5 per cent of group 3; and in a number of instances he observed a return to the normal blood-picture as a result of the inoculation of tuberculin.

Anatomical Changes Induced by Tuberculin.—The majority of morbid anatomists hold that there is nothing specifically peculiar in the inflam-

matory changes produced in the local lesions after the administration of tuberculin. In the series of cases published by Petruschky there appeared, however, to be a special predilection for the production of granulation tissue with consequent scar formation. This is of importance in estimating the value of tuberculin as a curative agent, as we know that this is the method by which nature heals tubercle under ordinary conditions, a complete *restitutio ad integrum* being practically impossible in a lesion of any magnitude. This being so, it is difficult to obtain any accurate post-mortem estimate of the value of tuberculin, and we are driven to the study of statistics, clinical observations, or animal experiments to answer the question. It must be admitted that tuberculin rarely arrests a tuberculous process in the animals mostly used for experimental purposes. In the case of the guinea-pig this is not surprising in view of the extraordinary susceptibility of this animal to tubercle bacilli, and negative results in this direction are no indications as to the value of tuberculin in much less susceptible man. In estimating the value of tuberculin as a therapeutic agent we have therefore to rely on clinical experiences only, and the judgment of its value may be decided by the standard of health obtained, the disappearance of symptoms, the absence of fever, the disappearance of tubercle bacilli from the sputum, and the maintenance of equilibrium in weight. A further rigorous test consists in the loss of reaction even on the administration of large doses of tuberculin. Where the value of tuberculin has to be compared with other methods of treatment, the percentage may be determined of those alive, after a certain period in good health, or at any rate capable of work as ordinarily understood, and in this respect the permanent result is of infinitely greater value as a criterion than mere temporary benefit. Now, in estimating the value of tuberculin in this way considerable difficulties are experienced; it is very difficult accurately to compare the results of different writers, as the class of case treated and many other factors must be taken into account. Perhaps the most accurate comparative estimates can be obtained when the cases of the same degree of severity are treated under the same local conditions by the same physician with and without tuberculin. Judging the matter in this way, Bandelier has recently reported a series of 383 cases treated by himself with perlsucht-tuberculin (178 cases) or bacillary emulsion (205 cases), the results being set forth in the accompanying table:—

Result.			First Stage.		Second Stage.		Third Stage.	
		Per cent.		Per cent.		Per cent.		Per cent.
Cured	59		21		38		0	
Completely fit for work	192		31		143		18	
	251	(65·5)	52	(88·13)	181	(75·10)	18	(21·69)
Partially fit for work within the meaning of the Insurance Law	114	(29·7)	7	(11·87)	56	(23·2)	51	(61·45)
Total positive results	365	(95·3)	59	(100)	237	(98·34)	69	(83·14)
Total negative results	18	(4·7)		...	4	(1·66)	14	(16·86)

Comparing 383 patients in the second stage, and treated with tuberculin, with 299 patients in the same stage, and treated by sanatorium methods only, Bandelier obtained the following results in the Cottbus sanatorium:—

Result.	Without Tuberculin.		With Tuberculin.	
		Per cent.		Per cent.
Cured	0	(0)	38	(15·77)
Completely fit for work	21	(25·3)	143	(59·33)
	21	(25·3)	181	(75·10)
Fit for work within the meaning of the Insurance Act	28	(33·7)	56	(23·24)
Total positive result	49	(59)	237	(98·34)
Total negative result	34	(41)	4	(1·66)

With reference to the permanency of the results, Bandelier's cases worked out as follows:—

Year.	Successful Results.		Maintained Success at End of			
			1 Year.	2 Years.	3 Years.	4 Years.
	No.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.
1902	204	88·31	81·82	71·43	67·53	61·90
1903	213	89·87	80·17	67·51	62·03	
1904	317	79·25	75·0	69·25		
1905	338	79·53	77·88			

Since 1893 Petruschky treated cases with the following ultimate result up to 1903, viz.: 58 severe cases with bacilli in sputum; 54 milder cases without bacilli in sputum. Of the 58, 23 (60 per cent) died; 15 (45 per cent) were cured. Of the milder cases all survived.

2. *Passive Immunisation—Anti-tuberculous Serum.*—The great success following the therapeutic administration of diphtheria antitoxin led many

to the belief that serum therapy might prove of service in the treatment of tuberculosis. With this object in view horses have been inoculated with tuberculin and with various other bacillary products, the serum being afterwards inoculated into tuberculous patients. Up to the present time, however, the results have been disappointing, although some have reported benefit or even cure. In particular, Maragliano has made a special study of such anti-tuberculous serum, something like 20,000 cases having been treated by it. Mircoli has recently published an analysis of 2897 cases treated by Maragliano's serum with the following results :—

	Cured.	Improved.
	Per cent.	Per cent.
250 cases of circumscribed non-febrile tuberculosis .	38	49
938 cases of circumscribed febrile tuberculosis . .	18	54
665 cases of diffuse tuberculous bronchopneumonia without mixed infection	14	43
332 cases of diffuse tuberculous bronchopneumonia with mixed infection	9	36
712 cases of consumption with cavity formation . .	6	40

It may be added, however, that Maffucci and di Vestea, and most recently Flick in Philadelphia have been unable to observe any beneficial effects from its use. Besides Maragliano's serum, which is prepared by inoculating horses with tuberculin and other toxin products obtained from tubercle bacilli, other serums of similar character have been used by Viquerat, de Schweinitz, Babes and Proca, Williams and Horrocks, and many others. Fisch inoculated horses with tuberculin T.R. for the production of anti-tuberculous serum. Marmorek prepares his serum in a different way. Believing that the true toxin of the tubercle bacillus is not developed in ordinary glycerin broth, he grows the culture in a medium containing extract of liver substance and leucotoxic serum. After a time the bacilli are filtered off, the filtrate being injected into horses, the serum of which is then used for treatment. Opinions differ with regard to the value of Marmorek's serum, but most writers are of opinion that it is without marked influence on the course of the tuberculous process. A few, however, have seen beneficial effects even in pulmonary tuberculosis (Frey).

Specific Treatment of Mixed Infections.—The question of specific treatment for the bacterial associations in consumption has been frequently raised. Anti-pneumococcic and anti-streptococcic serums have been used, but without striking benefit. From the results obtained by treatment with corresponding vaccins inoculation with killed cultures might prove of service; at the same time it must be remembered that it is by no means an easy thing to determine the special parts played by bacteria complicating the tuberculous process, and the state of the patient exhausted by a debilitating disease is not very favourable for an immunisation process.

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Bier's treatment of tuberculosis by passive hyperaemia has been applied to the lung by means of a suction mask. The use of this apparatus, which impedes the entry of air during inspiration while allowing free exit during expiration, excites hyperaemia and acceleration of the lymph stream in the lungs. Kuhn speaks well of the results of this method applied twice daily for a period of an hour.

Medicinal Treatment.—The number of drugs that have been vaunted as specifics for tuberculosis is legion. In recent years iodine, iodoform, carbolic acid, corrosive sublimate, formic aldehyde, creosote and one of its constituents, guaiacol, have been most largely used in virtue of their antiseptic properties. These have been administered by the mouth, by inhalation, subcutaneous and intravenous injection, inunction, and direct injection into the lung; and sulphuretted hydrogen gas has even been pumped into the rectum. The results have not differed greatly in respect of any of these methods. They have all passed through successive stages of exaggerated and hasty laudation, half-hearted approbation, and contemptuous neglect. Creosote is still used by some physicians, but I have not been able to see that it has any good effect on the disease. Unfortunately it is apt to derange the digestion in some cases. Urea has been recommended on the ground that gout is antagonistic to tuberculosis. Cinnamic acid, advocated by Landerer in virtue of its property of inducing leucocytosis, has been used mostly in the form of cinnamate of sodium or hetol. But, so far, no drug can be considered to be a specific.

Until we possess a reliable specific method of treatment our chief aim must be to increase, as far as possible, the resisting power of the patient, so as to put him in the best condition to withstand the inroads of the disease.

In order to maintain the nutrition of the body at as high a level as possible, the dietary must be liberal, and should include a large amount of fat in the shape of milk, cream, butter, fat bacon, and the like, in addition to a due proportion of nitrogenous and carbohydrate constituents. Patients with quiescent disease should take three good meals a day, avoiding, as far as possible, extras between meals with the exception of a glass of milk or a cup of afternoon tea. Zomotherapy, the use of raw meat, has been warmly praised by Richet and Héricourt, who claim excellent results from this method. These authors find that the beneficial effect is due to the muscle plasma, and they are inclined to attribute this to a special tonic action on the nervous system. Dr. Philip, in this country, has also reported good results from the use of raw meat.

A special distaste for fatty foods is manifested by some patients, but this aversion is by no means so general as certain writers would have us believe. Cod-liver oil is a valuable adjunct to the diet, but is possessed of no specific virtues. From an experimental comparison of its effect on healthy and on tuberculous pigs, Dr. Wells concluded that it increases the assimilation of other fats and diminishes body waste, as shewn by diminished exertion of nitrogen. This valuable food is sometimes prescribed in a manner calculated to bring it into discredit, that is, when it is administered in too large quantities. Two to four drams twice or thrice in the day is as much as most patients can digest, and it is frequently necessary to begin with even smaller doses. It usually agrees best when taken soon after a meal; but some people prefer a single dose at bedtime. In all cases of dyspepsia, and whenever the taste of the oil keeps rising into the mouth, it should be withheld. If persevered with in these circumstances it seldom fails to derange the digestion, It is better for the patient to enjoy his food without the oil, than to persist in its use and lose his appetite.

The taste of the oil may be disguised with peppermint, lemon juice, ginger or orange wine, cognac, liqueurs, and other flavourings. Many patients prefer to take the oil in the form of an emulsion, or in combination with malt extract. Malt is much used at present in England, and no doubt it possesses some digestive value, but it is no substitute for cod-liver oil or fats. Glycerin, in doses of three to four tablespoonfuls daily, has been recommended as a substitute for the oil by Jaccoud, but it has not found much favour with other physicians. Alcohol is not to be ordered in all cases indiscriminately; where the disease is quiescent, nutrition fairly well preserved, and the appetite good, it is not required; in conditions of debility, deficient appetite, and, above all, in pyrexial cases, alcohol is of great value.

The particular form in which stimulants are to be administered is largely a matter of taste. Ale and stout are preferred by many patients. In pyrexial cases, brandy, whisky, or some form of spirit, seems often to suit best, and the quantity that can be taken with advantage in these circumstances may be very large. Alcohol has no influence in promoting reparative sclerotic changes, as some have asserted. In cases of obstinate anorexia, forced feeding by means of the stomach-tube has been found useful by Debove and others. Massage is occasionally useful, especially where debility is a prominent symptom and is unaccompanied by pyrexia.

In addition to the utmost attention to the matter of food the rules of general hygiene must be carefully observed. The patient's house ought to be well drained, built on a light porous soil, and, if possible, it should face the south. The rooms, and especially the sleeping-apartments, must be well ventilated and suitably warmed. It is hardly possible to overestimate the value of fresh air and sunshine. Regular exercise, walking, riding, outdoor games of the less violent kind, such as golf, cycling, shooting, and fishing, may all be practised with moderation

if the patient's general condition be good, and if there be no pyrexia. Where this is not possible, the patient, in favourable weather, may go out in a bath-chair or in a carriage; or he may sit out of doors in a suitably arranged shelter. Even when he is entirely confined to bed with fever, wasting, night-sweats, and symptoms of progressive disease, much benefit may still accrue from wheeling the patient's bed out of doors into a sheltered spot, or into a sunny balcony, as is done at Falkenstein and other places; bedridden persons may, in this manner, spend the greater part of the day in the open air with great advantage. The clothing should be warm and yet light, and woollen garments should be worn next the skin. Comforters for the neck and chest-protectors, which encourage hyperaemia and increased sensitiveness of the skin to changes of temperature, are unnecessary and unadvisable. Woollen socks or stockings and thick boots are required to prevent the feet from getting chilled. Respirators worn over the mouth are not now so much in vogue as formerly. If the patient breathe through his nose, as he ought to do, a respirator is superfluous. When a strong, cold wind has to be faced, a light shawl or thick veil may be wrapped round the face for temporary protection.

The skin may be rendered less sensitive to changes of temperature by the daily use of the cold shower-bath or douche in the morning; but in the case of more delicate patients, with feeble circulation, a warm bath followed by cold sponging is preferable. Early hours, the avoidance of crowded rooms, theatres, and smoking-rooms, a life free from excitement, and occupation for the mind, such as reading, drawing, chess, billiards, and other indoor games are to be recommended. Instrumental music may be practised, but singing is not advisable, except for the more robust patients, in whom the disease is quiescent; though Walshe gives instances of singers continuing to take leading parts in the opera while suffering from pronounced pulmonary disease. Medical direction is most desirable; and the success of some continental health resorts is doubtless attributable in a large measure to the careful and strict superintendence of the physicians in charge. But the majority of English patients find such a rigid supervision irksome and disagreeable; and until comparatively recent times such establishments have not been in much request in this country. But owing to the success of the sanatorium treatment in Germany, in the first instance, this method has been widely adopted in Great Britain with excellent results. P. K.

Sanatorium Treatment.—The essentials of what is generally called the sanatorium or open-air treatment are: (1) abundance of fresh air, day and night; (2) a somewhat generous diet; (3) rest; and (4) regulated exercise.

Fresh Air.—The value of abundance of fresh air is inestimable, and to secure this the routine sanatorium treatment is largely directed. The patient should, so far as is possible, live continuously in the fresh air; this can be managed most readily at a sanatorium, but in the case of

patients living at home, even in large cities, a great deal can be done in this respect. The ideal is for a patient to be out of doors all day and all night: in practice a patient is kept out of doors for as long as possible, and his indoor life, by the plentiful provision of open windows, is made to approximate to the conditions of outdoor life. It is best for patients, when carrying out the open-air treatment at home, to have a room for their exclusive use. The chief difficulties of the open-air life are those due to climate. Although during the warmer months of the year it is possible for every patient to be out of doors all day, shelter must be provided against wind, rain, and excessive heat. Exposure to sun in the middle of summer is often prejudicial, and shelters, balconies, and the like with a southern exposure should be provided with sun-blinds. Patients' bedrooms should have plenty of window space, and preferably should face south. During the colder months of the year care must be taken that the patient does not become chilled when lying out in the open. A consumptive patient should never feel cold. The extremities especially require protection, as a precaution against chilblains. Warm clothes and rugs enable patients to lie out in the open air in the coldest weather without becoming chilled. It is advisable also to warm the consumptive's room in the coldest weather, preferably by an open fire. It is particularly important that the dining-room should not be too cold, as it is to the patient's disadvantage to get cold during his meals or to have his food rapidly chilled. The large majority of patients, especially those with early disease and good constitutions, rapidly become acclimatised to the open-air life even in the severest weather, and live under these somewhat rigorous conditions with the greatest advantage; but in patients somewhat advanced in years, in those with enfeebled constitutions, or much prone to bronchitis, the education up to this sanatorium standard should be a much more gradual and less complete process.

Diet.—The patient with tuberculosis requires a somewhat more generous diet than is suitable for him when in normal health. The increase in the several constituents of the normal diet (proteins, fats, and carbohydrates) should only be a moderate one, the so-called forced feeding or the ingestion of a very large amount of food being quite unnecessary, and in many cases definitely prejudicial. Experience shews that a good diet for any individual suffering from tuberculosis is represented by his physiological diet increased by 30 per cent in protein value, and 30 per cent in total caloric value. In practice, standard diets for men and women having the following nutritive values are found to be thoroughly satisfactory :—

	Proteins.	Fats.	Carbohydrates.	Calories.
Men . .	150	150	250	3000
Women .	126	150	220	2814

These standard diets must be modified according to individual requirements, and the diet prescribed should as far as possible resemble that taken by the individual when in ordinary health. The same food-stuffs should be used, and meals should be given at the usual times; for instance, breakfast, luncheon, and dinner. The food should be well cooked and varied as much as possible. The following is a good standard diet for sanatorium practice:—

	Amount.	Nutritive Value.		
		Protein.	Fat.	Carbohydrates.
	oz.	grams.	grams.	grams.
Milk	60	57	70	87
Bread	6½	16	2	88
Butter	1	...	23	...
Cream	1	1	6	...
Fish	4	20	10	...
Meat	6	44	22	...
Milk Pudding	4	9	16	50
Suet or Sponge Pudding	3			
Potatoes	5	1	...	30
Egg	one	6	4	...
Stewed Fruit, Green Vegetables, Soups, etc., from time to time	q.s.	1	1	7
Cake	1	1	2	12
Totals	...	156	156	274

The total caloric value of this diet is 3250.

With a satisfactory diet, patients, when appreciably below their normal weight, regain their lost weight at the rate of from one to two lbs. a week, and in the case of extremely emaciated patients, the gain during the first few weeks is very often considerably greater; speaking generally, however, very rapid gain in weight is not desirable. When patients have regained all their lost weight, and have reached a point a few pounds in excess of what is considered to be their proper weight, the disease at the same time being arrested, the diet can usually be somewhat reduced with advantage. This reduction is most readily made by omitting some of the milk from the diet. Care should be taken to prevent the addition of excessive body weight. Patients belonging to the working-classes, and especially men, when convalescent and engaged in some form of manual work, require a diet of higher nutritive value than the one just described. The increase in food is best made by giving larger amounts of bread and pudding, and adding some vegetable protein such as peas, lentils, etc. The following is a good standard diet for a sanatorium for the working-classes:—

	Amount. oz.
Whole Milk	20
Meat	9
Butter	1
Suet	½
Cheese	2
Bacon and Brawn	2
Bread	12
Potatoes	8
Pulses	3
Oatmeal	2
Sugar	2
Jam	1
Rice, etc.	½
Flour	1
Green Vegetables, Sundries	sufficient amounts.

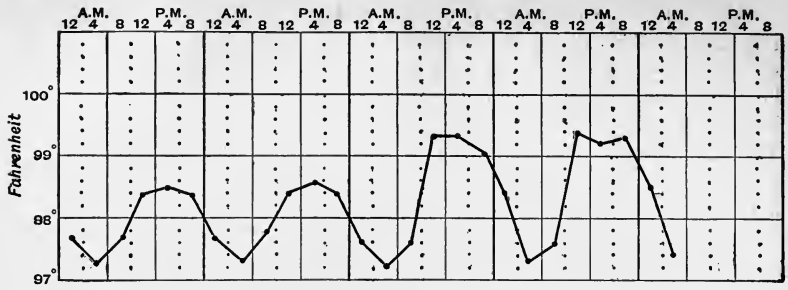
The nutritive value of this diet is: protein, 156; fat, 141; carbohydrate, 432; calories, 3722. Its cost is one shilling per day.

When there is persistent anorexia or digestive derangement, it is often advisable, for a time at least, to modify the diet in such a way that the requisite nutritive value is given in a form which is more readily taken. The diet, in short, should be somewhat concentrated. Food-stuffs of small nutritive value such as soups, potatoes, green vegetables, should be reduced in amount or omitted; bulky food-stuffs, also, such as porridge, pulses, bread, suet puddings, should be given in smaller quantities. The nutritive value of the eliminated food-stuffs should be given in a form that is more easily taken. To keep up the protein intake the milk should be "fortified," in other words, its nutritive value should be increased by the addition to it of a soluble casein, such as casumen, plasmon, sanatogen, or a similar preparation. Milk puddings and soups can be thus increased in nutritive value in a similar way. Egg, especially egg-flip, and raw meat, given either in milk or in sandwiches, are also easily-taken forms of protein food. The caloric value of the diet is most readily increased by the addition of Benger's food or some similar preparation, or by the addition to the diet of 4 or 5 ounces of cream daily. A bitter tonic taken before meals often has a very good effect in the treatment of patients with anorexia; perhaps the best is a mixture of sodii bicarbonat. gr. xv, tinct. nuc. vom. ♏vij, tinct. gentian. co. ʒss., aquam chloroformi ad ʒi.

Concentrated diets are often very useful in the treatment of patients with laryngeal disease associated with dysphagia. Many patients admitted to a sanatorium, with comparatively early tuberculosis, suffer from anorexia and dyspepsia, which, however, almost invariably disappear in the course of the first fortnight's treatment. The ordinary standard diet should be prescribed to these patients.

Rest; Regulated Exercise.—The regulation of the amount of rest and

exercise taken by patients is a most important part of the sanatorium treatment. The degree and character of the exercise that may with advantage be taken by a consumptive require very nice determination, the margin of error in the way of over-exercise being very much less than is the case in health, and the penalty of serious error much graver. The consumptive requires to be educated up to the requirements and limitations of his altered physical conditions. It is difficult to formulate exact rules for the regulation of rest and exercise, so many factors have to be taken into consideration. Absolute rest, preferably in the recumbent position and in silence, should form a considerable part of the routine treatment of every consumptive with active or but recently active disease. The greater the extent of the lesion, and the more active the process, the larger should be the amount of rest prescribed. Conversely, the smaller the lesion and the more complete the arrest of the morbid process, the more prominent a feature should exercise be in the routine. In practice the most important factor is the degree of activity of the disease, and in estimating this we rely on the daily temperature curve, the physical signs in the chest, and the pulse rate. The record of the daily temperature, though not free from fallacy, is perhaps our best guide as to the activity of the disease; for this reason the daily observation of the temperature forms an essential part of the routine treatment at a sanatorium. The temperature should be taken in the morning on waking, at midday (1 P.M.) after one hour's complete rest in the recumbent position, and at 7 P.M., after a similar hour's rest. In ordinary practice the temperature is usually taken in the mouth or axilla. Careful observation shews, however, that the temperature taken in these positions is not trustworthy in the case of patients treated out of doors. The skin and the cavity of the mouth become chilled by contact with the open air, and the temperatures recorded are, in consequence, appreciably lower than the true body temperature. The rectal temperature gives a much more faithful record of the body temperature, and is therefore more satisfactory in sanatorium practice. The rectal temperature is very sensitive and especially to exercise, very slight degrees of exertion raising it; hence the importance of the hour's rest before taking the temperature in this way, quite apart from the therapeutic value of this rest. The rectal temperature in fairly warm weather is, on an average, ·5° to 1° F. higher than in the mouth; in cold weather the difference between the two is very much greater, often amounting to several degrees. Temperatures taken in the mouth immediately after exercise also give a very erroneous record of the true temperature of the body. A knowledge of the normal fluctuations of the temperature in healthy persons is important as a standard for routine work. The following chart shews the daily temperature curve (rectal: 4 hourly) of the average normal person:—



1. At complete rest. 2. At work ; very slight muscular exertion.

CHART 5.—NORMAL TEMPERATURE CHART.—Temperature taken every 4 hours in the rectum.

The temperature records of the first two days on the chart represent the temperature curve of a normal person at complete rest. The records of the following two days represent the temperature curve of the same individual when engaged in his ordinary occupation. The individual was a medical man engaged in ordinary practice, an occupation which necessitates a slight amount, only, of muscular exertion. The temperature curves on the third and fourth day would have been the same as on the first and second days if the individual had rested an hour before taking his temperature at 12, 4, and 8 P.M.

Absolute rest, preferably in bed, should be prescribed so long as there are definite signs and symptoms of active disease. A temperature range which exceeds 100° F. to 100·5° F. (rectal) during the day, the patient being at complete rest for an hour before the temperature is taken, in the large majority of cases indicates the existence of active disease and contra-indicates any exercise whatsoever. When working on this rule, namely, that a patient should be kept in bed so long as his temperature touches 100° F. during the day, it is important carefully to exclude possible sources of elevation of temperature other than the tuberculous disease. When the temperature falls and does not reach 100° F. for some days consecutively, the patient can be allowed out of bed for an hour or two. When this amount of exertion on several consecutive days does not cause any rise of temperature the patient can be allowed up for a longer period, namely, from 10 A.M. to 5 or 6 P.M., and he should be allowed slight exercise, such as walking about his room or on the balcony of his room. If the improvement continue, a short walk, for instance a quarter of a mile, should be prescribed, the walk being taken slowly with occasional rests. This short walk should be repeated for several days, and if the temperature curve remain steady and the patient's general condition continue to be quite satisfactory, the exercise should be steadily increased. The amount of exercise to be taken during the day should be definitely prescribed, and the patient should rest throughout the whole of the day except for the periods of exercise ordered. If the temperature curve at rest shews signs of rising, the exercise must be reduced, or even discontinued for a time. It must be remembered that

exercise raises the body temperature, and often markedly so in the case of patients with imperfectly arrested tuberculosis. The temperature of a patient thus raised by exercise should fall to its normal level within an hour, if the patient rest immediately on completion of his exercise. When the temperature is steady, at a normal level, and the conditions of the general health, pulse, and lesion are all satisfactory, the amount of exercise should be steadily increased until the patient is walking some six to twelve miles daily. The secret of success lies in the exercise being gradually increased with the increasing convalescence of the patient. Experience has shewn that very large amounts of exercise and work requiring considerable muscular effort may be carried out with beneficial results by convalescent patients. This is an important consideration in cases in which it is essential to conserve or restore the capacity for manual work. In the working-classes a varying degree of actual muscular work can with advantage be prescribed to convalescent patients in lieu of the usual walking exercise. The care of gardens and grounds and many forms of outdoor occupation provide manual work of all grades, from very light work to that entailing great muscular exertion. The same principles apply to the regulation of manual work as to the regulation of walking exercise, and the training should be a gradual one. Speaking generally, patients with early disease which has not undergone caseation are best suited for such manual work. It is inadvisable to prescribe exercise of this kind to patients until they can walk some six miles daily with perfectly satisfactory results as regards temperature, physical signs, pulse-rate, and general health.

Recreation.—A part of the day should be allotted to recreation in the case of convalescent patients. Recreation should be expressly limited to certain hours, otherwise its value will be much discounted. Of outdoor games, croquet, putting, clock golf, deck quoits, and similar games requiring little exertion are generally suitable. Golf, cycling, riding, and shooting are permissible to patients with well-arrested lesions, but violent games such as hockey, football, tennis, and similar field-sports should not be allowed. Photography, music, and some card games such as whist and patience are suitable recreations under supervision. It need scarcely be said that recreations requiring a certain amount of muscular exertion should only be prescribed to patients who are sufficiently convalescent to be allowed a fair amount of exercise.

Baths.—Constant attention to the skin is of considerable importance. Every patient should have a tepid bath daily, and as convalescence is established, the tepid bath should be followed by a rub over with a cold sponge or by a cold douche.

Smoking should be carefully supervised, and the smoking of cigarettes should be altogether discountenanced. Smoking in any form is contra-indicated in patients with any catarrhal condition of the pharynx or larynx. Patients should be encouraged to give up smoking, and failing this, should be advised to limit it to a pipe after each meal. Smoking before meals should be especially avoided. Alcohol is not

required in the routine treatment, but is of use in the treatment of acute conditions.

Routine and Supervision.—One of the essentials of success of the sanatorium treatment is that the daily routine of each patient should be definitely prescribed, and loyally carried out. The regularity of the life is of the highest therapeutic value. Constant medical supervision is essential, both for the direction of the patients and to ensure that the orders given are faithfully followed. It is a good plan to write down for each patient the details of the manner in which his day should be spent, for when precise directions are given there is not the same risk that the patient may do something unwise, as when the patient is left to spend his spare time as he pleases. The precise daily routine naturally varies with the condition of the patients, but, speaking generally, the day is divided up into periods for rest, exercise, meals, and recreation. The following daily routine at present in force at the King Edward VII. Sanatorium is a good working model:—

DAILY ROUTINE

7.30 A.M.	Gong is sounded. Patients take their temperatures and get up. Baths, Hydrotherapy, etc.
8.15 „	First Breakfast Gong.
8.30 „	Breakfast Gong.
9 to 9.30 „	Leisure. Books can be obtained from the Librarian.
9.30 „	Gong is sounded. All patients must go direct to their rooms, or to that part of the balcony immediately outside their rooms, and rest on their chairs until they have been seen by their Medical Officers.
9.30 to 12 noon.	Rest or exercise as prescribed. On one day in each week, patients will attend in the Consulting Room at this hour.
12 „	Gong is sounded. All patients must go direct to their rooms.
12 to 1 P.M.	All patients must rest in the recumbent position in their rooms or on their balconies. No talking is allowed.
1 „	First Luncheon Gong. Patients take their temperatures.
1.15 „	Luncheon Gong.
2 to 2.30 „	Leisure.
2.30 to 4.30 „	Rest or exercise as prescribed.
4.30 „	Tea in Entrance Hall.
5 to 6 „	Recreation hour for music, games, etc.
6 „	Gong is sounded. All patients must go to their rooms as at 12 o'clock.
6-7 „	Rest hour.
7 „	First Dinner Gong. Patients take their temperatures.
7.15 „	Dinner Gong.
8 to 9.30 „	Recreation.
9.30 „	All patients must go to their rooms.
10 „	All lights out.

In sanatoriums for the working-classes the routine should be modified; for instance, the day's work should be begun earlier. During the periods of the day devoted to the treatment, excluding the hours for meals, patients should be either engaged in taking exercise or resting. Rest should be absolute, preferably in the recumbent position. The hour's rest before meals is of especial value, and is taken with advantage, in the patient's own bedroom, thus ensuring complete quiet. On the completion of their prescribed walks the patients should return to their long chairs and continue the rest-cure. In a sanatorium of any size constant supervision is necessary to maintain discipline and obedience to orders; and the more strictly observed the medical instructions, the better will be the results. It is a good plan to keep every patient, when first admitted, at complete rest or even in bed for a day or two, so as to allow a thorough examination to be made of the patient, and to enable an estimate to be formed of his recuperative power and constitution generally. The temperature, as already stated, should be taken on waking, at midday, and in the evening, the patient in each case being at complete rest, namely, not having taken any exercise for an hour. The pulse should be taken morning and evening. Patients should be weighed on admission, and subsequently once a week, and always in the same clothes and at the same time of day.

Education and After-Treatment.—The consumptive on his discharge from the sanatorium and return to ordinary life should be urged to embody the sanatorium principles of living in his daily routine. The necessity for doing so is especially great when patients, from financial or other reasons, have only been able to devote a short time to treatment in a sanatorium. A course of three months' treatment in a sanatorium is often long enough to teach a patient the principles on which he should live, and also very appreciably to arrest the disease; there are few cases, however, in which a stay of six months in a sanatorium is not desirable. Once a consumptive has been taught the routine treatment experience shews that he can do a very great deal towards curing himself, even when working and living under somewhat unfavourable conditions. Meals, more regular and of higher nutritive value than formerly, open windows all night and, when possible, also during the day, even when at work, avoidance of late hours and of anything calculated to over-fatigue, and a period of rest and open air every week-end are factors within the reach of the large majority of consumptives, and if taken advantage of, tend greatly to the preservation of life and capacity for work.

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N. B.

Climatic Treatment.—In selecting a suitable climate we must be guided by certain general principles. Purity of the atmosphere, and especially freedom from dust of all kinds, and abundant sunshine, are the fundamental requisites. Questions of altitude, temperature, and moisture of the air, and geographical considerations in general, are still matters of dispute, and are discussed elsewhere in this work. But it cannot be doubted that the success of sanatorium methods has tended to depreciate the importance of climatic treatment. It is obviously better, if possible, for a patient to undergo the necessary treatment in the climate in which he must live and carry on his work.

If the patient's surroundings satisfy the requirements just indicated, it is unnecessary, in most instances, to advise a permanent change of residence. In the case of wealthy people it may be desirable to send them away to some health resort, where they will be more ready to submit to strict medical supervision and direction than at home. When the patient lives in a large town he should be recommended to remove into purer air, if his means permit. It is useless and cruel to send patients with advanced disease to a distant health resort. To such persons the fatigue of a long journey may have disastrous consequences, and the loss of home comforts cannot be compensated even by the best of climates.

If the general health be well maintained, and the pulmonary disease be neither very active nor extensive, great benefit may be obtained by spending the winter, or better still, by continued residence at the high alpine stations, such as St. Moritz, Davos, and the like. Better results are generally obtained in men than in women, as the tastes and the habits of men impel them to take a fuller advantage of the opportunities of outdoor life and exercise presented by an alpine climate. Under similar conditions of health, emigration to Colorado, the Rocky Mountains, and the high levels of South Africa offers good prospects to young men.

Emphysema, laryngeal tuberculosis, and manifestations of nervous erethism are generally regarded as contra-indicating residence at the high alpine stations. Such cases are more adapted for Egypt, the Riviera, Madeira, the Canaries, or the south coast of England. For a detailed discussion of this subject the reader is referred to the article "Climate in the Treatment of Disease," Vol. I. p. 328.

Symptomatic Treatment.—In combination with the general hygienic measures that have been briefly sketched the exhibition of certain tonic

drugs is often very useful. The most valuable are strychnine or nux vomica, arsenic, and quinine. Opinions differ as to the relative value of these, but strychnine appears to deserve the first place. Arsenic has no specific influence on the disease, but it may do good service in its capacity of a nervine tonic; the same may be said of quinine. Iron has still a great reputation with some physicians; but it does not suit all patients, especially the large class that suffer from a tendency to gastric catarrh; and it has little effect on the anaemia of phthisis. In persons who can take a fair amount of exercise, and have a good digestion, a short course of iron, either alone or in combination with arsenic, is sometimes attended with good results. The hypophosphites of lime and sodium have been largely tried, and are still much used in this country. They are certainly not possessed of any direct action on the tuberculous process, and their tonic effects have been greatly overestimated.

Fever.—Quinine has been extensively used for the purpose of reducing fever, especially on the Continent; but it is generally allowed that in order to obtain this result 20 to 30 grains must be given in a single dose, or divided into four or five doses, to be taken at short intervals some hours before the temperature begins to rise. Even when administered in such quantities the antipyretic action of quinine is but slight, and the stomach is often deranged by the drug. The combination of quinine, opium, and digitalis, known as Niemeyer's Pill, has long enjoyed a great reputation in pyrexial cases; but, although its general effects are sometimes salutary, it is rarely very efficient in the reduction of temperature.

Of late no small number of antipyretic drugs have been employed—salicylic acid, salicylate of sodium, aspirin, antipyrin, thallin, phenacetin, antifebrin, and many others. The most effectual seem to be antipyrin and antifebrin, which, when given in sufficient doses, undoubtedly effect a considerable fall of temperature. Antifebrin is a very powerful remedy, but its action is somewhat uncertain. It is never advisable to prescribe larger doses than 2 or 3 grains to begin with: in these quantities it may be repeated at short intervals till 8 or 10 grains have been taken. Unfortunately the reduction of temperature produced is but temporary, and no further effect on the disease is produced. Moreover, the prolonged use of antifebrin and antipyrin is extremely depressing, and causes profuse sweating. Wilson Fox believed that the continued use of small doses of these remedies and of salicylate of sodium had a beneficial result on the general condition, although the range of temperature was not appreciably affected.

Tepid sponging during the pyrexial periods sometimes gives considerable relief, even if it fail to reduce the temperature of the body to any great extent. The use of the cold or tepid bath finds few advocates on account of the further depression which, in the prostrate condition of such patients, is apt to follow its use.

Sweats.—Atropine in doses of $\frac{1}{100}$th to $\frac{1}{60}$th of a grain, given at bedtime, is the most effectual agent we possess for checking sweats. A

combination of extract of belladonna and oxide of zinc is also useful, but it is inferior to atropine. Picrotoxin, $\frac{1}{100}$th to $\frac{1}{60}$th of a grain (Murrell); strychnine, 10 ♏ of the liquor (Lauder Brunton); and agaricin may also be employed with advantage in some cases. In the slighter cases, to sponge the skin with toilet vinegar and water may be sufficient. Arsenic is recommended by some authors, but when the sweats are profuse it has little influence.

Cough.—A moderate cough is the natural consequence of pulmonary disease, and needs no special treatment; moreover, where secreting cavities exist, effective cough is most desirable. But when the cough is very violent, spasmodic, or incessant, and the patient becomes much exhausted thereby, it is necessary to treat this distressing symptom directly. In order to do this with success we must first discover the source of the cough. The more violent the fits of coughing, the more likely are we to find that the cause is situated in the larynx or main air-passages. When the larynx is the seat of ulceration or inflammation local treatment is indicated. Among the most useful sedative remedies we may mention an intralaryngeal spray of cocaine (2 per cent solution), an inhalation of ten drops of oil of peppermint, or of a 20 per cent alcoholic solution of menthol in an ori-nasal respirator, and the use of 1 dram of glycerin of carbolic acid, with 10 drops of chloroform added to half a pint of boiling water in a steam-inhaler. Creosote or carbolic acid, diluted with rectified spirits, or spirits of chloroform, may also be used for inhalation in an ori-nasal respirator. In similar affections of the trachea and large bronchial tubes the same treatment may be applied; but the cocaine spray can only reach the upper part of the trachea at farthest.

Where the cough depends on bronchitis of the smaller tubes the treatment is that of ordinary bronchitis; an alkaline mixture containing bicarbonate of sodium, or citrate of potassium, with a few minims of ipecacuanha wine, may be described; and, if expectoration be difficult, 3 or 4 grains of carbonate of ammonium may be added. In some cases 5 ♏ of antimonial wine may be substituted for ipecacuanha for a few days with excellent effect. Similar drugs may be prescribed in an effervescing mixture. Iodide of potassium in small doses, squill, and senega may also be given when secretion is tough and difficult of removal. Warm drinks, like tea, cocoa, or milk, or a steam-kettle to moisten the air, may often be used successfully for the same purpose, and may be tried before resorting to expectorant remedies. But in many cases all the above-named measures fail to give more than temporary relief, and sedative drugs are required. A linctus containing tincture of belladonna, spirits of chloroform, and glycerin may sometimes prove useful; but in the worst cases opium in some shape is indispensable. A combination of morphine and hydrocyanic acid with glycerin, spirits of chloroform, or syrup of wild cherry, forms an effective linctus, which, however, must not be used too freely lest the digestion be deranged.

Heroin or codeia may be substituted for opium, as they interfere less

with the appetite; but their sedative effects are not equal to those of morphine.

In some cases of early disease, associated with a troublesome cough, much relief may be obtained from a small blister applied to the subclavicular region on the affected side.

Expectoration. — When the expectoration is very profuse, the administration of purified creosote or guaiacol in capsules is sometimes effectual in diminishing the excessive secretion of the bronchi and pulmonary cavities. Turpentine and various resinous drugs are sometimes given for the same purpose; but the expectoration is symptomatic of broncho-pulmonary disease, and rarely requires direct treatment.

Dyspnoea, though seldom a prominent feature, is occasionally very distressing. When due to acute miliary tuberculosis and rapidly advancing pulmonary disease it admits of little relief, and we must be content to administer stimulants, such as ammonia, ether, and brandy.

Attacks of dyspnoea, depending on violent and ineffectual attempts to remove tenacious secretion from the bronchial tubes, may be mitigated by the judicious use of expectorants, the best being ammonia and senega. Steam inhalations of carbolic acid may render good service. In some cases dyspnoea has been lessened by inhalations of iodide of ethyl, as suggested by Dr. R. E. Thompson. Dyspnoea arising from cardiac failure, with attendant oedema of the lung, must be treated by diffusible stimulants and hypodermic injections of strychnine. The dyspnoea of pneumothorax will be referred to presently.

Haemoptysis.—The pulmonary haemoptysis of tuberculous disease may be due to capillary haemorrhage, ulceration of vessels, or aneurysm of the pulmonary artery. The loss of blood in the first case is never extensive, and direct treatment is not required. In the second and third cases haemorrhage is the result of gross lesions of comparatively large vessels, consequently the amount of blood lost may be considerable; yet even in such circumstances spontaneous cure is not infrequently effected by the formation of a thrombus, which seals up the ruptured vessel.

In our treatment of haemoptysis we endeavour to imitate nature's method, that is, to promote thrombosis by lowering the pressure in the pulmonary artery.

It is important to recognise that the faintness which often attends the attack is a symptom of cardiac depression—a condition in itself favourable to thrombosis. In all cases, whether the haemorrhage be profuse or slight, absolute rest must be insisted upon. The patient must keep in bed in a cool airy room, and should maintain a semi-recumbent position. Talking, movement, or excitement of any kind must be avoided. Nothing more than iced milk, meat jelly, and small sandwiches of bread and butter should be given for the first few days, and alcohol in any form must be expressly forbidden. The cough, which

is rarely absent, may be relieved by sucking ice; but when it cannot thus be checked some preparation of opium must be administered. Small and frequent doses of morphia may be given by the mouth, or one-third of a grain may be injected under the skin. This remedy not only exerts a valuable local effect on the injured vessel by the rest which it gives to the lung, but it helps also to allay the restlessness and agitation of the patient. At the same time, seeing that in most fatal cases of haemoptysis death occurs from suffocation rather than from the amount of blood lost, it is clear that the indiscriminate use of morphine is not without its dangers.

When from flooding of the bronchial tubes with blood dyspnoea is very pronounced, cough should not be checked by sedative drugs. With the view of reducing the blood-pressure, sulphate of sodium or magnesium, in doses of 60 grains, should be given every three or four hours to begin with. Saline purgatives cause determination of blood to the intestine, and thus relieve vascular tension, but, unfortunately, their action is rather slow. Aconite has been recommended as a vascular depressant. I have not found any good results from its use. Amyl nitrite has recently been much used for its lowering effect on the general blood-pressure, and favourable reports of its action have been published, but it should not be forgotten that haemorrhage of the most alarming description is apt to cease spontaneously. Astringents, like gallic acid and lead, are still extensively used, but it is difficult to see what effect they can have on aneurysms or ulcerated vessels. Ergot is another popular drug, but, according to Bradford and Dean, it causes a rise of blood-pressure not only in the aortic but also in the pulmonary circuit; a result which must aggravate rather than check haemorrhage from the lungs. Clinical experience shews that the effect of ergot is as uncertain and unsatisfactory as those of gallic acid and lead.

The constipation which is produced by the last two remedies must tend, moreover, to raise blood-pressure, which is injurious. Oil of turpentine in large doses sometimes does good service, probably in virtue of the cardiac depression which it causes. Nauseating doses of ipecacuanha, recommended by Trousseau, seem to act in the same way; but the risk of vomiting is a serious one, and the remedy is now seldom employed. Suprarenal extract and subcutaneous injections of gelatin have been tried without much success. The application of ice to the chest appears to be of very doubtful utility, and in this country is little used.

The artificial induction of pneumothorax to cause collapse of the lung and pressure on the ruptured vessel was unsuccessfully employed by Dr. Cayley in one case of persistent haemoptysis. The cautious admission of nitrogen gas to the pleura is said by Loomis and others to arrest haemorrhage promptly. Attempts to increase the coagulability of the blood by a course of chloride of calcium have proved singularly disappointing in the treatment of haemoptysis. In any case great care is needed in the management of the patient after the haemorrhage has ceased. The diet should be very sparing, and the patient should not rise from

bed for three or four days at least. Free action of the bowels should be secured by the continued use of saline laxatives. Alcohol should be avoided altogether for some weeks.

Pleurisy.—For the relief of the pain of dry pleurisy Dr. F. T. Roberts's plan of strapping the affected side gives excellent results, and can be strongly recommended. But in cases in which one lung is extensively diseased, and pleurisy attacks the opposite side, it may not be possible to apply strapping without dangerously curtailing the already restricted respiratory surface. In such circumstances we must be content with counter-irritation, a few leeches, and poultices; if these fail, a hypodermic injection of morphine will be required.

Dr. Roberts's method is specially adapted for the treatment of pleurisy affecting the lower part of the chest, where the ribs are more yielding and their movement easily restrained. Pleurisy in the region of the upper three or four interspaces seldom causes such acute pain, as the range of movement of the upper ribs is limited; here counter-irritation is generally sufficient. In cases of sero-fibrinous or haemorrhagic effusion paracentesis should not be resorted to unless the quantity of fluid be so great as to cause embarrassment of the respiration. As a rule the fluid is slowly absorbed.

In the comparatively few instances of advanced phthisis in which empyema occurs, the pleura should not be opened unless the abscess point externally, or unless the effusion be so large as to constitute a mechanical hindrance to respiration. In the latter case aspiration is preferable to free incision. The empyema once opened will rarely close again; and free incision appears rather to hasten the patient's end. In cases of early or limited pulmonary disease empyema must be treated on ordinary lines. It occasionally happens that the pus spontaneously becomes inspissated, and undergoes a caseous change.

Pneumothorax.—When pneumothorax arises acutely, with severe dyspnoea and symptoms of shock, stimulants in the form of brandy, ether, or ammonia should be given at once. Morphia has been recommended by some writers to minimise the effects of shock, but in the presence of marked dyspnoea an opiate is contra-indicated. Where the opening is valvular, and air accumulates in the pleural cavity under great pressure, paracentesis may be necessary in order to withdraw a sufficient quantity of air to relieve the pleural tension. Sir R. Douglas Powell advises that the side be afterwards strapped to prevent reaccumulation of air. Paracentesis is sometimes followed by subcutaneous emphysema. In the event of sero-fibrinous effusion, tapping may be successfully employed, but seeing that spontaneous recovery may ensue, it is well to wait for a time before resorting to this measure. In pyopneumothorax incision is generally considered to be unadvisable, and this, no doubt, is true of advanced cases. But the practice of early drainage is worthy of further trial, where the general condition of the patient is fairly satisfactory and the lung is presumably not much affected.

Laryngeal Tuberculosis.—The treatment of this complication may

be general and local. The general treatment is practically that of pulmonary tuberculosis, with certain reservations as to climate. The best atmospheric conditions are a temperate climate, a moderate degree of moisture in the air, and an absence of dust. At the same time, it may be admitted that many cases do well in such a dust-laden and apparently undesirable atmosphere as that of London and other large towns. Tobacco-smoking requires a brief notice. Many patients have no desire to smoke, but some have a craving for tobacco: if so, the patient may be allowed to smoke once or twice a day after meals, provided it be out of doors or in a large, well-ventilated room; the object of these restrictions being to prevent the inhalation of smoky air into the larynx and lungs. The practice of inhaling tobacco smoke should be forbidden. Strong alcoholic drinks, spices, and highly-seasoned dishes irritate the pharynx and epiglottis, and are to be avoided. The practice of complete silence extending over long periods of time is stated to have given good results in some cases. The local treatment is fully described in the article on "Tuberculosis of the Larynx," Vol. IV. Part II. p. 200.

I may say here that to palliate the laryngeal irritation we may prescribe steam inhalations containing carbolic acid and chloroform; or at other times menthol or oil of peppermint on a respirator.

To soothe the pain so often present a 2 per cent spray of cocaine may be used a few minutes before meals, or, better still, insufflations of pure orthoform. The local application of menthol, in the form of a 10 to 20 per cent solution in olive oil, sometimes gives relief; or, again, the insufflation of one-sixth of a grain of morphia with a little starch powder or sugar of milk. Some patients find benefit from sucking ice. When, in spite of these measures, the patient is unable to swallow, Dr. Wolfenden's plan may prove successful; the patient is directed to lie on his face, with his head over the edge of the bed, and to drink through an india-rubber tube. It may ultimately be necessary to have recourse to nasal feeding, which, at times, does excellent service. The operation of tracheotomy is very rarely required, the only indication being afforded by the existence of severe laryngeal stenosis and impending asphyxia. The treatment of tracheal tuberculosis can only be palliative.

Tuberculous ulceration of the pharynx, palate, and tongue must be dealt with in the same way, and with the same reservations as in the case of the larynx. Good results sometimes follow the use of lactic acid when the ulceration is localised and the subjacent infiltration is not very great. Granular pharyngitis and other non-tuberculous affections of the pharynx, which may give rise to troublesome cough and other symptoms, must be treated on the principles laid down in the articles on Diseases of the Pharynx, Vol. IV. Part II. pp. 109-176.

Gastro-intestinal Symptoms.—Loss of appetite, cardialgia, and other symptoms of dyspepsia may be treated by alkaline and acid tonics; but for general use nothing can excel an alkaline mixture consisting of bicarbonate of sodium (15 grains), tincture of nux vomica (10 minims), and compound infusion of gentian (1 ounce), given before meals. If a

sedative action be desired, dilute hydrocyanic acid may be substituted for nux vomica. The good effects of this mixture are witnessed not only by increase of appetite and relief of the dyspeptic symptoms, but at the same time expectoration is facilitated, whereby the cough is indirectly relieved.

In other cases, especially where flatulence is a prominent symptom, better results are obtained by acids, with or without strychnine, given after meals. In cases marked by irritative symptoms—such as vomiting or pronounced epigastric pain and anorexia—a mixture containing bismuth, hydrocyanic acid, tincture of belladonna, or, if necessary, a few minims of liquor morphinae, given before meals, is to be preferred. Bismuth in powder, or in an effervescing draught with hydrocyanic acid, may prove more successful in particular cases.

In all instances of dyspepsia the diet requires a careful survey. The diet should be light and digestible, and the meals small and more frequent than in health. Freshly expressed raw beef juice flavoured with red wine or given with a little warm soup is sometimes well borne in such circumstances. In the comparatively uncommon form, distinguishable by a red glazed tongue, vomiting and anorexia, liquid food, especially milk with lime-water or soda-water, koumiss, veal- or chicken-broth, will be required; and complete rest in bed should be enjoined.

Inasmuch as this kind of gastric disorder mostly affects patients suffering from pyrexia and other symptoms of progressive disease, the outlook is very grave unless the gastritis can be speedily removed so far as to enable the patient to digest an adequate supply of food. If the symptoms resist the measures indicated, it may be necessary to rely exclusively on peptonised nutrient enemas for a few days, giving only a little iced water by the mouth, for the relief of thirst. Fortunately this form of gastric disturbance is not of very frequent occurrence.

In most cases of obstinate dyspepsia mild purgatives are called for such as a small dose of calomel (half a grain to a grain at bed-time), followed by a teaspoonful of Carlsbad salts, dissolved in 2 or 3 ounces of hot water, in the early morning, or a pill of aloin and cascara. Violent purgatives should be carefully avoided altogether, owing to the risk of setting up intractable diarrhoea. A tumblerful of hot water, sipped at bed-time for a few nights, often gives great relief by washing out the stomach and removing remnants of undigested food which are apt to undergo decomposition, and thus to aggravate the catarrhal condition of the stomach. Dilatation of the stomach occurs occasionally, and washing out may be required; though the cases in which this operation can be recommended are very few, as the disturbance caused by the passage of the stomach-tube in feeble patients may be attended with serious consequences. Gastric digestion may be assisted by the administration of pepsin or papain, but, except as a temporary expedient, little benefit is to be expected from this line of treatment.

Diarrhoea is a symptom that should never be neglected; it should be treated by rest in bed and the application of warmth to the abdomen

and extremities. In many instances it depends on slight errors of diet; and in such cases regulation of the diet, and a mild purge to free the intestine from irritating substances, may be all that is required in the way of treatment. For this purpose we may prescribe 2 drams to half an ounce of castor oil with 10 minims of laudanum, or a small dose of calomel. If the diarrhoea do not speedily yield, bismuth should be given, in 20-grain doses, with a few minims of laudanum. In the far more serious case in which diarrhoea is the result of tuberculous ulceration or lardaceous disease, powerful astringents, combined with opium, are indispensable. A mixture containing aromatic sulphuric acid, tincture of opium, and decoction of logwood, or again of subnitrate of bismuth, tincture of catechu, and tincture of opium, will often suffice to keep the diarrhoea in check. But in the most severe cases we must have recourse to stronger remedies, the best, perhaps, being a pill containing sulphate of copper ($\frac{1}{4}$ grain) and opium ($\frac{1}{2}$ grain), given once, twice, or three times a day, as may be required. In cases where the ulceration affects the lower end of the colon the enema opii (B.P.) gives more relief than anything else. It will generally be necessary to revise the diet carefully; the most suitable food in the acute cases being milk, koumiss, or carefully prepared beef-tea; but when the diarrhoea lasts for weeks, boiled fish and tender meat, freed from fat and pounded or finely minced, may be given in small quantities. Digestion may be aided by peptonisation of the milk, and by the use of pepsin or papain after meals. The slightly bitter taste of peptonised milk may be masked by the addition of a teaspoonful of rum, cognac, or liqueur.

If the diarrhoea be accompanied by much pain, hot fomentations should be applied to the abdomen, and the warmth of the extremities sedulously maintained. In the rare event of serious intestinal haemorrhage, an enema, consisting of a teaspoonful of oil of turpentine suspended in 2 ounces of starch mucilage, should be administered at once. Acute peritonitis must be treated on general principles by opium and hot fomentations. In the yet rarer instances in which perforation can be diagnosed the propriety of surgical interference must be considered; but the patient's general condition and the extent of the pulmonary disease may not justify such measures.

In chronic tuberculous peritonitis with effusion, whether serous or purulent, incision has, in several instances, been followed by arrest or cure. A similar result may also ensue without any surgical measures; in these cases, no doubt, the effusion is serous. Some physicians believe that the application of mercurial ointment to the abdominal wall promotes absorption of the fluid.

When suppuration has occurred, incision should not be delayed. Drugs seem to be of little use in this affection.

Renal Symptoms.—Albuminuria, whether due to nephritis or amyloid disease, is mostly found in advanced chronic cases. In such circumstances active treatment, by rigorous milk diet and purgation, is quite out of place. If possible, milk should be taken freely; but it is not advisable

to prohibit a certain amount of meat and fish if the patient can take them. The drug treatment may include digitalis and iron, mild saline diuretics, and an occasional small dose of blue pill. But treatment should be addressed primarily to the general condition rather than to the renal disease, which is probably a local consequence of the constitutional malady.

In the few instances in which nephritis occurs at an early period of the pulmonary disease, and in which the health is not seriously affected, treatment may be conducted on ordinary principles.

The tuberculous pyelitis and cystitis of advanced cases do not admit of more than palliative measures. If the lung disease be slight, surgical advice should be sought.

Nervous Symptoms.—For the treatment of meningitis, tuberculous tumours of the brain, and nervous complications in general, reference must be made to the proper articles.

It seems desirable, in conclusion, to sum up the general plan of treatment suitable for an ordinary case. In the first place, attention must be carefully directed to the rules of general hygiene; to the importance of spending as much time as possible in the open air, and the necessity of an abundant supply of food. For most cases a period of sanatorium treatment is advisable. Excepting in the more favourable instances, in which the disease is quiescent, some form of tonic medicine will be required from time to time, the best being an alkaline bitter mixture, such as that already indicated. Narcotic and sedative drugs generally should be employed with great caution, because of their prejudicial influence on digestion; and complications, as they arise, must be treated on general principles.

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P. K.

SYPHILITIC DISEASE OF THE LUNGS

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THE difficulty so long experienced in deciding in doubtful cases upon the nature of pulmonary lesions was chiefly due to the absence of any certain test of a tuberculous lesion. This difficulty has to a great extent disappeared since the discovery of the pathogenetic organism of tuberculosis. Still further aid has since been given by a like discovery with regard to syphilis, although it cannot be stated that the presence of the *Treponema pallidum* is proof of the syphilitic nature of a pulmonary lesion.

In a case reported by Max Koch of interstitial and desquamative white pneumonia occurring in a woman aet. 39, who presented numerous other syphilitic lesions, the lungs, in addition to the pneumonic changes, shewed diffuse bronchiectasis, bronchiectatic cavities, and fibrous peribronchitis. By treating portions of the right lung by Levaditi's silver method in its original form countless spirochaetae were found in the sections derived from the cavity walls. "These exactly resembled those which are found in such immense numbers in the organs of newly-born syphilitic children. In the narrow necrotic layer facing the lumen of the cavity there were found in sparse numbers, between the countless bacteria brought into view by the silver method, rod-shaped organisms that were mostly plump, somewhat curved and rounded at the ends. Further towards the periphery the bacteria became fewer in number and finally were altogether absent. In these areas only spirochaetae were found, disposed between the bundles of connective tissue, in the vessel walls and in the lumen of the blood-vessels; in the same way that the *Spirochaeta*

pallida is seen in congenital and acquired syphilis." In two cases of pulmonary gangrene in which there was no suspicion of syphilis, Küster, by using a similar method, discovered spirochaetae of the type of pallida. In these cases the microscopical appearances and distribution of the spirochaetae were precisely similar to those above described. Having seen Küster's preparations, Koch concludes that the discovery of spirochaetae of the type of pallida cannot, in any circumstances in the present state of our knowledge of that organism, "be taken as a criterion for estimating the syphilitic or non-syphilitic nature of pulmonary changes."

Morbid Anatomy. — The following pulmonary lesions have been attributed to syphilis: (*a*) gumma; (*b*) white hepatisation (Virchow, Weber), or "épithéliome" of the lung (Lorain, Robin); (*c*) grey infiltration (Welch, Pancritius); (*d*) lobular pneumonia or bronchopneumonia (Förster, Welch); (*e*) fibroid induration; (*f*) changes in the lymphatics (Hermann Weber); (*g*) a destructive disease, formerly called "Syphilitic Phthisis." It will be convenient to consider separately the lesions of the hereditary and the acquired disease.

Hereditary Syphilis.—The pulmonary changes in hereditary syphilis may be either circumscribed or diffuse; to the former the term "gumma" is applied; the latter are classified under the head of "pneumonia." It is, however, far more common to find the two changes associated than to meet with either separately.

A. *Gumma.*—As this lesion is of comparatively rare occurrence in congenital syphilis, and when present does not differ either in appearance or in microscopical structure from that found in the acquired disease, a more distinct picture of the morbid anatomy of the two affections will be obtained by describing it under the latter heading.

B. *Pneumonia.*—Two different lesions are included under this heading—namely, "white pneumonia" and "interstitial pneumonia"; but of these it must again be stated that they occur more often in combination than apart.

(*a*) *White Pneumonia* (Virchow, Weber), *Épithéliome* of the Lung (Lorain, Robin).—This lesion in its true form is rare, and is found only in the lungs of stillborn children, or of such as have survived their birth a very short time. Other unmistakable signs of congenital syphilis are usually present, and in such cases gestation has seldom proceeded to the full term.

It is a diffuse change affecting a lobe either as a whole or in part; or one or both lungs may be completely consolidated.

In stillborn children the affected part is bloodless and airless; even if force be used, it may be impossible to inflate it; but in infants several days old the lung always contains some air.

The lung is much increased in size, and its surface may be marked by the ribs. It is solid, dry, whitish-yellow or greyish-white in colour; but sometimes presents a reddish marbled appearance. The section differs from that of an ordinary pneumonic lung in that the granular appearance characteristic of the latter is absent, the surface being smooth and somewhat shining.

On microscopical examination in true cases the interstitial tissue is not increased. The alveolar walls are thickened, and the small bronchi and the alveoli are filled with masses of cells, of which some are round and others have more or less the character of epithelial cells: the cells are for the most part undergoing fatty degeneration and are beginning to break down. The alveoli are markedly enlarged. The colour of the affected area is due partly to the above changes, but in part also to diminished blood-supply the result of pressure upon the capillaries. The lung tissue surrounding the consolidated part may shew some degree of emphysema. Ecchymoses may be present in the pleura, pericardium, and thymus gland; but these appearances are probably incidental to the mode of death.

The bronchial glands are as a rule enlarged and on section dense, from a new formation of fibrous tissue enclosing cells arranged in a concentric manner.

White pneumonia is a lesion of purely pathological interest, as, owing to the filling of the alveoli with cells, the subjects of it, if not stillborn, are unable to maintain the respiratory function for any length of time, and soon succumb.

(*b*) *Interstitial Pneumonia.*—This is the most common pulmonary manifestation of hereditary syphilis; but it occurs more frequently in association with some of the changes described under "white pneumonia" than as a purely interstitial lesion. In its true form it is distinguished by a small-celled infiltration of the interalveolar connective tissue, the alveolar epithelium remaining unaffected. This change may be present to a very varied extent. In some cases lungs thus affected appear normal to the naked eye, the lesion being only discoverable on microscopic examination.

In well-marked cases the lungs are large and hard and of a pale or dark greyish-red tint. The change may be present throughout the organs, or a single lobe or portion of a lobe may be alone affected. To the naked eye the lung tissue presents a decidedly coarse appearance. On microscopical examination a marked increase is seen in the interalveolar and interlobular connective tissue, which forms broad meshes including small spaces wherein the alveoli are either crowded together or completely obliterated.

In some cases the interalveolar meshes appear to consist of a dense capillary network, the vessels being dilated and tortuous. Around the vessels and bronchi there is a marked increase of the connective tissue, and the tunica intima of the small arteries is thickened. The alveolar epithelium may shew desquamative changes, and brown and yellow pigment granules may be present.

Interstitial pneumonia is often found in association with congenital syphilitic lesions in the skin, with interstitial hepatitis, and with changes in the epiphyses; but it is also found in cases in which gummas are present in the lungs, liver, and other organs. The change begins during fetal life, and at birth may have affected the lungs extensively. In such cases

life is of short duration and death occurs from asphyxia, as is shewn after death by the frequent presence of ecchymoses in the pleura, pericardium, and thymus gland. When the change is less advanced at birth, such children may die at a later period by a slow process of carbonic acid poisoning, the first sign of which may be that a child previously fretful and noisy becomes quiet.

In cases in which the other organs are healthy, or nearly so, life may be prolonged for months or years; such subjects are, however, specially liable to acute disease of the respiratory organs, such as pleurisy, acute bronchitis, and bronchopneumonia.

From the above description it will be seen that the morbid processes concerned in the production of the gummatous and diffuse changes found in the lungs of syphilitic children chiefly affect the connective tissue and small arteries. They are:—(i.) A round-celled infiltration and proliferation of the interlobular and interalveolar connective tissue, originating in the cellular tissue around the bronchi, and leading to marked thickening of the framework of the lung. (ii.) An isolated perivascular cell-proliferation, which begins around the small arteries, and is accompanied by changes in the tunica intima (Hochsinger). Both the periarterial and peribronchial granulations may occur as separate nodules or node-like foci; or they may be diffused over large portions of the lungs. A well-marked desquamation of the alveolar and bronchial epithelium is almost always present, but it is quite a secondary process.

In the account here given of the pulmonary changes found in hereditary syphilis the descriptions of Heller, Spaundis, and Hochsinger have been followed, and to these authors I desire to acknowledge my indebtedness.

Association of Congenital Syphilis and Pulmonary Tuberculosis.—Syphilis, by lowering the resisting power of the individual, may dispose to tuberculosis; and it has been shewn by Hochsinger that the virus of syphilis and tuberculosis may be jointly transmitted from parent to offspring. This observation is of much importance, and throws a new light upon the nature of the pulmonary lesions found in infants the subjects of congenital syphilis. Hitherto it has often been assumed, on evidence which is now proved to be insufficient, that such lesions are of syphilitic origin; whereas it is clear that they may be due to an associated tuberculous infection.

In three infants suffering from congenital syphilis, and presenting symptoms of infiltration of the lungs, the pulmonary disease was found after death to be due to tuberculosis and not to syphilis. Tubercle bacilli were found in the lungs in all the cases.

The first case was observed in 1891 in a child not quite three weeks old; the second in 1891 in a child twenty-four days old; the third in 1893 in a child eleven weeks old.

Case I.—Anna B., aet. nearly three weeks. The parents had been married nine years. The father acquired syphilis shortly before marriage. The mother died from pulmonary tuberculosis three months after the

birth of the child. The first and second children of the marriage were stillborn; the third and fourth died during the first week; the fifth and sixth were living, aged four years and two years respectively. The case of the seventh child is here described. From the time of birth she was sickly and suffered from nasal obstruction, snuffles, and dyspnoea. Rales were present in the chest. At the end of the second week a bullous eruption appeared on the nates. The child presented all the ordinary external signs of congenital syphilis, and was shewn at the Vienna Dermatological Society as a case of gummatous disease of the viscera.

On examination of the chest there was marked dulness on the left side from the angle of the scapula downwards, with bronchial breathing over the dull area. The respiratory murmur was harsh over both lungs, with rhonchi and coarse rales. The spleen was enormously enlarged, extending as low as the anterior superior spine of the ilium; the liver could be felt four fingers' breadth below the costal margin, it was hard and the edge was rounded. The diagnosis was pulmonary and visceral syphilis. Mercurial treatment was prescribed. The child died on the thirty-first day after birth. On post-mortem examination the internal organs were found extensively infiltrated with tubercle. Both lungs shewed tubercles varying in size from a miliary granulation to a walnut. A nodule as large as a hen's egg occupied the right middle lobe. The left lobe of the liver was almost completely replaced by a caseous nodule; numerous tubercles studded the right lobe. The spleen was enlarged to nearly four times its normal size and contained similar deposits. Tubercles were also present in the kidney, pericardium, and peritoneum. The mesenteric and bronchial glands were enormously enlarged, and in many places caseous. Tubercle bacilli were present in all the lesions. None of the lesions in the internal organs was of syphilitic origin.

Case II.—Victoria S., twenty-four days old. The mother had previously brought three children suffering from congenital syphilis to the same clinic. She had previously stated that she had not had syphilis. Nothing was known of the father, and it is not certain that either parent was tuberculous. The child had snuffles and presented all the characteristic appearances of congenital syphilis. There was a confluent papular syphilitic eruption on the nates and elsewhere. The percussion note over the left lung was dull and the breathing bronchial, with consonating rales. The spleen was slightly, and the liver markedly, enlarged. The temperature was normal. Mercurial treatment was ordered.

The patient was shewn at the Vienna Dermatological Society as a case of syphilitic pemphigus and syphilitic pneumonia. The child died on the thirty-eighth day.

On post-mortem examination the left lower lobe was solid from greyish-white infiltration. There was acute catarrh of the bronchi of the left upper lobe and throughout the right lung, also of the larynx and trachea. The mediastinal and bronchial glands were enlarged, but not obviously caseous. The liver was large, reddish-brown, somewhat indurated and with rounded margin. On microscopical examination of the

lungs confluent peribronchial and perivascular tuberculosis was found, with tubercle bacilli. In the liver recent interstitial inflammation was present, with fatty degeneration of the liver-cells. No traces of tuberculous lesions were found in any other organ than the lungs.

Case III.—Auguste G., eleven weeks old. The mother, aet. 28, was suffering from pulmonary tuberculosis. She had had five illegitimate children and denied having had syphilis. Nothing was known of the father. The child presented the characteristic appearances of congenital syphilis, and had snuffles and a syphilitic rash on the buttocks. The rash appeared during the third week. The child had suffered from cough since it was five weeks old. There was doubtful dulness over the right lower lobe with bronchial breathing and abundant moist rales. The liver was very large and hard, with a rounded edge. The spleen extended four fingers' breadth below the costal margin. The temperature was normal. Mercurial inunction was ordered. The child died aged sixteen weeks.

Post-mortem.—The right lower lobe was solid from a homogeneous, greyish-white infiltration. Greyish-red and yellow tubercles were disseminated throughout the upper lobe. The lower half of the left lower lobe was collapsed. The bronchial glands were enlarged and caseation was beginning. The liver was fatty and slightly granular. In the portal fissure there was a caseous lymphatic gland the size of a hazelnut. The mesenteric glands were caseous. The spleen contained a large caseous nodule. Microscopic examination shewed the characteristic signs of "chronic tuberculous bronchopneumonia, tuberculosis of the spleen and mesenteric glands, and syphilitic interstitial inflammation of the liver with well-developed inflammation of the vessels."

It is clear from the perusal of these cases that it will be necessary in future, even when the evidence of syphilis in the fetus is undoubted, to examine carefully for tubercle bacilli before a pulmonary lesion is attributed to syphilis.

Acquired Syphilis.—To present a trustworthy account of the morbid anatomy of acquired syphilis of the lungs is a far more difficult task than that just attempted. In considering a matter of such uncertainty I have preferred to rely upon evidence which is at hand and may be put to the test, rather than upon that to be found in the records of a period when, owing to the absence of any certain test for tuberculosis, the difficulty of distinguishing between the pulmonary lesions of tubercle and syphilis was almost insuperable.

A study of the specimens of pulmonary syphilis contained in the London museums shews that the possibility of the changes being due to tuberculosis was in nearly all cases carefully considered. These specimens and the records connected with them probably constitute the most trustworthy evidence on which to base a description of the morbid anatomy of the acquired disease, and, as will be seen hereafter, they have been fully utilised.

Pathology and Morbid Anatomy.—Bronchial catarrh may occur as a

manifestation of the secondary stage of syphilis, and possibly also of the period of incubation (Walshe). The fact that bronchitis, occurring without obvious cause in syphilitic subjects, may be greatly alleviated or cured by the administration of mercury, is strongly in favour of this view. In the late secondary and tertiary stages gummatous infiltration of the submucous tissue of the trachea and bronchi is not infrequent, and may be followed by the formation of fibrous tissue which, subsequently undergoing cicatrisation, produces stenosis, one of the most characteristic syphilitic lesions in the main bronchi. (For Syphilis and Syphilitic Stricture of the Trachea see Vol. IV. Part II. pp. 333 and 340.)

No definite statement can be made as to the most common period of the occurrence of gumma in the lungs; cases of which the real nature could not be doubted have been recorded as early as two years and as late as twenty years after infection.

The pulmonary lesions of acquired syphilis belong chiefly to the late tertiary stage of that disease.

A. *Gumma.*—Gummas may occur either singly or in numbers, and may vary in size from that of a hemp-seed or a hazel-nut to that of a hen's egg, but the latter size is of rare occurrence. A gumma may be found in any part of the lung, but more commonly within its substance than upon the surface; and more often about the root, near the large vessels and bronchi, than elsewhere. The lower lobes are perhaps more often affected than the upper.

A gumma is rarely seen in the very early stage, of which alone the name is in any sense descriptive; but it is said then to present a gelatinous or glutinous appearance, thus resembling a similar growth in the liver. At a later stage it is of a grey colour, tinged with various shades of a red, white, or yellow, and presents on section a smooth and semi-transparent appearance. At a still later period a gumma forms a well-defined nodule of a yellowish colour, firm and dry. Inflammatory changes in the surrounding lung may lead to the production of a well-marked fibrous capsule, but this may be absent. The gumma may break down, and, its contents having been discharged, an irregular cavity may result; but this is, both absolutely and also in comparison with the occurrence of a similar change in caseous tuberculous masses, very rare.

The chief difference between a gumma of the skin, for example, and one of the lung is that whilst the former tends towards necrosis the latter tends to be transformed into a mass of scar tissue, the contraction of which causes puckering of the surrounding lung and overlying pleura. By the deposition of lime salts a gumma may become calcareous.

In histological structure a gumma of the lung does not differ essentially from a similar growth elsewhere. In the early stage it is seen to consist of a granulation tissue composed of small cells about $\frac{1}{2500}$ in. in diameter, arranged concentrically around the sheath of the small vessels, and in some cases around the small bronchi. At a later stage the nodule becomes opaque in the centre, and its cellular structure can no longer be recognised; but fatty and albuminous granules are seen instead in the

meshes of a dense fibrous stroma. Finally it becomes converted into a mass of dense cicatricial tissue. A gumma may form a centre from which a small-celled growth may infiltrate the surrounding tissue, spreading chiefly along the bronchioles.

The walls of the neighbouring alveoli are also infiltrated with small cells; and the alveolar spaces contain inflammatory products, due either to epithelial proliferation or to the presence of cells of a character similar to those constituting the nodular masses already described. Giant cells are occasionally present, but are not so characteristic a feature of gumma as of tubercle.

According to Councilman, the essential process in the production of a gumma in the lung is a pneumonia with fibrinous exudation, accompanied by fibrous change in the alveolar walls, the whole subsequently undergoing caseation. The first step in the process is stated to be a hyaline degeneration of the capillaries of the affected area; this is followed by atrophy of the alveolar walls. The alveoli become distended with large pale epithelial cells and fibrin; the cells also undergo the hyaline degeneration, forming smooth bodies staining with eosin, and varying in size from one-half the diameter of a red blood-corpuscle up to that of a large epithelial cell. The capillaries become converted into rigid tubes and their lumen is much narrowed. Similar changes occur in the small veins and arteries. Immediately around the bronchi and arteries there is a formation of connective tissue, and here the alveolar walls shew much thickening and contain many small round cells.

The whole of the structures thus altered tend to undergo necrosis, and when that change is complete a caseous-looking mass results.

The following descriptions of specimens in the Museum of Guy's Hospital well illustrate the appearances presented by gummas in the lungs. It will be observed that all the specimens here described were removed from the lungs of adults.

No. 254.—A portion of the upper lobe of a lung shewing on the cut surface two masses, one of which was described in the recent state as "consisting of a circumscribed nodule of a firm, yellowish, dry substance, corresponding in all particulars to that in the liver (a gumma), except in being somewhat less firm: the other is softening, breaking up, and in process of forming a cavity. Histologically the nodules are seen to consist of fibroid tissue with many areas of caseation and a few giant cells.

From the report of this case by Sir S. Wilks the following additional particulars have been derived:—The patient was a sailor, aged 29. No history was obtained; he was moribund from laryngeal obstruction when admitted, and there was profuse expectoration of mucus and blood. There was a scar in the groin, and phimosis from a contracting sore on the penis. The whole mucous membrane of the larynx and trachea was deeply ulcerated, and the walls thickened by an infiltration of fibrous tissue into the submucous structure, producing great induration. The thyroid cartilage was bare at one spot, the lymphatic glands in the neck were enlarged. The liver contained a dozen hard, round, fibrous tumours—the largest

the size of a marble—yellowish-white, tough, and of leathery consistence, dry, and emitting no juice on pressure. In two or three the circumference of the tumour consisted of a translucent structure; and this was evidently the more recent formation, the opaque and yellow parts being probably tissue undergoing a degenerative change. At one spot a deep cicatricial appearance was produced by the contraction of a group of these small nodules. Microscopically the nodules consisted of nucleated fibres and fibrous tissue.

No. 255.—The lower lobe of a left lung from a man, aged 27, who died from erysipelas of the larynx. The specimen shews at its hinder part a large yellowish mass partially separated from the surrounding tissue. Smaller nodules are seen in the adjacent lung. The pleura over the gumma is much thickened. Histologically the nodule consists of fibrous tissue which stains with difficulty. There were many gummas in the liver. With the exception of the above lesions and some bronchitis the lungs were healthy. There was a chancre on the penis and suppurating buboes.

No. 256.—A portion of lung shewing scattered through it several small masses of irregular shape, yellowish in colour, and firm on section. These masses are easily separable from the surrounding lung, which is healthy. Histologically the nodules shew a central area of caseous material surrounded by a narrow zone of fibrous tissue in which are many small round cells. The liver contained a single gumma, and was in a condition of diffuse syphilitic hepatitis. There were several gummas in the testes. From a man, aged thirty-nine, who had suffered from cough and dyspnoea for six months. He was admitted for hepatic ascites and slight jaundice.

The following specimen from the same Museum illustrates the appearances presented by a gumma which has undergone fibrous transformation:—

No. 253.—A section of a right lung. From a man, aged thirty-six, admitted for fracture of the cervical spine. At the upper part of the lower lobe is a circumscribed patch of fibroid material with radiating processes extending into the surrounding pulmonary tissue. The pleura over it is much thickened. The interlobar septum is thickened, and from its upper portion similar fine fibrous strands radiate into the upper lobe. Other portions are very emphysematous (also fibroid and pigmented). No tubercle was found anywhere. There was lardaceous disease of the liver, spleen, and kidneys. Both testes were good specimens of syphilitic orchitis.

The following description of a specimen in the Museum of St. George's Hospital illustrates a combination of the caseous and fibrous stages of a gumma (15):—

"Section of a right lung near the root. In the posterior and upper part of the lower lobe, close to the spine, there is an area shewing marked fibrosis; situated within it is a caseous mass the size of a marble, somewhat loose. The overlying pleura is adherent and

thickened; bands of thick greyish fibrous tissue pass inwards from the pleura, and joining with each other form a meshwork." No tubercle in any organ; surface of the liver scarred from perihepatitis. Large caseous gumma near the portal fissure, with smaller ones in its neighbourhood. Liver cirrhotic and lardaceous. Gummas in both testes. From a male patient who contracted syphilis in 1884, six years previous to his death. In 1886 he suffered from syphilitic disease of the testes and sores on the right elbow. Death was due to uraemia.

Lobular or Broncho-pneumonia.—A careful review of the evidence on which it is believed that inflammatory changes of the lobular or broncho-pneumonic type occur as the direct result of syphilis impresses me with the conviction that many of the cases described in the past as presenting such lesions were really cases of tuberculosis.

In the following case (5), however, such a possibility may be excluded. It will be observed that the pulmonary lesions were secondary to and in continuity with the growth of large gummas in the liver and spleen. The specimen is in St. George's Hospital Museum:—

Left lung.—The lower lobe is deeply congested and partially consolidated; the consolidation is in patches as in catarrhal pneumonia. Some of these masses appeared purulent, others fatty or caseous. The size varied from 3 mm. to $\frac{1}{2}$ mm.; each patch or nodule was surrounded by a deeply congested zone. Right lung.—The lower lobe presented changes similar to the above; it was adherent to the diaphragm, through which a large caseous gumma in the liver had extended into the lung. At the upper margin of the caseous mass there was much fibrous induration and exudative consolidation of the pulmonary tissue. For the microscopical changes, which are given in great detail, the reader is referred to the original article. There was a gummatous mass chiefly in the upper part of the right lobe of the liver measuring $5\frac{1}{2}$ in. by $4\frac{1}{4}$ in., and another occupying the upper third of the spleen. That organ was greatly enlarged, weighing 2 lb. 6 oz. Both liver and spleen were firmly adherent to the diaphragm, and the muscular tissue of the latter was in part destroyed by the extension through it of the gumma in the liver. The specimen was taken from a man, aged forty-three, who contracted syphilis in 1861, twenty-five years before his death. He had periostitis of the tibia in 1864; left hemiplegia in 1871, and again in 1876.

Fibroid Induration.—The following are the more important changes of this nature which have been attributed to syphilis: (*a*) thickening extending from the hilum around the bronchi and vessels; (*b*) isolated masses of fibroid tissue in various parts of the lung; (*c*) diffuse changes occupying the whole or the greater part of one lung.

The marked tendency of gummatous lesions to spread along the vessels and bronchi has already been referred to.

The following case (6) is an example of syphilitic fibrosis illustrating

the first variety of this lesion:—Woman aged fifty.—Thrombosis of cerebral artery; hemiplegia. Pigmented excavated scars on left leg, due to old syphilitic ulceration. Lungs.—Emphysema. Right lower lobe contained a deep depression and a much-puckered cicatrix due to pigmented fibroid bands running into the lung tissue. No caseous or calcareous nodules. No pleural adhesions. Microscopical examination.—The fibroid tissue is arranged chiefly around the vessels and bronchi with a more or less concentric disposition. The coats of the vessels are much thickened. There is a small-celled growth invading the alveolar walls, which are also much thickened. In places the cells and nuclei are aggregated in heaps.

The following case illustrates fibrosis in the form of scattered areas of induration (6):—Woman aged twenty-five.—Fracture of cervical spine. Pigmented and puckered cicatrix and syphilitic ulcers on left leg. Calcified gumma in the liver. Right lung.—Upper lobe healthy. Middle lobe presented in the centre large irregular patches formed by radiating bands of fibroid tissue; also smaller scattered patches of the same nature: the bands whitish, not pigmented. One patch contains a calcified nodule. No pleural adhesions. Left lung.—Adhesions over lower lobe; and whitish, puckered, depressed fibroid patches with irregular thickening of the pleura. On section extensive fibroid infiltration; bands appear to run into the lungs from the pleura. Some small rounded caseous patches are also present.

The following specimen from the Museum of Guy's Hospital (14) illustrates the appearances met with in "diffuse syphilitic fibrosis of the lungs." The patient a man, aged fifty-four, had suffered from winter cough for some years. No. 252.—A portion of a right lung in which there is a considerable excess of fibroid material appearing on the cut surface as a delicate network traversing the pulmonary tissue in all directions. The fibroid change is less marked at the apex than at the base, in which latter situation many of the air-vesicles are dilated; over this area the pleura is slightly thickened and is adherent. The dense fibroid tissue that pervades the lung shews, scattered through it, numerous collections of small round cells not undergoing caseation. No giant cells are present. The walls of the small arteries are thickened. One or two small cavities the size of peas, with soft caseous contents, were situated near the root of the right lung, probably softening gummas; no tubercle bacilli could be found in them. The condition of the left lung resembled that of the right. The liver was scarred; the testes were fibroid. Death was due to bronchitis.

Changes in the Bronchial Glands and Lymphatics of the Lung.—In a case of syphilitic disease of the liver, lungs, dura mater, cranium and sternum, recorded by Sir Hermann Weber, the bronchial glands and lymphatics of the lung presented the following appearances:—The bronchial glands were much enlarged—some being of the size of a pigeon's egg, some only that of a hazel-nut. From the greyish-white section of the larger glands, which were rather soft, a creamy fluid exuded, consisting of fat-globules,

granular corpuscles, and an abundance of large cells in a condition of fatty degeneration. The less enlarged glands were harder, their section offered a marbled appearance, large white patches, almost like bacon, being interspersed with greyish-red, very vascular tissue. No juice exuded spontaneously or could be squeezed from the section. Large nuclei and nucleated cells were the principal microscopical elements, with a very small proportion of fibres thickly studded with nuclei. The lymphatics leading from the lungs to the enlarged glands were dilated and their ramifications on the surface and throughout the lungs were distended with creamy fluid.

A similar appearance is described in the case of Drs. Delépine and Sisley already quoted. "Immediately under the pleura there was a network composed of ramified tracks. The appearance suggested lymphatics distended with cells or some fatty products." The lymphatics of the subserous layer of the pleura were considerably enlarged over areas corresponding to the yellow patches (? of syphilitic bronchopneumonia) within the lung.

Sir H. Weber rejects the view that the bronchial glands were first affected by the syphilitic virus, and that the engorgement of the pulmonary lymphatics resulted from obstruction to the passage of the lymph.

A progressive destructive disease, the so-called "syphilitic phthisis."

It appears to me that the question of the existence of a syphilitic lesion of the above form can only be settled by a careful study of cases which fulfil the following conditions:—(i.) The cases must be complete; that is, the symptoms observed during life must be considered in connexion with the lesions discovered on post-mortem examination. (ii.) The evidence of syphilitic infection must be undoubted. (iii.) Repeated examinations of the sputum must have been made, and tubercle bacilli invariably absent; and the absence of tubercle from the lungs (as the cause of the lesions) must be proved by post-mortem examination. (iv.) Syphilitic lesions about the nature of which there can be no doubt must be found in other organs.

From such evidence alone can we hope to construct the clinical history and morbid anatomy of advanced syphilitic disease of the lungs. The following cases illustrate this variety of the disease:—

Case I.—Charles N., aged thirty-eight, bricklayer. In 1892 he suffered from cough, with expectoration and pain on the left side of the chest. In 1893 he had night-sweats and dyspnoea. From January to May 1894 he was an in-patient of the Brompton Hospital under the care of Dr. Mitchell Bruce; the diagnosis then recorded was "Syphilis (?), tracheal stenosis, chronic bronchial catarrh, induration of the left upper lobe and of the left base with pleural adhesions over that area. Cicatrisation of the soft palate and adhesions of the right posterior pillar of the fauces to the back of the pharynx." There were no bacilli in the sputum. He continued fairly well until October 1894, when he expectorated a large quantity of offensive purulent material for two consecutive days.

Cough was very severe at this period. His health subsequently improved, and so remained until 20th February 1895; when in the course of a few days he brought up about a quart of blood-stained sputum. Haemorrhage then ceased and dyspnoea diminished. On 5th March, cough and dyspnoea increased and he became seriously ill, with constant headache and slight delirium. Oedema of the feet subsequently intervened. On 15th March 1895, he was admitted to the Brompton Hospital under the care of Dr. Percy Kidd. On admission he was reported to be fairly well nourished. He stated that he had not lost weight, and, beyond an occasional streak of blood in the sputum, there had not been any haemoptysis. There was marked stridor and severe cough. Right lung resonant everywhere; breath-sounds much exaggerated, expiration prolonged. Loud hoarse inspiratory and expiratory stridor all over the lung; sibilant rhonchi general. Left lung.—Expansion much diminished; resonance much impaired front and back; breath-sounds weak; expiration prolonged; fine crackling rales over the whole of lung; vocal fremitus and resonance diminished. Expectoration profuse and difficult to expel. No tubercle bacilli found. Temperature, 99° F. It varied between that point and 96° F. during the time the patient was in hospital. The dyspnoea gradually increased, and death occurred on 10th April.

Necropsy.—Scars on tongue, glans penis, and scrotum; and adhesions of skin to left testis. Marked thickening of the right tibia. Larynx normal. Trachea narrowed at the lower end. Recent ulceration from cricoid downwards for two inches; below this, down to point of bifurcation, there was extensive scarring of the cartilaginous portion; and also at its line of junction with the posterior wall. The submucous tissue was extremely thickened. Cartilages bare in several places. The main bronchi were much scarred and shewed extreme narrowing. The bronchus to the left upper lobe was impermeable to a probe. Right lung.—Old pleural adhesions over the upper lobe, recent pleurisy with effusion at the base. Emphysema, with reticular fibrosis especially around bronchioles. Deep in the upper lobe at the edge of one of the main bronchi there was a large black fibroid mass, with fibroid radiation into the surrounding tissue; elsewhere two small, hard, raised masses, one with fibrous strands running up to it. Base solid from bronchopneumonia. No appearance of tubercle. Left lung.—Upper lobe extremely contracted, containing no normal tissue. It consisted of deeply pigmented blackish-grey fibrous tissue surrounding the openings of bronchial tubes, and bronchiectasia. At the centre there was a smooth-walled cavity about the size of a small chestnut into which a bronchus opened. No appearance of tubercle. Lower lobe.—Emphysematous, with reticular fibrosis along the margin and at the base. Bronchi dilated, but not to a marked degree. About the centre point of the outer margin there was a small nodule, probably a gumma, white and firm, and surrounded by a pigmented fibrous capsule. The extreme base consisted of indurated fibrous tissue, extending from the pleura

to a cavity the size of a marble, into which a small bronchus opened. From this cavity fine fibrous bands radiated in all directions, producing extensive fibrosis of the surrounding lung. Perihepatic and splenic adhesions. Liver scarred and nutmeg. Spleen contained several calcareous masses surrounded by a fibrous capsule. Testes fibrous.

Case II.—R. D., aged thirty-six. At the age of eighteen he had a sore on the penis, for which he was treated for several months. In 1890 he suffered from cough and expectoration, and then had an enlarged gland in the inferior triangle of the neck on the right side, dulness at the right apex, with feeble breath-sounds, and bronchial breathing in the right supraspinous fossa. The liver was large, nodular, and very tender. He took iodide of potassium in gradually increasing doses and obtained some relief. In April 1893 he noticed oedema of the legs and scrotum. He had troublesome cough, accompanied by the expectoration of large quantities of extremely fetid pus. The breath was fetid.

Physical Signs.—Expansion deficient on right side. Relative dulness at right apex front and back, breath-sounds feeble over dull area. Absolute dulness from level of fifth interspace in nipple line and in axilla to base; behind from angle of scapula to base. Vocal fremitus and resonance diminished, and breath-sounds scarcely audible over dull area. Urine, sp. gr. 1004, neutral, contained albumin and fatty casts. The expectoration consisted of frothy greenish pus, forming thick masses in a watery fluid. It did not contain tubercle bacilli. On 17th May the chest was explored in the axillary and submammary region. No pus was found. 19th May.—Liver exposed by incision below costal arch, and a depressed cicatrix seen. The expectoration continued copious, green, and fetid. Absolute dulness appeared over whole of right side up to clavicle, with amphoric breathing and pectoriloquy below clavicle. 15th June.—Offensive pus was evacuated through a cannula inserted in third right interspace in mid-axillary line: a portion of the fourth rib resected, lung incised, more pus evacuated, drainage-tube inserted. 19th and 20th June.—Haemorrhage from wound. 21st June.—Death.

Necropsy. Abstract of notes:—Old syphilitic scar in trachea, six rings above bifurcation, more recent scar at bifurcation, producing stenosis of the main bronchi to the right upper and lower lobes. One bronchial gland enlarged. Pleura over right lower lobe adherent and much thickened. Bronchi much dilated beyond the site of stenosis. At the base of the upper lobe were two large irregular cavities with sinuous outlines communicating with large bronchi, lined by a distinct membrane, and containing sloughy portions of lung tissue. The anterior cavity had been opened by the incision. The section of the lung was smooth and presented a finely speckled yellow appearance. No pus exuded from the yellow spots on pressure. In the anterior part of the lower lobe there was a large irregular cavity, the walls of which shewed no sign of any mucous membrane; they were covered with yellowish-grey sloughy material. No tubercle present and no caseation. The lung puckered in many places and fibrous almost throughout. Liver enlarged (76 oz.).

Large puckered cicatrix on the upper surface of the left lobe and many similar cicatrices elsewhere. A cretaceous and caseous gumma on the posterior aspect of the right lobe. Liver substance fatty and amyloid. Kidneys large, pale, lardaceous, and fatty.

Case III.—T. H., aged fifty-nine. Chancre on penis in 1858 (aged twenty-five), secondary rash and sore throat subsequently. In 1864 ulcers on left leg and twice subsequently. In 1880 ulcer on right leg, near external malleolus. Dry cough since 1887, worse in winter. Since December 1892 severe paroxysmal cough with offensive muco-purulent expectoration. Marked emaciation during this period.

A pale, grey-haired, emaciated man. Breath very fetid. Extensive scars on left leg of old standing, more recent scars on right leg. Scar in right lumbar region where incision was made for "abscess." Right lung.—Hyper-resonant on percussion; breath-sounds at apex bronchial, front and back; crackling rales in supraspinous fossa. Bronchophony and pectoriloquy well marked in same area. Dulness over lower lobe to angle of scapula, breath-sounds bronchial, with coarse crackling rales over same area. Left lung.—Resonance impaired over clavicle and in supraclavicular fossa, elsewhere hyper-resonance. Bronchial breathing over upper lobe, front and back, with crackling rales. Breath-sounds bronchial over upper part of lower lobe, with bubbling and coarse crackling rales, the latter extending to the base. Expectoration copious, purulent, and offensive. Frequent examinations made for tubercle bacilli, but none found. Died 23rd February.

P.M.—Scar on corona of penis with some induration around. Calvarium thickened, dura mater adherent. Pleural adhesions over both lungs. Right lung.—Emphysema along anterior margin and at base. Apex pigmented and consolidated from pneumonia and oedema. In lower part an oval cavity measuring $2\frac{1}{2}$ inches by 2 inches, in communication with main bronchus, and containing greenish-yellow, offensive, shreddy material. Below this for $1\frac{1}{2}$ inches the lung grey in colour and almost solid, a few small cavities with curdy contents. No tubercle found. The pleura covering the consolidated area much thickened. Left Lung.—Upper lobe pigmented and "nodular." A cavity, from bronchial dilatation, occupies the posterior portion. The lower lobe emphysematous, and contained numerous encapsuled caseous masses about 2 mm. in diameter. Bronchial glands pigmented, but not caseated. No ulceration in air-passages. No gumma in liver or spleen. Testes scarred and fibrous. Small white fibrous nodule in right kidney.

Reference may be made to the article in the first edition of this work for the records of other cases of pulmonary syphilis which had not proved fatal (Vol. V. p. 325).

The following case shews that stenosis of a main bronchus may give rise to destructive changes in the lung. It will be observed that the case was one in which a recent tuberculosis supervened on old syphilitic disease:—Margaret S., aged twenty-five. Cough, expectoration, pain in left side, dyspnoea, night-sweats and emaciation have been present for eight

months. The fingers were clubbed; there was a large circular ulcer on the back of the left thigh with some scarring, and coppery staining about the knee and leg on the same side. Cough more or less paroxysmal; expectoration copious, nummular, and purulent. No tubercle bacilli. Dulness over left lung, absolute at base, where vocal fremitus is absent; elsewhere it is diminished. Bronchial breathing, pectoriloquy, and crepitation over left upper lobe. Breath-sounds absent at base, some rhonchus there. Slight crepitation at right base. The ulcer on the thigh yielded to antisyphilitic treatment. The physical signs remained much the same, except that the breath-sounds at the left apex became cavernous. There was well-marked pyrexia throughout. The expectoration remained copious, at times it averaged a pint in the twenty-four hours. Death occurred eight months later, and was preceded by anasarca, ascites, and profuse diarrhoea.

Necropsy.—A few small scars in the subglottic portion of the larynx. The lower half of the trachea marked by numerous stellate puckered cicatrices, involving both membranous and cartilaginous portions, but especially the latter. The origin of the left bronchus represented by a small opening just admitting a probe; the surrounding parts of the tracheal wall extremely fibrous and puckered. Slight scarring in the right bronchus about the origin of the upper lobar branch. Left lung excavated from apex to base. Numerous trabeculated cavities in the upper lobe intersected by tough pigmented bands: walls thin and smooth. The cavities larger behind than in front, in the latter region they were more numerous; and the intervening fibroid induration was more pronounced. Some bronchi appeared to expand uninterruptedly into the smaller cavities. Numerous small cavities in the lower lobe situated in indurated fibroid lung. The cavities contained extremely fetid reddish fluid secretion, and in some places some soft putty-like material. No tuberculous nodules in this lung. The contents of the pulmonary cavities, including the liquid and caseous parts, were carefully examined for tubercle bacilli, but none could be found. Right lung crepitant, but studded with large tuberculous masses which were most plentiful in the middle lobe and lower part of the lower lobe. Lardaceous disease of thyroid, mesenteric and mediastinal glands, also of the kidneys, liver, and spleen, and mucous membrane throughout the body.

Since lesions similar to those here described may occur when the narrowing of the bronchus is due to pressure from without, as by an aneurysm, it is clear that the bronchial obstruction is the main factor in their production. Stenosis of the bronchus is followed by retention of secretion in the tubes, and this by bronchiectasis. Decomposition of the retained secretion induces inflammatory changes in the surrounding lung, and finally the part so affected breaks down and cavities are formed.

The cases here described prove that in individuals undoubtedly the subjects of syphilis, widely-spread destructive changes may be found in the lungs; and that such lesions may occur independently of the presence of tuberculosis.

It may be of service to draw attention to the chief points of difference between the pulmonary lesions of tuberculosis and syphilis.

(i.) Tuberculosis usually affects the apex of the lung, and subsequently the apex of the lower lobe; and tends to progress along a certain route. The primary lesion of syphilis is often about the root and central part of the lung; the disease follows no definite line of march, and gummas may be found in any position.

(ii.) Both tubercles and gummas may undergo either necrosis and caseation, or fibrous transformation; but with caseous tubercle the tendency towards softening and cavity formation is the rule, whereas a caseous gumma very rarely breaks down.

(iii.) The progressive destruction of the lung by a process of disintegration leading to a gradual increase in the size of a cavity, a change so commonly observed in tuberculous disease, is rarely if ever observed in syphilis, except as a secondary result of stenosis of one of the main bronchi.

(iv.) In nearly all cases of advanced destruction of the lung occurring in the subjects of syphilis, stenosis either of the trachea or of one of the main bronchi is present, whereas this lesion is very rare indeed in tuberculosis.

(v.) The cavities found in cases of pulmonary syphilis are usually bronchiectatic, but not invariably so; whereas in tuberculosis they are commonly due to progressive destruction of the lung, but may be bronchiectatic.

(vi.) The tendency to the formation of pulmonary aneurysms, which is so marked a feature in tuberculosis, is rarely observed in pulmonary syphilis.

(vii.) Pulmonary lesions in tuberculosis are very common, whereas in syphilis they are extremely rare.

The necessity for prolonged specific treatment is certainly more generally appreciated now than formerly; and it is therefore probable that rare as these lesions have been in the past, they will be still rarer in the future. The conditions which favour their development are the neglect of mercurial treatment shortly after infection, and anything which, by lowering the general health, tends to diminish the resisting power of the individual.

Symptoms.—The only point worthy of mention in respect of syphilitic lesions of the bronchi is that the catarrhal signs which accompany the secondary stage are, as a rule, general in their distribution; whilst in the tertiary stage they are more often localised, owing to the tendency at that period to the formation of gummas in the main bronchi. Should stenosis occur, there may at first be bronchial breathing limited in area, and often most marked about the root of the lung posteriorly. As the lumen of the tube diminishes, the breath-sounds, over the pulmonary area which it supplies, become more and more feeble, and finally disappear when air ceases to pass the obstruction. If bronchiectasis is forming behind the site of stenosis there may be cough with profuse, purulent,

and fetid expectoration, accompanied by general signs such as emaciation and moderate pyrexia.

In the cases described in this article it will be observed that *cough* was, as a rule, the earliest and most prominent symptom. In the early stage it may be due to irritation, the result of laryngeal, tracheal, or bronchial lesions; at a later period it is probably chiefly due to the changes within the lung itself.

Dyspnoea comes next in point of frequency. It varies in severity with the nature of the lesion: slight when this is limited, in cases of extensive fibrosis or stenosis of one of the main bronchi it may be very severe. The dyspnoea tends to become paroxysmal and to assume the characters of bronchial asthma. *Haemoptysis* has not been of frequent occurrence in cases observed by myself, but it may occur and may prove fatal. In one case of syphilis of the bronchial glands, profuse and fatal haemorrhage occurred from softening of the gland and its rupture into a main branch of the pulmonary artery.

Expectoration may be profuse, purulent, and offensive. Fetor of the expectoration is common in cases of advanced pulmonary syphilis. The sputum will be free from tubercle bacilli.

Pain may be present, but is not a very prominent feature of the disease.

Emaciation is not, as a rule, nearly so extreme as in tuberculosis; but with advanced lesions in the lungs the difference is not so remarkable as to be of any value from a diagnostic point of view.

Night-sweats were present in several of the cases here described.

When extensive lesions are present, *pyrexia* may be considerable, and of the hectic type commonly observed in tuberculous disease of the lungs; but in the early stages of the disease there may be a complete absence of fever.

The general symptoms, as will be seen on reference to the cases described, do not, in the presence of widely-spread lesions, differ markedly from those of advanced tuberculous disease of the lung.

Physical Signs and Diagnosis.—The lesions of syphilis are rarely of such a kind as to produce signs by which they can be distinguished from others of an entirely different origin. Consolidation and excavation will be recognised by their ordinary signs, probably before their syphilitic origin is suspected; and it appears therefore unnecessary to describe them in detail, more particularly as in the cases here recorded the results of the physical examination are given in full. The features of pulmonary syphilis are certainly not as yet so clear that the disease can be recognised by any positive signs; but by a process of exclusion a diagnosis may generally be made.

The case will probably be regarded at first as one of pulmonary tuberculosis; but repeated examination of the sputum and the failure to discover tubercle bacilli will suggest another origin. A careful inquiry, previously perhaps omitted, will now be made as to syphilitic infection and as to the occurrence of any secondary or tertiary manifestations of

this disease. The absence of such a history in a hospital patient will not exclude syphilis; but it is rare in private practice for a patient to have had syphilis with tertiary symptoms and to be ignorant of the fact. Evidence of tertiary lesions in the larynx, liver, spleen, or testes is of importance as shewing that the viscera are affected. Careful search should also be made for lesions of the calvarium, of the dura mater, and of the sternum and ribs.

Speaking generally, the diagnosis of pulmonary syphilis from tuberculosis will depend far more upon the examination of the sputum than on the results of physical examination.

A careful examination of undoubted specimens of pulmonary syphilis does not bear out the statement that the lesions are generally limited to the middle part of the lung; they are so often found elsewhere that their more frequent occurrence in that part ceases to be a fact of much value in diagnosis. It would be rash indeed to diagnose pulmonary syphilis because of a lesion situated in and apparently limited to the middle of one lung, without having previously demonstrated, by frequent examinations, the absence of tubercle bacilli from the expectoration. Evidence of excavation and expectoration of a fetid sputum, which does not contain tubercle bacilli, should always suggest the possibility of pulmonary syphilis. When the physical signs indicate stenosis of the trachea, or of one of the main bronchi, and the presence of a growth or an aneurysm can be excluded, it is very probable indeed that syphilis is the main factor in the case. Those who neglect the systematic examination of the sputum, will almost certainly overlook a case of pulmonary syphilis if it should come in their way. A striking example of this may deserve mention. A military officer who had contracted syphilis some years back began to suffer from symptoms of laryngitis; and on examination of the chest well-marked signs of disease were found at the apex of the right lung. The laryngoscopic appearance did not suggest to several competent observers that the lesion was due to syphilis, and the case was regarded as one of "consumption of the throat and lungs." It occurred to a medical man who saw the patient at a later period to examine the sputa for tubercle bacilli, and, as none were found on repeated examination, doubt was cast upon the diagnosis; mercury and large doses of iodide of potassium were prescribed, and the patient rapidly improved; but the stenosis of the larynx remained.

Prognosis. — Extensive pulmonary lesions, particularly excavation, whether of bronchiectatic or disintegrative origin, and fetid expectoration are certainly very grave complications of syphilis. If, moreover, there is evidence also of gummatous hepatitis, albuminuria, and lardaceous disease, recovery is scarcely possible, and life is not likely to be much prolonged.

It is probable, however, that, with our present improved means of diagnosis of tuberculosis of the lungs, syphilitic cases, which formerly would have been considered tuberculous, may be recognised as syphilitic at an earlier stage, and the patients under appropriate treatment may

recover. In an undoubted case of pulmonary syphilis, which came under my own care at a late stage of the disease, the affection had been kept in check for many years by repeated visits to Aix-la-Chapelle, and by the active employment of antisyphilitic treatment. In any case seen in an early stage, great improvement, if not complete cure, may reasonably be expected from the use of similar measures. There are, however, limits to the action even of specific remedies; and it is not to be expected that lesions such as bronchial stenosis and dilatation, extensive fibrosis and excavation, or gummas in a state of fibrosis will disappear under the administration of mercury or iodide of potassium.

Treatment.—If the disease in the bronchi or lungs is recognised in an early stage, the patient should be advised to undergo a prolonged course of treatment with mercury. If, however, the disease is advanced, and the patient emaciated, it is better first to try the effect of iodide of potassium alone; giving at the same time cod-liver oil and tonics. To maintain and improve the strength and general nutrition of the patient are matters of as much importance in the treatment of syphilitic as of tuberculous disease of the lungs, and such desirable changes are, speaking generally, more likely to follow residence in a sanatorium than a visit to a health resort.

The warm sulphur baths of Aix-la-Chapelle, in association with mercurial inunction, enjoy a special reputation in the treatment of syphilis, and are to be recommended to sufferers from pulmonary syphilis who are able to go abroad for treatment.

When tuberculous disease of the lungs occurs in a syphilitic subject, the treatment will be mainly such as is suited to cases of tuberculosis. A mercurial course is rarely admissible, but iodine, in the form of the syrup of the iodide of iron, may be given with advantage.

In cases accompanied by fetid expectoration, creosote vapour baths and intratracheal injections of guaiacol should be tried.

Cases of syphilitic disease of the lung accompanied by bronchiectasis have not, in my experience, been benefited by surgical measures undertaken with a view to drain the cavities.

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PULMONARY ASPERGILLOSIS

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Short Description.—A destructive disease of the lungs due to their invasion by a fungus, the *Aspergillus fumigatus.* The disease depends on the inspiration of the spores of the fungus, and occurs chiefly in those whose occupation brings them in contact with infected grain. Clinically the disease presents itself under two forms: (i.) like chronic pulmonary tuberculosis; (ii.) like emphysema and bronchitis.

Besides attacking the lungs primarily, the aspergillus may become engrafted on pre-existing pulmonary lesions.

Historical.—Hughes Bennett, in 1842, described the first example of pneumomycosis, in which the sputum and cavities of a phthisical subject were found to contain a fungus. Gairdner, in 1853, shewed a specimen of a tuberculous lung which had given rise to pneumothorax, with small circular white areas of fungoid growth on the pleural surface, penetrating very slightly ($\frac{1}{16}$ inch) into the lung substance, and measuring $\frac{1}{8}$ inch in diameter. Rayer eleven years before, in 1842, had met with a very similar case. Bristowe, in 1854, recorded the case of a woman who died with signs of chronic bronchitis; in the apex of the left lung there were two communicating vomicae containing no secretion, but on the septum between them there was a powdery, velvety mass of mycelium; although there was no other evidence of tuberculosis, the vomicae were regarded as being tuberculous. Virchow, in 1856, gave an account of several cases of aspergillary broncho- and pneumo-mycosis in patients dying from other diseases. A number of other observers have recorded cases which, like the preceding cases, were regarded as being secondary infections of pre-existing pulmonary lesions. In 1890 Dieulafoy, Chantemesse, and Widal gave a clinical account of aspergillary pneumomycosis in persons engaged in stuffing and fattening pigeons for the Paris market, and struck out a new line in their view that it is a primary affection. In 1897 Rénon collected all the evidence bearing on the subject in his *Étude sur l'aspergillose chez les animaux et chez l'homme.*

At first and for a considerable time the occurrence of aspergillus was supposed to be no more than an accidental invasion of already diseased lung tissue, the fungus being merely saprophytic. Thus, in Bristowe's

case, although there was no sign of tubercle elsewhere in the lung, the lesions were regarded as tuberculous and not due to the activity of the fungus.

But subsequently the French school, and especially Rénon, whose conclusions are based on extensive experimental research, have successfully argued in favour of primary pneumo-aspergillosis; in England, Boyce and Arkle and Hinds, and in Italy, Baccarani, have described cases of the primary affection.

Aspergillary pneumomycosis may therefore be considered under the two heads—(*a*) primary; (*b*) secondary.

It is a difficult question, however, in many instances to settle whether the aspergillary affection be undoubtedly primary, and the cause of morbid lesions in a lung previously healthy; or whether it be a secondary infection only. In former times there was a strong and general impression that aspergillary occupation of the lung is essentially an accidental and secondary phenomenon. Max Podack has expressed doubts whether cases described as primary by the French observers are in reality of this nature; on the other hand, Rénon regards Wheaton's "case primarily of tubercle in which a fungus (aspergillus) grew in the bronchi and lung" as being an example of primary pulmonary aspergillosis. Thus different interpretations are put upon the same case.

Etiology.—Pulmonary aspergillosis is a trade disease in Paris; it occurs in persons whose calling is the artificial feeding of pigeons, and in those who comb and sort hair. The essential factor is the intimate relation to grain infected with the spores of the *Aspergillus fumigatus*. The pigeon-feeder fills his own mouth with a watery mixture of canary seeds and vetch seeds, and transfers the grain to the pigeon's mouth. Spores of aspergillus attached to the seeds thus get into the trachea and are conducted to the air-vesicles, through the walls of which they easily pass. It is remarkable that the alimentary canal of man seems immune to *Aspergillus fumigatus*. According to Rénon, there were only about ten persons engaged in this trade in Paris when he wrote.

The hair-sorters employ the flour of rye to enable them to separate the hairs more easily; this process impregnates the atmosphere in which they work with dust, which may contain the aspergillus of the rye flour. The atmosphere of their working-rooms is so poisonous that birds die after being exposed to it for a fortnight.

Aspergillosis is a rare disease; it appears more likely to occur in millers, agricultural labourers, and those brought in contact with grain, than in any other class of the community. Apart from the Paris cases a few sporadic examples of the disease have been recorded.

Pulmonary aspergillosis belongs to a class of lesions which, though comparatively little known, has been more studied in animals than man. The lesions of the class pseudo-tuberculosis are granulomas, and resemble those of true tuberculosis, except in respect of the causal agents, which include bacilli other than those of tubercle, fungi of various kinds, and even worms (vide *Paragonimus westermani*, Vol. II. Part II. p. 860). The

close resemblance (to the naked eye) of the lesions of pseudo-tuberculosis to genuine tuberculosis renders it very probable that they are often regarded as such; and that, being rarely recognised, this form of lesion is not so infrequent as our present experience would suggest. Systematic examination of pulmonary lesions might prove that some conditions generally dismissed as tuberculous are in reality pseudo-tuberculous, and are due to quite a different cause. Thus, Flexner has described the condition of Pseudo-tuberculosis hominis streptotrichia in a man who died with the signs of pulmonary tuberculosis, and whose lungs shewed consolidation with early excavation.

The aspergilli are true fungi and belong to the family Perisporiaceae, order Ascomycetes. Of the varieties of aspergillus, two, *A. fumigatus* and *A. niger*, are parasitic, and produce morbid changes in the human body.

Pulmonary aspergillosis appears to be almost always due to *A. fumigatus*; *A. niger* has, it is true, been described in some instances, but Rénon throws doubt on the accuracy of the observations, and regards them all as examples of *A. fumigatus*.

Both varieties have been described as attacking the external auditory meatus, and the skin.

It should be remembered that in order to determine the species cultures are necessary, and that without this no opinion as to the identity of the form of aspergillus is valid.

Aspergillus fumigatus flourishes best at the temperature 37° to 40° C., whilst *A. niger* grows best at 25° C.; and this might be thought to explain the pathogenetic qualities of *A. fumigatus*; but in Rénon's hands experiments on frogs do not support the simple view that it is merely a matter of the bodily temperature suiting the development of one species and not of the other.

Primary Pulmonary Aspergillosis.—*Symptoms.*—The clinical features presented by the recorded cases of primary pulmonary aspergillosis usually resemble either those of chronic pulmonary tuberculosis or those of emphysema. Recently Baccarani has described 3 cases in his own practice of acute primary aspergillosis of the lungs, in 2 of which the clinical picture was that of acute tuberculosis, the patients dying respectively in seven and nine weeks.

When the disease takes the first of these two forms there is recurring haemoptysis, cough, expectoration, becoming green and purulent, and signs first of bronchitis, and later of consolidation at the apex. Furthermore there is elevation of the temperature; and pleurisy may supervene. The resemblance, therefore, to pulmonary tuberculosis is so far exact; but if the sputum be examined, tubercle bacilli are absent, while the mycelium of *Aspergillus fumigatus* is present. The course of the disease is usually slow and prolonged; recovery takes place eventually by expectoration of the aspergillus, but the affected portion of the lung undergoes marked fibrosis.

A patient affected with pulmonary aspergillosis offers a suitable soil

for tubercle bacilli, and a secondary infection may take place, the aspergillus disappearing from the sputum and its place being taken by tubercle bacilli. Rénon and Sargent have recorded a case of primary pulmonary aspergillosis succeeded by tuberculosis, in which eventually both these infections became obsolete; but so much chronic pneumonia resulted that death from failure of the right side of the heart terminated the case. In another and similar case related by Rénon the sputum first contained the aspergillus alone; later very scanty traces of it, but numbers of tubercle bacilli were found, and eventually neither bacilli nor aspergillus persisted, the patient surviving with evidences of chronic pneumonia.

In the emphysematous form the disease may run a rapid course, as in the case recorded by Arkle and Hinds. Haemoptysis is infrequent, or may not occur at all; there is loss of flesh and strength, frequent cough and severe dyspnoea come on in attacks at night, and suggest spasmodic asthma. The physical signs are chiefly those of emphysema and bronchitis.

Intermediate forms between these two may occur, signs of apical consolidation supervening in the emphysematous varieties; and conversely cases which appeared like chronic phthisis may be marked by attacks of pseudo-asthma.

Morbid Anatomy.—The data at our disposal are somewhat scanty, but so far as they go they tend to shew that the morbid appearances in the lungs met with in the described cases of aspergillosis differ just as do the lesions of acute and chronic tuberculosis. This difference depends on the resistance offered by the lung tissue to the inroads of the fungus. It will be most convenient to describe the anatomical lesions in connexion with the two chief clinical types of the disease to which attention has already been called.

1. In cases in which the disease has run a very chronic course, resembling either chronic pulmonary tuberculosis or chronic pneumonia, the aspergillus may either (*a*) still be found in the lung tissue, or (*b*) it may have been entirely removed, and then have left behind it a chronic interstitial pneumonia which eventually proved fatal.

(*a*) Our knowledge of the lesions existing in primary aspergillosis when the aspergillus is still present in the lung tissue is particularly scanty. The lung tissue contains dilated bronchioles leading into cavities in pneumonic areas in which there are pseudo-tubercles composed of hyphae so arranged as to resemble actinomycosis. There is much phagocytic reaction in the pneumonic areas, shewing that very active resistance had been opposed by the lung tissue to the aspergillary invasion. Rénon associates the actinomycotic form adopted by the aspergillus with the active resistance of the tissues, and considers it as an indication of defensive powers on the part of the tissue and of lowered vitality on the part of the aspergillus. Hence this form of pneumo-aspergillosis is called by Rénon "abortive." The cavities also contain the aspergillus. The process is essentially the same as that in cases of actinomycosis; its clinical

features are those of emphysema and destruction of pulmonary tissue; but it is a local process which has become arrested at an earlier stage.

(*b*) In a case of primary pulmonary aspergillosis, described by Rénon and Sargent, in which true tuberculosis supervened with disappearance of the aspergillus from the sputum, death took place from failure of the right side of the heart, and examination of the lungs shewed chronic pneumonia; but no trace remained either of the aspergillus or of tubercle bacilli.

2. In cases in which the symptoms have been those of emphysema and dyspnoea the lungs contain patches of consolidation breaking down into cavities, while there is compensatory emphysema which may be well marked. The lesions in Hind and Arkle's case have some analogies with Dr. Tooth's case of multiple cavities in bronchopneumonia, though in the latter the causation had nothing to do with aspergillosis.

Microscopically the walls of the small bronchi are thickened, and both the lung substance and the alveolar cavities contain the aspergillus mycelium. In places the lung tissue is so disorganised as to be unrecognisable, and there is breaking down of the lung tissue leading to the formation of microscopic cavities. The mycelium is in extremely intimate relation with the lung tissue, and, as it is accompanied by phagocytic reaction, the aspergillary invasion of the lung tissue appears to be the direct cause of the lung lesions, not a merely accidental or post-mortem event.

It was formerly held that no toxin could be obtained either from the media in which the *Aspergillus fumigatus* is grown (Kotliar), or from the fungus itself (Rénon), and it appeared probable that the large quantities of the fungus in the lung tissue set up the inflammatory changes by mechanical irritation. Bodin and Gautier, however, have shewn that the *Aspergillus fumigatus* (like certain other fungi such as *Oidium albicans*) does produce a toxic substance. Animals differ in their susceptibility to this toxin; and it is remarkable that pigeons, which are extremely sensitive to the spores of the *A. fumigatus*, have a much more marked natural resistance to the toxin than rabbits have.

Generalisation of aspergillosis does not occur.

Diagnosis.—The physical signs are not in any way characteristic, and would point to bronchitis and emphysema or to chronic pulmonary tuberculosis. In Wheaton's case there was a growth of the fungus at first white, later black, on the tongue and palate. But this is the only help that ordinary methods of physical examination can be expected to supply, and, unfortunately as regards diagnosis, this coexistence of oral and pulmonary aspergillosis is almost unique.

The diagnosis depends on the presence of the fungus or its spores in the sputum. The fungus elements are more easily detected by mixing a small quantity of the sputum with a 20 per cent solution of sodium hydrate. In cases in which tubercle becomes engrafted on primary pneumo-aspergillosis, both organisms might be found in the sputum; and, unless the patient had been under observation from the beginning when the asper-

gillus alone was present in the sputum, there would be no means at first of distinguishing the primary form complicated by tubercle from secondary aspergillosis occurring late in the course of pulmonary tuberculosis.

The fungus, derived from dust, is occasionally found in the mouths of healthy persons.

Cultures of the aspergillus in appropriate media, such as Raulin's fluid, and inoculation of animals may be necessary to determine that the form of aspergillus is the pathogenetic *Aspergillus fumigatus*, and not the other non-pathogenetic varieties, such as *Aspergillus niger*, *A. glaucus*, and so forth. It must be distinguished from the streptothrix form of the bacillus tuberculosis; and, lastly, the lesions must be distinguished from other forms of pseudo-tuberculosis due to different factors such as bacteria, streptothrix, actinomyces, or *Paragonimus westermani*.

The prognosis of pulmonary aspergillosis is less grave than that of pulmonary tuberculosis, since the disease is usually much slower in its course, never sets up a general infection comparable to generalised tuberculosis, and tends to undergo a gradual and spontaneous cure. But there are several reservations to this general statement. For, even if the aspergillus disappear, the lesions of chronic interstitial pneumonia may lead to dilatation of the right side of the heart, and so to a fatal result.

It need hardly be said that the development of genuine tuberculosis renders the prognosis much graver.

The prognosis of the emphysematous form does not, from the few recorded examples, appear to be nearly so favourable as that of the more chronic variety which has been likened to chronic tuberculosis.

Treatment. — Although there is no specific remedy for pulmonary aspergillosis, nor any drug that can be employed to kill the fungus outright in this situation, experiments on animals shew that iodine, iodide of potassium, and arsenic increase the resistance of the organism to the invasion of *Aspergillus fumigatus* and inhibit its growth; their employment is therefore reasonable in this disease in man. The patient must avoid contact with dry grains and vegetable material, the removal from the poisonous atmosphere being an important essential, both in prophylaxis and in treatment. The general strength should also be improved by good and generous feeding, cod-liver oil, tonics, and fresh air free from dust; thus we may guard against secondary infection of tubercle, and assist the tissues in their struggle against the aspergillary infection.

Symptoms should be treated as they arise. When haemoptysis occurs the treatment is the same as in pulmonary tuberculosis. Attacks of asthma may be relieved by iodide of potassium, tincture of lobelia, and other appropriate remedies; while creosote, terpene, turpentine, may with other drugs be given for bronchitis.

When tuberculous infection has taken place, the course of treatment is that of chronic pulmonary tuberculosis.

Secondary Pulmonary Aspergillosis. — Here the *Aspergillus fumigatus* develops as a result of the inhalation of its spores; and finds a suitable nidus in lung tissue the resistance of which has been already

much lowered by pre-existing disease, or has actually undergone necrosis.

It has been found in the bronchi and in the lung substance. Thus the aspergillus may be engrafted on bronchiectasis of old standing; or may take root on the walls of vomicae due to tuberculosis; or in the lung under other conditions, such as malignant disease, pulmonary apoplexy, chronic bronchitis, bronchopneumonia, and gangrene of the lung.

In some of the cases in which it has been described as secondary, it may, as already hinted with regard to Bristowe's case, in reality have been primary.

In cases with multiple bronchiectases or vomicae in the lungs, the absence of the fungus from some of them and its presence in others are strong evidence in favour of the secondary nature.

It is remarkable that in gangrene of the lung associated with the presence of aspergillus there is no fetor. It seems that the growth of the micro-organisms of putrefaction is prevented by the aspergillus.

The actinomycotic form of the mycelium appears to occur where there is considerable reaction and resistance on the part of the tissues, and it is probable that it does not occur in secondary or terminal aspergillosis.

Clinically speaking, secondary aspergillary pneumomycosis, like thrush in the mouth of adults, is probably a precursor of death, and is not likely to be suspected or discovered unless the mycelium be found in the sputum. It is in fact a terminal complication.

The treatment is that of the primary disease on which the aspergillosis has been engrafted.

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A. L.

PNEUMOCONIOSIS

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ATTENTION was drawn to stone-masons' and miners' phthisis two hundred years ago by Ramazzini, Professor of Medicine in the University of Modena, in his treatise on trade diseases. He pointed out that in consequence of the inhalation of the sharp, rough, and cornered particles which fly off during the processes of cutting and polishing, stone- and marble-cutters became troubled with cough, then asthmatic and consumptive; after death the lungs were found studded with little stones, heaps of sand, so that in running the knife through the pulmonary vesicles it felt as if some sandy body was being cut. Thackrah, writing in 1831, says that the bronchial mucous membrane of masons often shews chronic inflammation, and that miners in the North of England suffer especially from chest complaints when employed in working ore in sandstone, but do not so suffer when the ore is in limestone. The explanation of the difference is that, as limestone is fissured vertically, water from the superincumbent beds percolates through the roof of the mine thus keeping the ore moist, whilst in the sandstone strata, which

are impervious to water, the ore is quite dry. Thackrah was thus one of the first to draw attention to the important point that the dust which is provocative of lung disease is dry dust. Valuable contributions to the literature of the subject were also made by E. H. Greenhow and J. C. Hall of Sheffield. In the first edition of this System the article on lung diseases caused by dust was written by the late Dr. John T. Arlidge, whose well-known work on *Diseases of Occupation* is a monument of research and experience. This authority spent most of his professional life in Staffordshire, and had therefore unusual opportunities of observing the effects of the local industries upon the lungs of the workpeople. To Dr. John Tatham we are indebted for a statistical review of the subject and for a comparison of the mortality returns of dusty trades.

Etiology.—Pneumoconiosis is a very complex subject, inasmuch as there are at the same time in the individual numerous co-operating factors, factors of occupation, housing, environment, the immoderate use of alcohol, and so forth. The physician is prone, moreover, to group together indiscriminately under the heading of "Inflammation of the Lungs" several forms of respiratory diseases, such as capillary bronchitis, bronchopneumonia, and pneumonia. This can only be obviated when medical practitioners give more time to diagnosis, and more care to the preparation of death certificates. It is far from easy to distinguish between lung disease consequent upon the inhalation of irritating dust, and that due, for instance, to breathing air contaminated with organic matter. The death-rate from phthisis and respiratory diseases is greater in some areas of male labour than in others; and this even in areas within districts where dusty trades prevail. Since Koch's discovery of the tubercle bacillus, medical opinion has changed in regard to the causation of pulmonary phthisis, which is now recognised as specifically due to the implantation of the tubercle bacillus in the lungs, intestine, or lymphatic glands. The problem is one of infection on the one hand, and of the recipient on the other; the malady to be discussed here, however, is a form of lung disease largely determined by a dusty occupation; so that, whilst the possibility of infection is admitted, the question arises whether the tubercle bacillus is a primary factor in the disease or only an accidental complication appearing late in the malady. In this case it may well be that the fibrotic changes of pneumoconiosis are due, in large part at any rate, to the irritation of the dust, rather than to that of the incidental microbe. Pulmonary consumption is so frequent in persons following dusty occupations that there is a danger of ascribing too much importance to dust, and of ignoring the possibility of infection. In this article an attempt will be made to assign as far as possible their proper shares to dust and infection respectively.

Both in home and in factory there lurks the possibility of tuberculous infection. Pneumoconioses occur at a period of life when men are still comparatively young, and should be in the vigour of health, with, to all appearance, many years of life before them. In ordinary pulmonary tuberculosis the highest death-rate in men is between forty-five and

fifty-five years of age; in women, between twenty-five to forty-five (*vide* Vol. I. p. 50); the earlier incidence of the disease in women being attributed to pregnancy and child-bearing. Except among women working in the potteries, the female sex is remarkably free from dust diseases of the lungs, and this, when it occurs, seems to be uninfluenced by child-bearing and pregnancy. It is to industrial pursuits indeed, apart from domestic occupation and maternity, that we must look for the chief cause of pneumoconiosis; herein we should as regards the age period of the disease, naturally expect a closer approximation between the two sexes than appertains in tuberculosis. In phthisis the mortality-rate was until recently greater in females than in males, but during the last two decades the death-rate from phthisis has been higher in males (*vide* Vol. I. p. 52); this raises the question whether some particular condition such as an occupation influence may not play a more important part now than formerly. And it is true that abundant evidence could be advanced to shew that all occupations, dusty or not, in which infection is presumably at work, give higher death-rates from phthisis than other trades. It is generally admitted that overcrowding, indoor occupations, imperfect ventilation, absence of sunlight, and the almost constant use of artificial light favour the onset of pulmonary tuberculosis rather than of pneumoconiosis.

Pneumoconiosis slowly but progressively advances. It is usually unattended by fever or by acceleration of the pulse; indeed, for a considerable time, it is quite consistent with fairly good health, though characterised by cough with expectoration and great dyspnoea. Haemoptysis is rare. In the less severe forms of the malady, patients follow their employment until the catarrh of the bronchi or of the smaller tubes of the lung is much aggravated. It is usually from an acuter attack of bronchitis that the patient dates his illness, although for months, or in some instances years previously, structural changes in the lungs must have been slowly advancing. Occasionally an acute inflammation attacks the damaged lungs, and death results from incidental pneumonia; or the tubercle bacillus finds its way into the lungs, and not only changes the clinical features of the disease, but hurries the illness to a fatal termination. In coal-miners killed by accident, who had not shewn any symptoms of disease, the lungs are often extremely black from the presence of carbonaceous pigment widely distributed, or collected here and there so as to form black masses of which the lung seems to be remarkably tolerant. Dust is absent from the lungs of newly-born infants. The deposit increases with age, but even in old people the amount of dust in the lungs is never equal to that met with in the respiratory organs of persons who during life had worked at a dusty trade. There is, therefore, a physiological as well as a pathological anthracosis; the one increases with age, and the other with exposure to dust. After early infancy there is always a certain amount of silica in the lungs: *e.g.* in an infant four weeks old no silica is found in the lungs, in an infant dying four months after birth there has been found 2·4 per cent of silica in the pulmonary ash; in a youth seventeen years of age, 13·3 per cent; in an elderly man sixty-

nine years of age, 14·6 per cent, and in a stone-grinder 45 per cent. The lungs may also contain a quantity of alumina. Greenhow by incineration of portions of the lungs of a buhr-stone mason obtained a considerable amount of white ash. Some of this dissolved in hydrochloric acid left a greyish-white residue, which, under the microscope, proved to be composed of minute angular particles. These, when treated with hydrofluoric acid, proved to be silica. By treating fine buhr-stone dust with hydrochloric acid, Greenhow obtained a residue with microscopic characters similar to those of the material from the incinerated lung, thus proving the identity of the two kinds of dust. From a coal-miner's lung, treated by hydrochloric and nitric acids, Greenhow obtained silica and alumina with a trace of iron; and from a potter's lung, silica, a trace of iron, and a larger quantity of alumina than in the coal-miner's lung. In pottery manufacture the chief sufferers from respiratory diseases are the china scourers, flat pressers, and hollow-earthenware pressers. During the scouring or cleaning of china, large quantities of very fine dust are given off. Opinions are divided on the question whether the power for harm lies in the size of the particles of dust or in their angular shape and hardness, but the nature and not the size of the dust particles is probably the important factor. Soft coal, for example, is much less irritating than coal that is hard and stony. Fine dust is readily raised into the atmosphere. When doing laborious work, men are obliged to make deeper inspirations, and, as a consequence, the finer particles of dust are more likely to be carried into the lungs than are the coarse ones; hence the freedom of the Aberdeen granite-cutter compared with the stonemason. Again, dust may do harm both locally and constitutionally by its chemical composition. Slag dust which is obtained from iron works is injurious to the lungs because of the large amount of lime it frequently contains. It therefore produces locally both mechanical and chemical effects, whereas white-lead dust when inhaled is dissolved in the secretions of the respiratory passages, and causes the constitutional symptoms of plumbism, the lung remaining practically unaffected.

Although the morbid changes in the lungs are more or less the same in all forms of pneumoconiosis, there are a few points in each which call for special notice.

Coal-Miners' Phthisis or Anthracosis.—In 1831, when Thackrah's book on the effects of occupation upon the health of workpeople appeared, colliers were as a class shorter-lived than now; coal-miners seldom lived more than fifty years. Many suffered from bronchitis and asthma, and some died from chronic lung disease, accompanied by "black spit" and emaciation. The conditions under which work was carried on in the coal-mines at this period were bad. There was only one shaft leading into the pit, and there was no thorough system of ventilation. The miners themselves attributed their attacks of bronchitis and asthma to the large amount of gunpowder reek in the mine, and to the smoke from the lamps. Sir John Simon drew attention to the relative freedom from

bronchial and pulmonary troubles enjoyed by the Northumberland coal-miners as compared with the workers in Welsh collieries, which were not so well ventilated. Seventy years ago debilitated colliers, men of middle age, bowed down, bent in the spine, and asthmatic, were no uncommon spectacle in mining villages; and even thirty years ago cases of miners' phthisis were always to be found in the Newcastle Royal Infirmary. Conditions, however, are now so completely changed that except as a result of some calamitous wrecking of a mine, as at Courrières in France or at Hartley in Northumberland, there is no mining village, such as Arkendale, described by Thackrah, in which the ravages of pulmonary disease and the effects of unhealthy occupation on the men have made widows of a large number of women under thirty years of age. So much have the conditions of labour in mines been improved that, apart from explosions, coal-mining is now a healthy occupation. The work is carried on in an abundance of fresh air, free from organic impurities; and coal-miners as a class, suffer less from phthisis than men in other occupations. So changed is medical opinion in this matter that some physicians assert that coal dust renders miners immune to tuberculosis; although this requires confirmation, the men certainly run very little risk of becoming infected in the mine. In the North of England, colliers often live to an advanced age. I have seen colliers upwards of seventy years of age in good health, and still at work. Coal-miners' phthisis or anthracosis is in this country on the decline. It is not, therefore, from coal-miners that a description of the characteristic form of pulmonary dust-disease should be drawn. Although colliers occasionally suffer from cough, shortness of breath, an abundant black and at times purulent expectoration, and shew progressive emaciation, the lungs after death being found black and excavated, and on section exuding an ink-like fluid on pressure, it is more than probable that, owing to the improved conditions of work in mines, the disease is not a pure pneumoconiosis due to dust, but a mixed tuberculous malady, the bacillary infection of which has been caught not in the pit but in the home or elsewhere. Overcrowding is not uncommon in the houses of coal-miners, hence the greater frequency of tuberculous disease in the wives and children of coal-miners than in the men themselves. It is noteworthy that whilst recent years have shewn a marked decrease in the death-rate of coal-miners below the age of fifty, no similar improvement has been observed in the Cornish tin-miners; during the period 1900-1902, the death-rate of all miners living in Cornwall increased, and was three to four times greater than that among colliers and iron-stone miners. The increase has been specially noticeable among the young men from twenty-five to forty years of age, in whom the death-rate is eight to ten times higher than among corresponding coal-miners. Since the home conditions have remained practically the same in Cornwall for decades of years, the rise in the mortality-rate can only be explained by the changed methods of working connected with the more frequent use of machine drills for boring the rock in mines.

Metalliferous Mines.—In metalliferous mines, such as tin, copper,

lead, and iron, the men are not exposed as are coal-miners to dangerous gases and the risk of explosions; but as the mines are not so well ventilated, are frequently deep, and the temperature therein high, the atmosphere is fouled by the respiratory products of the workmen and by the use of naked lights. Again, not only is the air in metalliferous mines less pure, but the work is dustier, and in many of the mines ingress and egress are only by ladders, up which a workman, fatigued at the end of the day, has to lift himself several hundred feet. It is in dry and dusty mines that the dangers are greatest. Experience has shewn that in moist mines the smoke generated by the explosives used for blasting purposes disappears more quickly, and that there is also less dust. Among the lead-miners of the dales of Durham respiratory diseases are extremely frequent, and the mortality from phthisis is high. In some instances the lungs of the men are converted into heavy tissue of stony solidity. The lungs shew primarily a fibrosis, but as the houses near the lead mines are bad and many of the men sleep during the week in overcrowded and ill-ventilated barracks close to the mine head, tuberculous infection is frequently grafted upon the pneumoconiosis. The symptoms, usually commencing as those of bronchitis, are cough, shortness of breath, and expectoration; after the malady has existed for a considerable length of time, tubercle bacilli will probably be found in the sputum. Haemoptysis is not common in lead-miners' phthisis, but these men are often short-winded and old-looking before forty years of age.

What has been said of lead applies to the tin-miners of Cornwall. In both cases the men when they commence work are strong and healthy, but, after following their employment for ten to fifteen years, many of them, especially those who use rock drills, succumb to pneumoconiosis and pulmonary phthisis before reaching forty years of age. Whereas the death-rate from lung disease in occupied males in England and Wales is highest between fifty-five and sixty-five years of age, in the Cornish tin-miners it is highest between twenty-five and forty-five. These miners, however, are not equally exposed to dust. Dr. Haldane found that whilst the average age at death of men who had never worked rock drills was 53, that of men who had worked rock drills was only 37·2; in other words, "the death-rate among machine men from respiratory diseases was about fifteen times, and their total death-rate eight times, that of the average occupied males in this country." Or to make another comparison, "the death-rate among machine men from respiratory diseases was about thirty times, and the total death-rate about ten times, as great as that among colliers or iron-stone miners of the same age." The deeply-rooted objection of the Cornish mining population to post-mortem examinations has thwarted investigation of this subject. During life, however, the physical signs are those of bronchitis, bronchopneumonia, or acute phthisis, marked even in its earlier stages by shortness of breath considerably in excess of that met with in ordinary tuberculous pulmonary phthisis. Dyspnoea is indeed one of the earliest symptoms, and it is usually accompanied by palpita-

tion and other signs of cardiac distress. Once the symptoms are fully developed emaciation progresses. Rock-drillers may present dyspnoea for many months before physical signs of consolidation are detected, although on auscultation of the chest dry creaking sounds may be occasionally heard at the base of one or other lung. In uncomplicated cases of tin-miners' phthisis, without acute catarrh or bacillary infection, the temperature is usually not above the normal.

Allusion has been made to the injurious dust produced by machines used in rock drilling. Arlidge believed that the great depth of the mine at which the men worked and the correspondingly high temperature, frequently 125° F. and higher, dispose to intercurrent catarrhal and inflammatory attacks owing to rapid changes of temperature. Others have held similar opinions since his time. Dr. Albert Bowhay, of Gunnislake, Tavistock, Cornwall, contributed to Arlidge's book the following notes on the diseases of tin- and copper-miners. The diseases of the respiratory organs "are due to the depth at which the miners work—often as much as 300 fathoms—the labour of climbing of the ladders, and the heat and impurity of the air. The diseases in the order of frequency are bronchitis, emphysema, phthisis, and asthma. Bronchitis can be easily accounted for, from the sudden change which they (the miners) undergo from the hot and moist atmosphere of the shaft to the coolness and often coldness of the surface atmosphere. Emphysema is frequently secondary to the bronchitis, but often primary as a result of the lung tissue giving way under the great strain which it undergoes during the act of climbing the ladders. The heart is in these cases hypertrophied. Phthisis is very common above the age of forty. The men are first subject to repeated attacks of bronchitis; after a time the lung substance breaks down and a cavity is formed. Or more common still is *fibroid phthisis*, affecting the base of the lung. Asthma in miners is nearly always secondary to emphysema."

China and Earthenware.—For more than two centuries the manufacture of pottery has been regarded as an unhealthy occupation. The men and women employed are particularly prone to lung disease, with emaciation and gradual loss of health; hence the terms "potters' rot" and "potters' phthisis." For this disease the use of clays and flints is in the main responsible. Cornish clay and Cornish stone when crushed yield a very fine white powder, rich in silex, the hard and sharp particles of which, resisting the defences of the tissues, irritate the lungs, into which they are carried. In the manufacture of porcelain the separate pieces of ware to be fired are placed in "saggers" or large coarse clay tubs that have already been baked in the oven. To keep the pieces separate in the sagger, fine white sand, which is really ground flint, is placed along with, and around the pieces of chinaware. On removal from the kiln the saggers are emptied, but as many particles of sand adhere to the ware it has to be brushed or "scoured," a process which is one of the dustiest and most dangerous in a pottery. Unless the

scouring is carried on over an open grating, down which there is a strong aspirating draft, the women who are employed are soon enveloped in a cloud of fine white dust, inhalation of which, after a very short exposure to the work, produces cough with signs of bronchitis and general debility. As the dust is silicious, it is more productive of injury to the lungs than are other forms of dust, unless an exception be made in favour of the metallic and stone dust inhaled by the Sheffield steel-grinder, and the rock dust breathed by the gold-miner on the Rand. Arlidge tells us that when potters' phthisis is uncomplicated by tuberculosis it "advances imperceptibly and without constitutional disturbance. One of its first symptoms is a clearing cough on first rising, but soon to be met with on any change of temperature, and accompanied by shortness of breath. Haemoptysis does not usher in the malady, and more frequently than not never makes its appearance. The appetite and the general bodily functions remain long intact; there is no febrile action, no accelerated pulse, no hectic, no rapid emaciation. Anaemia is no necessary adjunct. The sputa remain for long white and frothy, with specks or streaks of black matter, which is inhaled dust. Later on this mucous expectoration becomes purulent and heavy; it forms pellets, but is not green. The cough is more paroxysmal and violent than that of phthisis, and the urgency of the dyspnoea greater and out of proportion to the extent of consolidated lung. The signs of condensation are not so specially limited to the infraclavicular spaces as in a tuberculous lesion, and hence the sinking below the clavicles is not marked. Areas of dulness on percussion are often found distributed at different parts, particularly in the scapular region and near the base of the lungs. I would add that the general aspect and physiognomy differ from those of tuberculous phthisis. The features are rather those of asthmatical subjects; but we must never forget how frequently tuberculous deposit modifies the picture of fibrosis I have endeavoured to present." Arlidge found the mean age at death of male potters aged twenty and upwards to be 46½ years, whilst that of non-potters was 54. In potters the mortality from dust diseases was 12·29 per cent; in other workpeople in the neighbourhood only 7·86. The death-rate in potters from consumption was 12·9 per cent; in other workpeople 9·27. Dr. Tatham is of the opinion that potters succumb to non-tuberculous disease of the lungs much more rapidly than they do to pulmonary tuberculosis, and that much of the so-called potters' phthisis is pulmonary fibrosis.

Slate-Quarriers and -Dressers.—The quarrying of slate is carried on in two ways: (1) the open method as in ordinary quarries, and (2) underground. Underground quarries come under the "Metalliferous Slate Mining Act." It is with the underground methods of obtaining slate and the health of the workpeople concerned that I shall deal, also with the effects upon the health of the men when employed in cutting up the large blocks of stone, brought from the mine to the workshop, into slates of the proper length and dressed for the market. Dr. Richard Jones, of Blaenau Festiniog, has given a valuable account of the pulmonary

diseases met with in slate-miners and -dressers. It is among the men who dress the slates that the chronic form of pulmonary disease or fibrosis prevails, whereas in the men employed underground pneumonia is the more frequent malady. Were it not that in Merionethshire slate mills an average of 5000 cubic feet is allowed to each man and boy, "fibroid phthisis" would be much more frequent than it is. In slate-quarrying the methods used are as follows: quarrying is simply getting and removing to the surface large blocks of stone, often 3 to 5 yards long and 2 to 3 feet deep. These blocks are taken to the slate mills, where they are split up into smaller pieces, put on the sawing tables and sawn into different lengths. They are then by means of chisels split up into pieces about $\frac{1}{4}$ to $\frac{1}{8}$th inch in thickness, after which they are placed upon a machine, dressed, and thus made ready for sale. Slate is composed of 60 per cent of silica and 40 of alumina. Dr. Jones finds that many of the men are liable to low forms of pneumonia, from which most of them recover and return to work. Months or years afterwards these workmen are found to be suffering from cough, shortness of breath, and inability to follow their employment. On physical examination the chest wall is observed to be sunken and retracted, but there are no signs of excavation. At this stage, although carefully searched for, no tubercle bacilli are usually found in the expectoration; nor is haemoptysis common. When due to dust, the lung disease is as a rule bilateral, but when of tuberculous origin it is one-sided. Much of the lung disease met with in slate-dressers is the result of inhalation of the dust generated during the dressing of slates by means of machinery, for at Ballachulish, at the entrance to the Pass of Glencoe, where slate-quarrying and -dressing is an old industry, Dr. Lachlan Grant informs me there is no pulmonary fibrosis and very little pneumonia among the men, probably because work is all done by hand in well-ventilated buildings.

At the slate quarries at Fumay, in France, the work is underground, and Sejournet states that the men are exposed not only to dust, during the detachment of the blocks of stone, but also to the fumes from the gunpowder and dynamite used in blasting. The atmosphere of the workshops at the surface is cloudy with fine dust, which comes from the cutting and dressing of the slates by machinery. Whilst many of the slate-makers are strong, healthy-looking, and well-developed men, others are of short stature, bent in the spine, and rickety. Many of the men at Fumay commence work at the age of fifteen; they begin in the cutting and dressing departments, and subsequently go into the slate quarry. In France slate-miners' lung disease usually commences as a bronchitis or as a limited bronchopneumonia, which is recurrent and terminates fatally in from five to ten years. Both Sejournet and Hamaide consider the lung disease to be a form of phthisis, and attribute it to inhalation of dust. Pellets of a slate-like colour and of stony hardness are occasionally brought up in the expectoration, and are followed by fairly brisk haemoptysis. The malady is a genuine pneumoconiosis, the result of breathing slate dust. In the lungs are

found chronic interstitial pneumonia, lobular fibrosis or emphysema, and bronchitis. Ripert, while not considering the lung disease of slate-quarrymen and -dressers to be tuberculous phthisis, yet admits that if a workman is predisposed to tuberculosis he is less prepared to resist the bacillus. In the expectoration of only one of three patients examined did Ripert find tubercle bacilli. Slate-miners' phthisis, like other forms of pneumoconiosis, is so insidious in its progress that it may advance to a considerable extent without giving rise to symptoms which oblige the individual to give up work.

Ganister Mining and Ganister Crushing.—The valley of the Don is the principal centre of the ganister-mining industry in England. Ganister is an extremely hard, close-grained, silicious stone, usually found underneath coal seams. It is mined in Yorkshire, Durham, and North and South Wales. The rock, which possesses enormous fire-resisting properties, is crushed to make bricks to line Bessemer- and steel-converters. Dr. C. L. Birmingham has drawn attention to the effects of ganister mining and crushing upon the health of the men employed; so too has Dr. Robertshaw, the Medical Officer of Health for Stockbridge. The explosives used for getting the stone also create a considerable quantity of dust, but it is during the process of crushing that the larger quantity of fine dust is given off, inhalation of which is unavoidable unless jets of steam are made to play upon the ganister. The manufacture of bricks from the crushed stone is also a dusty process. Pulmonary phthisis of the fibrotic type is therefore frequently met with among ganister workers. In not a few of the patients the lung disease is a combination of fibrosis and tuberculosis.

Millstone Building, French Buhr-stone.—Men employed in millstone building are liable to pulmonary phthisis. The millstones used for grinding grain, spices, coprolites, etc., are made out of wedge-shaped pieces of buhr-stone, a hard flint-like stone which comes from France. Millstone masons are a short-lived body of men. Some of them succumb at an early age to phthisis and other pulmonary diseases, their death being too often hastened by exposure and alcoholic intemperance. The average number of years that a buhr-stone worker will follow his occupation is ten to fifteen. By this time he will probably have a cough and shortness of breath, attended by recurrent haemoptysis. Blood-spitting is a frequent symptom of the pneumoconiosis of millstone masons, in which respect it differs from the pneumoconiosis of some of the other dusty trades. In my visits to the millstone yards on the banks of the Thames, and to the quarries and buhr-stone works at Fierté-sous-Jouarre in France, I obtained the same story of the early development of pulmonary disease in the workmen; also that in consequence of lung disease and the drunken habits of the workmen few of the men reached the age of forty. In several instances the symptoms commence as those of bronchitis.

Steel Grinding.—The grinding of steel is done on circular stones turned by steam or water power. There are two kinds of grinding:

(1) dry, (2) wet method. Steel forks, needles, and gimlets are ground by the dry method; knives, scissors, and parts of razors by the wet. Dry grinding is the more dangerous from the point of view of health, for large quantities of fine steel and stone dust rise into the atmosphere and are irritating to the lungs and provocative of phthisis. The lungs of steel-grinders after death exhibit the characteristic lesions of fibrosis; imbedded in the thickened strands of fibro-connective tissue of the lungs can be seen particles which prove on chemical examination to be particles of iron. A few years ago the mortality of Sheffield steel-grinders from phthisis was high, but within recent years, owing to improvement of industrial conditions, including the introduction of means for the removal of dust, steel-grinders' phthisis has become less common. Mr. Sinclair White considers that the disease first appears as chronic bronchitis with emphysema. The symptoms may commence with a bronchitis that never quite disappears, or disappears during the summer months only. The malady surely recurs in the winter, and the cough and shortness of breath oblige the steel-grinder to give up work. The physical signs at this stage are those of chronic bronchitis, with insular areas of dulness over which the breath-sounds are loud and tubular, whilst at other places the respiratory murmur is deficient. Wasting, night-sweats, and haemoptysis mark the invasion of the lungs by tuberculosis. The shortness of breath is always greater than that observed in ordinary phthisis. In consequence of a certain amount of emphysema, which is invariably present, small areas of consolidation of the lung are not always readily detected. In the terminal stages of the disease tubercle bacilli are frequently found. When the late Dr. J. C. Hall of Sheffield read his paper on "Trade Phthisis" at the Social Science Congress in 1865, the average age of dry steel-grinders was 29 years; but in recent years the average age at death has risen to 43.

Slag Crushing.—Slag, the refuse obtained from blast furnaces in which the iron has been removed from the ore by the Gilchrist-Thomas or basic method, is, when crushed, made use of as a manure on account of the large amount of phosphate of lime which it contains. The slag which is crushed at Ruhrort on the Rhine contains 24 per cent of iron protoxide, traces of iron oxide, 40 per cent of phosphate of lime, and 30 of silicate of lime; the slag from the blast furnaces in Middlesbrough contains 41·58 per cent of lime, 6·14 of magnesia, 2·57 of alumina, 8·54 peroxide of iron, 13·6 of iron protoxide, and 14·36 of phosphoric acid. The slag is crushed by means of edge-runners and flint pebbles or heavy balls into a fine powder; and, although there have recently been considerable improvements in the methods of working, the crushing of slag still remains a dusty occupation, and not free from danger to the health of the workmen. In 1888 Middlesbrough suffered from an epidemic of pneumonia, which was at first attributed to slag dust; but Dr. Ballard, who was sent by the Local Government Board to make an inquiry, traced the disease to infected food. He was of the opinion, however, that although slag dust was not the cause of this outbreak of pneumonia,

yet when from any cause pneumonia became epidemic, persons exposed to slag dust were more liable to the disease, and more readily succumbed to it. In my own examination of the men employed in the slag-crushing works in and near Middlesbrough, I found the symptoms and physical signs to be those of chronic bronchitis and emphysema, and that many of the men had had one or two attacks of pneumonia. E. Aufrecht of Magdeburg also finds that slag workers are more liable to pneumonia than men employed in other trades. In 1887 at one particular slag works in his district 48 per cent of the men suffered from pneumonia, 25·5 per cent in 1888, and 21·5 in 1889. Aufrecht also found that several healthy labourers, within a fortnight after commencing work in the slag-crushing mills, were attacked by pneumonia, and that some of those men were seized as many as four times in succession; 30 per cent of the cases proved fatal. The difference in the chemical composition of the slag is probably the explanation of the greater prevalence of pneumonia among the slag-crushers in Germany than in Middlesbrough. The respiratory diseases induced by slag dust and those caused by the inhalation of coal, metallic, and mineral dust are not exactly the same in all respects. In slag-crushers the disease is not so much a true pneumoconiosis as an acute inflammation of the lower lobe of one of the lungs, which after death is found to be the seat of ordinary grey hepatisation. To what extent slag dust is responsible for the lung disease it is impossible to say; nor do we know whether the action is chemical or mechanical. It may be that the contemporaneous presence of the pneumococci in the lungs is only a coincidence; or it may be that the slag dust paves the way for the operation of the micro-organisms of pneumonia. It is noteworthy, and with this remark we shall dismiss the subject of slag-crushers' lung disease, that the inflammation of the lungs commences like pneumonia and runs a similar course, with rigor, pain in the chest, rusty sputa, and, in 30 per cent of the cases, herpes on the lips. On physical examination signs of pulmonary consolidation are to be noted.

Gold-Miners' Phthisis, Rand Phthisis, Silicosis.—In 1902 I drew attention to the large number of cases of miners' phthisis in men who, after having worked a few years in the South African goldfields had returned to this country, many of them only to die a few months afterwards. Shortly before the outbreak of the war these men, then all comparatively young and healthy, had gone from the Northumberland coalfields to the Rand in search of fortune. I was particularly struck by the bronzed and healthy appearance of the men on their return, yet on examining their chest I found evidence of extensive disease of the lungs which from its nature was likely to be progressive. Shortness of breath, aggravated by the slightest physical exertion, was the principal complaint. It was out of proportion to the extent of the pulmonary disease. Pain in the chest was only occasionally complained of, and cough was not frequent nor followed by expectoration. Haemoptysis was not common. Since 1902 a larger experience of the malady has led me to observe that

it is the shortness of breath which obliges a Rand miner to seek medical advice. Gold-miners on the Rand can follow the employment for a few years only, not more than five to ten; and they nearly all attribute their pulmonary disease to inhalation of dust. It is noteworthy that since the introduction of machine rock-drills into the South African mines the mortality from lung diseases in the men who work underground has enormously increased. Unless water spraying is carried on at the same time rock drilling by machinery gives rise to enormous quantities of very fine dust, which is composed of hard and sharp-pointed particles of silex; to the inhalation of this dust the lung disease is in all probability due.

There are other contributory causes. Many of the Transvaal mines are of great depth. They vary from 495 to 3916 feet, and the temperature runs, according to the depth, from 65° F. to 83° F. The increase in temperature is in direct proportion to the depth, being 1° F. for each 208 feet, *i.e.* 0·48° F. per 100 feet. In the deep mines the work is carried on in circumstances that are trying to the men. At the end of the day, by means of lifts, the miners are rapidly transported from a warm deep mine to the surface where the air is cold; consequently chills are not uncommon. Dr. Walter Summons, who has had experience of Australian mines, states that at Bendigo the temperatures are even higher than those of the Rand mines, and frequently reach 99° F. to 101° F. Miners when at work are fairly comfortable, if the air is circulating; it is when the air becomes stagnant and saturated with moisture that, unable to perspire freely, the men become fatigued. In addition to breathing the dust evolved during rock-drilling, gold-miners on the Rand return to the particular "working" in the mine too soon after the rock has been brought down by dynamite, when the atmosphere is not only charged with dust but contains large quantities of carbon dioxide and carbon monoxide gases, to the inhalation of which several South African mining engineers attribute, erroneously in my opinion, the special form of disease of the lung we are considering. The symptoms caused by "gassing" are not the same as those caused by an increasing pulmonary fibrosis. That Rand miners' phthisis is the result of exposure to dust in the mine the Report of the Miners' Phthisis Commission, Pretoria, amply demonstrates. Of 4403 miners, working underground in the gold-mines of Witwatersrand, 1200 were medically examined on behalf of the Commission; of this number 187 or 15·4 per cent were certified by the examining doctor to be suffering from miners' phthisis, and a further 88 were suspected. The average age at death of Transvaal gold-miners at the time of the war was 35·5 years. Most of the men who died from phthisis were rock-drillers, in whom as a class the disease prevailed to the extent of 91·98 per cent. The average length of time rock-drillers follow their occupation is 6·49 years. It is noteworthy that out of 93 males who died from disease of the chest in the Johannesburg Hospital 50 per cent were miners. The most dangerous dusty processes in the gold-mines are the blasting and boring of the rock, but a considerable quantity of dust is raised also during the shovelling of

the debris. A cubic foot of air, taken close to rock-drill machines boring dry holes, was found to contain 0·185 grain of dust on one occasion, and 0·083 grain on another; so that miners working in these atmospheres ran the risk of inhaling 2·38 grains of dust per hour. It is not contended, however, that the whole of this dust reached the lungs of the miners; most of it, caught by the ciliated epithelium, would be arrested in the mucus of the trachea and bronchial tubes, and finally expelled.

Morbid Anatomy.—Although towards the end of life the miners who had worked on the Rand, and who ultimately came under my care, had lost flesh, the emaciation was slight compared with that met with in pulmonary tuberculosis. After death, in fatal cases of chronic lung disease, there is not the amount of emaciation that might be expected. On removing the sternum with adjoining cartilages the lungs are found to be adherent to the costal pleura in places; some of the more recent adhesions separate readily, those at the base usually with difficulty. As a rule there is no pleural effusion. The lungs are here and there solid and of stony hardness, the hard areas being irregularly distributed and giving the sensation of solid balls scattered through the tissue. The lungs are black or bluish-black, and on section give a gritty feel. A considerable portion of the lung is solid, hard, airless, and when squeezed exudes a black ink-like fluid, especially in cases of anthracosis or coal-miners' phthisis. The cut surface of the lung may be smooth, except for the bronchial tubes with their rough and prominent walls, between which run coarse strands of greyish-white connective tissue extending to the pleura, which is often thickened. Characteristic pneumoconiosis does not present naked-eye evidences of tuberculosis. The bronchial glands are enlarged, black, and from periadenitis often adherent. Usually there are limited areas of emphysema, mostly marginal, but occasionally also in the body of the lung. The dulness detected on percussion of the chest during life is to be explained probably more by the patches of thickened pleura and adhesions to the chest walls than by the small areas of consolidated lung. In many instances indeed the pulmonary fibrosis is diffuse; this is most marked in the lower and posterior portions of each lung.

In the cases of uncomplicated gold-miners' phthisis which I have seen there were no cavities in the lungs save in one. In this instance there were in the centre of a mass of solid black tissue two small cavities with irregularly broken-down walls, but they were not secreting pus. Pulmonary excavation can take place apart from tuberculosis; it may, for example, be purely necrotic in origin.

In the lungs of a ganister miner who died from phthisis, Dr. Andrewes found definite evidences of tuberculosis in excavation, softening, and the presence of the tubercle bacillus. In several of my cases of pneumoconiosis tubercle bacilli have been found in the sputum during life, and in the lungs after death; but as in many others it was not found during life or after death, it would appear that the presence of tuberculosis was the result of an accidental infection and not a necessary

event in pneumoconiosis. Reference to this subject will be made on p. 462.

The hardness and solidity of the lung in pneumoconiosis are due to excessive fibrosis and to the deposition of gritty particles of stone in stone-miners' phthisis, of steel and stone in steel-grinders' phthisis, and of silica in miners' phthisis. The particles of grit in the lungs have been examined physically and chemically, and have been found to correspond exactly with the particles of dust that float in the atmosphere of the mine or factory where the patient had worked (*vide* p. 450).

Microscopical examination shews that large areas of the alveolar structure of the lung have disappeared, and that their place has been taken by a dense, unyielding fibrous tissue, scattered through which are myriads of black particles resembling carbon—some of these particles are of considerable size and are lying free in the tissue, while the more minute particles are imbedded in the large cells, the so-called "dust-cells." At places the fibrous tissue is arranged in concentric layers, so as to form small nodules; and between these layers, especially towards the periphery, the particles of pigment are especially numerous. The centre of these minute nodules is frequently found to be an obliterated and thickened blood-vessel. The nodules form round a small artery, vein, or bronchiole. In none of these masses have I found giant cells or the grouping of small cells suggesting tuberculosis. Fraenkel is of the opinion that the nodules form in consequence of chronic inflammation of the lumen of minute bronchioles and of the walls of the pulmonary alveoli. At first there is swelling, and this is followed by atrophy. Arnold speaks of the fibrosis commencing as an indurative bronchopneumonia in the peri-infundibular and peribronchial connective-tissue; or originating where blood-vessels bifurcate, the inflammation commencing in groups of cells in lymphoid tissue. The walls both of arteries and bronchial tubes are thickened; in the outermost rings of the fibrous tissue the pigment particles are usually most numerous. Between the nodules there are portions of lung which exhibit alveolar structure, but the air-cells are not quite normal; they either shew signs of proliferating catarrh or the walls are thickened, while lying free in the alveoli are large cells often quite full of black pigment granules. The septa of the lungs are enormously thickened, and can be traced outwards to the pleura, which is similarly changed. The pigment granules are frequently arranged so as to form long black lines or streaks which correspond to the course of the lymphatic vessels. The large bronchi shew catarrhal inflammation. As pigment particles are extremely numerous in the deeper portions of the mucous membrane of the bronchial tubes, the presumption is that these particles of dust effect an entrance through breaches of the superficial layer of cells. Normally the pulmonary alveoli are lined by a layer of flattened cells, between groups of which, according to some histologists, are stomata, through which particles of dust might find their way into the alveolar walls and lymphatic vessels. Although in anthracosis or coal-miners' phthisis the lung is perfectly black, the fibro-

connective tissue is not so much increased as in some other forms of pneumoconiosis; a condition which proves that carbon *per se* is but slightly irritating in its effects. When a coal-miner's lung shews pronounced fibrosis, it is generally an indication that the individual has worked in a coal-seam which contained a quantity of stone; it is the stone-dust in the coal, not the coal itself, which in the case of colliers' phthisis is the cause of the fibrosis, for the lungs of men who have worked in soft coal or at charcoal-burning, and who have inhaled the smoke from lamps, may be laden with carbon particles without much evidence of fibrosis and without the invasion of pulmonary phthisis, as is often seen in the bodies of miners who have been accidentally killed, and who had never had any symptoms of lung disease. A coal-miner in an acute bronchial attack will bring up large quantities of black spit, which will gradually lessen and cease on his recovery. Even though he never works again in the mine nor takes up any dusty trade, yet years afterwards, on the supervention of another catarrh, he will bring up black spit, a symptom which shews that the pigmented particles are deposited in the deeper layers of the bronchial mucosa, as well as in the alveoli. The heart is flaccid, but except that the wall of the right ventricle may be slightly thinner than usual, is otherwise healthy; the valves are natural, and the size and weight of the heart remain normal. The liver and spleen are usually normal in size; and on section the kidneys are healthy.

Dust Diseases of the Lungs and Tuberculosis.—Opinions are divided as to the relation of pneumoconiosis and tuberculosis. One party maintains that some of the structural changes met with in the lungs of persons who have worked in dust are tuberculous, and that pneumoconiosis is only the fibroid form of ordinary pulmonary tuberculosis. My own experience does not lead me to accept this conclusion. Pneumoconiosis is in its inception non-tuberculous; it may even run its course and end fatally without ever becoming tuberculous. In at least two necropsies which I made on the bodies of Rand miners the lungs were quite free from naked-eye and microscopical evidence of tuberculosis. The absence, during life, of fever, of sweating, and of emaciation, and the presence of a bronzed appearance of the skin, combined with a degree of breathlessness quite out of proportion to the physical signs of disease in the chest, all indicate that the disease is different from pulmonary tuberculosis. Yet in a considerable proportion of the patients the disease of the lungs becomes tuberculous; whether the percentage of such cases is as low as 47, as some pathologists maintain, or as high as 70, as others assert, the number of cases of miners' phthisis which become tuberculous is not so great after all, considering the length of time the illness lasts and the numerous opportunities for tuberculous infection. The records of any large Infirmary shew that evidence of pulmonary tuberculosis, latent or active, is forthcoming in nearly 70 per cent of all bodies examined after death. The presence of tuberculosis in from 47 to 70 per cent of cases of pneumoconiosis has given rise to the opinion that all cases are tuber-

culous, but this conclusion is not borne out by the clinical data, nor by results of naked-eye and microscopical examination of the diseased structures. As the disease progresses the patients run the risk of tuberculous infection, the onset of which is shewn by sweating, rise of temperature, presence of the bacilli in the sputum, rapid emaciation, a change in the symptoms, and by an alteration in the general conditions of the patient for the worse, as indicated by the more rapid course of the disease to a fatal termination.

There are two forms of pneumoconiosis: (1) the purely non-tuberculous form, and (2) that complicated with tuberculosis. A Committee of the Transvaal Medical Society inquired into this subject, and reported that "while in some cases a true tubercular phthisis may coexist or may be superadded, the conjunction is only seen in a minority of cases." Dr. Ernest Black, in the Report of the Royal Commission on the Ventilation and Sanitation of Mines in West Australia, February 1905, says: "Some of the cases investigated were of the purely tubercular type, but in the majority there had been apparently fibrosis of the lung followed by tubercular infection of the damaged lung." Prof. D. J. Hamilton considered that "coal-miners' phthisis is not a tuberculous process, but has more the character of an aseptic slough due to the altered condition of the organ. In the case of the stone-mason's lung, on the contrary, a complication with tubercle, at the time of death or for some time before it, is frequently met with, and according to Philip is accompanied by the expectoration of tubercle bacilli."

It is not easy to detect tuberculosis in lungs fibrosed from the effects of dust: bacilli are rare and giant cells are only occasionally observed. That tubercle bacilli and their toxins can *per se* give rise to an excessive development of fibrous tissue has long been known. Thus, in the case of the liver, Henri Claude experimentally produced a tuberculous cirrhosis with extremely dense fibrous tissue. He considered that the structural changes in the liver were set up by bacillary rather than by toxic action, and were the outcome of an exaggerated reaction due to increased local resistance. Stoerk also inoculated guinea-pigs with tuberculous products, and found that at first the liver shewed definite tuberculosis, but that subsequently fibrosis supervened and the tuberculosis receded, so that ultimately the liver shewed cirrhosis, the fibrous tissue being intersected by numerous biliary canaliculi. Since the experimental introduction of tubercle bacilli or their toxins into the blood-stream produces marked fibrosis of the liver, there is no histological reason, although the two organs are not exactly comparable, why similar changes should not take place in the lungs. The possibility that pulmonary fibrosis may be thus induced is not questioned, but experience proves that when tuberculosis is present in the lungs of persons who have died of pneumoconiosis the fibrosis is the result of a primary irritation induced by dust, and that the tuberculosis is secondary and accidental. H. Ribbert, on the contrary, regards the lesions in the lungs in pneumoconiosis as primarily tuberculous, and

considers that the tubercle bacilli weaken the lungs and so favour the entrance of dust into these organs. When pneumoconiosis and tuberculosis coexist there is in addition to the fibrosis slight catarrh of the remaining alveoli. The pigmentation of the lungs is much greater in pneumoconiosis than in tuberculosis. Where infection has been superadded there are minute tuberculous nodules, some of which are observed to be caseating in the centre, and among the round cells in the periphery may be seen one or two giant cells. The alveolar spaces usually contain large catarrhal cells.

While investigating the susceptibility of Bendigo miners to tuberculosis, Dr. Summons found the opsonic indices of ten miners with non-tuberculous fibrosis of the lungs, of ten tuberculous miners, and also of ten cases of consumption amongst adult males non-miners, to be as follows :—

Miners' Phthisis (non-tuberculous)	Miners' Phthisis (tuberculous).	Phthisis (tuberculous in non-miners).
1·16	1·3	·8
1·1	1·2	·75
1·1	·80	·65
1·01	·74	·6
1·0	·66	·6
1·0	·63	·5
·92	·62	·5
·88	·62	·46
·8	·57	·4
·7	·54	·4

In miners, as a class, the power of resisting tuberculous infection is much the same as in healthy adult males generally. "The great prevalence of tuberculosis among them is due to the lower vitality of the damaged lungs, and when infection does take place the opsonic index becomes subnormal and corresponds to that of ordinary consumptive cases." Where and how miners with pneumoconiosis become tuberculous it is difficult to say, but there is nothing to suggest that they become infected differently to other people. The infection must take place either in the mine, in the home, in the public-house, or in some place of amusement. In the case of the Rand miner the probability is that repeated chills by inducing recurrent catarrh of the bronchial tubes dispose the individual to infection by tuberculosis far more than the fibrosis itself does. Miners with tubercle bacilli in their sputum should not be allowed to work in the mine unless they are careful to carry a small spittoon to receive and disinfect the expectoration.

Most of the dust inhaled by people fortunately never reaches the lungs. Owing to the deflection of the currents of air at the sharp angle of the fauces the dust is arrested here, or if it succeeds in passing beyond this point, it is usually caught and deposited in the mucus secreted by the upper parts of the respiratory canal. Soluble dust may be absorbed.

Insoluble particles, on the other hand, may be expelled by the action of the ciliated epithelium or rejected in the mucus brought up by coughing. So long as the bronchial tubes are healthy the mucus and the ciliated epithelium form strong protective barriers to the entrance of dust into the lungs. Notwithstanding these obstacles, dust insidiously gains an entrance into the lungs, as shewn by the pigmented lungs of dwellers in towns as compared with the respiratory organs of an infant. Most of the pigmentation is due to the presence of particles of soot from smoke, and as no bad effects follow the presence of these particles in the lungs, we can only regard this form of anthracosis as coming under the category of the physiological condition alluded to on p. 449. The anthracosis of the coal-miner is harmless up to a certain point—this is equally true of the anthracosis caused by soot and carbon inhaled by miners when working in soft coal. It is different when the miners have been working in hard coal. This contains a good deal of stone, so that when pitmen in these circumstances become anthracosed, there is in addition to the pigmentation of the lung caused by carbon a degree of fibrosis of the lungs, the result of irritation from the particles of stone. Because uncomplicated anthracosis from carbon is consistent with good health, and of itself neither disposes to bronchial catarrh nor to tuberculosis, some physicians have asserted that anthracosis and tuberculosis are antagonistic to each other, and that particles of carbon in the lung exert a certain bactericidal influence. This is a subject upon which it is impossible at present to express a dogmatic opinion; leaving carbon out of the question, it may be said without hesitation that some other forms of dust frequently act as vehicles for micro-organisms, and that they prepare the tissues of the lungs for the reception and multiplication of microbes, especially if the dust provokes catarrh of the bronchial tubes and the alveoli. Inhalation of dust on a country road makes some people cough, in others it induces a catarrh. When persons have to work in a dusty atmosphere for several hours a day, the recurrent catarrh with frequent fits of coughing may obviously bring about a structural alteration in the lung, such as emphysema. The nature of the dust that is inhaled is not without a special influence on lung structure; hard and sharp-pointed particles of dust are much more likely to irritate the lungs and to be followed by a reactive inflammation than, for example, the soft and less angular particles of carbon. The lungs and the bronchial tubes are able to get rid of particles of dust. Thus, for a few days after a short exposure to a dusty atmosphere persons continue to bring up greyish-black sputum; and the lungs of animals kept for a few days in an atmosphere rendered thick by smoke from a lamp and at once killed, are found to be black, whereas the lungs of control animals which were removed from the sooty atmosphere and were kept alive for several days in good air, shew that the carbon has greatly diminished in amount. This is one reason why men engaged in dusty trades should, if possible, be allowed to have interrupted employment, so as to give the lungs the opportunity of getting rid of some of the dust.

A very minute quantity only of the inhaled dust reaches the lungs

and is retained there; the greater part is expelled by the expectoration and by mucus hawked up from the pharynx. It is chiefly the lighter and smaller particles of dust that reach the lungs, and yet in the experimental production of pneumoconiosis particles of considerable size can be seen in the pulmonary parenchyma. Under the influence of living cells many of these large particles of dust, if comparatively speaking soft, are gradually reduced in size by a process of erosion. The finer granules are absorbed by the large migratory phagocytes or "dust-cells" which are to be found in the bronchial mucous membrane and in the alveoli. These cells are aptly named scavengers, for having englobed the dust they themselves are thrown out in the expectoration, or, as they are endowed with powers of locomotion, they may penetrate the walls of the alveoli, where they remain or break up; or again, they may proceed by the lymphatics of the lungs to the bronchial glands, where they either unload themselves of the pigment particles or undergo a process of disintegration attended by liberation of the pigment,—hence the coal-black appearance on section of the glands at the root of the lungs. The removal of dust from the pulmonary alveoli by phagocytes is rapidly accomplished; in a few hours after the inhalation of red, blue, or black dust, similarly coloured dust will be found in the bronchial glands. The presence of dust in the lungs stimulates the phagocytes to activity, and for a brief period, if the dust is not too irritating, no other local reaction is observed. Although there is doubt as to the origin of these phagocytes, my own experiments lead me to regard them as derivatives from the alveolar epithelium and possibly the blood. Dr. J. C. Briscoe believes that the polymorphonuclear leucocytes of the blood and the alveolar cells are both capable of acting as phagocytic dust-cells. Phagocytes cannot and do not remove all the dust from the lungs; several of the sharp-pointed particles of dust penetrate the alveolar walls either through the stomata that normally exist or through lacerations of the alveolar epithelium, and here they may remain or are transported by the lymphatics. Much of the dust in the pulmonary lymphatics has entered these vessels not through the alveolar walls, but through the mucous membrane of the small bronchi. Particles of pigment are extremely numerous in the periphery of the minute bronchi and the blood-vessels. The particles of dust in the perivascular lymphatics reach these vessels by a less direct route than that followed by the particles in the peribronchial lymphatics. Repeated accessions of irritating dust into the lung will be followed by fibrosis, which, commencing as a peribronchitis or alveolitis, is apt to become progressive; but although it spreads through the lung it is not always evenly distributed, becoming accentuated in places so as to form nodules. The pleurae and the septa of the lung become thickened; in a miner's lung the blood-vessels are thickened, but this is due to periarteritis and not endarteritis, and in this respect the fibrotic lung of pneumoconiosis differs from that caused by syphilis. On microscopical examination of the bronchial glands, the place of the normal lymphoid structures is

found to be largely taken by fibrous tissue in which myriads of dust particles are imbedded.

Mode of Entrance of Dust: Aerial or Intestinal?—The question has recently been raised whether pulmonary anthracosis is the result of dust directly drawn into the lungs in inspiration or swallowed and passed through the intestinal walls into the lymphatics, and thus carried to the lungs. The intestinal origin of pulmonary anthracosis has been investigated by Calmette and by Vansteenberghe and Grysez. The results of their experiments lead them to advance the theory of the intestinal origin of anthracosis. The lungs of guinea-pigs, killed twenty-four to forty-eight hours after a meal of food mixed with Indian ink or carbon, contain islands of black material disseminated through the upper and lower lobes. The mesenteric glands are free, whilst those of the mediastinum are swollen and pigmented. According to Vansteenberghe and Grysez the results obtained vary with the age of the guinea-pigs. If the animals are young, the respiratory organs are found free from pigment, whilst the mesenteric glands are infiltrated with carbon. The explanation of the impregnation of the lungs with pigment particles is probably as follows: The carbon particles taken with the food soon reach the intestinal lymphatics, but in young guinea-pigs the mesenteric glands offer a barrier which the carbon particles cannot break through, whereas in adults the mesenteric glands do not arrest the particles, so that the dust, whether absorbed by phagocytes or lying free in the lymph in the form of granules, is diverted to the thoracic duct and thence into the general circulation, by means of which it reaches the lungs. Injection of Indian ink or particles of carbon into the peritoneal cavity is followed, but not quite so readily, by the same results; pulmonary anthracosis without any change in the mesenteric glands, can thus be produced in adult guinea-pigs, an anthracosis which gradually diminishes on cessation of the experiment, while the bronchial glands remain enlarged and pigmented. In young guinea-pigs, on the other hand, the lungs do not present any signs of pigmentation, but the mesenteric glands are of a deep black colour. From these results, which my own feeding experiments confirm, Vansteenberghe and Grysez conclude that pneumoconiosis may be of intestinal origin; they attach considerable importance to the absence of pulmonary anthracosis in animals which, after ligature of the oesophagus, had been exposed to a smoky or dusty atmosphere. They found that the carbon was arrested above the oesophageal ligature, and that although there was plenty of pigment in the nose, pharynx, and upper part of the oesophagus, none was found in the trachea. It would therefore appear that in many cases physiological anthracosis is the result of the intestinal absorption of carbon particles, especially as when one bronchus is occluded and the animal is fed with dust, the part of the lung corresponding to the occluded bronchus shews as much pigment as those portions of the lungs which are in free communication with the air. Calmette and Guérin apply these data to pulmonary tuberculosis (*vide* p. 305). In one of the hospitals in Lille,

George Petit administered small quantities of charcoal to tuberculous children whose mesenteric glands had lost their protective power through disease, but in none of those children was pulmonary anthracosis found after death. This subject is also discussed on p. 304.

The conception of the intestinal origin of pulmonary anthracosis has met with opposition. In young guinea-pigs placed in a dusty atmosphere for twenty minutes every morning and evening for three weeks, Kuss and Lobstein found marked evidence of pulmonary and glandular anthracosis, whilst in control animals which had received by ingestion amounts of carbon at least equal to the quantity respired, the lungs shewed nothing more than the slight microscopic anthracosis which is present in most animals. F. Feliziani administered to twenty guinea-pigs of various ages Indian ink, sometimes in food, sometimes by the stomach tube, and yet in none of the animals were the lungs found pigmented after death. In guinea-pigs and rabbits fed with Indian ink and killed forty-eight hours later Herman could not detect any signs of anthracosis in the lungs and internal organs by the naked eye, but on microscopical examination of sections of the lungs of two of the animals he found leucocytes containing granules of Indian ink in the interstitial tissue of the lungs. Carmine was also given by Herman, and although forty hours afterwards there were no coloured particles in the mesenteric glands or lungs, and no naked-eye evidence of such even seven days after the daily ingestion of carmine, yet after this period coloured granules were found in the so-called "dust cells," in the lungs, and in the bronchial glands. Herman's results, therefore, were not uniform. He does not adopt the theory of the intestinal origin of physiological anthracosis of the lungs. It is a question of degree between the physiological and pathological forms. Soot and carbon dust are not physiological elements. They do not correspond to any internal necessity. Although their presence in the body is an unavoidable consequence of our respiratory and digestive functions, we can scarcely regard physiological anthracosis as a pulmonary pigmentation of intestinal origin, and pathological anthracosis as a pigmentation of the lung, caused by inhalation of dust. Personally, I consider that pneumoconiosis is principally caused by inhaled dust, and while not denying the possibility of an intestinal origin, more convincing evidence is necessary before the widely accepted belief in its aerial origin is abandoned. Vansteenberghe and Grysez believe that the soot of smoke when inhaled only invades the pulmonary or alveolar epithelium without penetrating into the interior of the parenchyma. Two kinds of anthracosis might therefore be recognised—(1) intra-alveolar, corresponding to an enamelling of the pulmonary epithelium, and (2) interstitial, constituting a veritable tattooing of the lung. As a matter of fact, what happens when the smoke of turpentine, for example, is inhaled, is that the lining membrane of the bronchial tubes and the alveoli is invaded by the soot, but by degrees the intra-alveolar particles are taken up by phagocytes and carried into the parenchyma of the lung to such an extent that what was at first an alveolar anthracosis, rapidly passes

into an interstitial. An intestinal origin can scarcely, in my opinion, explain the pneumoconiosis of the stone-mason, of the buhr-stone worker, or of the steel-grinder. The lungs of millstone builders contain particles of stone and pigment, and the mediastinal glands are similarly affected, whereas the mesenteric glands are quite free. The same has been observed in men working in gold ore; their lungs are often black, owing partly to smoke and pigment, and though their bronchial glands are also black the mesenteric are unaffected. As a means of invading the lung, the intestinal method, whatever it may be for tuberculosis, must be, so far as dust is concerned, inferior to the aerial. That the intestine is a possible channel for the introduction of dust there is no doubt. When visiting one of the coal-mines in the neighbourhood of Valenciennes and Lille I came upon a group of French miners taking their forenoon meal in the pit. They were eating without having washed their hands, and thus giving themselves the opportunity of developing pulmonary anthracosis by the intestinal path, quite apart from aerial infection, for the atmosphere of the mine throughout was remarkably free from coal dust. No matter by what channel dust gains an entrance into the body there is always a local reaction in the form of phagocytosis, which is nature's earliest attempt to rid the part of dust.

The symptoms of pneumoconiosis are largely determined by the presence or absence of bronchitis in the early stages of the disease; thus, in slag-crushers since bronchitis appears early, cough and expectoration, shortness of breath, and a liability to asthmatic seizures are the usual symptoms. Notwithstanding the recurrent attacks of bronchitis the chest is, on the whole, less prone to assume the expanded form observed in emphysema than in ordinary bronchitis. Slag dust in some special way seems to dispose to pneumonia. The same is true of the dust in the Rand mines, and probably accounts for the high mortality from pneumonia among the Kaffirs employed in the mines. We are not, however, now concerned with the acute forms of pulmonary disease caused by dust, but with the more chronic forms in which definite structural alterations in the lungs, consisting in an excessive development of fibro-connective tissue attended by localised thickening and adhesion of the pleura. In many instances the fibrosis of the lungs develops so slowly and insidiously that, except for a sense of shortness of breath, the workman is unaware that he is already in the clutches of a fatal disease. He only becomes aware of it when he is accidentally injured, when he catches what at first appears to be a common cold, or when he is attacked by a pneumonia. In many persons employed in dusty trades, especially in Rand miners, whose occupation is extremely dusty, and when the particles inhaled are hard and angular, one of the first symptoms is shortness of breath, which is increased on the slightest exertion, and is out of all proportion to the organic changes in the lungs as revealed by physical examination. Except in the terminal stages of the malady it is unattended by cyanosis. Persons who are following a dusty occupation, such as the manufacture of pottery, usually suffer from morning cough

either on rising from bed or on their way to work. The cough is followed by the expectoration of mucus, occasionally of a bluish-black hue from the presence of particles of dust, which may be difficult to dislodge and bring up without considerable effort on the part of the patient. In addition, expectoration may be absent for a long time, even when physical signs of lung disease are present. For several months or a few years the malady may make little progress and the general health may not suffer in any way, until as a result of what is regarded as a simple catarrh, ascribed to catching cold on going to work on a winter's morning, the patient is attacked by cough with expectoration and difficulty of breathing, which does not entirely disappear with the subsidence of the bronchial affection. The patient continues to follow his occupation, but as the cough becomes more harassing his night's rest is broken, the expectoration becomes muco-purulent, the appetite fails, and progressive emaciation follows. The malady hitherto afebrile is now attended by a rise of temperature, which, with increasing cough and more abundant expectoration, gives the impression that the patient is the subject of pulmonary tuberculosis.

If the patient is a coal-miner he probably brings up large quantities of "black spit." In the early stages of Rand miners' phthisis cough is frequently absent, but later on with the advent of cough it is extremely hard and the expectoration is scanty. In pneumoconiosis generally there is, as a rule, no expectoration in the early stages; if present it is mucous and subsequently becomes muco-purulent; in uncomplicated cases there are no tubercle bacilli, but in advanced and very chronic cases they are often found. Occasionally, as the result of severe coughing or of the dislodgment of some hardened pellet from the lungs, there is haemoptysis, but this is an equivocal symptom, and as it occurs more frequently in some forms of pneumoconiosis than others it is probably dependent upon the character of the dust inhaled. Pain is an uncertain symptom. When complained of it is seldom severe, notwithstanding the almost constant presence of thickening and adhesion of the pleura in these cases. It is more a sense of tightness that is complained of, or a feeling as if the chest could not be inflated. Anaemia is not a necessary adjunct. The bronzed appearance of the Rand miner whose lungs are fibrotic creates a deceptive appearance of good health, but the bronzing disappears as the disease progresses, and may be followed by slight desquamation. The appetite remains good for a long time, and in uncomplicated cases there is neither fever nor night-sweating.

Physical Signs.—In the early stages of pneumoconiosis physical signs are few. Unless there is bronchitis there are usually no physical signs until consolidation of the lung or thickening of the pleura is established. In the case of workpeople who have been inhaling dust for years and whose lungs shew but slight structural alterations, it is not uncommon for symptoms and physical signs to be absent. There is, however, great variation in this respect, for health is seriously affected in some persons compared with others after a relatively short exposure to dust. It is

more than probable that a person's habits and his constitution are not without influence in the development of symptoms. There may be distinct flattening of the percussion-note under one or both clavicles or at the bases. When the disease is fully established there is usually dulness over a limited area, or over several small areas in the chest wall, not necessarily confined to one side. In my own cases the commonest seats of dulness have been the front of the left chest, extending from the clavicle to the third and fourth ribs, the base of the lung in the axillary line, and a small area two inches from the spine over the fifth, sixth, and seventh ribs. The affected side is usually retracted and moves but little during respiration, so that circumferential measurement of the whole chest shews barely one inch of difference between inspiration and expiration. On auscultation the breath-sounds over the affected areas are coarser than usual and the expiratory murmur is prolonged, or the inspiratory murmur is interrupted, jerky, and whiffing; sometimes the respiratory murmur is coarse and dry, or there are dry clicks at the end of inspiration. Usually the breath-sounds are dry and tubular over limited areas, accompanied by friction, or a small, high-pitched musical rale is heard here and there in the chest. In well-marked cases crepitation can be heard at the end of inspiration or during both inspiration and expiration, with or without cavernous breathing. What the physical examination reveals depends upon the stage of the disease, and whether the pneumoconiosis is uncomplicated or not. The physical signs of an uncomplicated pulmonary fibrosis due to dust are, when the disease is established but not too far advanced, a moderate degree of dulness on percussion, dry, coarse breathing amounting to tubularity, dry clicks or crepitations at the end of inspiration, with probably dry friction over a limited area at the base of one or other lung. The voice-sounds and vocal fremitus are usually exaggerated. When the apex of the left lung has been affected for a long time, the base of the heart is exposed by the retraction of the fibrosed lung, and pulsation can be seen and felt over the second and third left costal cartilages, a click synchronous with the closure of the pulmonary semilunar valves being palpable. On auscultation, the second sound over the pulmonary artery is loudly accentuated, but in other respects the heart's sounds are healthy. The apex beat of the heart is displaced outwards and upwards as far as the left nipple. Occasionally the superficial veins of the neck are distended, and those on the front of the chest are more prominent than in health. In well-established cases the pulse and respiration are quickened, even when the patient is sitting quietly. The slightest exertion brings on dyspnoea and, but by no means always, audible wheezing. With all this there is an absence of fever, of night-sweats, and of any appreciable loss of flesh. The supervention of these indicates that a change has taken place, and that what was previously a case of uncomplicated pneumoconiosis has become tuberculous. In uncomplicated pneumoconiosis I have usually found that the blood shews leucopenia with eosinophilia, and about the normal number of erythrocytes. Dr. Summons examined the blood of extremely

healthy-looking miners at Bendigo with uncomplicated pulmonary fibrosis, and found a high count of red corpuscles, *e.g.* 5,700,000, which he regarded as possibly an effort to compensate for interference with the respiratory processes in the lungs. The onset of bronchial catarrh is followed by a diminution in the number of red blood-corpuscles, and tuberculous infection gives rise to an increase in the number of leucocytes, a fall in the number of red blood-corpuscles with poikilocytosis, with loss of the power of taking up stains. The urine remains free from albumin and sugar.

The three features in the comparatively early stages of pneumoconiosis which attract attention, are dyspnoea far in excess of physical signs, deficient movement of the chest, and absence of rales, with here and there jerky and interrupted respiratory murmur. Some patients give a history of recurrent colds in the chest with mild attacks of bronchitis, but even in them the dyspnoea is always greater than in those who are the subjects of ordinary bronchitis. It is difficult to explain the dyspnoea, for though it might be explained by emphysema, this is usually too limited in degree to interfere with respiration and the pulmonary circulation. Due in some way or other to a diminution of the respiratory area, the dyspnoea can hardly be explained by bronchial catarrh, and the presence of excessive secretion in the tubes, for rales are frequently absent. The beat of the heart is readily quickened, but there is no evidence of incompetence on either side of the heart. Restriction of the respiratory movements is no doubt partly due to the firm pleural adhesions; and the fibrosis of the lungs, which, starting as a peribronchitis leads to thickening and narrowing of the bronchi, so impairs the elasticity of the bronchial tubes that the respiratory movements are unable to transport the normal amount of atmospheric air. From examination with the fluorescent screen of the chests of three cases of advanced pulmonary fibrosis at Bendigo, Drs. Summons and Jackson found that "Abnormal shadows, extremely irregular in distribution, were present in all; but dark lines in the situation of the interlobular septa stretched outwards from the roots in several, indicating interlobular pleurisy with adhesions. Interspersed between the dark patches were light areas, suggesting changes in parts of the lung not so densely fibroid. The dust particles, being chiefly of silica and alumina, did not increase the density of the shadows thrown by the lungs." In one of my patients, a Witwatersrand gold-miner, the well-marked shadows of the upper two-thirds of the left lung and of a small area at the right apex completely confirmed the limitations of the disease as determined by auscultation and percussion. Notwithstanding the extent of the disease the expectoration, which was examined on several occasions, remained free from tubercle bacilli.

It is difficult to say how long a miner, a potter, or any person employed in a dusty trade will follow his occupation before symptoms develop. Nearly all the Rand miners whom I examined, also perusal of the records of 68 other cases which these men supplied me

with, lead me to the conclusion that six years is the average for a rock-driller in South Africa. The length of time will vary with the amount and character of the dust, the ventilation of the mine, and habits of the workmen. Thus, at Bendigo the average working life of the miners is much longer, namely twenty-two years; the explanation of this may be that bronchitis being more frequent in the Australian mines, the miners are obliged to give up work and take temporary rest at more frequent intervals than is the case with the gold-miners in the Transvaal.

Prognosis.—When once the disease is thoroughly established the prospect is not good, and yet in the earlier stages, if the conditions of life and occupation are altered, the outlook is not altogether hopeless. Pneumoconiosis, probably from the accompanying catarrh, favours tuberculous infection; hence, though the resemblance in the physical signs may give rise to some difficulty in distinguishing between pneumoconiosis and the fibroid forms of pulmonary tuberculosis, the diagnosis is important in order to avoid infection spreading to other patients with uncomplicated pneumoconiosis. The advance of pulmonary fibrosis caused by dust is very slow, and at first it scarcely interferes with the patient's health at all, but its progress is so sure that gradually difficulty of breathing is induced on the slightest exertion. The lease of life of the patients with pulmonary fibrosis caused by dust, varies with the character of the dust inhaled, the environment, and the previous habits of the patient. As just mentioned the Rand rock-driller seldom lasts more than six or seven years, whereas the Bendigo miner may survive for twenty-two. The occurrence of haemoptysis increases the gravity of the prognosis. The downward path of a patient with pneumoconiosis is marked by great dyspnoea, cough, and sleeplessness, and by hectic fever when tuberculous infection has supervened. Occasionally life is rapidly brought to a close by acute pneumonia.

Treatment.—As soon as there is the slightest evidence of any pulmonary mischief, which, if unchecked, will lead to pneumoconiosis, the workman should, if possible, abandon his dusty occupation for other employment in the open air. As the disease is due to the inhalation of dust, it is obvious that measures should be taken to remove dust in all trades wherein it is known to give rise to the malady. In dry and dusty mines proper ventilation is called for, and no rock-drills should be used unless they automatically spray water at the same time as they bore. The use of water-spraying in gold and other mines where the rock is hard not only allays dust, but keeps down the temperature, and in this way favourably affects the health of miners.

As regards medicinal treatment, a mixture of iodide of potassium, nux vomica, and carminatives answers on the whole fairly well. Easton's syrup, or syrup of glycerophosphate of calcium with formates, maintains the nutrition of the nervous system. The subcutaneous injection of nuclein has been recommended in order to stimulate leucocytosis, but I have had no experience of its utility. To arrest wasting, cod-liver oil or virol may be given, whilst to relieve cough and sleeplessness glycoheroin,

codeine, or small doses of morphine may be administered. When there is catarrh with abundant and yellow expectoration, inhalation of cinnamon oil deserves a trial. When pneumoconiosis is complicated by tuberculosis, a mixture of guaiacol carbonate with tincture of chiretta or nux vomica will improve the staying power of the patient. Sanatorium treatment, outdoor life, and gentle muscular exercise should be recommended when the course of the disease is slow. Since Rand miners with pulmonary fibrosis do badly both on the coast of Natal and on board ship when returning home from South Africa, it is clear that on reaching England they should not settle down at the seaside.

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T. O.

EMPHYSEMA OF THE LUNGS

By J. KINGSTON FOWLER, M.D., D.Sc., F.R.C.P.

Definition.—A disease of the lungs characterised by over-distension of the alveoli and atrophy of the alveolar walls.

It has been the custom to describe under this heading two essentially distinct morbid conditions; the one, corresponding in anatomical details

to the definition above given, having nothing in common with the other but the name. An account of this latter affection, *interlobular or interstitial emphysema*, will be found at the end of this article.

The description of emphysema of the lungs given by Laennec, accurate though it was as regards both anatomical characters and clinical history, remained incomplete until supplemented by the microscopical researches of Rokitansky and the clear exposition of its pathology which we owe to Sir William Jenner. Our knowledge of the disease has been mainly derived from their writings, and few additions of importance have been made to it in recent years.

Etiology.—*Age.*—It is a matter of common experience that the disease may be met with at any age. Some of the most marked examples are seen in young children. The atrophic form of the affection (see Varieties of Emphysema, p. 479) is most often met with in old people.

Sex.—Men are naturally more subject to the disease than women, as they are more exposed to the conditions which favour its development.

Occupation.—Any occupation involving severe muscular effort, especially if performed with the lungs distended and the glottis closed, tends to produce emphysema. In all such efforts the chest is forcibly compressed by muscular contraction, and the act is equivalent to one of forced expiration. The classical example of an occupation involving the latter condition is that of a cornet-player. Smiths, hammermen, and porters engaged in lifting heavy weights are all liable to emphysema. Omnibus- and cab-drivers, and all persons whose occupations involve exposure to inclement weather, are prone to attacks of bronchitis, whence comes emphysema. The inhalation of dust, a condition almost inseparable from many occupations, necessarily induces catarrh of the bronchi; upon this cough and emphysema follow.

Diseases such as whooping-cough and chronic bronchitis present the conditions essential to the production of emphysema to the fullest extent. The violent respiratory acts in many forms of dyspnoea may lead to extreme over-distension of the lungs, which may be either temporary or permanent. The same is true in cases of extensive collapse of the lungs as regards those parts into which the air is free to enter. The mode of production of emphysema in asthma and allied conditions will be considered later.

The onset of emphysema will naturally be favoured by any conditions, such as chronic congestion from valvular disease and chronic bronchitis, which tend to diminish the natural elasticity of the lungs. Advancing age is a factor which operates in a similar manner.

Hereditary Predisposition.—It has been suggested that there exists in some individuals and families an hereditary tendency to the disease; and this opinion still meets with some support. Various observers have investigated the question, the result being the supposed discovery of the hereditary tendency in a proportion of cases varying from 12 per cent (Lebert) to about 60 per cent (Fuller, Jackson) in adults, and 100 per cent of cases in children (Jackson). It is probably true, as pointed out

by Sir William Jenner, that the tendency is not to the disease itself, but to conditions which dispose to it.

Although, however, we may not admit heredity in its most absolute sense to be a cause of emphysema, it does not follow that what, in the absence of precise knowledge, we call the "constitution" of the patient has no influence in determining its occurrence. The tone of muscle and its capacity for energy vary enormously in different persons, though no structural differences can be demonstrated; and the same may be true of the elastic tissues. That such is the case is certainly possible, and in my opinion probable; if so, the occurrence of dilatation of the pulmonary alveoli may well be brought about in certain persons by a degree of increased pressure within the air-passages, such as accompanies ordinary straining efforts, which we are not accustomed to regard as adequate to the production of emphysema, and which, in persons of firmer fibre, are not so.

All who have studied the subject of emphysema from a clinical standpoint must have met with cases in which the ordinary proximate causes of the disease seemed to be absent. In many of these the absence has, it is true, been but apparent, for it is difficult to realise how slightly a chronic winter cough impresses itself upon the memory of some patients; hospital patients, indeed, rarely mention such an ailment unless directly questioned about it. But due weight having been given to this source of error, there undoubtedly remains a certain small proportion of cases in which no adequate exciting cause can be discovered. This lack of resisting power on the part of the elastic tissues of the lung may certainly be acquired, it may possibly be inherited, and is probably a common result of the degenerative processes incidental to advanced age. A case recorded by Hugner proves clearly that after recovery from an attack of pneumonia emphysema of the affected part may ensue upon the resumption of an occupation, such as that of a cornet-player, which favours the occurrence of the disease, but which had been previously followed without injury to the lungs.

Normal Anatomy of a Pulmonary Lobule.—A lobule of the lung may be regarded as a lung in miniature; a clear notion of the structure of a single lobule will therefore enable us without much effort to construct the whole organ.

Each lobule, more or less cone-shaped, is surrounded by areolar tissue; at its apex the lobular bronchus, the blood-vessels, lymphatics, and nerves unite to constitute it. The bronchus, after a short course within the lobule, divides and subdivides, with at first but slight diminution in size, forming passages which are termed the interalveolar or intervesicular passages. The course of the bronchus is at first fairly straight, but as the divisions increase in number and diminish in size the direction constantly changes. As the alveolar passages approach the surface of the lobule they cease to diminish in size. Each passage beyond the final division ends in a blind extremity, which, if not dilated, often appears to be so, from the fact, above stated, that the passages do not

diminish in diameter. In some cases, however, the ends of the alveolar passages are really dilated, and from this appearance the name "infundibula" has been applied to them; but a distinctive name is scarcely necessary. As the bronchus enters the lobule rounded orifices appear upon its walls. These are the openings of the alveoli, which may be regarded as the radicles of the bronchial tree. They are at first but few in number, but gradually increase. As the air-channel passes onwards through the lobule, and the interalveolar passages are formed, their walls become more and more thickly studded with the orifices of the air-vesicles, until, by the time the surface of the lobule is reached, the blind ends of the passages are found to consist entirely of the orifices of these small recesses.

From the foregoing description it will be seen that the air-vesicles of the terminal passages open into a common space, adjacent vesicles being separated by incomplete partitions; and that all the air-cells of a single lobule are, to a considerable extent, confluent one with another. Adjacent interalveolar passages are separated by partitions formed at the site of branching of the air-vessels.

The interalveolar passages and their terminations are chiefly composed of unstriped muscular fibres, arranged circularly, and supported by a delicate fibroid tissue mingled with elastic fibres. The walls of the air-vessels consist of a delicate membrane crossed by a network of elastic fibres.

The capillaries on the terminal passages are covered by epithelium only on the surface looking towards the cavity; those in the septa project into the cavities on either side.

Morbid Anatomy.—The primary lesion in emphysema consists in an enlargement of the terminal interalveolar passages, which increase in size at the expense of the alveoli opening into them. Sometimes, however, the alveoli appear to be the first to undergo dilatation. In any case the effect is, by pressure and stretching, to diminish the blood-supply to the epithelial and vascular structures in their walls. The alveolar epithelium undergoes fatty degeneration, the granules being aggregated round the remains of the nuclei. The septa between adjacent alveoli are reduced to small projections by a gradual process of wasting; subsequently the partitions between neighbouring alveolar passages are perforated, and they become fused into rounded spaces, the size of which tends to increase with the continued operation of the immediate cause of the disease. It is obvious that this process must be accompanied by a great destruction of the pulmonary capillaries, an important factor in determining some of the effects of the disease. In addition the extensive destruction of the lymphatics interferes with the rapid absorption of inflammatory products and so contributes to the long, irregular, and not infrequently fatal course of pulmonary inflammations in emphysematous patients (Oertel). According to Rindfleisch, wide communications are formed between the pulmonary artery and the pulmonary and bronchial veins, thus relieving the tension of the former vessel, but allowing the blood to pass through the lungs without undergoing proper aeration.

Varieties of Emphysema.—Certain varieties of the disease may be recognised both clinically and pathologically; the morbid changes by which they are characterised will now be considered.

Large-lunged Emphysema (*Chronic Hypertrophic Emphysema*).—The objection to the term hypertrophic as applied to this condition is that its use connotes increased functional activity, whereas in emphysema the opposite condition prevails. The name here adopted, which was first suggested by Jenner, appears preferable, as it describes the condition and involves no hypothesis.

When the thorax is opened the lungs not only fail to collapse, but remain fully distended, and, when the smaller bronchi have been obstructed from inflammation, may even bulge forward. The apices fill the supraclavicular regions, and the enlarged anterior margins may be in contact beneath the whole length of the sternum, the precordial area being occupied by the distended auricular process of the left upper lobe. The diaphragm is depressed owing to the permanently inflated condition of the lungs. After removal, when the organs are held with the base upwards, the distended and rounded edges of the lower lobes form the sides of a deep cup. Pigment is sometimes entirely absent in certain areas. (Pulmonary albinism, Virchow.)

The lungs in emphysema were likened by Laennec to a pillow of down, and the simile can scarcely be improved upon. They are soft and non-crepitant; when compressed a deep pit forms and remains. They are pale grey in colour, and are marked by black pigment, scattered over the surface in lines and spots, the lines in some cases mapping out the lobules. On close inspection the superficial portions have the appearance of a very fine froth, consisting of very minute air-bubbles covered by the pleura. This is rendered more obvious by the use of a hand-lens.

In some cases large rounded air-containing bullae are present, usually along the anterior margin of the upper lobes or around the bases, but they may be absent when the disease is advanced and widely disseminated. Some are attached to the lung by a narrow peduncle only, the auricular process of the left upper lobe being a common site of this particular lesion. They collapse when opened, and delicate fibrous bands, the remains of alveolar septa and obliterated vessels, may then be found crossing the interior.

These two forms, the "local" or "bullous" and the "general," are too frequently associated to justify a separation in nomenclature; but it is important to bear them in mind, as will appear when we come to consider the physical signs of the disease.

On section the lungs are bloodless and dry, except perhaps at the bases, where oedema may be present. This, however, pertains more to some complication, such as bronchitis or cardiac failure, and is no necessary effect of the disease.

If the section be made from the extreme posterior margin forwards, the portion of the lung which occupies the hollow beside the spine will often be found in an advanced condition of emphysema; large spaces

being present beneath the pleura, and extending for perhaps half an inch or more into the lung.

The smaller bronchi are in some cases dilated to a slight degree, but bronchiectasis is by no means frequently associated with emphysema.

Atheroma of the pulmonary artery is commonly present, and in advanced cases patches may be found throughout the vessel, not even the smaller branches escaping; it is a result of the increased strain on the walls of the vessel from the obstruction to the passage of the blood through the lungs. There is very often a complete absence of pleural adhesions, a condition rarely observed in adults unless they are subjects of emphysema.

Small-lunged Emphysema; Senile Atrophic Emphysema (Synonym: *Senile Atrophy of the Lungs*).—The most striking clinical and pathological characteristics of this condition of the lungs are indicated by its name. It appears to be primarily an atrophic change, incidental to advanced age, and shared by the lungs equally with the other organs of the body. Its title to be considered either as a substantive disease of the lungs or as a distinct variety of emphysema is doubtful. It never occurs apart from a general condition of atrophy; and the slight degree of emphysema which accompanies it is probably induced by the cough of a bronchial catarrh, from which the very aged are rarely quite free. It is, however, convenient and in accordance with custom to describe it as a variety of emphysema. The subjects of senile emphysema present a wasted, shrivelled, and withered-up appearance; the thorax is rigid, the space within is small, the lower ribs are almost in contact and very obliquely placed. On opening the chest the uncovered area of the heart is not diminished, it may even be enlarged; the lungs readily collapse, falling back towards the spine; they are smaller than normal, deeply pigmented, almost black in colour, light, dry, and easily compressible. On section they present a coarsely reticulated structure. The vesicles are enlarged by a process of fusion, the result of wasting of the septa; and this change may in places be so advanced as to involve adjacent lobules. Large bullae are rare, but the margins are in some cases much dilated. The bronchi are thin-walled, and have undergone dilatation; the lining membrane is commonly inflamed, and the tubes contain puriform fluid. Collapse and oedema are often present, and are generally most marked on the posterior aspect of the lower lobes.

Local Emphysema; Compensatory Emphysema.—This form of the disease is invariably secondary to some pulmonary lesion, most commonly to tuberculosis which has undergone either complete or partial arrest. In the presence of a contracting lesion within the lungs—for instance, a cavity or an area of fibroid tuberculosis—either the surrounding tissue becomes emphysematous or the pleura thickened; the result being determined by the nature, site, and extent of the lesion. In the case of a lesion situated close to the surface, if the lung intervening between it and the pleura be condensed, airless, and incapable of expansion, the visceral and parietal layers of the pleura, partially united by fine fibrous

bands, tend to become separated. The space is at first filled with yellow serous exudation, which ultimately undergoes transformation into a thickened fibroid tissue almost cartilaginous in density. The apex of the lung, in cases of very chronic pulmonary tuberculosis, when the upper lobe is almost completely occupied by a contracted thick-walled cavity, shews such a thickening of the pleura as is here described. If, on the other hand, the lung tissue around the lesion is not the seat of such advanced changes, and still admits of the entrance of air, the surface vesicles enlarge, coalesce, and form bullae, sometimes of considerable size. Such a condition is commonly seen at the apex of the lung, and is a certain guide to a contracted lesion within. The surface may be scarred and puckered, and on section dense pigmented fibrous bands are seen surrounding old fibrous, caseous, or calcareous lesions, and extending into the neighbouring emphysematous tissue. The vessels and bronchi in such an area are usually obliterated, but on its confines the latter may be found dilated.

Another common site of local emphysema is the posterior and upper part of the lower lobe. Here the change is secondary to a contracting lesion, usually a cavity, at the apex of the lung; and may occupy a considerable area. In one such case observed by myself the posterior aspect of the contracted upper lobe was completely covered by the upper part of the lower lobe. No bullae are formed, but on section a coarsely-reticulated structure is seen, replacing the normal tissue and reaching downwards along the posterior aspect of the lobe.

In cases of fibroid transformation of tubercle the densely pigmented contracting fibrous nodules are often found embedded in emphysematous lung; the whole presenting appearances which shew unmistakably that the fibrosis has preceded the emphysema.

Acute Vesicular Emphysema.—The definition of the disease given at the head of this article does not include a lesion consisting merely in an over-distension of healthy alveoli, such as is present in the above-named condition. Atrophy of the alveolar walls is an essential part of the morbid anatomy of emphysema, and in its absence we cannot recognise acute vesicular emphysema as a true variety of the disease. It is sometimes found after death from acute bronchitis, or from asphyxia, which had been accompanied by violent inspiratory efforts; or when, from collapse or other cause, the air has been prevented from entering portions of the lung, thus throwing an increased strain upon the alveoli of other parts.

It may be demonstrated, however, by physical examination that a similar condition is present in cases which are not fatal; and also that after a time the lungs return to their normal size, a proof of the absence of structural damage.

The lung in such a condition of over-distension is large and pale, and with a hand-lens the increase in size of the surface alveoli can be readily seen.

Lesions associated with Emphysema.—*Lungs.*—Although, in the

majority of cases, bronchitis and emphysema stand related to one another as cause and effect, it is nevertheless true that when emphysema has become established it increases the tendency to bronchitis.

The over-distended air-vesicles compress and obstruct the capillaries and impede the circulation through the pulmonary and bronchial vessels. The bronchial mucous membrane becomes congested, and the condition thus established greatly increases the liability to inflammatory attacks. Rupture of dilated vesicles may lead to pneumothorax; but if the pleura overlying the site of rupture remains intact, interlobular emphysema results. Death is rarely due to pneumothorax so caused, but one such case has been observed by myself, and others are on record.

Bronchi. — As already described, the bronchi are often found obliterated and forming thin fibrous bands in large emphysematous bullae; they are, however, occasionally, but not commonly, found dilated to a moderate degree in less advanced cases of general emphysema, and more often in localised emphysema. In the atrophic form the bronchial walls are usually thin; in other forms they may be somewhat thickened, as may also be the walls of the vesicles and interalveolar passages.

Heart.—The obstruction to the flow of blood through the capillaries of the lungs naturally increases the pressure within the pulmonary artery and requires a more forcible contraction of the right ventricle. This leads to hypertrophy of the ventricle, and thus for a time equilibrium may be restored. But when, from any cause, the structural integrity of the new muscular tissue is impaired, particularly if at the same time greater stress is thrown upon the right ventricle, dilatation follows, the tricuspid orifice enlarges, and the valve becomes incompetent.

The right auricle, probably already somewhat enlarged, now undergoes still further dilatation, and the superior and inferior venae cavae are similarly affected. Congestion of all the organs which are drained by the systemic veins necessarily follows. The portal system may become involved at a later period. This sequence of events is not uncommonly initiated by an attack of bronchitis.

The dilatation and hypertrophy of the right ventricle, including the conus arteriosus—for the latter is always involved—are usually found on autopsy to be associated with similar but less advanced changes in the left ventricle; a result probably due, at least in part, to their intimate association both in structure and functional activity.

Degenerative changes are often observed in the heart in emphysematous subjects, and the impaired nutrition of the muscular walls may be due to obstruction to the return of blood by the coronary veins.

As a result of the enlargement of the lung and the permanently depressed state of the diaphragm, the position of the heart becomes altered. It lies lower in the chest, and its axis is more nearly horizontal. The front of the heart is formed entirely by the enlarged right ventricle and auricle. The altered position and size of the organ account for the pulsation commonly observed in the epigastrium in well-marked cases of

emphysema; but of these two factors the change of position is the more important.

Secondary changes of a fibroid character are not infrequently found in the tricuspid and mitral valves; and, more rarely, in the aortic valve also.

Liver.—The changes in the liver resulting from chronic venous congestion are too well known to require complete description. The organ is enlarged and the hepatic veins are dilated. The section presents the "nutmeg" character, and there is some degree of induration; but emphysema alone is as powerless as chronic mitral disease to produce a true cirrhosis.

The kidneys may be enlarged and cyanotic, but in a considerable proportion of cases they are granular from the presence of chronic interstitial nephritis, a disease with which emphysema is not uncommonly associated. The *spleen* is as a rule enlarged and hard, but its condition varies.

Chronic venous congestion of the *stomach* may give rise to catarrh and haemorrhage into the mucous membrane. The *brain* also shews evidence of venous congestion. The *costal cartilages* are often calcified.

Pathogeny.—Various hypotheses have been advanced to explain the origin of emphysema, some of which meet with but little support at the present time. It would serve no useful purpose to enter upon a detailed discussion of the problem, as it is exhaustively dealt with in the original papers of Sir William Jenner, to which reference may be made. It will be sufficient to mention those views which have at any time received considerable support, and to discuss in greater detail that which is now generally adopted.

Primary Degeneration Hypothesis.—The view that the general cause of emphysema is a primary fatty degeneration of the alveolar walls was first stated by Rainey, and subsequently received support from Villemin. The latter writer describes the changes as beginning in an excessive proliferation of the intercapillary nuclei, followed by secondary fatty degeneration of the nuclei and other structures, the result of pressure upon the capillaries. It is now generally considered that the degenerative changes in the alveolar walls are secondary to the distension of the air-vesicles and interalveolar spaces, and to the diminution in the blood-supply thereby induced.

It is possible, however, that in the form of emphysema met with in old people, primary degenerative changes may play a more important part. Reference will be made to this point subsequently.

Inspiratory Hypothesis.—The hypothesis that emphysema is due to distension of the lungs during inspiration was really first advanced by Laennec. He believed that the air drawn into the lung in inspiration was retained, being unable to escape during expiration, owing to the obstruction caused either by catarrhal swelling of the mucous membrane of the bronchi or by accumulation of mucus in the tubes; and that as a consequence the lungs became over-distended with air.

Sir W. Gairdner, in 1850, stated the inspiratory hypothesis in a different form. According to his view, some change in the lungs, such as collapse or retrocedent tubercle, leading to a diminution in size in one part, preceded the establishment of emphysema. As the air-vesicles within the area of disease or collapse did not expand during inspiration, an undue strain was thrown upon those in the immediate neighbourhood by the incoming air, and in consequence they became enlarged.

This opinion, as regards the general disease, has been completely displaced by that to be next mentioned; and as an explanation of the conditions found around patches of collapse or of fibroid tubercle—compensatory emphysema—it is believed that the distending force of inspiration, although possibly not without effect, is subordinate to that of forced expiration.

Expiratory Hypothesis.—In 1845 Mendelssohn first advanced the opinion that emphysema is produced during a forced expiration. He believed that the air is prevented from escaping from the upper lobes by the compression of the lungs during forced expiration; that consequently the pressure within the lung is increased, and the air-vesicles undergo dilatation. In 1857 Sir William Jenner stated the above-named hypothesis in the following terms: "The lung during expiration is compressed at different parts with different degrees of force. The parietes of the thorax, in consequence of their anatomical constitution, yield to the same force at different parts with various degrees of facility. The chosen seats of emphysema are exactly those parts of the lung which are the least compressed during expiration, and which are situated under those portions of the thoracic parietes that give way the most readily before pressure." In a footnote to his paper on "Emphysema of the Lungs," in Reynolds's *System of Medicine*, Sir William Jenner stated that he was unacquainted with Mendelssohn's paper when he advanced this hypothesis in 1857; and that, so far as he was aware, the existence of that paper was unknown in this country until 1867, and rarely, if ever, referred to abroad until that date. Having regard to the above facts, to the singular completeness of Jenner's papers, and to his demonstration of the exact sites of emphysema, we may fairly regard him as having been the first to make known the true mode of origin of the disease.

The increased pressure in the air-passages, which we have seen to be a common antecedent of emphysema, may be induced in various ways.

Cough.—The almost invariable association of some degree of emphysema with chronic bronchitis points to cough as the most frequent cause of the disease. The chest having first been filled with air, the glottis is closed, a violent expiratory effort is made during which the tension within the air-passages is enormously increased, the glottis then relaxes, the air passes rapidly through the narrow orifice, and a cough results. It is the frequent repetition of this act which eventually induces a permanent dilatation of the air-vesicles and interalveolar passages. The effect of the compression of the lungs during a violent expiratory effort, such as that above described, is to drive the air in all directions from the central

to the peripheral part of the lungs; the result is the distension of those parts which are least supported. As pointed out by Sir William Jenner, these parts are the apices, the anterior margin of the upper lobes, and the margins of the bases of the lungs. These are the sites of the primary lesions; but, in the course of the enlargement of the thorax which they entail, the relative position of a given area of lung and the chest wall gradually changes, fresh portions being brought into contact with the intercostal spaces, the resisting power of which is less than that of the ribs, and thus in course of time the change may become general throughout the lungs.

Muscular Effort.—It is probable that next to cough violent muscular effort is the most common cause of emphysema. The mechanism is as follows:—The lungs having been completely expanded by a deep inspiration, the glottis is closed; any severe and sustained muscular effort with the thorax in this position necessarily subjects the lungs to strong compression, the increase in pressure within the air-passages being most effectual in distending the lung in those situations where the organ meets with least support. Straining in constipation may have the same effect.

Reference has already been made to other causes of over-distension in describing the etiological factors of the disease.

It will be convenient here to refer to those conditions of a temporary nature which lead to over-distension of the air-vesicles. In such cases when the cause is removed the effect may disappear; but whether it does so or not depends upon the duration of the exciting cause and the integrity of the elastic tissue of the lung.

The best example which can be given of this temporary over-distension of the lungs is the condition observed during a paroxysm of asthma. At the height of the attack the lungs may be found distended with air to a degree equal to that present in the most advanced cases of emphysema; but when the attack has passed off, the organs may return to their previous size. It is rare, however, to meet with patients whose asthma is of long standing who are not also the subjects of emphysema.

The mechanism by which this state of over-distension is produced appears to be a matter of doubt; the explanations vary with the hypotheses concerning the cause of the asthmatic paroxysm. If the hypothesis of a spasm either of the diaphragm or of the muscles of inspiration be held, there is little difficulty in understanding why the chest is in a condition of extreme inspiratory distension; if, on the other hand, we reject both these views and accept that now generally received, namely, that the asthmatic paroxysm is due to bronchial obstruction, the result either of a spasm of the muscular fibres of the bronchi or of a fluxionary hyperaemia of the bronchial mucous membrane, the explanation of its mode of occurrence is not quite so obvious.

It is, as a rule, gradual in onset and also in decline, and is apparently brought about in the following manner:—

(i.) The bronchial obstruction induces increased inspiratory effort.

(ii.) The entering air passes the obstruction with difficulty, but the gradual increasing prolongation and force of the expiratory act shew that the air meets with still greater difficulty in escaping from the lungs.

(iii.) Expiration, although prolonged, is not sufficiently so to produce an equilibrium between the incoming and outgoing air; a fractional addition is therefore made to the residual air by each completed act of respiration, and in time the lungs become over-distended.

It may be objected that, as the force of expiration is greater than that of inspiration, the obstruction should be more easily overcome by the outgoing than by the incoming current of air; but it would appear that experience teaches us to rely upon forced inspiratory efforts to remedy a defective aeration of the blood, whereas the condition really requires for its relief forced efforts limited to the period of expiration.

Another possible factor in the production of this state of extreme distension is the compression of the smaller bronchi by the distended alveoli, an effect necessarily more felt during expiration.

Other causes of temporary over-distension of the lungs are laryngeal obstruction, from whatever cause arising, whooping-cough, acute bronchitis in children, and severe muscular strain.

Symptoms of Large-lunged Emphysema.—The symptoms strictly referable to emphysema are very few, the condition, apart from its complications, being one of which patients have little or no knowledge, and one of which therefore they rarely complain.

Dyspnoea is the most important symptom, but even this is seldom mentioned until it has become somewhat urgent: it is in proportion to the extent of the disease. At first slight, and only experienced on exertion, especially on walking uphill, it may gradually increase, until in the end not only exercise, but even movement becomes impossible.

It is always much increased during an intercurrent attack of bronchitis, and tends, as the disease progresses, to occur in paroxysms, a condition to which the term "bronchial asthma" is usually applied. The asthmatic element in such cases may either arise directly from the emphysema—the more common order—or the emphysema may be a consequence of asthma. The difficulty of breathing is increased by anything which interferes with the descent of the diaphragm, such as flatulent distension of the stomach or intestines, stooping, or sitting in a low chair after a meal. Orthopnoea follows as the disease progresses, the patient sleeping either propped up with pillows or in a sitting position.

Cyanosis may be considerable, even while the patient is still capable of movement—a combination rarely met with except in this disease. The polycythaemia due to cyanosis may mask the secondary anaemia usually present in advanced cases.

Cough.—Sufferers from emphysema are rarely free from cough for long intervals, although cough is, strictly speaking, due rather to the condition of the bronchi than to the change in the lungs. It is loud, harsh and wheezing, and, like the dyspnoea, may occur in paroxysms.

It is always more troublesome in the winter, and particularly so when the weather is cold and damp, or when fog is present.

Expectoration.—Emphysema does not of itself give rise to secretion, but it is by no means uncommon for patients to expectorate a small quantity of mucus to which the descriptive word "pearly" is usually applied. When bronchitis occurs, expectoration becomes profuse, and passes through the various phases usual in this disease.

Haemoptysis, although an unusual complication of emphysema, may occur, and may even prove fatal. It is generally small in amount. Having regard to the frequent association of atheroma of the pulmonary artery with emphysema, it is perhaps surprising that rupture does not more often happen.

The appetite is often poor; complaint may be made of flatulent distension of the stomach and intestines, and constipation is not uncommon.

The deficient aeration of the blood may give rise to drowsiness and headache.

The arteries are badly filled owing to the distension of the venous system, and consequently the pulse is small and weak. The blood-pressure is low, but may be observed to rise during the act of coughing (Jenner). In the later stages, when the muscular tissue of the heart has undergone degenerative changes, its action often becomes irregular and intermittent. Arteriosclerosis is often present.

The veins of the neck are usually distended, and they may pulsate and fill from below. Filling from below is a sign that the valves at the orifice of the jugular veins are incompetent. Forcible pulsation usually indicates that the tricuspid valve is incompetent, but a slight impulse may be the result of the impact of the blood against the tricuspid valve being transmitted through a distended right auricle to the over-filled jugular vein, or it may possibly be due to the systole of the auricle. An impulse may also be produced in a distended jugular vein by the systolic wave in the underlying carotid artery.

The physiognomy of emphysema is characteristic. In the earlier stages of the disease the face is full, the lips are thick, and the mucous surface is congested. At a later stage, when emaciation has occurred, the appearance alters. The lines of the forehead are now deep, the brows knit, the naso-labial folds distinct, the expression careworn. The face is of a faintly bluish tint, the colour being well marked in the lips, which are thickened; the eyes are prominent, and the conjunctivae injected. At a still later stage there may be well-marked cyanosis of the face. The signs of venous congestion always become more obvious on exertion.

Clubbing of the fingers and toes is often well marked, especially when emaciation has occurred.

The abdomen is usually somewhat distended; the liver and spleen assume a lower position than normal, and the liver is enlarged and may be tender and pulsate from tricuspid incompetence; catarrh of the stomach and intestines is apt to cause dyspepsia and flatulent distension. Oedema of the lower extremities is often present in the latest stages of

the disease, and dropsy of all the serous cavities with anasarca may occur when there is pronounced failure of the heart. All the symptoms above described become more marked during intercurrent attacks of bronchitis; some, indeed, are present only at such times.

Physical Examination; Inspection.—The chest tends to undergo enlargement in all its diameters, but particularly in the antero-posterior, owing to exaggeration of the dorsal curve, and to the curvature of the sternum in the opposite direction.

The angulus Ludovici, marking the junction of the manubrium with the body of the sternum, is prominent, and the costal angle is much widened. The vertical measurement is increased by the downward displacement of the diaphragm, and the "oblique diameters" by the ribs becoming more nearly horizontal and the interspaces wider. This form may be modified by the presence of any of the deformities of the chest due to rickets or other causes, to which reference has already been made; but otherwise the general tendency of the chest is to assume a rounded form—the so-called "barrel-shaped chest" of emphysema. The rounded outline is often more marked in the upper part of the chest, whilst in the lower the increase of the transverse diameter is more obvious.

The clavicles are thrown forward, and the sterno-mastoids and other muscles of the neck are tense, giving the neck a short and thick appearance. The supraclavicular hollows may be deep; but if the apices of the lungs are markedly affected the normal depressions here may have disappeared. The curvature of the spine causes the shoulders to be round, and in extreme cases the shoulder-blades may assume almost an horizontal position.

The upper intercostal spaces may present an even surface, but the lower are often depressed. This becomes more marked on inspiration owing to the non-expansion of the emphysematous lung. Bulging of the spaces may be well marked when the patient coughs. The respiratory movements are restricted, and the expiratory act is much prolonged notwithstanding the forcible contraction of the abdominal muscles. The gradual expansion of the chest during inspiration, which is characteristic of health, tends to be replaced by a uniform upward lift, during which the accessory muscles of inspiration stand out in strong relief. In some cases, however, the infra-axillary regions are drawn inwards and the sternum projected forwards, whilst at the same time the epigastric region, instead of bulging during inspiration, may be visibly depressed. This recession of the lower ribs during inspiration is often well marked, and may accompany the deformity of the chest called the "transversely-constricted" thorax, which is usually a relic of infantile rickets. The downward and axial displacement of the heart, combined with the hypertrophy and dilatation of the right ventricle, to which reference has already been made, are jointly the causes of the epigastric impulse commonly observed in emphysema. An horizontal sulcus is observed in some cases to extend across the body from side to side about the level of the lower part of

the costal arch. A broad line of dilated venules is often seen in emphysematous subjects tending obliquely upwards on either side along the line of the lower costo-chondral junctions, and across the base of the ensiform cartilage, and therefore corresponding roughly with the attachment of the diaphragm. It is rarely complete posteriorly.

Palpation.—The vocal fremitus is diminished.

The impulse in the precordial area is generally feeble owing to the cushion of lung intervening between the heart and the chest wall; but the hypertrophied right ventricle, in the absence of much enlargement of the lung, may cause a heaving impulse in the lower sternal region.

Percussion.—A hyper-resonant note will be found in regions such as the precordial and hepatic, which are normally dull; or dulness may still be present, but over a much diminished area; whilst behind it is by no means uncommon to find well-marked resonance as low as the twelfth rib. Inspiration and expiration make but little change either in the area of resonance or in the pitch of the note on percussion.

By *skiagraphy* a diagnosis of emphysema can be made; the lungs appear brighter and larger than normal, the excursion of the diaphragm is shorter than normal and low down in the chest, and the long axis of the heart is vertical (*vide* Vol. I. p. 498).

Auscultation.—The character of the respiratory murmur varies with the form of the predominant lesion, whether this be of the bullous type or general in its distribution. If "bullous," the breath-sound is weak near the sternum and along the margins of the upper lobes, but harsh beneath the outer half of the clavicle; whilst in the "general" form the breath-sound over the upper lobes is everywhere feeble. It is right to state, however, that the opposite opinion is held by some authors. In place of the normal vesicular murmur audible on inspiration the continuous low-pitched rumbling sound produced by the contraction of the muscles is often very distinct.

When the disease is fully established the expiratory sound is almost invariably prolonged, often very markedly so; in fact, during an intercurrent bronchial catarrh its duration may be so prolonged as to be nearly four times that of inspiration.

These changes in the respiratory sounds are usually most obvious over the upper part of the chest; but when the posterior aspect of the lower lobes is affected the breathing will be weak at the bases, and fine crackling rales may be present there also. These signs are important both as evidence of advanced disease and of oedema of the affected parts of the lung.

At the apex of the heart the sounds are feeble, the characters of the first sound being determined by the relative preponderance of hypertrophy or dilatation of the right ventricle. In the former case it is low-pitched and prolonged, in the latter short and sharp, but weak. The point of maximum intensity of the sounds at the base is lower than normal, and, owing to the increased pressure in the

pulmonary artery, the second sound is accentuated, and may be reduplicated.

A rough murmur is often audible in cases of emphysema about the sternal end of the sixth left interspace and over the seventh rib, close to the base of the ensiform cartilage. It is systolic in time, usually short, sharp, localised, and superficial, and it often more nearly resembles a rough reduplication of the first sound than a murmur. It may be due to a "white patch" on the anterior surface of the right ventricle, a condition often present in emphysema. The effect of change of position of the body on this sound is variable. It may disappear or remain unchanged. The only importance of the sign is that it is very likely to be mistaken for the murmur of mitral regurgitation.

Symptoms of Small-lunged Emphysema.—In this form of the disease the symptoms are much less pronounced. The most important change in the lungs—the atrophy—is but a part of a general process of wasting in which all the tissues of the body, including the blood, share alike. The respiratory needs are therefore less, and they may be adequately met by a smaller pulmonary area. The capacity for exertion is limited because of the feebleness of muscular power; and, in the absence of effort, there may be little or no dyspnoea.

Another point of difference from the variety just considered is that atrophic emphysema is rarely complicated by attacks of bronchial asthma; but intercurrent bronchitis may induce dyspnoea which, although differing in its mode of onset, is hardly less in degree than that which characterises the asthmatic paroxysm.

Physical Examination; Inspection.—The emaciated and withered appearance of the subjects of this form of the disease has already been mentioned. The evidences of venous obstruction, such as cyanosis and clubbing of the fingers, are absent; as also are the effects which that condition produces in the size, shape, and position of the heart. The chest assumes the barrel shape as a result, not of a process of enlargement, but of "shrinkage" in all its diameters, and especially in the lateral. The gradual diminution in the size of the lungs is necessarily accompanied by a recession of the ribs, which assume a more oblique position. The interspaces from the first to the fourth on the front of the chest are often both wide and deep; but the increased obliquity of the lower ribs tends to approximate them, so that the interspaces may be obliterated, or adjacent ribs may even overlap each other.

Inspiration is shallow, the rigid thorax moves as a whole, the upper interspaces recede, and descent of the diaphragm is restricted.

Percussion.—The note is hyper-resonant, but it tends to be clearer in tone and more tympanitic in quality than in the large-lunged variety. The area of precordial dulness is not diminished and may possibly be increased. The former statement applies also to the hepatic dulness.

Auscultation.—The breath-sound is weak, but the expiratory sound is not prolonged to nearly the same extent as in large-lunged emphysema. Adventitious sounds are not necessarily present, but the coexistence of

chronic bronchitis is so common as to make their complete absence very rare; fine and medium bubbling rales may be heard over the bases of both lungs. Fine crackling rales may be audible over the same area if oedema is present.

Other pulmonary complications will give rise to the auscultatory signs by which they are usually characterised, modified to some extent by the presence of emphysema.

Symptoms of Localised Emphysema.—On reference to what has been stated as to the mode of production and common sites of this variety of emphysema, it will be seen that the symptoms must necessarily depend upon the condition to which it is secondary. It may, however, be repeated that it is frequently a sequence of tuberculosis, and its presence at the apex of a lung should suggest the possibility of such a connexion.

An enlargement of one lung or of a portion of it, consequent on disease and contraction of the opposite lung, is not necessarily due to emphysema; it. may be a true hypertrophy. The test by which the two conditions are distinguished is that of functional activity. If this is increased, the enlargement must be regarded as hypertrophy; if diminished, as probably due to emphysema: in the former case the breathing is puerile, in the latter it is usually feeble with prolonged expiration.

Symptoms of Acute Vesicular Emphysema.—As already stated, this condition is only recognised as a form of the disease in deference to tradition.

It originates during a state of extreme dyspnoea, the urgency of which it doubtless increases; but the result to the patient is probably determined almost invariably by the nature of the exciting cause and not by the effect produced upon the lungs. Cyanosis may very likely be observed during the attack.

The chest will be in a condition of extreme inspiratory distension. The nature of the breath-sounds and adventitious sounds will vary with the exciting cause.

The diagnosis of the large-lunged form of emphysema rarely presents much difficulty. It is suggested by a history in which cough and dyspnoea are prominent features, or by the patient being engaged in some occupation known to involve severe muscular effort; it is confirmed on examination by the alteration in the form of the chest, the hyper-resonance on percussion, diminished movement, and feeble respiratory sounds—signs which are present on both sides of the chest.

Error has apparently arisen at times from pneumothorax being mistaken for this form of emphysema. In such cases the methodical examination of the chest has probably been neglected, and undue reliance placed upon one step in the process, possibly on percussion. In pneumothorax the enlargement of the affected side, the obliteration of the interspaces, the absence of movement contrasting with the increased movement of the healthy side—if it be healthy,—the displacement of

the heart to the sound side, the more amphoric note on percussion, and the absence of the breath-sounds, or their amphoric quality, are signs which combine to form a picture that, in well-marked cases, should be unmistakable.

It is possible, however, for a collection of air, confined by firm adhesions to a very small part only of the pleural cavity, to give rise to signs which may be mistaken for those of emphysema. Such a case, due to the rupture of an emphysematous bulla near the base of the lung, came under my own notice. It is sufficient to mention it as a possibility to be borne in mind without discussing in detail the diagnosis of a condition of such rare occurrence. Pneumothorax may, however, be due to rupture of an emphysematous bulla; it is very rare; Zahn has collected six cases confirmed by autopsy.

Aneurysm of the transverse part of the arch of the aorta compressing the trachea may be mistaken for emphysema with bronchitis. The tracheal stridor and brassy cough, the dulness, or at any rate the absence of increased resonance over the manubrium, and the loud tracheal breathing over the same area usually suffice to prevent error.

"Emphysema and bronchitis" is occasionally the diagnosis on admission to hospital of cases in which the primary disease is really stenosis of the mitral orifice; cardiac failure, pulmonary engorgement and oedema have supervened, and the murmur has disappeared. After a few days of rest and treatment considerable improvement as a rule takes place, the murmur again becomes audible, and the true nature of the case is then obvious.

True cardiac dyspnoea is distinguished from that accompanying emphysema by its "panting" character; but failure of the right heart often follows upon long-standing emphysema, and the dyspnoea is then the resultant of the two conditions and partakes of the characters of both.

An examination of the sputum for tubercle bacilli should always be made in cases of emphysema and bronchitis, particularly in such as are accompanied by marked emaciation. In the fibroid form of pulmonary tuberculosis, which is often associated with emphysema (not so-called "fibroid phthisis"), bacilli may be absent and the true nature of the disease may only be discovered on autopsy. The absence of pyrexia in such cases is not a distinguishing symptom of much value; fibroid tuberculosis being often unaccompanied by fever, at any rate for intervals of considerable duration.

The diagnosis of the atrophic form of emphysema is but rarely attended with difficulty.

Prognosis.—True emphysema, that is, dilatation with atrophy, is a permanent condition, with a decided tendency to advance. But whether it increase, and if so, at what rate, depends chiefly upon the continuance of the exciting cause, which, in the great majority of cases, is the cough of catarrh or bronchitis. If the patient is able, by change of residence or in other ways, to shield himself from adverse conditions of climate,

the disease may remain stationary. In any circumstances its course is chronic, and life only becomes endangered when complications arise.

The extent of the lesions will naturally influence the prognosis; but the effect produced upon the heart and circulation is a far more important factor in determining the probable duration of life. As dyspnoea is the chief evidence of this effect, its degree during rest and on exertion becomes one of the main elements in prognosis. The condition of the veins of the neck as to over-distension, pulsation, and filling from below, is an important guide to the state of the right side of the heart.

The existence of enlargement of the liver, oedema of the legs, ascites, and albuminuria marks an advanced stage of cardiac failure.

The presence of renal complications, particularly chronic interstitial nephritis, is of especial importance in prognosis.

Treatment.—Sufferers from emphysema rarely ask for advice on this ground alone, as the laity may be said to be ignorant of the existence of the disease. As a rule, no complaint is made of the accompanying dyspnoea; the patient has become so habituated to it that he has ceased to regard it. In the majority of cases the condition is discovered when an intercurrent attack of bronchitis leads to an examination of the chest. Atrophy of the alveolar walls, destruction of the capillaries, and wasting of the elastic tissues are changes which cannot be repaired; and a return to the normal state is only possible in the cases of temporary over-distension which occur for the most part in young subjects, as a result either of laryngeal obstruction, spasm, or whooping-cough, or of bronchitis accompanying an acute disease, such as measles.

Much, however, may be done to stay the progress of the disease by shielding the patient from further attacks of bronchitis, or by advising a cessation of any occupation which necessarily involves a strain upon the respiratory organs. Treatment may also be usefully directed towards the relief of the secondary effects upon the heart and circulation.

Emphysema once established undoubtedly disposes to bronchitis; it is therefore of the first importance that all known causes of catarrhal inflammation should be carefully avoided. Those whose means permit will be well advised to spend the winter and spring in a warmer climate than is to be found in this country at such times; many sufferers, however, although they know this full well, are prone to delay their departure unduly, and an early November fog finds them still here; the result too often is a severe attack of bronchitis and much increase in the emphysema. Persons who are unable to leave home, if they hope to escape an attack of bronchitis, must exercise the greatest care in avoiding cold north and east winds, foggy and damp air, over-fatigue, or sitting in draughty rooms, and anything likely to give rise to a chill. Notwithstanding its unsightly appearance, a respirator, or woollen "comforter" covering the mouth, by warming the incoming air is of real service in warding off attacks of bronchial catarrh.

The conditions which give rise to increased pressure within the air-passages have already been described; it will be sufficient, therefore, to

state that it is absolutely necessary for the sufferer from emphysema to avoid them if he wishes to escape an increase of his disease.

The effect upon the respiration is a useful test as to whether any form of exercise is harmful either in kind or degree; if it causes dyspnoea it should be avoided. The bowels should not be allowed to become confined, as, in addition to the gastro-intestinal derangements likely to ensue, much harm may be done by straining efforts in defecation.

In the article on "Aerotherapeutics" (p. 35) a full description is given of the various forms of apparatus used in the application of condensed air to the body as a whole, and of condensed or rarefied air to the respiratory surface in emphysema. Notwithstanding that much has been done in recent years to render our knowledge of this branch of treatment more exact it is still but little used in this country. This is doubtless due to the fact that patients are rarely under treatment for emphysema apart from its complications; and also to the small number of compressed air baths available for use.

The condition of the lungs in emphysema indicates that expiration into rarefied air should afford relief. This proceeding causes a diminution in the amount of residual air, and an increase in the volume of inspired air; thus a partial retraction of the lungs and a rise in the position of the diaphragm are brought about. These changes are accompanied by a lessened circumference of the chest, and by an increase in the vital capacity and of the force of inspiration and expiration. The apparatus of Waldenburg, of which a description will be found in the article on "Aerotherapeutics" (p. 35), is most suited for this form of treatment. Expiration into rarefied air produces a sense of extreme constriction within the chest and certainly diminishes the amount of residual air. The "vital capacity" of patients with emphysema under treatment by this method undoubtedly increases; but this result cannot be accepted as an absolute proof of its value, as it also follows the use of the apparatus by those whose lungs are structurally sound, practice enabling the individual to obtain a better result.

The results obtained from expiration into rarefied air are, however, much less satisfactory than those which attend the use of compressed air applied to the body as a whole.

I have given a prolonged trial at the Brompton Hospital to the use of the compressed air bath in the treatment of emphysema associated with bronchitis, and am able to support the favourable opinions expressed by Dr. C. Theodore Williams and others as to its great value (*vide* p. 42).

Patients almost invariably state that they breathe more freely whilst in the bath; and after a considerable number of baths (from 20 to 30 or more) have been taken this feeling becomes continuous, and has remained whilst the patients have been under treatment. The greater capacity for exertion which follows the use of compressed air baths in emphysema has been tested by observation of the gradually increasing facility with which patients thus treated have been able to mount a flight of steps which leads from the basement, where the bath is situated,

to the "gallery" (wards) occupied by them. Patients who at first were obliged to use the lift to return to their ward, or were only able to climb the stairs with many halts to take breath, have been enabled gradually to reduce the number of stoppages on the ascent; and many have at length been able to return from the basement to the uppermost floor without stopping once.

In addition to the greater freedom of respiration and increased capacity for exertion, the cough becomes less frequent and the quantity of expectoration is reduced.

It is not quite clear how these favourable results are produced. In a healthy person the effect on the respiratory organs of submitting the body as a whole to air gradually condensed to the extent of three-sevenths or one-half an atmosphere is to cause diminished frequency of respiration, enlargement of the lungs, increase of the vital capacity, and probably also an increase in the amount of oxygen absorbed. The change is attributed to the greater density of the air, and consequently to the increased amount of oxygen supplied to the lungs. The respiratory power and the elasticity of the lungs, both during and after the bath, are increased; the chest is enlarged in all its measurements, and the diaphragm assumes a lower level. In the subjects of emphysema, however, the effect of the bath is to cause a reduction in the size of the chest, as ascertained by measurement of the circumference; and also in the amount of distension of the lungs, as proved by the reappearance of dulness in the precordial and hepatic regions. The diaphragm is raised instead of being lowered, and epigastric pulsation may be replaced by an impulse more nearly in the normal situation of the apex-beat of the heart. It appears probable that the condensed air penetrates into parts of the lungs which have been long unused in respiration, and in which air has been, so to speak, imprisoned at a high pressure; the escape of this air is facilitated and contraction of the lung follows.

In some cases the improvement following the use of the bath is but temporary, and in cases of emphysema accompanied by asthma I have observed very severe attacks of dyspnoea to follow very shortly after a bath. If this should occur after the second bath, it is generally better to discontinue its use. Many cases of asthma are, however, greatly benefited by this method of treatment.

For the details of this method the reader is referred to the article on "Artificial Aerotherapeutics," p. 39.

The treatment of an attack of bronchitis occurring in a patient the subject of emphysema is not materially modified by the latter complication; but the duration of the attack is sensibly prolonged, and the danger to life is much greater, owing to the loss of power of expectoration which results from the diminished elasticity of the lungs.

Spasmodic dyspnoea often accompanies an attack of bronchitis, and requires the use of such remedies as stramonium, lobelia, belladonna, grindelia, or iodide of potassium in large doses, in addition to the ordinary drugs used in the treatment of bronchitis. The desirability of

employing morphine in such cases will depend chiefly on the relative preponderance of the spasmodic or the catarrhal factor. The nearer the attack approaches in character to one of true asthma the greater is the probability of relief from a subcutaneous injection of morphine; whilst, on the other hand, if the dyspnoea be chiefly due to the accompanying bronchitis, the use of morphine will be attended with the greatest danger. The history of previous attacks, the mode of onset, the presence of pyrexia, the character of the adventitious sounds—for instance, the presence of fine or medium bubbling rales, indicative of an affection of the smallest bronchi or of the alveoli,—and particularly the condition of the bases of the lungs, are some of the points to be considered in determining such a question. In the treatment of the attacks of wheezing, so often met with in emphysema, apart from any serious bronchial attack, a stimulating liniment containing turpentine and iodine rubbed into the chest is often of much service. Iodide of potassium in doses of five, eight, or ten grains three times daily, in combination with extract of stramonium and carbonate of ammonium, generally affords relief. In the intervals of comparative freedom from such attacks, and often throughout the winter months, the administration of cod-liver oil is hardly of less service than in cases of pulmonary tuberculosis. It is of special benefit when nutrition is failing, as is commonly the case in advanced stages of the disease, and in the atrophous emphysema of the aged. Iron in combination with spirits of chloroform is often taken by patients with emphysema with much benefit.

Turpentine, terebene, and balsamic remedies are of service where expectoration is excessive; this symptom is, however, due to the accompanying bronchitis, and its treatment is described in the article on that subject.

Cyanosis is an indication for venesection, and the necessity is urgent when there is evidence of great over-distension of the right side of the heart, with tricuspid regurgitation, pulsation in the jugular veins, and oedema of the feet. Digitalis should be given as soon as the blood has been drawn; and its use may be necessary in cases which are not so advanced as to require venesection.

When, as is not uncommonly the case, emphysema supervenes on bronchitis of gouty origin, the existence of this factor in the case must not be overlooked in the treatment. The same statement applies to the coexistence of chronic interstitial nephritis. It must not be assumed at once that the presence of a small quantity of albumin in the urine is due merely to renal congestion; search should be made for casts.

It is of great importance in cases of emphysema accompanied by attacks of dyspnoea, occurring at night, that the patient should not take a heavy meal at seven or half-past and retire early to bed; by so doing he is very likely to induce an attack. Full time should be given for digestion, and the lighter the evening meal the better; such patients should dine in the middle of the day.

Few conditions apart from bronchial catarrh are so likely to induce

an attack of dyspnoea as flatulent distension of the stomach. This is chiefly to be avoided by attention to diet; and these patients are nearly always well aware what food suits them and what does not. A mixture containing bicarbonate of sodium, tincture of nux vomica, compound tincture of cardamoms or tincture of ginger, with a bitter infusion, taken half an hour before meals, may prevent such an attack. A dose of blue pill, taken twice a week at bedtime and followed in the morning by a saline purge, is often beneficial in middle-aged subjects of the disease who are well nourished and have a tendency to gout.

Interlobular or Interstitial Emphysema

The escape of air into the connective tissue of the lung produces a condition to which the above name is applied.

As stated in the previous section, it has nothing in common with emphysema of the lungs but the name.

The air appears as rows of beads beneath the pleura and in the substance of the lung.

Wounds of the lung or rupture of the air-vesicles from overstrain during violent cough are the most common causes of the affection.

I have specially observed it in connexion with laryngeal diphtheria, generally after tracheotomy had been performed; but it may occur independently of that operation. The air, as pointed out by Dr. Champneys, passes from the tracheotomy wound downwards into the thorax behind the deep cervical fascia. From the mediastinum it may spread along the connective tissue surrounding the bronchi and vessels, and may appear on the surface of the lung as small beads of air beneath the pleura.

Mediastinal and interlobular emphysema may occur in diphtheria when tracheotomy has not been performed, probably from rupture of vesicles upon the surface of the lung; and pneumothorax, from perforation of the pleura, may follow.

Pathology.—The following extracts from the post-mortem register of the Middlesex Hospital (2) illustrate the changes met with in cases of interstitial and mediastinal emphysema:—

Case 1.—Male, age 3½ years. Diphtheria; tracheotomy. Extreme subcutaneous emphysema of the face, neck, and trunk; collapse of both lungs; mediastinal and subpleural emphysema.

Case 2.—Female, age 5 years. Diphtheria; tracheotomy. Lungs fully distended; no collapse; air in anterior mediastinum; membrane on fauces and in larynx, trachea, and bronchi.

Case 3.—Female, age 5 years. Diphtheria; tracheotomy not performed. Emphysema of root of neck; mediastinal, interlobar, and interlobular emphysema; pneumothorax (R); pulmonary collapse.

Case 4.—Male, age 5 years. Diphtheria; tracheotomy. General emphysema of subcutaneous cellular tissue of neck, trunk, and arms; lungs almost completely

collapsed from double pneumothorax; air in mediastina and around roots of lungs; membrane on tonsils and in larynx, trachea, and large bronchi.

Case 5.—Male, age 2 years. Diphtheria; tracheotomy. Larynx completely blocked with membrane, which extended throughout the trachea and main bronchi; lungs collapsed in patches; emphysema of anterior mediastinum.

Case 6.—Male, age 11 years. Diphtheria; tracheotomy. General emphysema; membrane in trachea and bronchi of left lung, latter collapsed; marked emphysema of anterior mediastinum.

Case 7.—Female, age 4 years. Diphtheria; tracheotomy. Interlobar emphysema on right side; air in anterior mediastinum; membrane as far as secondary divisions of bronchi; numerous areas of pulmonary collapse.

The preceding cases illustrate the lesions commonly found in association with interlobular emphysema when that condition occurs in diphtheria; the most important being general emphysema, pneumothorax, and pulmonary collapse.

Symptoms.—In all the cases above described in which tracheotomy was performed there would necessarily be urgent dyspnoea at the time the trachea was opened. The dyspnoea would then be relieved, but the occurrence of mediastinal and interstitial emphysema is accompanied by an increase in the dyspnoea. If pneumothorax supervene, the dyspnoea becomes extreme.

Double pneumothorax is necessarily quickly followed by death.

The breath-sounds would almost certainly be weak or absent if the connective tissue of the lung were infiltrated with air. Pneumothorax would be characterised by its ordinary physical signs.

Interlobular emphysema is rarely recognised during life. It may be suspected when subcutaneous emphysema is present, or when pneumothorax occurs. The latter is a serious complication. It is probable that the condition here described is often present but is unsuspected, and that the air is absorbed when recovery takes place.

No definite *treatment* can be adopted for the condition.

J. K. Fowler.

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NEW GROWTHS OF THE LUNG

By Frederick T. Roberts, M.D., F.R.C.P., and J. J. Perkins, M.B., F.R.C.P.

Non-Malignant New Growths.—Before discussing malignant disease of the lungs, it may be mentioned that these organs are in exceptional cases the seat of growths which are undoubtedly benign, though some of them, for example chondroma, may occasionally exhibit malignancy.

Hydatid cysts (*vide* Vol. II. Part II. p. 1019) and gumma (*vide* p. 426) are discussed elsewhere.

Enchondroma, ossifying enchondroma, and osteoma now and then occur as primary growths, but fibroma does not affect the lungs. Cases of adeno-rhabdomyoma in a stillborn child (Zipkin) and rhabdomyoma (Helbing) have been described; the patient in the latter case lived till the age of twenty-three years, and at the necropsy the place of the left lung was found to be occupied by an airless mass composed of small round cells, cartilage, fibrous bands, and muscular fibres. The tumour was considered to be derived from the embryonic residue of the absent left lung and to be allied to a teratoma. Though a "dermoid cyst" or teratoma may appear to be directly associated with the lung or embedded in its substance, it is affirmed that it never originates there, but must have extended from the mediastinum.

As a rule the non-malignant tumours do not give any clinical evidence of their presence; but if a benign growth attain a considerable size or encroach on the mediastinum, it may cause more or less pronounced symptoms and physical signs.

The malignant growths involving the lung may be primary or secondary. Direct invasion of the lung by tumours originating in adjacent structures is rare, except from the pleura and from the root of the lung.

In *secondary malignant* disease of the lungs the chief seats of the primary growth are said to be the breast, bronchial glands, oesophagus, stomach, liver, peritoneum, testes, and bones. The lung is the place of election for the secondary growths in primary sarcoma of bones and in chorion-epithelioma. The structure of the metastases is the same as that of the original growth: the chorion-epitheliomas shew their marked tendency to haemorrhage and necrosis.

The primary growths are chiefly carcinoma and sarcoma. Malignant enchondroma (Dalton), lymphadenoma as a part of the generalised disease, and lymphosarcoma (Davies) have been described.

Round-, spindle-, and mixed-celled sarcomas and chondrosarcoma (Scott) have all been found. The carcinomas are usually columnar- or cubical-celled, with a well-marked tendency to polymorphism. Squamous-celled carcinomas have been described (Gougerot, Neumeister), due to a

metaplasia of the epithelium, and columnar-celled carcinoma with ciliated epithelium (Horn). In the squamous-celled growths cornification is the rule. Cystic adeno-carcinomas have been reported by Coats (the cysts containing colloid material) and by Labbé and Boidin. In both these cases the formation of cysts was seen in all the secondary growths, and was not confined to those in the lung; in one of these cases there was a large cyst in the cerebellum (Labbé and Boidin).

Incidence.—Primary malignant disease of the lung is rare; in 21,034 necropsies at Munich, Perutz found 17 cases only of primary carcinoma of the lung (Horn); in Pässler's series (Breslau) there were in 9246 necropsies 1000 malignant tumours (870 carcinoma, 130 sarcoma), of which 16 were carcinoma and 4 sarcoma of lung. Pässler collected 78 recorded cases, but among these he avowedly included cases arising in a bronchus. Drs. Rolleston and Trevor, from a critical examination of this list, conclude that the figures are too high for pure primary carcinoma of lung, and from an analysis of a large mass of material argue that in the vast majority of cases the description is a mistake on the part of the older observers, and that there is no reason to believe that primary carcinoma of lung is more frequent than primary sarcoma. In 3983 autopsies at St. George's Hospital no example of carcinoma occurred, and 3 only of sarcoma. In their opinion all primary malignant disease of the lung is sarcomatous, spindle-celled when arising in the body of the lung, endotheliomatous in the root. It has, indeed, long been contended that carcinoma of the lung so-called really always arises in a bronchus (Pässler, Langhans), and the question is made the more difficult by the presence of bronchioles in the substance of the lung. Tumours containing ciliated epithelium must certainly have so arisen. Malassez was the first to demonstrate the origin of carcinoma from the epithelium of the alveoli, and the general belief at present is in favour of that view. In Neumeister's case (squamous-celled carcinoma) the bronchi and glands did not shew any trace of disease on the most careful examination; whilst the figures of Musser's sections carry conviction as to the actual conversion of alveolar cells to a malignant type.

Age and Sex.—In 60 collected cases 47 were males and 13 females (Rolleston and Trevor). The early *age* at which primary malignant disease of the lung occurs compared with malignant disease elsewhere has always been insisted on. In Benckert's table of 90 cases (Horn) 5 were between thirty and forty; 15 between twenty and thirty; 3 under twenty. In Drs. Rolleston and Trevor's series 50 were over forty, 10 under; the lowest limit being 13 for sarcoma, 19 for carcinoma. Cases in early childhood have been reported.

Metastases in sarcoma are rare, and often or usually absent: in carcinoma they may be widespread (Rolleston and Trevor), standing in order of frequency as follows:—Bronchial and mediastinal glands, liver, lung, pleura, kidneys, bones, suprarenals, spleen, brain, cervical glands, axillary glands, thyroid, dura mater, muscle of diaphragm, skin, pancreas, gall-bladder, and peritoneum.

Association with Tuberculosis.—Most writers agree, in opposition to Kurt Wolf and a few others, that the coexistence of active tuberculosis with cancer of the lung is very rare, Dr. J. K. Fowler finding the association in 2 only out of 30 recorded cases. Dr. Batty Shaw, criticising Wolf's list of 13 cases of tuberculosis in 31 of malignant disease of the lung, accepts only 8 of these as being even possible examples, and regards most of these as doubtful: he holds that if the demonstration of the tubercle bacillus be made the criterion, the combination of the two will be found to be exceedingly rare. A few instances, however (Gougerot and others), have stood this test.

Anatomical Characters.—Malignant growths in the lungs may take the form of infiltrations, distinct tumours, or a combination of both. Malignant disease of any of the varieties already mentioned may occur in the lungs, or rarely two kinds are present in the same case. The general distinction between separate tumours or nodules and infiltration must be recognised in growths of this nature, though they present considerable differences in detail in different cases. Primary malignant disease is not infrequently confined to a single lung; secondary growths as a rule affect both organs. The latter, moreover, generally assume a tuberous or nodulated form, being most abundant near the periphery; whilst the infiltrating variety is in the majority of cases primary, being limited to one lung. It will be convenient to deal further with the more important points relating to this class of morbid conditions under the following heads.

(*a*) Mode of Distribution and Extension.—When malignant disease in the lung occurs in the form of tumour, there may be but one such growth, of large size, which generally extends from the root into the central portion; but it may be quite distinct. In other cases the growth is multiple and disseminated, varying in size from a hazel-nut or walnut to a Maltese orange; such cases might be described as the "nodular" and "tuberous" group. These growths are at first isolated; but in their progress and development, which in the softer varieties is sometimes very rapid, they often become so incorporated together, that a large portion of, or even a whole, lung may ultimately be involved. In a third group malignant disease presents a miliary appearance and mode of dissemination in the pulmonary tissues—"miliary carcinomatosis"—resembling tuberculosis, but differing from this morbid growth in that the apices and upper parts of the lungs are not specially implicated, and may be quite free. The malignant growth is then more or less thickly scattered through the lung, in small nodules, ranging in size from a lentil or millet seed to that of a pea. A class of case occasionally met with consists of those in which the growths are chiefly subpleural, occurring either as flattened masses, from a quarter of an inch to an inch in diameter, semi-transparent or dull white, and compared to drops of wax; or extending more deeply into the lung, and acquiring a cupped, umbilicated, cupulated, or mushroom-like appearance. From these growths bands may also proceed into the interior of the organ for a variable distance.

The infiltrating form of malignant disease was described by Wilson Fox under two chief types. One is a general infiltration of the pulmonary tissues, which may fill large tracts of the lung with an almost uniform mass, in which, however, traces of the lobular tissue of the lung are still preserved; the other, even more uniform, in appearance and firmness may closely resemble the grey pneumonia attending tuberculisation. These conditions may involve the whole or nearly the whole of a lung. In the other variety the infiltration proceeds in the course of the interlobular septa, from which the growth may extend directly into the pulmonary tissue, or along the bronchi and blood-vessels, contracting their calibre, and greatly thickening their walls. These modes of extension may coexist. While recognising the general distinction between malignant tumours and infiltrations, it must be understood that they may occur together in various combinations.

(*b*) Effects on the Lung.—Malignant disease of the lung is likely to cause either an increase or a diminution in the bulk of the organ, but it may remain of normal size. Enlargement is usually associated with single or disseminated growths, or when these are incorporated together into a large mass, but is occasionally observed in connexion with infiltration. The latter more commonly tends to produce contraction and puckering, with alteration in shape. The lung may be so contracted and puckered as to give it an appearance resembling that of a hobnailed liver. These changes are especially pronounced when there is a great thickening of the pleura, and when a hard growth extends inwards along the septa and bronchi, or in bands from subpleural tumours. There is always increase in weight, which may be very considerable, and the lung feels remarkably heavy. The effect of malignant disease upon the pulmonary tissues not actually involved is usually to cause congestion and compression, but they may be quite normal. Possibly inflammation may be set up occasionally, or even suppuration around cancerous masses. In one of J. L. Steven's cases, a primary growth at the root of the lung had set up a widespread grey hepatisation. The condensation of lung is sometimes very well marked, and the investment of a tumour by a "condensed zone" may give it the appearance of being "encysted," a condition which does not occur in connexion with malignant growths in this organ. In individual cases the compressed lung has been described as forming a kind of cap to a tumour growing from below, or as a thin layer covering a tumour occupying nearly the whole substance of the organ. Haemorrhages or infarctions occasionally supervene; and diffuse pulmonary apoplexy has been found around tumours in the lung. It may happen that a growth projecting from a lung presses on the main bronchus, and produces the changes in different degrees which result from such pressure from any cause. With the extension of cancer into the pulmonary tissue all distinctions of its structures tend to disappear; but the vessels and bronchi resist the longest. The lymphatic vessels around isolated tumours may be distended with malignant growth; and it is affirmed

that the disease may be limited to these vessels, and may nowhere extend into the tissue of the lung.

(*c*) Secondary Changes.—Malignant growths in the lung sometimes undergo destructive changes, which must be duly recognised. They may thus become the seat of necrosis and softening; or abscesses may form, followed by cavities. Suppuration around malignant masses may give rise to an appearance like metastatic abscesses, and the lung may be found riddled with cavities. Such abscesses in rare instances have dissected the pleura from the lung over a considerable area, or have even perforated the pulmonary pleura. A cavity in the lung has been found as the sole evidence of malignant disease. A destructive process with suppuration may take place at the base of a lung, and simulate empyema. Extravasation of blood into malignant pulmonary growths occurs not uncommonly. The pleura often becomes involved in a growth, and extensive pleuritic adhesions are often observed, or there may be effusion which may be haemorrhagic. The portions of lung which are not involved in the growth are often the seat of collapse or more rarely of gangrene.

Sarcoma in the lung may appear as independent growths; or as an evident extension from a mediastinal tumour of similar nature. In the latter case the encroachment takes place along the bronchial tubes, which may be entirely destroyed; but sometimes the tumour moulds itself directly to the edge of the lung, and spreads up over the organ. Primary sarcoma in the lung may form very large tumours. They are, as a rule, soft and friable, white or yellowish-white. They may, however, present different degrees of firmness, due to intermixture of the fibrous element. Tumours secondary to remote sarcoma are generally of the round-celled or spindle-celled variety; but they may be ossifying or chondrifying. In a case described by Dr. Arthur Davies the whole left side of the chest was filled by a hard mass of new growth, scarcely any lung substance being visible. The left lung cut with difficulty, and presented a mottled appearance and yellow colour; the growth was most distinct along the pleural cavity. Microscopically it was a lymphosarcoma, which completely filled up the alveoli.

Clinical History.—The phenomena to be discussed come naturally under the groups of symptoms and physical signs, but before dealing with them individually, there are certain general points to which it is desirable to call attention.

1. Small, isolated, and deep-seated pulmonary growths obviously need not be accompanied with any symptoms or physical signs whatever, and this happens not uncommonly when they are secondary. Cases, however, which are thus latent at first, may during their further progress be attended with more or less definite indications of the presence of such growths.

2. There is a remarkable group of cases of secondary malignant disease of the lung, in which, although symptoms are either entirely absent, or so slight and indefinite as scarcely to attract notice, yet physical

examination of the chest at once reveals the existence of a tumour, it may be of large dimensions and of rapid growth. Some striking examples of this nature have come under my notice (F. T. R.), in which very extensive pulmonary growths, immediately and easily detected by physical signs, gave rise to no symptoms whatever, except some degree of shortness of breath on exertion, and occasional cough of no special character.

3. When malignant growths develop on an extensive scale in one or both lungs, they will probably give rise to more or less pronounced pulmonary symptoms and physical signs; and such cases come under observation as those of lung disease. The phenomena are, however, not uncommonly anything but characteristic; and various other pulmonary affections may be simulated. Thus the symptoms are in some instances merely of a bronchitic, emphysematous, or asthmatic character, with very indefinite physical signs; or they may resemble acute pneumonia or pleuritic effusion. This point will be further considered in relation to diagnosis, and in the meantime it will suffice to state that though difficulties in this direction must be fully recognised, in not a few instances the clinical phenomena, if duly studied and understood, are at least suggestive of malignant disease of the lungs, whilst in others they are sufficiently distinctive, or even quite characteristic.

4. So long as malignant growths are confined to the lung, they do not, in the large majority of cases, give rise to any of the recognised intrathoracic pressure-symptoms; but it must be remembered that occasionally a growth projects from the organ, and may thus interfere with one or more of the adjacent structures; or it may in its progress definitely encroach upon the mediastinum, and thus originate the more characteristic pressure-phenomena of mediastinal tumour.

Symptoms.—*Local Symptoms.*—Cases of secondary growths in the lung are usually characterised by the absence of any pain in the chest. This symptom may not be present from first to last even in primary cases, but a localised pain is usually complained of, which may be extremely severe, of a lancinating character, and accompanied with tenderness or superficial hyperaesthesia.

Some form of dyspnoea is generally present in cases of pulmonary malignant disease, and so long as the mischief is confined to the lungs, its nature and degree depend chiefly on the extent to which these organs are implicated and their functions interfered with, and on the arrangement of the growth. There may be some shortness of breath, hurried or excessive respiration, even at rest; or actual difficulty of breathing of different kinds. In secondary cases there may be very extensive growths, with but little obvious disturbance of breathing. Dyspnoea is also absent in some cases of infiltration; but it forms a prominent feature when any considerable area of lung has been affected, and in some cases the dyspnoea is very intense.

Cough is a probable symptom in connexion with growths in the lungs, if they reach any size, but it may be practically absent even with a large tumour. It is often, however, very distressing. It may be peculiarly

hard and dry. If the main air-tube is interfered with, the cough assumes the usual peculiar features.

Sputa.—Occasionally expectoration has been absent entirely. When present its naked-eye appearances cannot be considered as in any way characteristic (Ebstein). Mucoid sputa as in bronchitis; muco-purulent or purulent as in pulmonary tuberculosis; bright green as observed in some cases of pneumonia; or gelatinous and reddish- or blackish-brown from blood intimately diffused, may all occur. With gangrene the sputa will become fetid. In Musser's case there was an almost constant mucoid expectoration due to pressure and congestion. Only the presence of recognisably malignant cells or particles of growth can be considered as characteristic, and in 9 recorded cases a correct diagnosis has been made by this means, a number which may be increased with a more regular or routine search. Claisse was thus able to arrive at a diagnosis several weeks before symptoms or signs even suggestive of new growth appeared. In his case two small lumps, of which sections could be made, were brought up, and shewed a characteristically malignant epithelial structure including cell-nests. Ménétrier also diagnosed 2 cases in the same way. In other cases individual cells or microscopic groups of cells have been recognised. Hampeln lays down as criteria of malignancy that the cells shall be free from pigment, polygonal, and polymorphic. Betschart describes carcinomatous cells in the sputa as very large, with single or multiple nuclei containing three or four nucleoli, the cells being single or in groups. Mitosis has been observed in sarcomatous cells.

Haemoptysis is an important, and may be the earliest symptom of intrapulmonary growths; to some extent it occurred in 72 per cent of Walshe's series of malignant disease of the lung of all forms. It may be profuse and even fatal. Much importance has been attached to expectoration resembling red-currant jelly or prune-juice, due to the intimate admixture of blood. When present, it seems to be highly characteristic, but as a matter of fact it is extremely rare. So long as a growth is confined to the lungs, disturbance of the heart's action is seldom complained of, except such as may be due to weakness of the myocardium. Enlargement of the superficial veins, with oedema, may supervene during the progress of a malignant growth originally pulmonary; and possibly dysphagia, but not so long as the growth is limited to the lung.

General Symptoms.—A patient suffering from malignant disease of the lungs may present a more or less cyanotic aspect, as the result of interference with the respiratory functions. The general system may not be materially affected even when there is obvious and extensive mischief of this nature; and constitutional symptoms are not as a rule so pronounced as might be expected, especially in secondary cases. The cancerous cachexia may be sometimes evident, but on the whole cachexia is a much less marked feature in pulmonary than in abdominal malignant disease. Probably there is always more or less loss of weight, and wasting is in some instances extremely rapid. Other symptoms to be looked for are

more or less pyrexia, sweating, and weakness. Exceptional acute cases of malignant disease of the lungs are characterised by rigors, high fever, profuse sweating, rapid emaciation, albuminuria, with possibly delirium or coma before the fatal termination.

Apart from these exceptional cases fever, reaching 102° or even 103° has been noted in many cases of pulmonary growth (Jackson, Musser, Rolleston and Trevor) even of the type of a single large solid tumour. A leucocytosis of 22,000, 26,000, or in a unique instance 75,000 has been noted in these cases. It is unnecessary to insist how close the resemblance may be between malignant disease and an acute effusion or consolidation of the lung, especially when, as not infrequently happens, the symptoms of the former may have an acute or subacute onset. In Kappis' case, with a leucocytosis varying between 40,000 and 50,000, the eosinophils numbered from 14,000 to 19,500.

Physical Signs.—The clinical phenomena coming under this category, when present, exhibit much variation in cases of pulmonary malignant growths, according to their seat and distribution, number, extent and size, mode of formation, secondary effects, associated conditions, and other circumstances. Hence, as in the case of mediastinal growths, it is by no means an easy matter to give a definite comprehensive description of the abnormal physical signs associated with the chest to which they may give rise. As already stated, they may be entirely absent, or in no way characteristic. They will be discussed on the same plan as that adopted in relation to mediastinal tumour, except that no particular reference will be made to the superficial structures, which are not likely to shew any signs of venous obstruction or other changes, so long as growths are limited to the lungs. Modifications of the physical signs, due to pleuritic conditions, must always be borne in mind.

Changes in Shape and Size.—In cases of malignant disease of the lungs, the chest may exhibit:—(1) General enlargement, either associated with an extensive tumour distending the whole of one side, with compensatory distension of the healthy lung; or with disseminated growths on both sides, accompanied by an emphysematous condition. (2) Unilateral enlargement, due to extensive implication of one lung, which is more common, the intercostal spaces being widened and flattened, and the surface feeling unusually smooth and even. (3) Rarely unilateral retraction, with depression and narrowing of the spaces, accompanied by distension of the opposite lung (Kidd, Habershon), the result of the infiltrating malignant disease causing contraction of the organ, or of obstruction of the main bronchus, and consequent collapse of the lung. It is interesting that retraction has been noted on the side opposite to that on which the lung was the seat of malignant growths, owing to compression of the bronchus on the healthy side. (4) Local prominence, or even definite bulging in connexion with a circumscribed tumour of the lung coming to the surface; or possibly, on the other hand, local depression from limited infiltration or collapse.

Respiratory Movements.—The general effect of intrapulmonary

growths is to interfere more or less, and often to a marked degree, with these movements, usually unilateral or local. Should both lungs be invaded, they will be proportionately diminished generally. As a rule the most striking disorder is deficiency or abolition of inspiratory expansion. This is generally due to the growth itself, but may be partly the result of obstruction of a bronchus or lung-distension. Occasionally retraction of the lower part of the chest on deep inspiration is observed, as a rule unilateral, but possibly bilateral, when extensive areas of both lungs are implicated by malignant growths. When retraction of one side is associated with malignant pulmonary disease, some degree of movement of the intercostal spaces can in most cases be detected; but when the side is enlarged, they are practically motionless.

Tactile Sensations.—When a tumour in the lung comes to the surface, the sensation to the fingers is that of abnormal firmness and resistance, which may be very pronounced and characteristic. Vocal fremitus frequently persists in the case of pulmonary growths, and may even be intensified in different parts, when the growths are diffused or there is only moderate infiltration; as well as when the pulmonary tissue is more or less condensed or consolidated. Should, however, a lung be the seat of dense infiltration, or be converted into one large solid tumour, the vocal fremitus will be diminished over a corresponding area on one side, or even entirely abolished; though on careful palpation it may sometimes be noted that there are islets here and there over which the fremitus can still be felt. A combination which may be met with is the total extinction of this sign over the site of a tumour, with exaggeration over adjacent condensed lung.

Percussion.—The chief deviations from the normal which may affect the percussion sounds in cases of pulmonary malignant growths may be summed up as follows:—(1) There may be unilateral hyper-resonance or a more or less tympanitic sound, due to the effects of obstruction of a main bronchus by a growth. (2) A remarkable and general rise of pitch in the percussion-note over both lungs has been described by Fraentzel in a case in which a growth chiefly extended along the lymphatics of these organs. A similar change, of unilateral distribution, may be associated with a diffuse growth in one lung, when not too abundant. In connexion with tumours lying deep in the lung the sound may be hyper-resonant or actually tympanitic. (3) Dulness is the usual and more characteristic percussion-sign of pulmonary malignant disease, and it is often pronounced or absolute. Careful percussion may even then bring out isolated spots or islets which are more or less resonant, and correspond to unaffected portions of lung tissue. The opposite lung is often hyper-resonant, but it may itself be the seat of less extensive growths, and the percussion-sound would probably be modified accordingly. Dulness may extend from the affected side across the sternum to its opposite margin, or even for some distance beyond; and this has been looked upon as an important sign of malignant disease of the lung, but it is by no means invariable, and

may occur with a large pleural effusion. The dulness is localised in connexion with a limited growth in the lung, and is then chiefly observed either over the upper part of the chest in front; in the middle region posteriorly; or at the base. With a basal growth the infra-clavicular region may yield a high-pitched or possibly a cracked-pot sound. When a tumour in the lung comes to the surface the sensation felt on percussion is that of peculiar firmness or hardness and resistance, which is often highly characteristic.

Auscultation.—The breath-sounds are not necessarily affected in cases of growths in the lungs, even when these are revealed by other definite signs. Malignant disease infiltrating the septa may give rise to harsh breathing, or harsh breathing above and indeterminate breathing below, which in the later stages may pass into simple weak breathing. Diffused miliary nodules may also only cause harsh breathing, with prolonged expiration. When a lung becomes converted into a solid mass, the respiration will be practically inaudible over the whole side; or it may be feebly heard here and there; or possibly some circumscribed hollow breathing may still continue in the infraclavicular region; or the sound may be bronchial or tubular in the interscapular region. One of us (F. T. R.) has had the opportunity of watching a few cases in which the breathing on one side, at first harsh, then weaker but of tubular quality, became by degrees more and more obscured, until finally it was completely suppressed and inaudible over the whole side. Implication of the pleura, or pleuritic effusion, will help to weaken or abolish the respiratory sounds, often very extensively. Should the opposite lung be healthy and free to act, puerile breathing will probably be observed on that side.

When a portion of lung is consolidated by a growth, or a definite tumour exists in its substance, the breath-sounds are generally bronchial or tubular over the corresponding area, and may be excessively loud, being conducted from the larger air-tubes; in exceptional instances they may even approach a cavernous quality. Different modifications of the respiratory sounds may be observed over different parts of the same lung. Thus, with a tumour in its upper part and collapse below, it may be bronchial above and weak or inaudible towards the base.

Should cavities form in connexion with malignant growths in the lungs, the respiratory sounds will probably exhibit a corresponding hollow quality, but this is by no means always the case. Cavernous respiration in different parts of the chest was noted in a case of Stokes's, with dissection of the pleura from the lung by abscesses originating in cancer.

Malignant growths in the lungs do not of themselves directly originate any adventitious sounds. In cases of infiltrating growths and also where there are diffused miliary nodules, dry or moist rales may be present; or there may be definite bronchitic sounds. Coarse crepitation has been described over lung nearly solid from cancer and coexistent pneumonia, due to abscesses forming in the pneumonic parts, or to dilated bronchi. Various rales, which may be of hollow quality, may be

audible in connexion with cavities resulting from the breaking down of malignant growths in the lung, especially in the infraclavicular region. If the lung is the seat of consolidation by new growth up to a certain point, the vocal resonance will be increased; and it may be very loud, bronchophonic, or even pectoriloquous. In connexion with a definite tumour conducting vibrations from the main air-tube, it may be very intense, and of aegophonic, tubular, or amphoric quality. When the growth becomes excessive, the vocal resonance becomes impaired, and it may ultimately be suppressed practically over a whole side; though perhaps still audible in spots here and there. Sometimes, in connexion with an infiltrating pulmonary growth, it is intensified or pectoriloquous above, but absent below.

Cardiac Signs.—The impulse of the heart is sometimes felt extensively over a lung infiltrated with cancer. Displacement of the organ is less frequent, and usually less marked when growths are limited to the lungs than with mediastinal growths, but it is sometimes observed, especially when pleural effusion is superadded, even to a considerable degree. The cardiac action is disturbed in different ways in some cases.

Special Examination.—It will suffice to mention that in the investigation of certain cases of doubtful or obscure malignant disease of the lung it may be desirable to use an exploring needle; or to employ the *x*-rays, which may be of decided help in revealing the presence of growths, but it is difficult to distinguish infiltrations or scattered nodules from tuberculous lesions. As already stated, special examination of the sputum may be needed, and may possibly afford valuable information (p. 504).

Course and Termination.—Malignant disease of the lung is, as a rule, essentially chronic in its course, and steadily progressive. Carcinoma is said to last as a rule from 6 months to 2 years, and seldom goes beyond 4 years. Walshe, in a small number of cases, found the mean duration to be 13·2 months; the maximum being 27 months and the minimum 3·5 months. Several cases, however, are on record in which malignant disease of the lung ran an acute course of a few weeks from the first appearance of symptoms. "The ordinary course of growths limited to the lung is that of a gradual death by means of mingled conditions of asphyxia, hectic, and exhaustion in relatively varying degrees, in which, however, asphyxial symptoms usually predominate, being sometimes rapidly intensified by the supervention of acute oedema of the lung" (Wilson Fox).

Diagnosis.—When growths are confined to the lung, the difficulty of diagnosis is obviously much greater than when they occupy the mediastinum, either entirely or partially. Under such circumstances it may be almost impossible to come to a positive conclusion, especially when the disease is primary; though due consideration of the case in all its aspects may at any rate lead to a suspicion of its nature. In not a few instances, moreover, pulmonary malignant disease can be fairly recognised by the signs of extensive and marked consolidation of the lung, attended either with enlargement or retraction of the side, and, it

may be, shewing little or no disposition to break down. Among the symptoms which may be significant, associated with such conditions, are severe pain in the side; disproportionate or paroxysmal dyspnoea; and repeated haemoptysis, especially if the blood resembles currant jelly or prune-juice. Evidence of obstruction of one bronchus, or any indication of pressure signs, would materially assist the diagnosis of a growth. When malignant disease of the lung is secondary the local phenomena are not uncommonly highly characteristic.

In dealing further with the diagnosis of malignant growths in the lungs, it is necessary to refer briefly to the chief morbid conditions which may cause a difficulty or lead to error. The relations of pulmonary and mediastinal tumours are sufficiently considered elsewhere, and if it should happen that it is impossible to make a definite differential diagnosis between them, the result is of no practical moment.

Acute Pulmonary Diseases.—As has already been pointed out, acute disseminated or infiltrating cancer in the lungs may closely simulate other acute pulmonary affections; namely, bronchitis, pneumonia, tuberculous phthisis, or acute tuberculosis. The course of events may also much resemble that of tuberculous meningitis, cerebral symptoms being prominent, which may or may not be associated with cerebral metastases. It is impossible to lay down any definite rules for establishing a diagnosis in cases of this kind, and it must suffice to warn the practitioner of their possible occurrence. The probability is that even the most experienced would in the circumstances fall into error, and fail to recognise the nature of the disease. Wilson Fox refers particularly to acute caseous pneumonia, affecting chiefly the base, and consolidating the whole or the greater part of one lung, as in some cases presenting a striking resemblance to infiltrating cancer when the latter does not retract the side. "The most distinctive features are the high fever, the more abundant expectoration, and the rapid emaciation. Diarrhoea, if present, would be still more in favour of the diagnosis of caseous pneumonia. Malignant infiltration is more likely to be mistaken for caseous pneumonia than that the converse error should occur." I (F. T. R.) have not seen any acute case exemplifying this difficulty. Sir Clifford Allbutt met with a very instructive case of a patient who died of primary malignant disease of the left lung in Addenbrooke's Hospital. As she was in hospital during an examination week she was seen by some six physicians of large experience. Four of them took the case to be caseous pneumonia, two of them made the correct diagnosis. A remittent febrile temperature had been present since admission.

Chronic Pneumonia.—One of us (F. T. R.) has met with cases of what he believed to be extensive unilateral chronic pneumonia, in which the lung was not retracted, but appeared even to be enlarged, and in which the phenomena were very like those of a pulmonary growth. Their prolonged duration was one of the points in favour of this diagnosis, but in neither instance could a necropsy be obtained. By far the more important condition, however, to be mentioned under this head is the fibroid lung,

which may be confounded with infiltrating pulmonary cancer causing retraction of the side. In most instances the history would materially help in the diagnosis; and probably any obscurity would be cleared up sooner or later by the course of events. The differences in the physical signs are, as a rule, sufficiently distinctive, though by no means wholly to be trusted. Those in favour of malignant disease are absolute dulness with much resistance, especially if it extends across the middle line; suppression or marked weakness of breath-sounds; absence of adventitious sounds; abolition of vocal fremitus and resonance; and depression of the liver—if the retraction be on the right side. As the fibrotic lung is often accompanied with cavities or dilated bronchi, bronchial or tubular breathing is likely to be audible, with moist rales, which may be of more or less cavernous quality. Severe pain in the side is in favour of cancer; as well as pyrexia in a case of considerable chronicity, and where the disease is manifestly advancing.

Emphysema and Bronchitis.—True vesicular emphysema may precede or coexist with growths in the lung, which are then apt to be overlooked or obscured; as they may also be by secondary pulmonary distension. The association of bronchitis with disseminated or infiltrating malignant disease of the lung is apt to make the diagnosis very difficult or uncertain. Only very careful investigation and thoughtful consideration can obviate mistakes in diagnosis in relation to these conditions, which, however, are very likely to happen in any circumstances.

Chronic Pulmonary Tuberculosis.—There is a real danger of mistaking malignant disease affecting the lung for chronic tuberculosis, although, of course, only in the very exceptional cases when the growth happens to involve the upper part of the organ, and especially if it should break down and form a cavity or cavities. The local and general symptoms may be very similar in both classes of cases; and even diarrhoea may be a prominent symptom in those of cancer. Implication of both apices, with absence of pressure-symptoms and presence of fever, would be practically positive evidence of tuberculous mischief. Extensive consolidation of one lung, without signs of softening or cavities, but with gradual suppression of the respiratory sounds and extension of dulness across the middle line, are strongly in favour of malignant disease. Prolonged absence of pyrexia is also very suggestive; as well as "unusual" symptoms, such as extreme debility, marked anorexia, and a slow, feeble pulse, coupled with a limited amount of disease at one apex (Wilson Fox). With regard to haemoptysis, its comparative frequency is of little value in diagnosis. Frequently recurring haemoptysis in a man past middle age and without signs of emaciation, was noted by Stokes as characteristic of malignant disease. In unilateral pulmonary tuberculosis haemoptysis is said to be rarely profuse or often repeated, but I (F. T. R.) have met with not a few exceptions to this statement. The curability of this symptom in any given case is in favour of tuberculous rather than of malignant disease. It has been stated that enlargement of the supraclavicular glands is probably associated with malignant disease, whilst enlargement of the

submaxillary glands is in favour of tubercle; but this distinction cannot be positively relied upon in diagnosis. Systematic examination of the sputum would be likely to afford valuable information in doubtful cases, by revealing the presence of tubercle bacilli on the one hand, or fragments of growth on the other. Its absence might in certain circumstances point rather to new growth. The possibility of the coexistence of malignant disease and tuberculosis must be borne in mind.

Pleuritic Conditions.—Possibly some difficulty might be experienced in the diagnosis between a pulmonary growth and an adherent and much thickened pleura; these pleuritic changes may be associated with such a growth. The most important point, however, in the present connexion is the danger of mistaking a malignant tumour originating in the lung, so extensive as to occupy the whole of one side of the chest, for a chronic pleuritic effusion or an empyema. In many recorded cases this mistake has been made; it is favoured by the absence of cachexia and the subacute onset noted in many cases of growth. Fever, too, may be present in either. Repeated haemoptysis, especially of the red-currant jelly or prune-juice type, would be strongly in favour of growth; as well as profuse offensive expectoration, and fetor of the breath, if a perforating empyema could be excluded, as it might be by the presence of elastic tissue or fragments of growth. A careful search for enlarged glands in the neck might materially help in clearing up the diagnosis in doubtful cases.

In distinguishing between the conditions at present under consideration, physical signs demand special attention and study, and to these reference will now be made. (*a*) Oedema of the subcutaneous tissue of the chest is suggestive of intrathoracic tumour, though it does rarely occur in connexion with empyema. In the latter case, however, it is almost always unilateral, and the superficial veins are not enlarged. When the oedema is more extensive over the thorax, involving also the neck, face, or arm, and accompanied with any appearance of cyanosis, or with dilated veins, the diagnosis is strongly in favour of growth. (*b*) The affected side is more or less enlarged as a whole in both kinds of cases, but extreme enlargement would be rather indicative of pleural effusion. In this condition the dilatation is likely to be uniform, and any want of regularity, or a local bulging, would suggest a tumour. Empyema may, however, cause a limited prominence. Another point of distinction is that fluid tends to make the intercostal spaces prominent, whereas a growth will only lead to stretching without protrusion, or may affect them but little. (*c*) A feeling of fluctuation over any of the intercostal spaces is in favour of fluid, but this sign is liable to fallacy. On the other hand, a pulmonary growth may yield a remarkable degree of resistance on palpation, which is very suggestive. (*d*) Careful investigation of the vocal fremitus may afford indications in diagnosis; especially as revealing, in connexion with tumour, islets where it can be felt, though it is generally abolished or markedly deficient. (*e*) The percussion-signs demand particular study. In both conditions dulness is very pronounced and

extensive, but there are certain points relating to the percussion-sound which may be of diagnostic significance in difficult cases. Those in favour of tumour are extension of dulness from above downwards, if the case happens to have been under observation, or it may be less marked below than above; absolute and general dulness, without such a degree of enlargement of the side or other signs as would point to an effusion sufficiently abundant to produce this effect; irregularity and inequality in the degree of dulness in different parts of the chest, possibly with resonant spots, not varying with change of posture; and its irregular extension across the middle line at the upper part of the thorax. It has been stated that the absence of Skodaic resonance under the clavicle, in a case of extensive unilateral dulness, is characteristic of malignant disease as distinguished from pleuritic effusion; but I (F. T. R.) can affirm from personal observation that such a distinction cannot be relied upon in either direction. The marked sense of resistance elicited on percussion is often highly significant of a solid intrathoracic growth, as compared with the feeling associated with fluid. (*f*) Auscultation signs are also worthy of attention. Breath-sounds and vocal resonance may be practically abolished over the whole side both in connexion with pleural effusion and pulmonary tumour, but in the latter condition they will probably be audible over some spots, at any rate; and there may be bronchial breathing and bronchophony over considerable areas where dulness is pronounced. Absence of respiratory sounds and vocal resonance below, with auscultatory phenomena indicative of condensed lung above, would probably point to effusion. Undue conduction of the heart sounds is much in favour of growth in the lung. (*g*) Displacement of organs, and especially of the heart, is likely to be decidedly more marked in cases of pleural effusion than of tumour. Moreover, the latter tends to push the heart more downwards than laterally, and this is especially characteristic when the left side is affected. (*h*) An exploratory puncture should always be made in doubtful cases, and it may clear up any obscurity at once. It should be remembered, however, that a pleural effusion may be but a symptom of underlying malignant disease. (*i*) Possibly the *x*-rays might help in the differential diagnosis of obscure cases.

Prognosis.—In all cases of malignant disease of the lung the prognosis is absolutely hopeless. The duration will vary according to circumstances, within the recognised limits, but it is out of the question to venture on any definite opinion on this point. It must be remembered that in some instances the progress is acute and rapid; whilst untoward events may occur which bring about a speedy or sudden termination in chronic cases.

Treatment.—The treatment of pulmonary malignant growths can only be palliative and symptomatic, and must be guided by general principles, carried out according to the judgment and discretion of the practitioner. Venesection and the inhalation of oxygen may be of value for the relief of dyspnoea. No vaunted treatment for malignant disease can be of the slightest use in these cases; and operative interference is practically out

of the question, except that it might be necessary to perform paracentesis for pleural effusion. The patient must be made as comfortable as possible, and be well looked after in every respect.

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DISEASES OF THE PLEURA

INTRAPLEURAL TENSION

PLEURISY

PNEUMOTHORAX

NEW GROWTHS

INTRAPLEURAL TENSION

By Samuel West, M.D., F.R.C.P.

In health the two layers of the pleura are in close contact, but they are subject to a constant strain, which tends to separate them; this is called the intrapleural tension. It is for all practical purposes equal to the elasticity of the lung, but opposite in direction; and thus the elasticity of the lung is positive and the intrapleural tension negative.

Whether in health there is any force existing between the layers of the pleura—such as that of cohesion, as I suggested some years ago (12), which neutralises the elasticity of the lung when fully expanded—is a matter which is open to question. It is possible, and I think it probable; but the question need not be further considered here.

The forces, of which the intrapleural tension is the resultant, are, first, the rigidity of the chest walls; secondly and chiefly, the elasticity of the lungs; and, thirdly, the movements of respiration.

So far as the condition of the chest walls is concerned, where they are fairly rigid, as in the adult, this factor may practically be disregarded; but not so in infants or little children, in whom the chest walls are soft and yielding; for then, under pathological conditions, part of the force which would otherwise tend to separate the two layers of the pleura is spent in drawing the chest walls in.

The condition of the chest walls and the elasticity of the lungs cannot vary while observations on intrapleural tension are being made; but the third factor, namely, the movements of respiration, is one which is constantly varying, and introducing variations in intrapleural tension which have to be reckoned with. Thus during inspiration the lungs are placed more on the stretch, and consequently the intrapleural tension is greater; during expiration the lungs are less on the stretch, and the intrapleural tension is therefore smaller.

If the air in the tubes were stationary, as it is after death, the pressure in the air-tubes would be that of the atmosphere; but, during respiration, the air, as it passes in and out through the air-tubes, meets with some obstruction, which on inspiration amounts to about half a millimetre of mercury, and on expiration from 2 to 3 millimetres. Thus an oscillation in pressure is produced during the different phases of respiration, which amounts to 2 or 3 millimetres of mercury; that is, $1\frac{1}{2}$ to 2 inches of water. This is called the respiratory oscillation.

If the movements of respiration were left out of account, the intrapleural tension would be equal to that of the atmosphere, minus the elasticity of the lungs; that is to say, it would always give a negative reading on the manometer. It would then be equal to the elasticity of the lungs with the sign changed, that is, −6 to −8 millimetres of mercury.

During ordinary respiration the intrapleural tension is also negative throughout; for, if it is negative when the air is stationary, it will be more negative still on inspiration, the lung being more on the stretch; and during quiet expiration, even when from the normal elasticity of the lung the 2½ to 3 millimetres of mercury be deducted which represent the obstruction in the tubes to which the air is subject on expiration, there are still left 4 to 5 millimetres of negative pressure.

During violent expiration, of course, the pressure may rise considerably, even to so much as 70 to 100 millimetres (3 to 4 inches) of mercury; but it must be remembered that under normal conditions this pressure does not fall directly upon the pleura, but is immediately supported by the chest walls. Under pathological conditions, on the other hand, when the two layers of the pleura are not in contact, but are separated by air or by fluid, pressure of any kind will make itself felt directly by the contents.

There are two methods of determining the value of the intrapleural tension. (1) In the one the elasticity of the lung is determined, and the result, with the sign changed, is transferred to the pleura; (2) in the other the intrapleural tension is estimated directly by means of a trocar introduced between the layers of the pleura.

In man both these methods of investigation are available after death, but the latter only during life, and this under pathological conditions.

In either case the reading is made upon a mercury- or water-manometer. Water has been more commonly employed, because the oscillations are larger and are more easily read; but the conversion is easily made from the one to the other: thus 1 inch is equal to 25 millimetres, and 1 millimetre of mercury is approximately equal to half an inch of water or 12½ millimetres of water.

Intrapleural tension is often spoken of as "intrapleural pressure," and thus confusion is introduced both in thought and in expression. This confusion will be avoided if it be remembered that the values stated are not actual pressures but readings on the manometer. For instance, if the pressure in the pleura were equal to that of the atmosphere it might be called 1, but as this would be indicated on the manometer by the position of equilibrium which is marked zero, it is usually spoken of as zero; 1, 2, or 3 inches or millimetres would then represent 1, or 2, or 3 above or below the atmospheric pressure, as the case might be.

The elasticity of the lung was estimated by Donders to be from 6 to 8 millimetres of mercury; this, therefore, with the sign changed, would represent the intrapleural tension.

An important series of observations of a similar kind was made by

Perls. After a tube connected with a manometer had been fixed into the trachea, first one pleura and then the other was opened and the pressures registered. The observations were made upon the dead body of a man under a variety of different conditions, and the results are very interesting.

Sir J. Barr's observations, made on himself by means of a tube in the mouth or nares respectively, give similar results. The readings, in millimetres of water, were :—

	Inspiration.	Expiration.
Oral breathing, quiet .	− 5 to − 8	+ 3 to + 5
„ deep .	− 24 to − 34	+ 20 to + 30
Nasal breathing, quiet—		
„ 2 nostrils .	− 10 to − 16	+ 6 to + 10
„ 1 nostril .	− 16 to − 22	+ 12 to + 16
„ deep—		
„ 2 nostrils .	− 40 to − 60	+ 30 to + 40
„ 1 nostril .	− 180 to − 200	+ 160 to + 180

Müller's experiment, expanding the chest after deep expiration, the mouth and nostrils being closed, gave − 80 mm. of mercury.

Valsalva's experiment, by forcible expiration after deep inspiration, the mouth and nostrils being closed, gave + 100 mm. of mercury.

Aron induced a healthy man to allow a manometer to be inserted into his chest, and found as the average of thirty-six observations that the maximum reading for quiet inspiration was 5·1 mm. Hg, and the minimum for expiration − 2·5 mm. Hg.

Seeing how closely intrapleural tension is connected with the elasticity of the lung this will be the natural place to consider various pathological conditions under which the normal elasticity of the lung is altered.

When one pleural cavity is laid freely open to the air there will then be atmospheric pressure on both sides of the visceral pleura ; the elasticity of the lungs will come into play, and the exposed lung will collapse. But this is not all, for the alterations in pressure do not affect the one lung only ; the mediastinum being not a fixed partition, but a movable one, the elasticity of the opposite lung also comes into play ; with the result that the mediastinum and the organs therein are drawn over to the sound side. Thus it follows that the opening of one pleura not only satisfies the elasticity of the one lung, but goes a long way to satisfy the elasticity of the other. If, for example, the pressures be reduced to figures, and we assume for the sake of illustration that in a healthy man the total elastic contractility of the two lungs together amounts to 50, the opening of one pleura may satisfy this elasticity to the extent of 40, leaving only 10 for the unsatisfied elasticity of the opposite lung.

Thus, in pneumothorax, which is the corresponding pathological

condition, if the lungs are healthy and their elasticity at its maximum, the total respiratory capacity will be suddenly reduced by four-fifths. If, however, the lungs be previously diseased or the pleura adherent, the elasticity of the lungs will be either reduced or prevented from coming into play; and thus the change in respiratory capacity consequent on the pneumothorax will not be so extreme. For these two reasons it is evident why the sudden admission of air to the pleura should produce more severe results in a healthy person than in one whose chest has been previously diseased; and a clinical paradox is explained.

Where the pleura is completely adherent the elasticity of the corresponding lung may be almost abolished; but it is frequently retained, though of course when retained it is unable to come into play. Under these conditions the opposite lung often becomes greatly enlarged. This has often been called "complementary emphysema," but in these cases the elasticity of the enlarged lung is not diminished, as in ordinary emphysema, but actually largely increased, so that the elasticity of that one lung may be almost equal to the combined elasticity of two healthy lungs. Thus it is made evident that this condition is not emphysema, but hypertrophy, as there are also the best of clinical reasons for maintaining It should therefore be called, not complementary emphysema, but complementary hypertrophy.

There is good ground for believing that the contractility of the lung is not simply elastic, but is due in some measure to the muscular fibre with which it is so richly provided. If that be so, we may fairly speak of "pulmonary tone" in the same way as we speak of "vascular tone"; and we may expect it to vary not only with local conditions of nutrition in the lung, but also with defects of nutrition which are general.

Thus, in various local affections, of which pneumonia is the most important, Perls found the elasticity of the lung greatly reduced; as well as in general diseases without any local affection of the lung, as for example in enteric fever, delirium tremens, erysipelas, phosphorus poisoning, and after severe haemorrhage.

If, then, pulmonary tone be not simply elastic in origin, but in part neuro-muscular, the loss of it may be met with under two different clinical conditions: first, as the result of general causes—as an evidence, for instance, of general neuro-muscular failure; and, secondly, as a result of local nutritive disturbance.

As a neuro-paralytic phenomenon it might be placed in association with the like condition in the abdomen (acute tympanites), which in the same way may be due to general or local causes. For example, just as in pneumonia, acute abdominal tympanites may suddenly manifest itself —a phenomenon of fatal significance; so with typhoid fever, or any other specific fever, a similar condition may appear in the lung which is likewise of fatal import.

The loss of pulmonary tone is indicated during life, just as it is after death, by change in the percussion-note; the resonance becoming more tympanitic and of that character which is generally known under the

name of "Skodaic resonance." Without any local disease of the lung, I have on several occasions seen this acute pulmonary tympanites set in; whatever the explanation of its occurrence, there is no doubt as to the existence of the condition.

Where there is local disease in the lung, the other parts of the lungs, as is well known, frequently yield a tympanitic percussion-note. There are several conditions under which this is met with: the commonest and easiest to explain is that which occurs with pleural effusion, when the lung floating on the fluid yields this Skodaic resonance. The conditions and the percussion-note are the same as are presented by the lung removed from the body.

With complementary emphysema, where one part of a lung is diseased and the other parts proportionately distended, similar hyper-resonance is obtained. In this case the hyper-resonance is due to the over-distension of some of the air-vesicles.

But besides these there is another condition which requires a different explanation. Nothing is commoner in pneumonia than to find the parts of the lung above or in front of the affected portion yielding a highly tympanitic note; yet the pneumonic portions of the lung are certainly not collapsed or smaller than they should be, nor are they much larger: thus neither of the explanations just given is applicable; the part of the lung where the hyper-resonance is obtained is not collapsed on the one hand, nor over-distended on the other. This condition, it appears to me, can only be explained on the assumption of loss of lung-tone of neuro-paralytic origin and dependent on nutritive disturbance. This view also obtains support from some of Perls' observations, for among his cases are several instances of pneumonia as well as some of embolism and gangrene; and in all of them the elasticity of the lung was very greatly reduced.

It is possible that the elasticity of the lung diminishes after death, but there are no direct observations to prove this. We may assume at any rate that for some hours after death the elasticity of the lungs is not materially affected.

In estimating the elasticity of the lung and the intrapleural tension the condition of the abdominal muscles and of the diaphragm must not be overlooked. We have to reckon on the one hand, during life, with their respiratory action, and on the other, after death, with rigor mortis; but it is not necessary here to do more than refer to these complicating factors.

THE PLEURAL CAVITY UNDER PATHOLOGICAL CONDITIONS

Under pathological conditions the two layers of the pleura may be separated either by air or by fluid, and each of these presents its own peculiarities and difficulties: thus, fluid has weight, but is practically incompressible; air is compressible, but its weight may be disregarded. With fluid, therefore, the height of the column above the point of the

trocar will affect the manometer readings, while with air the position of the trocar is immaterial. As in many respects the problem is simpler in the case of air than of fluid, it will be well to begin with pneumothorax.

Intrapleural Tension in Pneumothorax.—Air may gain access into the pleura either from without through the chest walls, as by a wound, or internally from the lung; and in both cases we have to consider, first, the condition in which the air enters more freely on inspiration than it finds issue on expiration, and, secondly, the condition in which there is no abnormal obstruction either on inspiration or on expiration.

A. Where the air finds entrance through the chest walls.

(i.) *By a Punctured Wound.*—In this case, where the wound is a small one and merely a puncture, though the lung be injured the air does not, as a rule, find access to the pleura, but crosses the pleura and reaches the subcutaneous tissue. The reason of this is very difficult to find, but of the fact there is no doubt. The explanation which I suggested in 1887 was that the cohesion between the two layers of the pleura is such that a considerable force is required to separate them. This was adopted by Sir W. MacEwen in 1906, and need not be further considered here.

(ii.) *Where the opening is a small one*, so that the air finds easier entrance than it finds exit. This condition will be the same as that in which the air gains access to the pleura through the lung, and will be better considered later.

(iii.) *Where there is a large opening through the chest walls*, at least as large as the cross-section of the trachea. The air then enters and leaves the pleura without obstruction, that is to say, the pressure on both sides of the visceral pleura is the same—namely, that of the atmosphere—during all phases of respiration. Under these circumstances the elasticity of the lungs comes simply into play, so that the lungs collapse.

It is no doubt true, as Donders said, that in course of time under these circumstances the lungs will become completely collapsed by virtue of their own elasticity; yet we have daily experience that this does not usually occur, and when we consider the matter the reason is clear. It is found in the fact which has already been stated; namely, that the air in the tubes is not subject simply to the atmospheric pressure during the phases of respiration; on inspiration it is under a pressure somewhat less than the atmosphere (by half a millimetre of mercury), and on expiration under a pressure above that of the atmosphere (to the extent of $1\frac{1}{2}$ to 2 millimetres of mercury).

During expiration, therefore, the lungs will always be subject to the distending force of $1\frac{1}{2}$ to 2 millimetres of mercury. There are no observations to shew how far the lung will be expanded under such a pressure, but it cannot well be less than a half, and is probably more; at any rate we have daily demonstration of the fact that the lungs do not collapse completely as the result of opening the side: on the contrary, on opening the side for empyema it is a common experience to find the lungs which have been completely collapsed by the effusion expand again as soon as the pus has evacuated, so as to reach close to the chest walls

immediately after the operation. This may at first be the result of the violent respiratory efforts or of the coughing which very frequently follows the operation; but this is not the only explanation, for it occurs when there is no violent expiration or coughing, or persists when they have passed off.

Two cases which I have recorded are of interest in this respect, because the lung had been compressed by fluid for a long time — eighteen months and five months respectively, one being a case of serous effusion and the other of pyopneumothorax; in both, immediately after the operation, the lungs were close to the chest wall, and within a week had come into close contact with it everywhere except just round the incision (14).

B. Where the air gains access to the pleura from the lung.

(i.) Theoretically it is possible that the opening through the lung should be large enough for the air to pass freely in and out during inspiration and expiration without obstruction; yet this is a condition which can hardly ever arise, and almost all the cases of pneumothorax therefore come into the second category.

(ii.) That in which the opening through the lung is of such a kind that though the air gains free entrance into the pleura during inspiration it cannot find free issue from it during expiration. The result of this is that during expiration the pressure rises and compresses the lung, which gradually becomes more and more collapsed. Although it is true that the mediastinum may be displaced to the maximum and the lungs be completely collapsed in cases where there is no expiratory compression, still in the great majority of cases this rise of pressure during expiration plays a very important part in the production of both these phenomena.

The division of pneumothorax into open, closed, and valvular, interesting as it is in some respects, is of no practical importance from the present point of view—that of intrapleural tension; for in a case of recent pneumothorax as soon as the lungs are completely collapsed the hole becomes closed, whether it be permanently sealed or not. During the early stages pneumothorax is always more or less valvular; in other words, the air finds easier access during inspiration than it finds issue during expiration.

The intrapleural pressures during inspiration and expiration require, in the case of pneumothorax, to be considered separately.

1. *The Inspiratory Pressure.*—When the lung has ruptured, air finds access to the pleura during inspiration so long as the pressure in the pleura is below that of the pressure in the air-tubes; that is, below the atmospheric pressure:—although this has to be reduced, as already stated, by half a millimetre of mercury, being the value of the obstruction which the air meets with on its way into the lungs. The inspiratory pressure, therefore, can never rise in pneumothorax above that of the atmosphere except under one condition, namely, that in which there has been much dyspnoea; for as the inspiratory efforts are then considerable the air will consequently continue to enter the pleura as long as the pressure at the

end of each inspiration is below that of the atmosphere and until it equals that of the atmosphere, after which no more air can enter. It follows, therefore, that if the patient survive and the dyspnoea pass off, the inspiratory pressure might be above that of the atmosphere to the extent of the difference between the pressure on deep inspiration and the pressure on ordinary inspiration. This is not very much, and in all probability the excess of air, which represents the difference of pressure, is rapidly absorbed.

In ordinary simple pneumothorax the inspiratory pressure is therefore not, as a rule, above that of the atmosphere. If it be, some other factor is required to account for it, and this almost without exception proves to be the presence of fluid; we may therefore conclude that whenever the inspiratory pressure is much raised we shall probably find that fluid is present as well as air.

2. *The Expiratory Pressure.* — The expiratory pressure in pneumothorax is always positive. It is true that the mediastinum may be displaced to its maximum in a case in which the pressure in the pleura is zero. Still the raised expiratory pressure tends to make the displacement extreme or to produce it more rapidly; whilst, as already stated, it is the expiratory pressure which probably chiefly accounts for the complete collapse of the lung.

3. *The Respiratory Oscillation.*—As this is the difference between the pressure on inspiration and the pressure on expiration it will vary according to the amount of dyspnoea or the violence of the respirations at any given time.

It might be thought, considering the violence of respiration in many of these cases, that the respiratory oscillations would always be considerable. As a matter of fact this is not found to be so, and a little consideration will shew why this is the case: on the affected side the chest is in a condition of maximum inspiratory expansion and cannot alter from this on expiration; while on the opposite side the lung is prevented from expanding fully, by the amount of the reduction of its volume by the displacement of the mediastinum and the organs connected with it; thus its elasticity also is reduced, being, as already stated, partly satisfied. It is evident, therefore, that the total respiratory excursion of the chest will be very considerably diminished and the respiratory oscillation therefore small.

I have recorded a series of observations upon the pressures in pneumothorax in eleven cases, some of which were tapped several times; so that there are records of twenty different paracenteses (15).

The *inspiratory pressure* varied from zero to + 9, the several pressures being 0, $\frac{1}{2}$, 1, $1\frac{1}{2}$, $2\frac{1}{2}$, 4, $4\frac{1}{2}$, 5, $6\frac{1}{4}$, $6\frac{1}{2}$, $6\frac{3}{4}$, 7, $8\frac{1}{4}$, $8\frac{1}{2}$, 9 inches of water.

In two cases the inspiratory pressure was that of the atmosphere; that is, the reading of the manometer stood at zero. In both of these cases fluid was present as well as air. From this it is evident that as soon as the fluid formed the air must have been absorbed, since the opening into the lung in both cases was closed.

In another case the inspiratory pressure, after having been in the two first paracenteses positive, fell in the last two to zero; and the change in pressure was due to an opening of considerable size having formed into the lung.

In all the other cases the inspiratory pressure was positive, and fluid (sometimes pus, sometimes serum) was present as well as air; thus the statement already made is confirmed, namely, that when the inspiratory pressure is much above that of the atmosphere the conclusion may be drawn that fluid is present as well as air.

It is no matter of wonder that the inspiratory pressure rises when fluid forms; but it is surprising that the pressure is not much higher than we find it. The highest pressure that I observed was 9 inches of water, but pressures as high and even higher have been met with in serous effusions. It follows, therefore, that when fluid forms in pneumothorax a large amount of the air present must be absorbed as the fluid forms.

We know, both as the result of experiments on animals and of operations upon man, as well as from observations of pneumothorax in man, that air may be very rapidly absorbed from the pleura.

Even when fluid is present the pressure may not be above that of the atmosphere, as we have already seen; and I think we may possibly even go so far as to say that if the intrapleural pressure remains unusually high in pneumothorax it may be taken as an indication that there is extensive disease both of the lung and the pleura; so that the absorption of air which would ordinarily occur is prevented from taking place.

The *expiratory pressure* also varied considerably from zero up to $13\frac{1}{4}$, the actual figures being 0, 0, 1, $1\frac{1}{2}$, $2\frac{1}{4}$, $2\frac{1}{2}$, $4\frac{1}{2}$, 5, 7, 8, $8\frac{1}{2}$, 9, and $13\frac{1}{4}$. The highest expiratory pressures are, as already stated, due to dyspnoea; that is, to violent expiratory efforts.

The *respiratory oscillations* in the same way shewed great variations, and fluctuated from zero up to 8. The largest were 8, $6\frac{5}{8}$, $6\frac{1}{2}$, 6, and 4. In all these cases there was dyspnoea, and the large respiratory oscillation was the result of the high expiratory pressure.

The lower respiratory oscillations were 0, $\frac{1}{2}$, $\frac{1}{4}$, 1, $1\frac{1}{2}$, $1\frac{3}{4}$, and $3\frac{1}{4}$.

Even where the inspiratory and expiratory pressures are high, the respiratory oscillations may be small or absent; thus in one instance where the inspiratory pressure was + 9, the expiratory pressure was the same, and the respiratory oscillation therefore 0. *Per contra* even where the inspiratory pressure is low, the respiratory oscillation may be considerable if there be much dyspnoea; for example, in a case in which the inspiratory pressure was 0, the expiratory pressure was + 8, and the respiratory oscillation therefore 8.

Where there is no dyspnoea the respiratory oscillations are apt to be small, and may be completely absent.

These observations shew that, in pneumothorax, whatever general statements may be made, they have to be applied with caution in

individual cases, for it is impossible in any given case to forecast what the actual pressures will prove to be; and, finally, that although the results obtained will have to be explained according to the peculiar circumstances of each case, yet if this be done carefully, much information may be obtained concerning the actual condition of the lung and pleura.

Intrapleural Tension in Serous Effusion.—In health the pleural cavity contains no fluid, and we often speak of it as dry; yet this description is somewhat inaccurate, for there is in fact a constant circulation of fluid into the pleura and out of it, the fluid being effused by the blood-vessels and carried away by the lymphatics. The mechanism by which this is performed has been described as "the lymphatic pump." It consists of the lymphatic vessels with their stomata and valves, and is worked by the respiratory movements. The course of the circulation in the lung is from the pleural surface towards the root of the lung, as has been determined by experiment; and there is a similar circulation from the pleural surface through the diaphragm and through the chest walls. It is partly through the action of the lymphatic pump that the negative pressure is maintained in the pleural cavity and the lungs kept fully expanded.

There are two ways, therefore, in which fluid may accumulate in the pleura: either it may be poured out into the pleura in larger quantities than the pump can remove, that is, its amount may be abnormal, or the amount of fluid not being above the normal, the pump may be defective.

In the case of pleural inflammation both these processes come into play; the amount of transudation is considerable, while the stomata and smaller lymphatics are often plugged by deposits of fibrin. Thus in inflammatory cases the fluid may accumulate with very great rapidity and soon reach a large amount.

In the case of dropsy of the pleura consequent, let us suppose, on heart disease, the explanation is probably also in great part mechanical. Exudation under these conditions takes place from the blood-vessels into the lymphatics of the lung, which become water-logged or choked; thus it is impossible for the pleural cavity to be freed from the fluid, which consequently accumulates. With dropsy, however, the accumulation of fluid is much slower and the amount as a rule much less.

When fluid collects in the pleura it falls by its weight to the lowest part; and although the tension in the whole pleural cavity is diminished in proportion to the amount of fluid present, still the effect upon the different parts of the lung is different: thus, the lowest parts suffer most and become collapsed, while the upper parts of the lung remain distended; yet the tension in the upper part of the pleural cavity is also lower than it otherwise would be, as is shewn by Dr. Calvert's observations. The diminished tone in the lung or tension in the pleura explains the hyper-resonant note which is obtained in those parts of the lungs which are floating upon the fluid.

In determining the intrapleural pressure in cases of fluid effusion

something will depend upon the seat of puncture. This Dr. Calvert has also demonstrated; for if the mouth of the trocar be 1, 2, or 3 inches respectively below the level of the fluid, there will be the pressure of a column of fluid of this height to allow for. If, for example, the intrapleural tension be equivalent to – 3 inches of water, and the amount of fluid exuded into the pleura be sufficient to reduce this 3 inches negative pressure to 2 inches negative pressure, it follows that if the mouth of the trocar be 2 inches below the level of the fluid, a positive pressure of 2 inches will have to be added to the negative pressure in the rest of the pleura, which will reduce the pressure-reading to zero; or, if the height of the fluid be 3 inches instead of 2 inches, it would convert the pressure at the point of puncture to a positive pressure of 1 inch. It is very difficult to make due allowance for these variable conditions, so that the pressure records in pleural effusions have not anything like the same value as those in pneumothorax.

It might be supposed at first that with large effusions the pressure would be high, with medium-sized effusions moderate, and with small effusions low; but actual observation shews that this is by no means the case, for whatever be the bulk of the effusions the pressures may be high, moderate, zero, or even below zero. Thus, among my own observations, where the effusion was large and a considerable quantity of fluid was drawn off, the pressures were – 1, $2\frac{1}{2}$, 4, 6, 8, $11\frac{1}{2}$, and 18; where the effusion was moderate – 1, 0, 4, 5, $8\frac{1}{2}$; and where it was small, 0, $\frac{1}{2}$, $1\frac{1}{4}$, 3, 5, 11.

The pressures, therefore, vary in a curiously irregular way, and it is difficult to see what the explanation can be. It is natural to attempt to refer these variations to the different stages of the inflammation. Thus in the early ingravescent stage, when the effusion is rapidly forming, the pressures might be high, and low in the later stages when the fluid is being absorbed. There is some evidence in favour of this view, but the matter is by no means as simple as it would seem.

Respiratory Oscillations.—For the reasons given when speaking of pneumothorax the respiratory oscillation with serous effusion is likely to be small; as a matter of fact it is so, and not infrequently it is entirely absent.

Now, as the action of the lymphatic pump depends upon the respiratory movements, and as these are indicated by the respiratory oscillations, it is evident that in these cases the mechanism for the removal of the fluid is at a standstill.

It is interesting to observe in some cases, though the respiratory oscillation is absent when the puncture is first made, that after fluid has been withdrawn the respiratory oscillation begins to return, and at the end of the operation may be fairly considerable. This is important, as it explains what is often observed at the bedside, namely, that the removal of a small quantity of an effusion may lead to the rapid spontaneous disappearance of the rest. What it really means is, that the lymphatic pump has been set to work again.

The intrapleural pressure in serous effusions is the resultant of three forces:—1. The respiratory movements. The effect of these has been already sufficiently considered. 2. The force of inflammatory exudation. We do not know much of the pressures under which the exudation of inflammatory fluid takes place in the pleura; but if we may compare it with the knee-joint, which is more accessible to observation, we may be quite sure that it occurs under very considerable pressure when we remember how tense the synovial sac becomes during the early stages of inflammatory effusion. 3. The action of the lymphatic pump; this is opposed to the first. We may presume that it is practically equivalent to the elasticity of the lung, and therefore equal to 6 or 8 millimetres of mercury, when the lung is fully distended; but it is a rapidly diminishing force as the lung becomes compressed, the stomata closed, and the lymphatics collapsed; and when the chest is full of fluid it vanishes, for, as the respiratory oscillations shew, the lymphatic pump comes to a stop.

In the early stage of acute inflammation we may conclude that the pressure may be very high when the effusion is a large one, or when the effusion, if a small one, is encapsulated, that is, localised and not general.

When the acute stage of the inflammation has passed and exudation ceases, if the fluid begins to be slowly removed the pressure will fall; and it is obvious, since the fluid is ultimately removed completely, and the lungs come out into contact with the chest walls again, that in course of time the pressure will even become negative. I do not see any way in which this can be brought about except through the intervention of the lymphatic pump.

Intrapleural Tension in Empyema.—This is a much simpler problem than in the case of serous effusions. The pressures here are in accord with what we know of suppuration elsewhere; for the formation of pus goes on under considerable pressure. It is only in the very chronic so-called "cold" abscesses that the tension is low; but even then the pressure is probably above that of the atmosphere.

Thus, among my own observations the pressure was considerably raised in all cases, the lowest being + 3. The highest was + 16, and this was found with a very large effusion; but, as I have said, small effusions may have a very high pressure if they be loculated or encapsulated. An interesting example of this was observed among the cases of serous effusion; for in one in which the pleura had been tapped twice, and the pressure found on each occasion to be not raised, on the third paracentesis the pressure was + 3; the effusion, however, was no longer serous, but had become purulent: in other words, the general serous effusion had been followed by a small localised empyema; this was incised and then recovery became complete.

The respiratory oscillation in empyema is always small and frequently entirely absent.

From what has been said it is evident that the problem of intrapleural

tension, especially under pathological conditions, is a very complicated and difficult one, and requires much further investigation.

SAMUEL WEST.

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S. W.

PLEURISY

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THE name pleurisy (ἡ πλευρῖτις νόσος, morbus lateralis, side-sore of early English) formerly denoted that acute disease which is characterised by fever and severe pains in the side; and the meaning of the word was wholly clinical. After the time of Morgagni, when the influence of morbid anatomy became predominant, the name acquired that anatomical signification which it has since retained; and for the last century or more, pleurisy has been defined to mean inflammation of the pleural membrane.

Inflammation of the pleura may lead to the effusion of coagulable lymph with or without serum, or of pus. It is convenient to describe these two forms of the disease separately, because there are important differences between them in regard to etiology and treatment. But it should be remembered that this division of the subject is merely dictated by convenience and not by any essential difference in the pathological processes underlying the disease; still less is it dictated by any difference in symptoms or in physical signs. Some authors make a further division of the disease and separate the condition of pleurisy without liquid effusion ("dry pleurisy") from that of pleurisy with liquid effusion ("pleurisy with effusion"). This, however, is not necessary;

"dry pleurisy" is often but an early stage of "pleurisy with effusion," and it is seldom possible to be sure that there is an absence of liquid effusion in any given case of pleurisy. Indeed it is probable that a small amount of liquid is present in many cases which are classed as "dry pleurisy."

A. Sero-Fibrinous Pleurisy

Etiology.—1. *Age and Sex.*—Pleurisy occurs at all ages: one of us (S. G.) has evacuated pleural empyemas in infants aged one month, three months, and five months; and has drawn off three pints of serum from the chest of a woman eighty-seven years old. Sero-fibrinous pleurisy, however, is uncommon in infants. Dr. Thursfield, in an unpublished analysis of 100 cases of pleurisy extending over a period of three years at the Hospital for Sick Children, Great Ormond Street, found that of the cases occurring under ten years of age 82 per cent were empyemas; of those occurring over five years of age 77 per cent were sero-fibrinous pleurisy. The mean age of the cases with empyema was 2·1 years, and that of the cases with sero-fibrinous exudation 6·1 years. The annexed table, drawn from the records of St. Bartholomew's Hospital for twenty years (1884-1903), shews in two periods of ten years each the number of patients in whom sero-fibrinous pleurisy was the main and foremost disease; it does not include the cases in which pleurisy was secondary to some other disease no less serious. The figures shew (*a*) that pleurisy is much more frequent in males than in females (in the proportion of 2·5 to 1·0); and (*b*) that pleurisy is most common in patients between twenty and forty years old, more than 48 per cent of the cases being within these age-limits. The age-incidence shewn by these figures corresponds with that obtained by Lord at the Massachusetts General Hospital, where, out of 760 cases, one-half occurred in these two decades (20-40).

	Males.	Females.	Deaths.	5 yrs. and under.	10 y.	15 y.	20 y.	30 y.	40 y.	50 y.	60 y.	Over 60.	Totals.
1884-1893 .	465	186	48	25	59	50	54	179	149	85	35	15	651
1894-1903 .	565	218	11	30	62	56	103	185	176	103	49	19	783
Totals .	1030	404	59	55	121	106	157	364	325	188	84	34	1434

2. *Occupation*, as judged by the above series of 1434 cases, has no special bearing upon the disease.

3. *Season.*—The cases in this series were distributed almost equally throughout the year, with a slight preponderance during the months of May and November. In America Lord found the maximum monthly incidence during March.

4. *Exposure.*—Pleurisy, like pneumonia, will sometimes follow so

speedily upon great exposure of the whole body, or of the chest in particular, to cold, that it is carrying scepticism to excess to doubt that the exposure plays some part in causing the subsequent disease: in this case the cold may be supposed to bring about such an altered nutrition of the parts as favours invasion by specific microbes.

5. *Injury.*—A heavy blow upon the chest, not leading to more than bruising of the parts, and not bringing about any solution of continuity, will sometimes be followed by constant pain, and at length by serous effusion into the pleural cavity: in this case, also, it is reasonable to suppose that the injury affords an opportunity for infection.

6. *Bacteria.*—Pleurisy is due to irritation of the pleural membrane by certain microbes. It is difficult not to believe that this proposition is universally true; and true, even in the case of pleurisy following upon an injury to the side, or upon exposure of the chest to cold. In by far the greater number of cases the disease is spontaneous, and arises apart from the operation of any obvious antecedent cause. Bacteriology has thrown great light upon this spontaneous or idiopathic pleurisy. The microbes which will account for most pleurisies are three—the tubercle bacillus, the pneumococcus, and the streptococcus.

(i.) Tubercle Bacillus.—Even before the discovery of the bacillus of Koch, it was suspected that many cases of pleurisy with serous effusion were due to tuberculosis of the pleura; and now it cannot be doubted that tuberculosis is the commonest cause of pleurisy with serous effusion. This opinion is based upon the following data: (*a*) Many of the patients who die are found at necropsy to be tuberculous. Of 131 patients thus examined, Prof. Osler found this to be the case in 32 (24·4 per cent). Dr. Theodore Fisher, in an analysis of 240 recent necropsies, found old pleural adhesions present in 41; of these 28 shewed evidence of old tuberculosis of the lung. (*b*) In a considerable number of the cases clinical evidence of tuberculosis is found in the lungs or in other organs. Signs of phthisis, which were not previously detected, may be clearly manifest after drawing off the fluid. Prof. Osler found that in 195 cases in which the sputum was examined tubercle bacilli were demonstrated in 30 (15·3 per cent). (*c*) The demonstration of bacilli in the fluid removed by paracentesis has hitherto been notoriously difficult, even in cases which are undoubtedly tuberculous. But more recent methods have given a larger proportion of positive results; this is true both as regards the isolation of the bacillus direct from the exudate and also as regards the inoculation of guinea-pigs with the exudate. By a simple process of sedimentation Zebrowski demonstrated the bacilli in 55 per cent of 22 cases; by his method of *inoscopy* (*vide* p. 546) Jousset states that he can demonstrate the bacilli constantly. In the inoculation experiments Eichhorst advises the use of large doses of the fluid—15 c.c. at least. Le Damany used much larger quantities than this (up to 300 c.c.), and produced tuberculosis in the pigs as often as 51 times in 55 cases. (*d*) Widal and Ravaut's method of *cytodiagnosis* (*vide* p. 545) favours the view that most of the cases of sero-fibrinous pleurisy are tuberculous, the cells

present in the fluid being chiefly lymphocytes, often to the extent of 100 per cent in a count of 100 to 200 cells. (*e*) A positive reaction is given by the tuberculin test in about three-fourths of the cases. Beck found it present in 73·7 per cent of cases examined and Lord in 76·5 per cent. It must, however, be remembered that the reaction may be due to a tuberculous lesion elsewhere in the body. (*f*) The subsequent history of the patients supports the conclusion. Many of those who recover from the effusion suffer afterwards from tuberculous disease, and especially from pulmonary tuberculosis. Bowditch was the first to adduce figures in this connexion; of 90 cases traced during the years 1849-1879, 32 died of pulmonary tuberculosis. Dr. Hedges followed up 130 cases treated at St. Bartholomew's Hospital, and found that 40 per cent of these had become tuberculous within seven years. Of 300 cases from the Massachusetts General Hospital investigated by R. C. Cabot, 117 were found to have died within five years. (*g*) Many of the patients have inherited a tendency to tuberculous disease. It is now generally considered that this bulk of evidence is sufficient to justify the conclusion that most cases of spontaneous pleuritic effusion are due to the tubercle bacillus. Dr. Gibson and other physicians contest this.

(ii.) Pneumococcus.—The pleuritic effusion which is secondary to pneumonia is not always purulent, but is sometimes serous; in this serous effusion pneumococci are found. Moreover, serous effusion, which is not secondary to pneumonia, is due in a few cases to pneumococci.

(iii.) Streptococcus.—This micro-organism is occasionally found in pleuritic effusions which are serous in character. Dr. Andrewes and one of us (T. J. H.) met with two instances and Dr. Mervyn Gordon with one. In all three cases the streptococcus was a variant of *S. pyogenes.*

(iv.) The *typhoid bacillus* is an uncommon cause of pleuritic effusion. T. M'Crae was able to discover only three instances of pleurisy in 1500 cases of enteric fever (0·2 per cent). Pure cultures of the bacillus have been obtained from the pleuritic fluid by Achard and Gordinier, by Fernet, and by Lartigau. In the case described by the first of these authors the agglutinating power of the exudate was ten times that of the blood serum. Mariotti has reported a case in which the effusion was haemorrhagic. Lord's criticism that the generalisation of the typhoid bacillus is such that its mere presence in a pleuritic effusion is not enough to prove its causal relation to the serous inflammation seems scarcely warranted. In the pleurisy which not infrequently occurs during convalescence from enteric fever the operation of the tubercle bacillus must always be suspected. Even if the typhoid bacillus be present in the effusion the inoculation of a guinea-pig with the fluid may shew the presence of the tubercle bacillus also (H. Vincent).

7. There are some other causes of pleurisy, but the specific manner in which they operate is not so clear; such are superficial *haemorrhagic infarcts* of the lung, *nephritis*, *rheumatism*, and *gonorrhoeal rheumatism.* In the case of the last-named disease the direct operation of the causal microbe has been clearly demonstrated in one case by Bordoni-

Uffreduzzi. The occurrence of pleurisy, both with and without serous effusion, is not at all uncommon in association with rheumatism. Most often the patient shewing this association is suffering from a severe attack of rheumatic fever, and there is usually also present endocarditis, or pericarditis, or both. Occasionally, however, the rheumatic process appears to shew itself as pleurisy only. But rheumatic pleurisy must not be diagnosed in the absence of physical signs, for pleurodynia of rheumatic origin is a more common disease, especially in children. In rheumatoid arthritis pleurisy also occurs, indeed it may be a conspicuous feature of the disease; but here it is probable that etiological factors other than the rheumatic poison are at work. In most of the cases of pleurisy complicating acute rheumatism and rheumatoid arthritis the operation of the tubercle bacillus can almost certainly be excluded. Careful search for bacteria in pleuritic effusions found after death in fatal cases of rheumatic fever has mostly yielded negative results to one of us (T. J. H.), and in the few cases in which micro-organisms have been isolated these have been streptococci without any special characters. Those workers, however, who consider the *Diplococcus rheumaticus* to be the cause of rheumatic fever have found this micro-organism in the effusion in cases of rheumatic pleurisy. The pleurisy occurring in the course of nephritis, like the pericarditis which is such a common terminal event in this disease, is often proved to be of streptococcal or of pneumococcal origin.

8. Stinzig considers that pleurisy without liquid effusion is not seldom due to *syphilis*. This opinion seems to be based very largely upon the good effects which are sometimes seen to follow the administration of iodide of potassium in such cases—evidence too slender to carry conviction.

9. Pleurisy with effusion is said to have been caused by the application to the chest of *x*-rays (C. Quadrone).

10. *Pleurisy by extension* of inflammation from adjacent organs. (i.) Pericardium. When pleurisy and pericarditis concur it is often impossible to say which is the primary disease. The diagnosis of pericardial effusion in the presence of pleural effusion is often very difficult. The nature of the combined inflammation of these two serous membranes is, with a few exceptions, either rheumatism or pneumococcal infection. (ii.) Oesophagus. Pleurisy may complicate malignant disease of the oesophagus. Occasionally a malignant ulcer of the oesophagus perforates into the pleural sac, causing pneumothorax.

(iii.) From the abdomen. Pleurisy is often secondary to inflammation below the diaphragm, and may occur either with or without the formation of subphrenic abscess. The possibility that pleurisy is due to the spread of infective processes from the abdominal viscera must constantly be borne in mind, for the primary disease may remain latent or may yield symptoms which seem insignificant. The chief abdominal conditions which deserve mention in this connexion are the following:—(*a*) Gastric and duodenal ulcers. Pleurisy arising insidiously in a patient (especially if a woman) who is suffering from dyspepsia should always

raise a suspicion of gastric ulcer. Pleurisy so arising usually means that the ulcer has perforated but that adhesions are present which prevent infection of the general peritoneal cavity. Early recognition of the pleurisy is of the utmost importance, as a subphrenic abscess is almost certainly in course of formation. From the concurrence of perigastric adhesions and adherent pleura over the diaphragm in the post-mortem room it is probable that the pleura not seldom becomes infected in gastric diseases, without perforation of the stomach. (*b*) Hepatic abscess. Actinomycosis of the liver often spreads to the pleura and lung. (*c*) Splenic infarct, by perisplenitis and inflammation of the diaphragm. In this way pleurisy has been the first evidence of infective endocarditis. (*d*) Appendix abscess is an instance of remote abdominal suppuration which sometimes leads to pleurisy. (*e*) After operations upon the stomach and intestines pleurisy may be the first sign of "sepsis." A slight leak from a perforated ulcer which has been sutured, or from a gastro-enterostomy wound, not seldom reveals itself first in this manner. The surgeon may fail to discover anything amiss with the abdomen, and the functions of the stomach and bowel may be carried on satisfactorily. A second laparotomy, however, or a necropsy if the patient die, will reveal the track by which the infection has spread, and usually one or more collections of pus below the diaphragm.

Morbid Anatomy. — The changes produced in the pleura by the action of the irritants enumerated above are those of inflammation of serous membranes generally. These changes are more or less intense according to the stage of the disease at which the inflamed structures are examined; they vary but little according to the nature of the irritant. Almost the only macroscopic feature which suggests to the experienced observer the kind of micro-organism at work is the character of the inflammatory exudate; abundance of fibrin, leading to the production of a false membrane which can be peeled off the inflamed pleura, is commonly due to the pneumococcus; a haemorrhagic exudate, if not manifestly connected with injury or new growth, is most often due to the tubercle bacillus. But these points will sometimes mislead, and perhaps the only certain characteristic by which a specific cause of the pleurisy may be recognised is the presence of miliary tubercles on the pleural surface. Even here, however, the converse does not hold, for it not seldom remains for the microscope to demonstrate the presence of tubercles which are not apparent to the naked eye.

The earliest change found in the membrane is a loss of lustre, with slight roughness, as easily palpable as visible. Increased vascularity is not usually very apparent to the naked eye, though it is a striking feature under the microscope. Small haemorrhages into the pleura are most often seen in the pleurisy associated with massive bronchopneumonia, and are not uncommon in the fatal pulmonary complications of influenza. At this stage the microscope will shew, besides the congestion of the blood-vessels, proliferation and detachment of the endothelial cells lining the sac, increase of the sub-endothelial connective-tissue cells and leucocytic

infiltration of the inflamed part. The further changes observed have to do with the character and amount of the exudate and the occurrence of adhesions. The characters of the exudate are dealt with elsewhere (p. 545); they can be studied as well during life as in the post-mortem room. Adhesions vary with the duration of the disease, from easily friable bands of coagulated lymph to stout fibrous tissue which, in extreme cases, may be universal in disposition, and may necessitate the enucleation of the lung from the thorax together with the parietal pleura and diaphragm. The commonest situations of old adhesions are about the apex, on the diaphragmatic surface of the pleura, and where this membrane lies adjacent to the pericardial sac. Some degree of adhesion is almost invariable if death has occurred during the course of a pleuritic attack; hence, if liquid effusion be present, some loculation of this is also very common. Such loculation is one mark of distinction between an inflammatory exudate and a mere transudate such as occurs in connexion with morbus cordis.

In effusions of moderate size the base and posterior border of the collapsed lung are found to be of a bluish tint and airless; there is still blood in the vessels, and often a considerable quantity of oedema fluid escapes from the cut surface of the organ. In large effusions, when a positive pressure is exerted by the fluid, and especially when the effusion has been present for some time, the lung is forcibly compressed, and is seen to lie packed against the spine; the viscus is now empty of blood as well as of air, and is of a pale grey colour. On section of such a lung its parenchyma is found to be smooth and firm, and pinkish-grey in colour ("carnified"). In the section are seen the cut ends of the bronchi lying in groups close together.

Bacteriology.—In cases of "dry" pleurisy the operation of bacteria, though in many cases strongly suspected, cannot often be proved; for paracentesis gives no material for examination, and the disease is rarely fatal. But several of the reasons for regarding serous pleurisy as being most often due to the tubercle bacillus (see p. 533) also hold good, but to a less degree, in "dry" pleurisy. Lord found the tuberculin test was positive in 4 out of 12 cases (33·3 per cent) of "dry" pleurisy, as against 36 out of 47 cases (76·5 per cent) of serous pleurisy. In the case of pleurisy with effusion, the argument for the responsibility of the *tubercle bacillus* has already been set out at length on p. 533. Undoubtedly the micro-organisms found next in frequency in serous pleuritic exudates are the *pneumococcus* and *streptococci*. Out of 49 consecutive cases examined bacteriologically at St. Bartholomew's Hospital, 40 were sterile on cultivation, 7 yielded a growth of pneumococcus, and 2 a growth of streptococcus. It is thus seen that in over 80 per cent of cases the fluid removed from the chest in pleurisy with effusion is sterile when tested by ordinary culture media. This is, of course, what might be expected if the great majority of such cases are due to the tubercle bacillus. If to these three micro-organisms be added the occasional occurrence of *B. typhosus*, *Pfeiffer's bacillus*, and the *gonococcus*, the flora of non-purulent

pleural inflammation, so far as present observations are concerned, is exhausted. Nor does this statement fail to take account of the results of the positive school of observers in the matter of pleural effusions occurring in rheumatic fever; for it must be conceded that, even if the *Diplococcus rheumaticus* be eventually proved to possess a definite causal relation to this disease, it still belongs to the genus streptococcus.

Symptoms.—1. *Onset of the Disease.*—(i.) Latent.—The occurrence of one or more symptoms marks the onset of the disease in most cases. But in other cases the onset is not perceived: the disease at first is latent; and it is most likely to be latent when it is secondary to other serious disease, the symptoms indicative of the onset of pleurisy being masked by pre-existing symptoms dependent upon the primary disease.

(ii.) Manifest.—When the onset of the disease is not latent, the indicative or invasion symptoms either (α) occur suddenly and decisively, clearly marking the time at which the state of health passes into the state of sickness; or (β) they occur gradually, so that it is not easy to say precisely when the disease began. Whether they occur suddenly or gradually, these symptoms, denoting the onset of the disease, are no other than more or fewer of the symptoms which attend the confirmed disease, and which will be described in the next place. The commonest invasion symptoms are fever (with shivering or not), pain in the side, vomiting, cough, quickness and shortness of breathing; in children sometimes convulsions.

2. *Fever.*—Fever is not a constant symptom; being slight and temporary in pleurisy with small innocuous exudation; being present in most, and yet not in all cases of larger effusion. Some degree of fever is so commonly present in acute pleurisy that it should be allowed to weigh heavily in favour of this disease in any case of pain in the side of doubtful nature.

(i.) In acute pleurisy the temperature seldom rises above 103°. In pleurisy, as compared with pneumonia, the fever is not so high, shivering at the onset is less common, and the duration of the fever is indefinite.

(ii.) In chronic pleurisy no distinction can be drawn between serous and purulent effusion by means of the characters of the fever. What is called serous effusion is not serous in the strict meaning of that word, but is really a dilute lymph or liquor sanguinis[1] not free from leucocytes. In pleurisy with serous effusion the temperature is often (but not always) persistently raised; and the fever not less or less constant than that of a purulent effusion. When fever is present it lasts until the effusion is wholly absorbed; indeed, in cases of febrile serous effusion defervescence is the best evidence that the effusion has been absorbed, for physical examination is often of no avail in determining this point. The type of fever tends to be quotidian remittent.

[1] A fact first recognised by B. G. Babington in 1830; see *Med.-Chir. Trans.*, vol. xvi. p. 303.

Local Temperature.—That the affected side is sometimes hotter than the other was known to ancient Greek physicians, who employed an ingenious means of discovering the fact (see Hippocrates, *De Morbis*, iii. chapter 16).

3. *Pain.*—Severe pain in the side was the main and constant sign of the disease called pleurisy in the ancient sense of the word; but the pain of pleurisy, in the modern sense, may be severe, or may be not severe, or there may be no pain at all. The pain is usually felt in the side of the chest; sometimes about the nipple, or above the clavicle, or in the hypochondrium; sometimes about the navel, or even in the iliac fossa and lower belly, on the same side as the disease. The onset of the pain may be very abrupt. The skin over the affected side is often very tender. Marked spinal tenderness, in some part of the vertebral groove in the dorsal region, is common.

The nature of the pain is a matter for debate; probably there are different causes of the pain. Intercostal or diaphragmatic cramp has been suggested as an explanation of the stitch in the side. The pain felt at a distance (namely, in the abdomen) is probably conducted along an intercostal nerve.

The occurrence of severe abdominal pain in acute pleurisy, as in pneumonia (in which the same cause is probably at work), especially if it be associated with tenderness of the skin, and rigidity of the muscles of the abdomen, not seldom suggests the presence of peritonitis. So much so that there are few surgeons of great experience who have not performed laparotomy in these circumstances.

4. *Dyspnoea.* — Dyspnoea, manifested by frequent or laboured breathing, is common. Patients kept in bed are apt to become accustomed to the want of breath, and so their dyspnoea may diminish or even disappear; although the quantity of pleural effusion (if present) remain unchanged. Dyspnoea is in some cases greatly due to associated disease; for instance, to chronic pneumonia on the same side as the pleurisy. The dyspnoea of pleurisy without liquid effusion is chiefly shortness of breath; that is to say, inability to breathe freely and deeply because of the pain caused thereby.

5. *Cough and Expectoration.*—Cough is usually present: in most cases it is short, painful, frequent, and ineffectual. But in rare cases there may be no cough, even in pleurisy going on to effusion.

Concerning the Sputa.—The terms dry and humoral pleurisy, in the old sense of these words, relate to the absence or presence of expectoration. For sometimes there is no expectoration, and therefore no exspuition. But commonly there is expectoration, although the humours coughed up are not always spat out. (i.) The sputa sometimes consist of mucus nearly pure, judging from their colour and transparency: when the mucus is thin and watery, like gum water, it is called pituitous. (ii.) More often the sputa are muco-purulent. (iii.) More or less blood in the sputum is not uncommon at the onset of the disease, especially if a liquid effusion collect rapidly. (iv.) It is a very uncommon event for a

serous effusion to burst through the lung, and so to be expectorated. Yet this seems to have happened in a case narrated by Dr. Vincent Harris; and Sahli refers to another instance of the same event. Less uncommon is the muco-serous (or albuminous) expectoration, which sometimes occurs during or soon after paracentesis thoracis, and which will be described in connexion with that operation (see p. 559).

6. *Vomiting and Diarrhoea.* — Vomiting is common at the onset, especially in children. Diarrhoea is not uncommon in pleurisy with serous effusion, but it is rarely so marked a symptom as may be the case in empyema (see p. 563).

7. *Latent Pleurisy.*—Pleurisy is sometimes latent, in the sense that the symptoms of the disease are slight, nay almost absent; and this even in the case of large effusion. But it is only in the neglect of physical examination that pleurisy, unless its extent be very small indeed, can ever be really latent.

Signs.—Signs which are pathognomonic, signs by which pleurisy can, with certainty, be distinguished from other diseases, are of two kinds; namely, physical signs and the result of puncture. These signs do more than this; they enable us to distinguish two kinds of pleurisy, which it is important should be distinguished; namely, pleurisy with exudation of coagulable lymph only, and pleurisy with liquid effusion. Moreover, puncture enables us to distinguish the different kinds of liquid effused.

A. *Pleurisy with no Liquid Effusion.*—1. This condition often exists unattended by physical signs of disease, or at most attended by signs which are not distinctive; such as some degree of retraction of the chest, some loss of clear tone on percussion, some weakness of breathing sound.

2. The only sign which is quite distinctive is friction sound. But it is very far from being a constant attendant upon pleurisy, even when the effusion is nothing more than coagulable lymph. Indeed it might be said, and probably with truth, that even under these conditions friction sound is more frequently absent than present. Friction-sound is to be recognised by its peculiar friction quality, giving the notion either of rubbing to any degree between lightest grazing and harshest scraping, or of creaking like that of leather. Friction is usually a very local sound, heard over a small part of one side only; and that part is mostly where the rib movements are freest, namely, the lower part of the chest, below the nipple or armpit, or about the angle of the shoulder-blade.

B. *Pleurisy with Liquid Effusion.*—1. Before the effusion becomes abundant enough to gravitate, a friction-sound is sometimes (but seldom) heard. Still more uncommon are signs which attend the onset of pleurisy with effusion in rare cases, and which closely resemble those of bronchitis. The distinction between the two diseases is to be found in the fact that bronchitis very seldom affects one side only, and that pleurisy with effusion very seldom affects both sides.

The signs referred to are these:—The affected side moves less freely than the other; the percussion-note is raised in pitch and muffled over the greater part or the whole of the side; the sense of resistance to percussion is increased; the breathing sound is weak and attended by widely-spread rale, which is quite indistinguishable from the rale of bronchitis. This rale has been called friction-rale, thereby to indicate the belief that the sound is produced in the pleural sac. But it seems more probable that the rale really is a bronchial and mucous rale produced in the air-tubes, and that the catarrhal or bronchitic state of the lung is due to its relaxation or deficient expansion consequent upon the pleural effusion, small though it be. But if the assertion of Galvagni be correct, that this "pleuritic rale" is not transmitted to the mouth, whereas the rale of bronchitis is, the above explanation cannot be true.

2. Much more frequently, however, the earliest signs of pleurisy with effusion are those which indicate that the effusion is already abundant enough to have sunk to the lowest place. What constitutes the lowest place depends upon the attitude assumed by the patient while effusion is going on. At first, when the quantity is small, the lung is simply relaxed by virtue of its own elasticity, and swims upon the effusion; but as the liquid accumulates, it compresses the lung and renders it more or less empty of air.

(i.) The great sign of liquid effusion is a coextensive dulness to percussion. This dulness is not wholly due to the effusion, but is partly dependent upon associated collapse of lung; that is to say, a layer of liquid an inch or more thick would transmit percussion resonance of the lung were the lung resonant. Dulness begins at the lowest part of the chest behind, the note being natural elsewhere. When the effusion has risen higher than the angle of the scapula, the lung will have relaxed to such an extent as to give a clear tracheal[1] note above the nipple of the same side in front—a sign not always present even in cases watched day by day from the onset. Whether, by further increase in the quantity of the fluid, the whole back become dull before the front is so at all, or whether the upper level of the fluid be comparatively horizontal, depends upon the attitude assumed by the patient while the effusion is going on. Hence, when the effusion is small the dulness may be wholly posterior, and sharply defined in front by the posterior axillary line, the lateral region remaining resonant. On the other hand, the upper limit of a dulness which occupies the lower rather than the hinder part of the chest often rises higher in the axillary region than in the back. Even when absolute dulness is confined to the base, there is usually some impairment of resonance all over the back on that side. The dulness over the effusion may be far from absolute. The anterior clear resonance, when present, is sometimes of cracked-pot quality. The effusion, even when partial and

[1] What the Germans call "tympanitisch." For the exact meaning of the technical terms used in these pages with reference to percussion and auscultation, the reader is referred to the book on those subjects by one of us (S. G.).

recent, does not shift its position easily or at all with changes in the position of the body. In a patient under the care of one of us (S. G.) at St. Bartholomew's Hospital, with the effusion at its height, the upper level of dulness behind only reached to the angle of the scapula, whilst in front it reached to the clavicle. The percussion dulness last to disappear with absorption of the effusion was that in front of the chest. It was noticed that this patient invariably slept lying upon his belly.

(ii.) In proportion to the amount of effusion the side is enlarged, diaphragm depressed, and mediastinum displaced. (*a*) The side, compared with the other, will possess these characters: shape, on horizontal section, rounder; antero-posterior diameter longer; length from above downwards diminished; shoulder raised; spine curved towards the unaffected side. The antero-posterior enlargement becomes very obvious when the physician stands behind the patient so as to look obliquely over the shoulders and the front of the chest. Circumferential measurements of the two sides are often made for the sake of comparison, but be it remembered that, by the passage of the elliptical form into the circular, considerable increase in the sectional area of the chest may occur, whilst the length of the periphery remains the same. Moreover, the displacement of the mediastinum thrusts the heart into the unaffected side. Add this consideration, too, that the walls of the healthy side must follow the antero-posterior projection of the diseased side; and then it will be plain why, as a matter of fact, the perimeter of the affected side often measures very little more, nay, sometimes even less, than that of the side which is not diseased. The cyrtometer, by indicating shape as well as circumference, affords us the true means of recording the amount of unilateral enlargement. (*β*) Displacement of the mediastinum is indicated by displacement of the heart. Effusion into the right pleura may displace the heart so as to cause its impulse to be felt in the left axillary line, and in any interspace from the second to the sixth. Effusion into the left pleura may displace the heart so as to cause its impulse to be felt anywhere between its natural position and the right nipple line, and in any interspace from the fourth to the seventh, or in the epigastrium. When the impulse is felt to the right of the natural position, it is often some part of the heart, other than the apex, which strikes against the chest; and this part is usually the right conus arteriosus. When the heart is displaced to the right, there is, in most cases, no considerable change in the relative position of base and apex; that is to say, the heart does not swing to the right upon its base as a fixed point. Yet such a change in the attitude of the heart does sometimes occur, and the very ventricular apex may beat in the right nipple line. The displacement of the heart is often more or less than might be expected; for instance, it may remain unmoved by an effusion of not less than a quart of serum into one pleura. According to C. L. Greene the displacement of the heart may be rhythmical, the organ moving towards the affected side during inspiration and away from it during expiration; the amplitude of the movement may be as much as

two inches. Percussion of the sternal region above the heart sometimes affords evidence of displacement of the mediastinum: the upper part of the sternum naturally yields a clear resonance; under the pressure of a copious liquid effusion into either pleura, the mediastinum bulges so much towards the unaffected side as to afford absolute dulness to percussion in the sternal region, and even somewhat beyond it. (γ) Displacement of the diaphragm downwards is determined by ascertaining the position of the liver, spleen, and stomach. When the quantity of fluid in the left pleura is very great, the left half of the diaphragm may possibly be depressed to such a degree that not only can the lower margin of the spleen be felt, but even its upper margin, in fact its whole outline. At the same time, the thrusting of the mediastinum and heart into the right side of the thorax may depress the right wing also of the diaphragm to an almost equal degree; a point ascertained by examination of the liver.

(iii.) Vocal thrill is diminished where dulness to percussion exists, and is wholly abolished in great distension of the side.

(iv.) The respiratory sound is at first weakly vesicular, and sometimes remains so throughout the disease. But often the breathing soon becomes bronchial, sometimes even before the dulness becomes absolute. With progressive increase of effusion the bronchial breathing tends to become less and less loud, until, at last, it is wholly suppressed. But sometimes, although the quantity of fluid be very great, loud bronchial breathing is heard all over the affected side: the fact being that the loudness depends, not inversely upon the quantity of liquor effused, but directly upon the openness of the air-tubes; for liquid is a good conductor of sound.

(v.) Vocal resonance is weak or bronchial in much the same manner as the breathing sound. When the effusion is partial, with clear resonance in front, the bronchophony is sometimes aegophonic about the angle of the scapula. Aegophony is a sign of little or no value. In the first place, well-marked aegophony is seldom heard; next, it is sometimes heard over simple consolidation of the lung, such as is left by absorption of pleural effusion; and, lastly, aegophony certainly does not always attend thin layers of liquid in the pleural sac.

(vi.) By percussing the chest in front with two coins, and auscultating behind as for the bell sound, a pleural effusion will sometimes be found to transmit a clear metallic sound (penny sound, *signe de sou*) quite unlike that heard through healthy or solid lung.

(vii.) A small protrusion, in the lateral region, distended during expiration, receding during inspiration, and due to perforation of the pleura and intercostal space, may be met with even in moderate serous effusion. In rare instances the protrusion may pulsate: pulsating serous effusions have been described by Cruveilhier, Flint, Broadbent, and others. More rarely still the effusion may discharge externally (Sahli).

(viii.) A systolic murmur, having the characters of a pulmonary obstructive murmur, sometimes concurs with pleural effusion; dis-

appearance of the effusion being attended by disappearance of the murmur.

(ix.) The *diaphragm phenomenon* first described by Gerhardt and later by Litten, may be observed. In thin persons in a state of health, if examined in the supine position and with an appropriate light, a transverse shadow may be seen at the lower anterior and lateral regions of the chest; descending with inspiration and ascending with expiration; commencing above, about the seventh rib, its highest level lying in front, curving downwards towards the axillary line. In the presence of pleural effusion this shadow is often absent, or may be abnormally low, and its excursion may be much diminished in amplitude. In pneumonia, pulmonary tuberculosis, pleural adhesion, and some other morbid pulmonary conditions, similar changes from the normal may be observed; the sign is therefore not of much value in the differential diagnosis of pulmonary lesions. In the diagnosis of pleural effusion from subphrenic abscess, however, it may be of service; in the latter condition the shadow lies abnormally high (compare Vol. III. p. 1002). It is also said that the sign serves to distinguish pneumothorax from diaphragmatic hernia, being absent in the former disease and present in the latter.

(x.) The *paravertebral triangle of dulness* (Grocco's triangle) was first described by Korányi. Its existence in cases of pleural effusion has been confirmed by several observers, particularly by Thayer and Fabyan, who investigated its presence in 32 cases and were able to demonstrate it in 30. Hamburger found that the sign was present in children with pleural effusion. According to the above authors the triangle, which is usually present when the effusion reaches as high as the eighth dorsal vertebra, consists of an area of *relative* percussion dulness on the side opposite to that of the effusion. The vertical line of the triangle joins the vertebral apophyses and reaches slightly above the level of the effusion; the base extends directly outwards along the lower limits of normal pulmonary resonance for a distance varying from 2 to 7 cm.; the hypothenuse joins these two lines. The degree of dulness over the triangle is more marked as the observer approaches the spine. The respiratory murmur is often suppressed over the area and aegophony may be present. If the patient lie on the affected side the dulness disappears. As this triangle of dulness would seem to occur very infrequently in pneumonia, its discovery in a case of doubtful consolidation or pleural effusion may be a point of diagnostic value. Several explanations of the phenomenon are forthcoming: Baduel and Siciliano think that the liquid in the opposite pleural sac acts as a mute in suppressing the sonorous vibrations of the spine; both Korányi and Grocco supposed that the dulness is due to the displacement of the contents of the posterior mediastinum; but Rauchfuss finds that the dulness does not disappear for one or two days after paracentesis, a discovery which favours the view that it is due to congestion or collapse of the lung lying immediately beneath.

(xi.) Inequality of the pupils has been observed by Chauffard and Laederich and by Ledroit. The first-named authors state that the in-

equality was witnessed in seven out of seventeen cases investigated. The larger pupil is on the affected side. Paracentesis does not affect the inequality. It is probable that the condition is due to changes at the apex of the lung or in the bronchial glands.

(xii.) Skiagraphy shews the presence of an effusion and the displacement of the heart (*vide* Vol. I. p. 499).

C. *Puncture.*—Puncture of the chest, by means of a fine tubular needle adapted to a small exhausting syringe, is the most decisive means of determining the presence of pleural effusion. Moreover, puncture ascertains the quality of the effusion. The bare suspicion of a pleural effusion, however small it may seem to be, is a sufficient reason for exploring the chest by puncture, inasmuch as we know that to pierce the lung with a clean, fine needle is harmless.

Puncture is made where the signs of effusion are most marked; due regard being paid to the anatomy of the parts within, so as to beware of wounding the heart, diaphragm, or great vessels. But, if possible, let the puncture be made somewhere between the angle of the scapula and the edge of the pectoralis major, and not much below the nipple level. As matter of fact, the puncture is most usually made somewhere about the angle of the scapula.

D. *Different Kinds of Liquid Effusion.*—It is by means of puncture that the kind of effusion is discovered.

1. Serous Effusion.—It has been already remarked that what is called a serous effusion consists of diluted liquor sanguinis. The specific gravity is usually from 1018 to 1024; but in proportion as the effusion approximates to the nature of hydrothorax the specific gravity falls, and it may be so low as 1006. Reaction, alkaline. Colour, yellowish from serum-lutein. Proteins present: fibrinogen, serum-globulin, and serum-albumin. In inflammatory exudates the amount of protein may be as high as 4-5 per cent. Bence-Jones' protein is occasionally present. A small quantity of sugar is often found. The liquid is seldom or never quite clear and transparent. Opalescence, when slight, is due to a few leucocytes, endothelial cells, particles of fibrin, albuminous particles, minute oil-globules, or cholesterin. When the turbidity is great the effusion is called opaline or chylous, a condition which will be described further on (see p. 547). The fibrin present coagulates soon after the effusion is drawn off. The quantity of fibrin differs much in different cases; it may amount to no more than a few filaments floating in the serum, or it may be so abundant as to coagulate into a firm jelly.

Nature of Cells present; Cytodiagnosis.—It is in connexion with pleural effusions that most of the researches into the cytology of exudates and transudates have hitherto been directed. The pioneers in this work were Wida and Ravaut, who, as a result of their observations, stated the following cytological formula:—*When the dominant cells present in a pleural effusion are small lymphocytes the probable cause of the inflammation is the tubercle bacillus; when the dominant cells are the polymorphonuclear leucocytes the probable cause is some pyogenetic micro-organism.* If the effusion from a tuber-

culous pleurisy is examined very early, the predominance of the lymphocyte is less marked than as the effusion progresses. The polymorphonuclear cells may even be present in excess; Dr. Gulland considers that this is limited to the first three days of the effusion. To these original conclusions of Widal and Ravaut's little has since been added by other observers. The main statement has been amply confirmed in many quarters, and the cytological investigation of pleural exudates has now become a routine addition to clinical pathology. As also observed by the above authors, pleural transudates are mainly characterised by the presence of endothelial cells; if of long standing, however, the lymphocyte may predominate (Naunyn). A secondary infection will alter the cell content readily, whether it be a tuberculous exudate or a transudate. In 28 cases at the Massachusetts General Hospital, proved to be tuberculous, lymphocytes were present in the effusion to the extent of 90-100 per cent in 24; in 1 they were present to 88 per cent; in 3 to 70-75 per cent (Lord). (For a full *résumé* of the subject, with additional observations, see a valuable paper by Dr. Athole Ross.)

Eosinophil pleurisy has been studied by Barjou and Cade, who met with five cases; as inoculation tests in guinea-pigs were negative in all five cases there is reason for regarding the presence of eosinophil cells in pleural exudates as evidence against tuberculosis. Another case was very fully investigated by Drs. Perkins and Dudgeon, who found an accompanying leucopenia with eosinophilia; the patient died, and at the necropsy no evidence of tuberculosis existed. In none of these cases did the percentage of eosinophils rise above 30.

Occurrence and Isolation of Micro-organisms.—In serous effusions, when bacteria are present they usually exist in such small numbers that it is advisable to adopt some special method of isolation. In the case of pyogenetic microbes centrifuging generally suffices, or even simple sedimentation. In the case of tubercle bacilli, however, elaborations are necessary. (*a*) The method of Jousset, unnecessarily designated "inoscopy"; the effusion is allowed to clot, the clot is digested with artificial gastric juice, the residue is centrifuged, and films are prepared. (*b*) The method of Zebrowsky; the exudate is mixed with a solution of 0·5 per cent of sodium fluoride, the mixture is centrifuged, and films are made. Jousset found bacilli in 25 out of 25 cases of primary sero-fibrinous pleurisy by his method; although other observers have not all had such complete success the technique should be given a good trial in all cases of doubtful tuberculous pleurisy.

Of the toxicity of the fluid apart from the action of contained bacteria, little is known. Fede found that in one case of proved tuberculous origin the injection into the unaffected side of 1 c.c. of the effusion produced a general reaction similar to that seen in a positive tuberculin reaction; Fede suggests that this procedure may be a means of differentiating the tuberculous cases. Mergoni has attributed convulsions in a patient to the rapid absorption of a pleural effusion from which he suffered.

2. Blood mingled with Effusion.—Not haemothorax, which signifies extravasation of pure blood into the pleural sac. The effusion, which is bloody, is either serous or purulent, and the proportion of blood differs much in different cases.

The conditions under which an effusion becomes bloody are these :— (i.) Simple uncomplicated pleurisy, the haemorrhage being probably due to rupture of embryonic vessels in the false membranes ; the hydrothorax of heart disease, especially when associated with pulmonary "apoplexies"; the pleurisy of scarlatinal renal dropsy. (ii.) Acute tuberculosis of the pleura. (iii.) Cancer, sarcoma, lymphadenoma of the pleura. (iv.) Aortic aneurysm. (v.) Haemorrhagic diathesis. The patient is sometimes markedly anaemic from the loss of blood, sallow, cachectic. The prognosis depends upon the cause, the presence of blood in the effusion makes no difference. Malignant disease of the pleura is by no means the most frequent cause of bloody effusion, and the effusion in malignant disease of the pleura is sometimes clear yellow serum.

3. Opaline Serous Effusion.— The effusion is opaline, milky, in consequence of abundant molecular matter suspended in it ; a few leucocytes are often present, and sometimes a few red discs : these latter may be numerous enough to give a reddish colour to the effusion. The specific gravity is the same as that of ordinary pleural serum. The conditions of opaline effusion are these :—

(i.) Sometimes the opacity is really chylous ; for instance, if the thoracic duct be torn across, so that chyle is effused into the right pleura : in this case the molecules are all fatty, and rise to the top of the effusion like cream. Obstruction to the duct may have the same effect ; and the cause of the obstruction may be nothing more than dense fibrous adhesions ; the demonstration of the route taken by the chyle under these conditions is only to be made out by careful dissection after injection of the vessels with coloured fluid. The chylous effusion may be loculated, the rest of the effusion being clear, as observed in a case examined after death recently by one of us (T. J. H.). In this case the portion of the pleural sac containing the chylous effusion was interposed in the course of the main thoracic duct. The distal part of the duct divided into several branches which entered the sac below. From the upper part of the sac several tributaries arose which united to form the proximal part of the duct. Extensive mediastinitis was present, due to tuberculosis.

(ii.) But in most cases there is no reason for suspecting any lesion of the chylous system. The particles are often by no means all fatty, indeed very few may be fatty ; they seem to be some ill-known form of protein. Whence they come is quite uncertain ; disintegration of pus globules has been supposed to be the source. Cholesterin crystals may be present, usually very few, but now and then they are very abundant, so that the opacity is chiefly due to them. No deduction can be drawn, as to the nature of the pleurisy, from the opaline character of the effusion.

4. Chalky Effusion.—The effusion is white and opaque, due to the presence of calcium phosphate. Dr. S. West described an extraordinary case of this kind in which several pints of this creamy fluid were present. A large calcareous bronchial gland was found after death, but it did not appear to have ulcerated into the pleura; the lung had been completely destroyed, and when the fluid part of the exudate was removed the appearance of the pleural sac was exactly that of a miniature chalk-pit.

E. *Quantity of the Effusion.*—This varies from a few cubic centimetres up to three or more litres. It can only be estimated by direct removal. Neither the chromometric method of Achard, Schifone, and others nor the cryoscopic method of Korányi can be relied upon to measure the amount of the effusion (Usoff).

F. *The Blood.*—A moderate degree of simple anaemia is present in severe cases of sero-fibrinous pleurisy. The *leucocytes* do not shew any great increase in number. In a study of 89 cases at the Johns Hopkins Hospital, Emerson found that in only one was the count above 15,000, whereas in 26 it lay between 10,000 and 15,000, and in 12 it was less than 5000. Lord points out that in "dry" pleurisy the count is higher than in serous pleurisy; out of 48 cases of "primary fibrinous pleurisy," investigated at the Massachusetts General Hospital, the figure reached 12,000 in 39·5 per cent; out of 33 cases with sero-fibrinous effusion it reached 12,000 in only 9·09 per cent. These figures contrast strongly with those obtaining in empyema (see p. 566).

Course and Termination.—1. *Adhesions.*—When pleurisy terminates favourably, it is by the formation of more or less extensive adhesions between the opposed pleural surfaces, the pleural cavity being proportionally obliterated. The patient has recovered, and it is assumed, for this reason, that adhesion has occurred. Yet the recovery from pleurisy without effusion, and even from pleurisy with effusion and empyema, is often complete so far as physical signs are concerned; and the most careful examination fails to find contraction of the chest or any other signs of past disease. If adhesion be attended by physical signs, they are those which indicate unilateral contraction of the thorax and imperfect expansion of the lung. The more marked these signs, the more dense and tight may the adhesions be assumed to be.

2. *Serous Effusion.*—(i.) Absorption. Serous effusion tends to be spontaneously absorbed; a large effusion may thus disappear in a week or two.

The temperature, if it have been raised, usually remains raised until absorption is complete.

The physical signs which indicate the progress of absorption are these:—The diaphragm and mediastinum go back to their natural positions; to follow the retreating heart, liver, and spleen is the best means of marking the process so long as the quantity of effusion remains great. The distension of the affected side becomes less, and accurately to register this fact is an important service rendered by the cyrtometer.

When the effusion has so far diminished that the lung again comes into contact with the chest wall, percussion usually enables us to follow the falling level of liquid. And, at the same time, auscultation will sometimes inform us when and where actual contact of the opposed surfaces of the pleura has occurred, friction-sound being heard.

The manner in which the effusion is absorbed is not constant, but usually the liquid disappears in something like the following order :— From the vertebral groove near the root of the lung; from the supramammary region; from the rest of the vertebral groove and infrascapular region; from the inframammary region; and, lastly, from the lower lateral region, concerning which it is important to remember that the lowest part of the pleural cavity, in the erect position of the body, is in the axillary line. Thus, the upper surface of the liquid, when it reaches as high as two inches above the nipple level, is horizontal; when lower than this, the dulness forms irregular parabolic curves, which become smaller and smaller, and last of all disappears in the lowest parts of the thorax. But we must be prepared to meet with exceptions to these rules, and to find the residue of liquid in almost any part of the chest. Moreover, a large pleural effusion is sometimes absorbed, not from above downwards, according to the rule, but equally all over the side at once, friction or pleuritic rale becoming audible all over the side at once.

Disappearance of effused liquid at any spot is sometimes attended for a day or two by friction-sound, indicative of restored contact between the pleural surfaces, redux friction as it is usually called.

Dulness, practically absolute, and due to unexpanded lung, often remains for a long time after all the effusion has been absorbed. For this reason it is often impossible to say, from physical signs alone, when the effusion has been absorbed. The physician must judge from all the signs and symptoms taken together, and especially from permanent defervescence, if the patient have been febrile. More or less dulness often remains for the rest of life.

The latest physical sign, dependent upon absorption, is retraction of the affected side. Cup-like sinking of the lower part of the sternum occasionally ensues. In some cases these deformities tend to disappear gradually, in others they are permanent.

When one side of the chest is left contracted a permanent systolic murmur is sometimes heard.

(ii.) Rupture.—This may occur, as already stated, through the lung (Vincent Harris, Sahli); or externally (Sahli). Both are rare events.

(iii.) Permanence.—If the whole lung be very much reduced in size and quite inexpansible, a serous effusion will probably be permanent and endure to the end of the patient's life. It is possible that, in these circumstances, the chest walls may contract, and the mediastinum and diaphragm be displaced to such a degree as to allow of absorption of the liquid and obliteration of the pleural cavity; but these events seldom happen in the case of serous effusion. The conditions of lung which

lead to its complete inexpansibility are two: carnification (see p. 552), associated with tight, unyielding thickening of the pulmonary pleura; and contracting new growth, which may reduce the whole lung to a mass not larger than the pancreas.

Associated Diseases.—Pleurisy is often accompanied with other diseases which impede or prevent recovery.

1. *The pleura of the other side* sometimes becomes inflamed, and the patient suffers from double pleurisy. Recovery, and quick recovery, is not uncommon.

2. *Collapse of the lung* on the other side may occur in an infant and be necessarily fatal.

3. *Grey induration* (fibrous change, cirrhosis) will sometimes ensue upon collapse of the lung. But collapse may last for many years without being followed by fibrous change, a fact proved by examination post-mortem.

4. *Pneumothorax* is often associated with pleural effusion, and in one of two ways. Either the pneumothorax and effusion occur simultaneously, in consequence of rupture of the lung, in which case the effusion is usually purulent, but may be serous; or the pneumothorax is secondary to the pleural effusion: a pleural effusion has been removed by paracentesis, and air has passed out of the lung into the pleural cavity, not through puncture of the lung, but through rupture of it by atmospheric pressure from within.

5. *Tuberculosis of the lung* associated with pleurisy has been already referred to, and it has also been pointed out that many cases of pleurisy are due to tuberculosis of the pleura, the source of infection being, in some cases, the bronchial glands, which lie at the root of the lung covered in places by nothing but pleura. Tuberculous pleurisy is attended by exudation of organisable lymph, or serum, or pus, or by haemorrhagic effusion. But pleural liquid effusion is sometimes concurrent with progressive pulmonary consumption, a complication which cannot be detected by physical examination until the effusion has been absorbed. Examination of the sputa for bacilli affords the only certain means by which pulmonary disease can be discovered during the presence of pleural effusion; but skiagraphy may be of some help in this connexion. When, as is sometimes the case, there is phthisis on the side opposite to that of the effusion, diagnosis is less difficult. More distant organs sometimes become tuberculous during the course of pleurisy, and thus the patient's death may be hastened; the meninges of the brain are especially apt to be so affected in the young.

6. *Pericarditis* often coexists whether the pleurisy affect the left side or the right. Sometimes, but seldom, perforation of the pericardium has taken place. In any case pericarditis is apt to go on to large effusion. The pericardial effusion is usually not detected during life, the physical signs of that condition being hidden by those of the pleurisy. This is unfortunate, because the complication is very serious, and the patients generally die.

7. *Peritonitis* may occur. It is sometimes acute, and is then usually part of a pneumococcal infection. Or it is chronic, and in this case is often tuberculous, ascites or universal adhesion being the result: the patient may recover even after his pleural effusion has been complicated by ascites. The certain diagnosis of acute and of chronic peritonitis is often impossible during life. When ascites is present the legs are sometimes anasarcous; this condition also may end in recovery.

8. *Dilatation of the heart* sometimes follows pleurisy, especially when both pleurae are obliterated by old adhesions, and when the lungs are imperfectly expanded. Under these conditions universal dropsy may ensue.

9. *Dropsy*, that is to say, anasarca and ascites, sometimes occurs even in acute pleurisy with effusion on one side only, there being no evidence of nephritis or of disease of the heart, and the patient recovering completely in about three months. In such cases the dropsy must be due to stagnation of blood in the right side of the heart.

10. *Nephritis* is frequently complicated by pleurisy, with or without liquid effusion.

11. *Clubbing of the finger-ends*, although appearing earlier, and becoming more marked, in empyema, may be present in sero-fibrinous pleurisy. It may, or may not, disappear with the disappearance of the disease.

Diagnosis.—Pleurisy is simulated by certain other diseases in respect either of symptoms or of physical signs.

1. The *pain* of *pleurodynia* is, by itself, indistinguishable from that of pleurisy. Diagnosis becomes possible when there are other signs or symptoms of pleurisy; for pleurodynia is mere pain, and pleurisy is sometimes indicated by pain alone. The great frequency with which old pleuritic adhesions are found after death in the bodies of persons who have given no history of pleurisy should make us refrain from denying the existence of this disease in cases of pain in the side without physical signs. In this connexion the existence of fever, of however mild a degree, is of great importance. The pain which occasionally precedes the eruption of *herpes zoster* can mislead for a few days at most. Persistent pain in the chest without physical signs should always lead to careful examination of the spine for evidence of *Pott's disease*.

2. The *rale* (not friction sound) which in rare cases attends the onset of pleurisy closely resembles the rale of bronchitis (see p. 541). The difference lies mainly in this, that the rale of pleurisy tends to be heard over one side only of the chest, and the rale of bronchitis over both sides. Pleuritic rale is soon superseded by other signs of pleurisy. The *rhonchus* of bronchitis is sometimes mistaken for pleuritic friction-sound, although the resemblance is never so close as it may be between the rale of bronchitis and the rale of early pleurisy. The difference mentioned above is also to be noted here, and also this further difference: that whereas rhonchus is commonly altered in position or in quality or in both these respects by deep breathing or by cough, friction sound usually remains unaffected by these movements. Friction sound due to *perihepatitis* and

to *perisplenitis* set up by an infarct must now and again be distinguished from pleuritic rub. The beginner is not seldom confused by hearing *muscular rumbling* on auscultating the chest; his difficulty ceases with the recognition that this sound, unlike pleural and pulmonary sounds, is continuous. This muscular sound is probably the "pseudo-pleuritic friction" of some authors.

3. *Acute collapse* of extensive portions of lung is a condition which is very apt to occur in young children as a result of obstruction to a bronchial tube. The case of obstruction by an inhaled foreign body need not be considered here, for the whole course and symptoms of this accident are not at all like those of pleurisy with effusion. But bronchial catarrh, and even slight bronchial catarrh, will sometimes cause extensive collapse in a young child, or in a very feeble patient who is not a young child. Bronchitis setting in suddenly, with fever, cough, tightness of the chest, vomiting, and followed in a day or two by the signs of collapse at the lower part of one lung (namely, dulness to percussion and weak breathing), counterfeits pleurisy with effusion very closely. Diagnosis may be impossible at first. Usually the collapsed lung soon expands; if it be deemed necessary a puncture may be made.

4. *Chronic collapse of lung and fibrosis* are two conditions which closely resemble each other in the living subject, and which often cannot be distinguished except upon the post-mortem table. Nor is it of any practical importance that they should be distinguished; the useful term carnification (invented by Laennec) may be taken to include them both. The physical signs of carnification of the lower lobe of a lung and those of a small pleural effusion are the same, excepting that the chest may be distended on one side, and the heart be displaced away from the disease in some cases of local pleural effusion. But now and then the chest is contracted and the heart not displaced even in a pleural effusion. The symptoms afford no help to diagnosis, and the right understanding of a case may be rendered all the more difficult by the fact that carnification is not only a constant result of pleural effusion, but often persists long after the effusion has disappeared (see p. 550). The chief means of distinguishing between the two conditions is puncture. Yet, in these circumstances, puncture sometimes fails to detect pleural effusion, and chiefly for this reason, that carnification is often much more extensive than the effusion which causes it. For instance, a small pleural effusion, lying upon the diaphragm or in the posterior mediastinum, will sometimes be attended by collapse of the whole lower lobe of a lung; and this carnified lung being the only portion of disease which is in contact with the chest walls, the physical signs will be wholly dependent upon the carnification, and if puncture be made it cannot hit the effusion unless the needle go right through the lung. Wherefore it may be impossible to say whether there is an effusion or a mere carnification. Sometimes the expectoration of a small empyema occurs so as to clear up our doubts.

5. *Tuberculous phthisis* of a lower lobe resembles a small pleural

effusion in many respects which it seems hardly necessary to enumerate; puncture and microscopic examination of the sputa are the most trustworthy means of distinction. But there is an especial form of pleurisy which, for a time, is indistinguishable from pulmonary tuberculosis. In this case the pleurisy involves the whole of one side, which is retracted, it may be considerably, and moves much less freely than in health. The percussion-note is raised in pitch and muffled over the greater part or the whole of the side; the sense of resistance is increased; when the disease affects the left side the superficial area of cardiac dulness is extended. The respiration generally is weak, and attended by friction sound at some part, or by widespread rale indistinguishable from the mucous rale of catarrh or phthisis (see p. 541). At places the breath-sound may be bronchial, in all degrees of intensity, up to perfect cavernous resonance. Add to these signs hectic fever with diarrhoea and vomiting, and it is easy to understand why pleurisy of this kind is apt to be mistaken for phthisis more or less advanced. The pleurisy terminates in one of two ways. Either the physical signs of disease gradually disappear, excepting perhaps that a slight unilateral retraction of the chest, or a cup-like depression of the sternum, is left behind, the patient recovering at the same time his former state of health; or signs of a small effusion slowly appear at the base, and, when the chest is punctured, a little pus is withdrawn and the case comes into the category of empyema. Whenever the signs of a case of supposed phthisis are in some respects peculiar; whenever they indicate advanced and extensive disease, but limited to one side of the chest; whenever cavernous signs are heard in unusual places;—it is well to weigh the possibility of simple pleurisy, and not to rest confidently in the diagnosis of phthisis until tubercle bacilli have been found in the sputa.

6. *Acute pneumonia* is seldom mistaken for pleural effusion unless the tubes of the pneumonic lung be so plugged with mucus that conduction of the breath-sounds is obstructed. It much more often happens that a small pleural effusion is mistaken for pneumonia. The physical signs of the two diseases may be the same, and even puncture is not always decisive; should an empyema be confined to the apex of a pleural cavity, so infrequent an occurrence, compared with the frequency of apex pneumonia, will render diagnosis unusually difficult (see p. 569). The symptoms of the two diseases may be the same, especially in the pleurisy which is due to the pneumococcus; not seldom in this case the patient dies before certain diagnosis becomes possible: a physician well read in the book of nature knows that he cannot always distinguish between pleurisy and pneumonia.

Chronic pneumonia—that is to say, hepatisation slow to resolve—will resemble in many respects pleural effusion supervening upon pneumonia (*vide* also p. 265).

7. *Malignant tumour* of the lung closely resembles pleural effusion in respect of the physical signs. A tumour does not often cause

enlargement of the affected side, or displace any organs, yet now and then a quickly-growing tumour will produce these effects. When dulness begins not at the bottom of the chest; when there is a great extent of absolute dulness in front and none behind; when, in the midst of a great extent of dulness, we detect one or more small insulated patches of resonance (perhaps quite clear or even cracked-pot), we may debate the existence of solid tumour. The crucial test is puncture.

A large serous effusion is sometimes the necessary result of contracting new growth of the lung. Removal of the fluid is usually followed by more or less rapid recurrence of the effusion. The nature of the case may be suspected if cancer can be discovered elsewhere, and especially if large hard glands can be felt above the collar-bone or in the armpit. The possibility that cells indicating a new growth may be found in the fluid removed by puncture should be borne in mind.

8. *Primary malignant disease of the pleura* may for some time shew itself merely as pleurisy with effusion. As in malignant disease of the lung, so here, the effusion tends to recur: this very tendency should always raise a suspicion that pleural effusion may be due to malignant disease, either of the lung or of the pleura.

9. *A large hydatid cyst* will yield most of the signs of pleural effusion; namely, unilateral distension of the chest, displacement of the diaphragm and mediastinum, dulness to percussion, and weak or absent breath-sounds. An exploratory puncture is the most decisive means of diagnosis; the fluid of hydatid being free from albumin and more watery than that of pleural effusion, to say nothing of the possible discovery of echinococcus hooks. But if the hydatid have suppurated, the nature of the disease is sometimes not suspected until a free opening has been made, such as to permit the escape of hydatid membrane. (For a full discussion of Thoracic Hydatid, *vide* Vol. II. Part II. p. 1019.)

10. *Actinomycosis* of the base of the lung simulates pleurisy with effusion, and is, indeed, sometimes attended therewith. The diagnosis cannot be made until the fungus is discovered in the sputum, or in fluid removed by puncture, or until the growth perforates the wall of the chest (*vide* Vol. II. Part I. p. 329).

11. *Aortic aneurysm* is almost invariably, sooner or later in its course, associated with pleurisy. That this must be so follows from observations made in the post-mortem room. But this pleurisy does not often yield signs unless it go on to serous or haemorrhagic effusion. Like the effusion accompanying malignant disease of the lung, that which accompanies aneurysm is apt to recur.

12. It is sometimes hard to decide whether *friction-sound* heard over the heart region is *pleural or pericardial.* Pleural friction may be produced by movement of the heart alone; as pericardial friction may be under the influence of breathing movements.

13. Large effusion into the left pleura may cause bulging of the chest in the heart region, such as to raise the question of *concurrent pericardial effusion*; for the two diseases are often associated (see p. 550).

The diagnosis depends mainly upon the result of emptying the left pleura by paracentesis, whereby alone can the signs of pericardial effusion become manifest.

14. When pericardial effusion is attended by extensive collapse of lung, and the chest is punctured with a view to determine the cause of the dulness, the needle may go right through the lung and discharge liquid from the pericardium; and, until examination post-mortem, the physician may rest in the unshaken belief that the liquid came from the pleura.

Prognosis.—Of 129 cases of pleurisy without effusion treated at St. Bartholomew's Hospital during the five years 1899-1903 the average duration of stay in hospital was 23·8 days. Of 238 cases of pleurisy with effusion treated during the same time the average duration of stay was 33·7 days. Thus it is seen that the course of a case of "dry" pleurisy generally lasts from three to four weeks, whilst the course of a case of pleurisy with effusion generally lasts from four to five weeks. The mortality in 651 cases of pleurisy treated at the above hospital during the ten years 1884-1893 was 10·3 per cent; in 783 cases treated during the next decade (1894-1903) it was only 1·4 per cent; the total mortality in the 1434 cases treated during the twenty years ending with 1903 was therefore 4·1 per cent. The lower mortality during recent years is undoubtedly explained by the growing tendency to early aspiration of the effusion and by improved treatment generally. It seems unnecessary to reiterate many prognostics, which will be found in their appropriate places in the foregoing and following pages. But one point of great importance demands special attention, namely, the occurrence of *unexpected and speedy death* in cases of pleural effusion. The conditions of this unexpected death are not always the same.

(i.) The effusion is usually large, filling up the whole or greater part of the pleural cavity. Whether it be on the right side or on the left makes no difference. Suddenly, and often after a little exertion, the patient is seized with dyspnoea or faintness, or both. The lipothymial symptoms soon predominate: the skin becomes cold and clammy or sweating, the face and lips assume the wan, dusky, livid colour of a dying person, the pulse is small and irregular; death ensues within half an hour or an hour. The explanation of the speedy death is mostly found post-mortem in thrombosis of the right side of the heart, consequent upon stagnation of the circulation through it, dependent upon the collapsed state of the lung. This heart thrombus has one of two results: either the thrombus is propagated into the pulmonary artery, and thence into that branch of it which supplies the unaffected lung; or an embolus, derived from the heart thrombus, is driven into the pulmonary artery, or a large branch of it. But thrombosis meet to explain the death is not always found: sometimes a latent pericardial effusion is present; but sometimes nothing sufficient can be found, and in cases of this kind hypothetical explanations have been offered, such as twisting of the large vessels at the root of the heart, bending of the inferior vena

cava at an acute angle, compression of one auricle of the heart, degenerative changes in the muscular tissue of the heart.

(ii.) Frothy serous expectoration sometimes suffocates the patient during or soon after paracentesis of the chest (see p. 559); or, in very rare cases, may even supervene upon large effusions apart from paracentesis.

Treatment.—A. In the treatment of pleurisy with no liquid effusion, the main indication special to the disease is to relieve pain. The most effectual means of doing so are two: subcutaneous injection of morphine at the seat of pain, or the application of a few leeches. In many cases much less decisive means are sufficient: warmth by hot water fomentations or linseed-meal poultices; a mustard poultice, or a turpentine fomentation.

Some physicians speak highly of fixation of the side by means of strips of plaster or by bandages: the limitation of respiratory movements on the affected side relieves the pain. An objection to this mode of treatment, if plaster be used, is that local applications to the skin, such as counter-irritants, cannot be employed at the same time.

B. The treatment of pleurisy with effusion relates almost wholly to removal of the effusion.

When the effusion is believed to be recent, not large, and not purulent, it is best to defer operation for a week or two, so as to see whether the liquid can be removed spontaneously without operation. It is probable that absorption may be assisted by sundry means; iodide of potassium in moderate doses should be given; the affected side of the chest should be painted with tincture or liniment of iodine two or three times a day; blisters, the size of the palm of the hand, or less according to the size of the patient, may be employed, one blister at a time, and the sore allowed to heal as soon as possible. In the case of children blisters should not be used. W. Carter recommends the use internally of oleum terebinthinae in doses of ℥x. Purges, diuretics, and a dry and salt-free diet may all be invoked as aids to absorption.

But the question of paracentesis is always foremost in the mind, and may be discussed under four heads: when, where, and how the operation should be performed; and lastly, certain dangers which sometimes attend the operation. The age of the patient is never taken into consideration.

I. *When should Paracentesis be performed?*—Paracentesis should be performed in all cases which present an effusion so great as to fill the pleura, or which are attended by any distress of breathing, or which shew no signs of being absorbed after a week or ten days of the other treatment already described.

Some physicians are content to leave an effusion, even a large effusion, untapped for a period much longer than this; but there is a growing tendency amongst the majority, fully justified by results, to favour early paracentesis. Let it be clearly understood that we are here speaking of simple pleuritic effusion, uncomplicated by more serious diseases. Our remarks do not apply, for example, to pleural effusion

complicating pulmonary tuberculosis—a common and important association, the appropriate treatment of which is discussed on p. 415.

II. *Where should Paracentesis be performed?*—1. When the effusion is small the puncture must be made where the effusion is believed to be.

2. When the effusion is great, so that the pleural cavity is full or almost full, the best place for puncture is in the middle line of the axillary region, about the horizontal level of the nipple or a little below it, where the intercostal spaces are wide and the muscular integuments thin. Another part of the chest which is often chosen for puncture is a spot just below the angle of the scapula, but the lung is sometimes adherent to the chest wall here, and will therefore be pierced by paracentesis; in this case pneumothorax is apt to ensue, and, what is a result far worse, but less frequent, sloughing of the perforated lung. Probably no part of the chest can be chosen as being entirely free from the risk that paracentesis may perforate collapsed and adherent lung, but the risk is less at the spot first recommended for the place of puncture than at any other situation.

III. *How should Paracentesis be performed?*—The patient should be in the semi-recumbent position, the back well supported by a hard bolster placed parallel with the patient, the arm on the affected side being drawn well forward. The effusion should be removed by means of a trocar and cannula. Whether suction be employed or not is, in most cases, a matter of no great consequence. If suction be not employed, a cannula connected with a long india-rubber tube should be used, the free end of the tube being kept under liquid, so that no air can enter the chest. On the whole, suction is to be preferred, for in this way small obstacles due to fragments of lymph floating in the serum can be overcome. It is best to make no more vacuum than is necessary to maintain a gentle flow of liquid. As much liquid is to be drawn off as possible without causing any serious discomfort to the patient. But in the case of very large effusions it is well to desist after the removal of 2 litres. The suction should be suspended for a few minutes if the patient feel faint (when a little brandy may be given), or if he cough a little; but neither of these things calls for removal of the trocar: they will probably cease if no haste be shewn in performing the operation. Suction is to be stopped, however, if the fluid become blood-stained, if the patient feel much pain in his chest, or if he cough much; in which last case there is the risk of serous expectoration (p. 559).

The pain of puncture is diminished if the skin be previously frozen by ice, or by an ether or ethyl-chloride spray.

It happens sometimes, but not often, that the most powerful suction can extract no more than a small quantity of the effusion. The usual cause of this difficulty is found in a fragment of lymph which blocks the cannula or obstructs its orifice. But sometimes, even when the effusion is free from floating lymph, it is impossible to evacuate the chest. Cases of this latter kind, which are uncommon, are probably to be explained by a lung rendered inexpansible by thickened pleura or by obstructed

air-tubes. Nothing more can be done than to draw off as much serum as possible, and to repeat the paracentesis in a day or two.

Very often a single paracentesis cures the patient, the little liquid left being soon absorbed. But sometimes the effusion returns, and the rule of practice is to repeat the operation as often as seems necessary. In Lord's series of 369 cases, 75 per cent shewed no recurrence of the effusion, and of the rest 20 per cent recurred once only. In R. C. Cabot's series of 300 cases, re-accumulation of the fluid occurred in 1·3 per cent only. In rare cases an abundant effusion will continue for an indefinite time, but even then the only treatment is paracentesis repeated as often as necessary. Drainage by a permanent opening is out of the question, and would be certain to convert the serous effusion into empyema, to the great danger of the patient's life. Repeated recurrence of the effusion should raise the question of the existence of pulmonary tuberculosis, malignant disease, aneurysm, lymphadenoma, or of actinomycosis.

There is no reason for fear lest paracentesis alone and without drainage should convert serous effusion into pus, provided that all the instruments used be surgically clean.

Injections of Air into the Pleural Cavity. — Since 1903 Sir James Barr has been a strong advocate of the principle of substituting air for the effusion; he states that this method, by allowing a slower expansion of the collapsed lung, obviates the tendency to sudden congestion and oedema, and diminishes the risk of recurrence of the effusion. Several years before Sir J. Barr's papers appeared, air had been injected into the pleural sac by Potain in a case of pyopneumothorax, and shortly after Potain's observation several Italian physicians had experimented with the injection of air and oxygen into the pleura. Immediately before the publication of Sir J. Barr's first paper, Vaquez and Quiserne gave an account of two cases of recurring pleuritic effusion treated by this method with success. Since Sir J. Barr's advocacy of the principle several other observers have published results (Dufour and Foix, and Ewart and Murray). The infrequency of recurrence of the effusion in uncomplicated cases makes this mode of treatment of doubtful value. It certainly does not seem to be indicated as a routine measure.

Injection of Other Substances.—Sir J. Barr originated the introduction of suprarenal extract into the pleural sac after paracentesis. His usual procedure is to replace the effusion by two-thirds to three-quarters of its volume of sterile air, and to follow this by the injection of 4 to 8 c.c. of a 1 in 1000 solution of adrenalin. Amongst other substances that have been injected are physiological salt solution and formalin (1 ounce of a 2 per cent solution in glycerin). In regard to the use of these substances the same comment applies; in the great majority of cases no such addition to the usual practice of simple paracentesis seems necessary. Moreover, the injection of chemical solutions into the pleural sac is not unattended by danger (see 572). Sir J. Barr suggests the use of liquid paraffin as a means of preventing adhesions; there appears, however, little or no reason for regarding pleural adhesions as prejudicial to the patient.

Dangers of Paracentesis.—1. Serous (or albuminous) expectoration. Paracentesis, by suction, of a pleural effusion is sometimes followed by expectoration of blood-serum. If a patient begin to cough much during the operation it must be stopped at once, and the patient be carefully watched. It is very probable that a small amount of serous expectoration in these circumstances is not uncommon; it is only when the secretion is abundant that the condition is dangerous and apt to end in speedy death. Serous expectoration mostly ensues during or directly after the operation, but sometimes an hour or two will elapse before the secretion becomes dangerously abundant; the latter cases are less grave. When abundant serous expectoration follows rapidly upon paracentesis the patient may die suffocated within half an hour. The fluid expectorated is frothy, viscid, transparent, neutral or alkaline, yellow or yellowish-green, with a specific gravity of about 1020, and rendered almost solid by heat and a drop or two of acetic acid. Chemically the sputum consists of serum-albumin and a little mucin. On standing there falls a scanty deposit of pus and blood-corpuscles. Post-mortem the lung is oedematous, and usually fully expanded. Concomitant disease, such as disease of the heart, mediastinal tumour, or haemoptoic infarcts, favours the occurrence of serous expectoration. Dr. Horton-Smith Hartley has collected over 40 cases from the literature, and has described a case with chemical analyses; his paper gives a full account of this interesting condition.

2. Pneumothorax sometimes follows withdrawal of a pleural effusion. Dr. Ewart considers this event to be by no means uncommon. The cause is not always the same. (i.) In some cases the lung has been injured by the operation, an accident especially apt to occur when collapsed lung, undiscoverable by physical examination, is adherent to the chest wall, so that the trocar goes through the lung. (ii.) Sometimes the air comes from a spontaneous rupture of the lung; softened tubercle may give way; or merely collapsed lung may burst in some small spot in the process of expansion during paracentesis by suction.

3. Haemorrhage from the pleuritic membranes is sometimes the result of paracentesis. If the blood flow at all freely, the operation must be stopped, and it is seldom that any bad consequence follows. But death has been due to this cause, the pleural cavity being found post-mortem to contain a large quantity of blood.

4. The needle or trocar may pierce an intercostal artery, causing haemothorax, which may be fatal: a rare accident, but witnessed by one of us (T. J. H.) in a case in which the punctured vessel was found at the necropsy.

5. Embolism of distant arteries, by coagula dislodged from the pulmonary veins, may be the result of paracentesis. The most common result is hemiplegia (see p. 569), which is usually incomplete. Embolism of both iliac arteries has been known to occur.

6. Death may follow paracentesis in rare cases. It may be sudden, or it may follow a state of collapse in a few minutes up to five days. In

1891 Wilson Fox collected 17 cases in which death occurred within 48 hours after paracentesis. Dr. A. E. Russell has described 4 cases, in 2 of which death took place suddenly, 1 on the third and 1 on the fifth day. Sir T. Oliver described 2 cases, 1 occurring suddenly and 1 the day following the operation, and a third case in which the patient rallied from the collapse. Sears described 1 case, death taking place in 15 minutes. In most of the cases no satisfactory explanation of death is forthcoming. It is possible in these cases that the vagus fibres are rendered unduly sensitive by compression or inflammation, for experimentally stimulation of these fibres is known to produce inhibition of the left ventricle. But in all operations there is the possible contingency that the patient may die suddenly.

Subsequent Deformity. — Not much can be done to expand the collapsed lung, and to counteract the deformity of the thorax and spine which is apt to follow upon chronic pleurisy. Exercises for the arms should be prescribed, especially such as tend to open the chest in front; for instance, drawing the body up by the arms clinging to a horizontal bar, skipping backwards, the use of a chest-expander behind the back, or of dumb-bells and appropriate drilling.

B. Empyema

I. **Etiology.**—(1) *Age and Sex.*—Pleural empyema is most common in patients under 10 years of age, 50 per cent of the cases occurring during the first decade of life; the decade shewing the next greatest incidence of empyema is between 20 and 30 (17·4 per cent), undoubtedly following the age-incidence of lobar pneumonia, of which it is so often a complication or sequel. As in sero-fibrinous pleurisy, males are affected between two and three times as often as females. These points are seen in the following table, drawn up from the records of St. Bartholomew's Hospital for the twenty years 1884-1903 :—

	Males.	Females.	Deaths.	5 yrs. and under.	10 y.	15 y.	20 y.	30 y.	40 y.	50 y.	60 y.	Over 60.	Totals.
1884-1893	155	61	48	53	32	15	22	48	17	23	6	0	216
1894-1903	197	86	62	108	48	17	21	39	26	15	7	2	283
Totals	352	147	110	161	80	32	43	87	43	38	13	2	499

(2) *Exposure.*—The remarks on pp. 532-3 apply equally here.

(3) *Bacteria.*—Like sero-fibrinous pleurisy, empyema is, in the great majority of cases, spontaneous, and can be accounted for by the action of certain microbes. In Netter's series of 109 cases, the pneumococcus was found in 53·6 per cent, streptococcus in 46·7 per cent, the tubercle bacillus in 11 per cent, and staphylococcus in 1 per cent. In Lord's series

of 137 cases pneumococcus grew in 39·4 per cent, streptococcus in 20·4 per cent, staphylococcus in 3·6 per cent; the infection was mixed in 16 per cent, and the pus was sterile in 18·2 per cent. In the remaining 2·4 per cent rare micro-organisms were present. In the last 32 consecutive cases examined at St. Bartholomew's Hospital pneumococcus grew in the cultures in 75 per cent, and streptococci in 20 per cent. Fraley, at the Pennsylvania Hospital, reports pneumococcus in 52 per cent and streptococcus in 21 per cent. Netter's figure for streptococcus is certainly much higher than that obtained by English and American workers. It may be concluded that pneumococcus accounts for a half to three-quarters of all empyemas, streptococcus for a quarter of the cases, and staphylococcus for a much smaller number.

(i.) *Pneumococcus.*—In the empyema of childhood this micro-organism is found with even greater frequency than that stated above for empyema at all ages.

(ii.) *Streptococcus.*—Relatively more common in the empyema of adults than of children. The type of streptococcus is usually *S. pyogenes.*

(iii.) *Staphylococcus.*—In a few cases this is the sole microbe present, but perhaps as often as part of a mixed infection. If empyema complicate osteomyelitis this is the micro-organism most often present, the type being *S. aureus.* So also for other forms of staphylococcal pyaemia.

(iv.) *Tubercle bacillus.*—Most English pathologists consider empyema as rarely due to this cause. And it may be predicted, in a case of empyema occurring in a tuberculous subject, that one or other of the pyogenetic microbes will be demonstrated on examination of the pus, whether or not the tubercle bacillus be there also.

(v.) *B. coli communis, B. typhosus, Pfeiffer's bacillus; actinomyces.*—These have all been found in the pus from empyemas. They are perhaps as often found in mixed infections as they are in pure culture. Diphtheroid organisms are said by some authorities to occur not infrequently; but it must be remembered what common contaminations of the skin are the xerosis bacillus and allied microbes. The occurrence of these micro-organisms in cultures made from pus sent to the laboratory is familiar to most clinical bacteriologists.

(4) Empyema is often the result of *extension* of an infective process from adjacent organs. All the modes of extension detailed on p. 535 may lead as well to purulent as to sero-fibrinous effusion. Some of these cases of extension of disease, indeed, notably those concerned with gastric ulcer and appendicitis, are more apt to appear as empyema than as sero-fibrinous pleurisy. In these cases pyopneumothorax not infrequently appears, associated with the growth of *Bacillus coli* and *B. aerogenes capsulatus.*

Morbid Anatomy.—Too rigid a distinction is often drawn between serous pleural effusion and empyema. Both during life, as the result of paracentesis, and after death, effusions are met with which are neither the one nor the other. These border-line effusions are most often pneumococcal in origin. As seen in the post-mortem room the liquid

effused in these cases is usually accompanied by a large amount of coagulated lymph, sometimes lining the whole pleural sac. The condition, especially if it be localised, is wont to be called "early empyema." But the effusion is not, strictly speaking, purulent, and it is certain that such effusions occur not infrequently in pneumonia and pneumococcal pleurisy and resolve without the formation of true empyema.

Certain differences, other than those connected with the quality of the effusion, are seen after death between serous effusion and empyema. (i.) Loculation of empyema is much more common than of serous effusion (see p. 537). (ii.) In proportion to the amount of liquid present the associated collapse of lung is often more extensive in empyema. (iii.) Ulceration of the pleural membrane is more common in empyema; on this account pneumothorax occurs more often in empyema than in serous effusion. For the same reason abscess in the lung is by no means a rare complication. In most of the cases it is apparent that the suppuration in the lung is secondary to that in the pleura; in not a few cases, however, it is extremely difficult for the observer to say whether he is dealing with an empyema which has ruptured into the lung or with a pulmonary abscess which has extended to the pleura. Primary abscess of the lung is seldom seen (*vide* p. 268); empyema is a very common disease; this must be borne in mind in estimating the sequence of events in any case. (iv.) Multiple empyemas are not at all uncommon; multiple pleuritic effusions are rare. (v.) Associated pericarditis (usually with pyopericardium) is more often seen to complicate empyema than serous effusion.

Bacteriology.—Owing to the great importance played by microbes in this disease our knowledge of their incidence and action has been discussed under etiology (see p. 560).

Symptoms.—1. *Onset of the Disease.*—As in sero-fibrinous pleurisy, this may be latent or manifest, and the statements made in respect of the non-purulent form of pleurisy apply equally here (see p. 538). The empyema which follows pneumonia is particularly apt to be latent.

2. *Fever* is a more constant symptom than in sero-fibrinous pleurisy; yet even in empyema it is sometimes absent. As already observed, the character of the fever in a case of pleurisy does not serve as a distinction between serous and purulent effusions, for in serous effusion, as in purulent, the type of temperature may be quotidian remittent with evening exacerbations. If colliquative symptoms (heavy sweats and diarrhoea) attend the fever the probability of empyema is increased. In fistulous empyema the temperature is usually almost or quite natural; and a rise of temperature means that pus is pent up somewhere. In some cases of small empyema, even when undrained, the temperature remains normal. As in sero-fibrinous pleurisy, the affected side may be hotter than the other.

3. *Pain, Dyspnoea and Cough.*—The remarks made in connexion with non-purulent pleurisy apply equally here (see p. 539).

4. *The Sputa.*—These may be the same as with serous effusion (p. 539). But the expectoration may be fetid, the result of one of two conditions: either a fetid empyema has burst through the lung—by far the more

common cause; or a fetid empyema, which has certainly not burst through the lung, communicates an offensive smell to the secretions of the air-passages in the neighbourhood, just as abscesses near the alimentary canal often acquire, for this reason, a disgusting odour.

5. *Vomiting and diarrhoea* are both common at the onset, especially in children; should vomiting, pain referred to the belly, and tenderness of the belly concur with diarrhoea, peritonitis will at first be closely simulated. This diarrhoea tends to be very obstinate, and in many cases cannot be stopped until the empyema is cured. Diarrhoea and marasmus may be the main symptoms of a small empyema. Should the patient die, post-mortem nothing amiss with the intestines will be discovered by the naked eye: it is an infective diarrhoea.

6. *Infection of the Whole Body.*—(i.) Symptoms which were formerly called "typhoid" or "putrid," and which are indicative of infection of the whole body, are apt to accompany fetid empyema. The tongue is dry and brown, the secretions become offensive to smell, the eyes are yellowish, the face is dusky, the pulse soft and weak, consciousness blunted, and muscular debility, or prostration, great. (ii.) Like symptoms sometimes occur from the very onset of empyema which is not fetid. In a state of good health sudden shivering occurs, headache, cough, in some cases much pain in the side, in others no pain at all. The fever is high, the temperature often reaching 104° or more; respiration frequent; sputa not rusty. Consciousness becomes affected; in some cases so much that even as early as on the second day the patient is deeply comatose; but the degree of coma is apt to vary, so that the patient, after deep unconsciousness, may become fairly sensible. More or less delirium occurs in some cases, but in others none at all. Morbilliform mottling of the skin (not much like the rash of typhus), temporary redness, swelling, and tenderness of one or several joints; enlargement of the spleen and diarrhoea may occur in some patients. The urine may be albuminous or not. The physical signs of effusion are sometimes late to appear, and are apt to be mistaken for those of pneumonia. The patient will die within ten or twelve days; and whether paracentesis be employed or not seems to make small difference. The pus has been found to contain pneumococci, and it is highly probable that the condition is one of general pneumococcal infection, with or without endocarditis. But pneumococcal pleurisy is seldom attended by these grave signs of universal poisoning.

Signs.—A. *Physical Signs.*—These are independent of the nature of the effusion; the section dealing with the signs of pleurisy with fluid effusion on pp. 540-548 therefore holds good in this place.

B. *Puncture.*—In the case of empyema puncture may lead us into error. (i.) In small old empyemas the enclosing walls are sometimes very thick, and it demands some faith in our power of diagnosis to enable us to push the needle boldly through them so as to reach the pus. (ii.) Pus is sometimes so thick that it will not pass through a fine needle: in this case a small quantity (less than a drop perhaps) will

probably have entered the needle, and can be blown out and examined; if there be pus, a larger needle must be used next time. (iii.) Pus can sometimes be drawn from a bronchial tube, or from a suppurating cavity within the lung, such as is produced by tuberculosis, destructive pneumonia, or actinomycosis. (iv.) The needle may draw off pus from the pericardium or a subphrenic abscess, after perforating the lung or the diaphragm.

C. *Characters of the Effusion.*—Pleural empyema is probably such from the first in most cases. Yet a serous effusion may possibly become purulent, a change which is either spontaneous or the result of operation. Spontaneously the change takes place slowly, a serous effusion becoming gradually purulent in the course of about three weeks. When the change is due to operation upon a serous effusion (that is to say, to infection of the effusion by septic matters), suppuration occurs more quickly, in a few days instead of weeks.

Pus is sometimes remarkably glutinous, so that, as it escapes during paracentesis, it stands in a heap when drawn into an aspiration bottle.

Pus sometimes contains much gas in solution, so that it effervesces in an aspiration bottle. Such pus is not necessarily offensive.

Pus is sometimes very fetid, and the cause is not always the same. (i.) The cause is sometimes obscure, the pus is fetid from the first; such a case may end in recovery after a single paracentesis, without draining. (ii.) The cause is sometimes manifest; the pus becomes offensive through contamination with putrefactive microbes in such manner as the following:—gangrene of lung, perforation of lung, perforation from without (for example, an operation), perforation of diaphragm by hepatic or subphrenic abscess, mere contiguity of an offensive abdominal abscess without actual operation. Fetid empyema is sometimes associated with:—(i.) Sloughing of pleural false membranes, and even of the pleura itself (an offensive slough lying loose in the empyematous cavity may be the cause of the fetor); (ii.) necrosis of one or more ribs.

D. *Loculated Empyema*, or pleural abscess; the purulent effusion not occupying the whole of the pleural cavity, and being enclosed by adhesions, the rest of the pleural sac being natural or obliterated by adhesions.

1. The commonest seat of a circumscribed effusion is in the lateral or posterior part of the lower half of the chest on one side. In this case the diagnosis is easy enough by physical examination and puncture.

2. Loculated empyema sometimes lies between the base of the lung and the diaphragm; mostly on one side only, but occasionally on both sides, without communicating. The diagnosis depends upon the situation of the pain felt, namely, at the attachment of the diaphragm around the lower margin of the thorax, upon immobility of the diaphragm and hypochondrium on the affected side; upon increased resistance of the hypochondrium to pressure; upon the signs of more or less extensive solidification of the base of the lung on the same side, in consequence

of collapse of the lung and associated congestion (a small empyema will sometimes cause very extensive collapse), indicated by loss of percussion tone (now and then the tone is clear and tubular, the lung being relaxed only), and weakened breath-sounds. The breathing is apt to be painful and difficult. Diaphragmatic empyema is often associated with subphrenic or hepatic abscess, and is often quite latent, found on post-mortem examination only. When a loculated empyema of this kind contains gas, diagnosis is often difficult.

3. Abscess between the lobes of a lung is less common. The pus is very often discharged through the lung and expectorated, as early, it may be, as three or four weeks from the onset of the pleuritic symptoms. As a rule, it is only when the patient has begun to spit pus that the disease can even be suspected; physical signs, if any, are inadequate to the diagnosis.

4. Empyema at the apex only of the pleural cavity is an uncommon event, but one which sometimes occurs. Diagnosis is rendered all the more difficult on account of the reluctance with which we make a puncture in this dangerous region.

E. *Pulsating Empyema.*—That is to say, empyema which pulsates rhythmically with the heart.

The empyema is commonly very large, occupies and fills the left pleural cavity. (i.) The effusion usually points in one or two places, which alone pulsate. This bulging occurs in the normal heart region or in the lowest interspaces. In rare cases the protrusion has been seen in the loin below the ribs. The bulging is never larger than an orange. (ii.) Less commonly, the effusion nowhere points or bulges through the chest wall. However, in these cases also, the pulsation is usually limited to the normal heart region (to the left of the sternum), or to the lowest three or four intercostal spaces. But sometimes the pulsations are seen and felt over almost the whole of the left side.

Whether the empyema bulge or not, the heart is much displaced to the right. Pericarditis may concur, but usually the heart remains healthy. Auscultation of the pulsating heart may detect conducted heart-sounds. Palpation detects no thrill and no expansion like that of an aneurysm.

Paracentesis very much helps the diagnosis. By removing part of the liquid the pulsation ceases; but the heart, being fixed by external pericardial adhesions, does not return to its normal position. The puncture need not be made at the spot which pulsates.

The effusion is mostly chronic, and the lung wholly collapsed. Pneumothorax often concurs; in this case, pulsation is conveyed by the liquid only. The effusion is purulent in the great majority of cases, but now and then a serous effusion has been known to pulsate: this was so in one case only out of 95 recently analysed by Sailer.

Very seldom the empyema does not fill the whole pleural cavity, but is loculated and enclosed in adhesions—13 cases in Sailer's collected series. This kind of pulsating empyema always bulges; it may

be to the right of the sternum, but still in close neighbourhood to the heart.

The diagnosis is from intrathoracic aneurysm, and from the very uncommon condition of a pulsating malignant tumour. Aortic aneurysm and pulsating empyema may coexist.

Pulsating empyema is, in most cases, incurable.

F. *The Blood.*—The degree of anaemia seen in empyema is usually more marked than in sero-fibrinous pleurisy; in severe cases, or in cases of long standing, the reduction in red cells and in haemoglobin may be very considerable. The leucocytes are invariably increased in number and the increase is usually considerable. Some of the highest leucocyte counts recorded have been observed in cases of empyema: Prof. Osler refers to a case in which the figure reached 115,000. In Lord's series of 28 cases the figure exceeded 12,000 in all but 6. The duration of the empyema is of importance in estimating the value of the leucocyte-count in diagnosis: in chronic cases the number may not be much raised. Another point must be borne in mind: that in children a high leucocyte-count does not possess the significance that it does in adults.

Course and Termination.—(i.) External Rupture.—An empyema, left to itself, will usually perforate the thoracic wall in course of time. The opening mostly occurs in front; a common situation is the fifth interspace in the nipple line. But an empyema may point almost anywhere, from just below the collar-bone to the loin or even the buttock. The first effect of a pointing empyema in some cases is to produce what looks like a mere subcutaneous abscess; in fact an abscess of this kind over the ribs is often due to the perforation of a pleural empyema, even if there be no signs of pleural effusion. In a few cases there is an abscess in the wall of the thorax at a place remote from, and unconnected with, the empyema.

The course of an empyema (unless it be very small) which has been allowed to discharge spontaneously through the chest wall, and which is left to itself, is very tedious. If the opening close, it takes a long time in doing so, but often it never closes. In either case the patient runs the risk of a ruined state of health, complicated by lardaceous changes in the viscera. Necrosis of a rib may also occur, and erosion of an intercostal artery has been described.

(ii.) Rupture through Lung.—In this case a small hole, which allows of direct communication between the empyema and a bronchial tube, is made through the lung by ulceration; or else, more seldom, the pus filters through a small portion of lung which is spongy and penetrated by many minute passages.

Empyema, which perforates the lung, is usually loculated, and often so small and deeply seated that it cannot be detected by physical examination. Such loculated empyemas often occur between the lobes of a lung, or between the lung and diaphragm, or in the mediastinum close to the root of the lung.

The expectorated pus is sometimes fetid, sometimes not. It is sometimes fetid at first, and afterwards spontaneously ceases to be fetid. In some cases the opened cavity contains air, in others not.

Recovery often occurs, and in no great space of time, even when the patient is left to the unassisted powers of nature, as is very often the case, it being impossible to open a deeply-seated abscess by simple paracentesis. In some of the cases recovery is tedious and both the signs and the symptoms are those of bronchiectasis; for the differential diagnosis, see p. 147. It is tempting to invite the help of surgery in order to get a more speedy drainage than that afforded by nature. But two considerations arise: first, that even these patients commonly do well at last; and, secondly, that as no planned operation meets all cases, the extent of healthy lung and pleural tissue opened up by the knife and the surgeon's finger is apt to constitute a grave danger to life.

Death, if it occur, may be very unexpected, the patient being choked by the sudden discharge of a large quantity of pus into the air-passages. Or death may be the termination of a long period of purulent expectoration and gradual exhaustion of the patient's strength.

(iii.) Rupture into other Parts.—Empyema will sometimes perforate the pericardium, and in the case of pyopneumothorax the pericardial sac may contain air as well as pus. The peritoneum may be perforated. The empyema may discharge through the oesophagus, and a pleuro-oesophageal fistula may result. It is probable that the cases narrated by older physicians, cases in which empyema has been accompanied by a discharge of pus from the intestines or with the urine, were really cases of empyema complicated with subphrenic abscess.

(iv.) Incurable Empyema.—Empyema is sometimes permanent and incurable because associated with certain local conditions which prevent recovery. The lung may be quite inexpansible, either carnified or tightly bound by thickened pleura. Tubercle may have invaded the lung extensively. When empyema follows upon pneumonia the pulmonary inflammation sometimes is never resolved, the lung remains hepatised, and if the patient live long enough the hepatisation will tend to pass into cirrhosis. The corresponding branch of the pulmonary artery may be closed by a thrombus. And, lastly, extensive necrosis or erosion of the ribs may ensue, in which case the pus is not necessarily offensive.

(v.) Great Deformity.—More or less contraction of the affected side is an almost necessary result of a healed empyema which has occupied the whole or the greater part of the pleural cavity. When the lung is totally unexpanded the contraction will be great, the spine much curved, the mediastinum, heart, other lung, and diaphragm displaced towards the affected side. In course of time the heart will become dilated, especially the right chambers, and this is one way in which the patient may die at last from the consequences of his empyema, even although it may have closed long ago.

Associated Diseases.—Empyema is often accompanied with other diseases which impede or prevent recovery.

1. *Double empyema* is not uncommon; a less serious state of things than might be supposed; for appropriate treatment will usually cure the patient.

2. *Collapse of lung* with, or without, subsequent fibrosis. If collapse occur on the other side, as it may do in an infant, it is necessarily fatal.

3. *Gangrene* of a portion of the lung may occur when fetid pus penetrates it from an empyema—a serious complication.

4. *Pyopneumothorax* may occur in one of two ways. Either (i.) the lung has ruptured or (ii.) an empyema has opened up a bronchus by ulceration or has discharged through the thoracic wall, or has been evacuated by paracentesis and air has passed out of the lung into the pleural cavity, not through puncture of the lung, but through rupture of it by atmospheric pressure from within.

5. *Pericarditis* or *Peritonitis*, or both, may concur. The remarks concerning the complications of sero-fibrinous pleurisy on p. 550 are true of empyema also.

6. *Nephritis*, indicated by the appearance of blood and tube-casts in the urine, sometimes occurs suddenly in the course of empyema under treatment by drainage. The nephritis usually lasts four or six weeks and ends in recovery.

7. *Abscess of the brain* is a not very uncommon consequence of empyema as it is of bronchiectasis and of other forms of intrathoracic suppuration. The abscess is usually single, and occupies either the occipital or temporo-sphenoidal lobe: in a few rare cases many abscesses have been found. The abscess sometimes bursts into the lateral ventricle; and in this way even the subarachnoid space of the spinal cord may become filled with pus. This cerebral abscess is probably metastatic, and due to the transportation of a microbic embolus from the thoracic disease; but any other signs of pyaemia are seldom observed either before or after death: why the white matter of the brain alone should be selected for embolism is unknown. The onset of cerebral abscess is very insidious: for a long time the only symptom is headache of varying severity, sometimes little, sometimes much: so far as any distinctive symptoms go, the disease is latent. Towards the end, a few days or a week before death, much more decisive signs of disease are superadded to the headache; namely, vomiting, optic neuritis, general convulsions, coma. Or, as sometimes happens, the patient dies very unexpectedly, without the occurrence of any grave warning symptoms. Even when the abscess is diagnosed, treatment by operation rarely, if ever, saves the patient's life; and this seems equally true, whether there be localising signs or not. One reason for this very grave prognosis may lie in the frequency with which there exists, around the abscess, an area of softened brain tissue of considerable size.

8. *Hemiplegia* due to softening of the brain is another possible con-

sequence of empyema. No doubt the softening is sometimes caused by embolism of the middle cerebral artery; the embolus being derived from a thrombus which has formed in the heart or pulmonary veins during the stagnation of the circulation which is a necessary result of the compression of the lung and displacement of the heart. Sometimes hemiplegia occurs during or soon after paracentesis, a thrombus or a portion thereof being dislodged during the commotion of parts which must follow upon removal of much liquid. In rare cases this hemiplegia is temporary, and the patient recovers in a few hours or days. But the softening of the brain which causes hemiplegia is not always to be explained by embolism; it may be that no arterial lesions of any kind are to be found after death; and a local metastatic encephalitis, not going on to suppuration, seems to afford the most probable explanation. Other symptoms may depend upon the softening, according to its locality; namely, aphasia and associated defects; amaurosis, with a natural condition of the retina. Or the softening may involve both sides of the brain, with the consequences of general paralysis and dementia.

9. *Lardaceous disease* is a consequence which nowadays is seldom met with. In this case the empyema is usually chronic and fistulous; but even a small empyema which has never been discharged may be attended by this form of degeneration.

10. *Clubbing of the finger-ends* attracted much attention from the ancient physicians. The symptom may be well marked at the end of a fortnight from the beginning of an empyema. Clubbing will sometimes disappear gradually when empyema has been cured. The enlargement may not be confined to the ends of the fingers and toes, but may involve the hand or foot or even the greater part of a limb. This condition, first described by Marie under the name *chronic pulmonary osteo-arthropathy*, is usually found in cases in which there is progressive fibrosis of the lung and pleura. (See Vol. III. p. 64.)

Diagnosis.—Reference should be made to the section dealing with diagnosis of pleurisy in general on p. 551. The simulation of empyema in particular may, however, be so close in the following diseases that special comment is called for in respect of them.

1. *Acute Pneumonia.*—Mention has already been made of the fact that the physical signs of pneumonia and pleurisy may be the same. Should an empyema be confined to the apex of a pleural cavity, so infrequent an occurrence compared with the frequency of apical pneumonia, diagnosis becomes unusually difficult. It is perhaps a sound clinical rule to observe, that in any case diagnosed as pneumonia, in which unusual physical signs are present after the tenth day and in which the temperature has not fallen satisfactorily, puncture of the chest should be made. Some careful physicians, remembering the experience of the post-mortem room, make a practice of puncturing the chest in every case of pneumonia in which the patient's condition becomes alarming; an unsuspected empyema is thereby occasionally brought to light. A dry puncture need never be a matter for shame, whereas the discovery of an

undiagnosed empyema after death is certain to cause regret, although it may call for no remorse.

2. *Subphrenic abscess* is much more common on the right side than on the left, for reasons which become clear when the antecedents of the abscess are considered. It is often, if not always, associated with pleurisy on the same side, and usually with empyema, due to perforation of the diaphragm or not. Hence empyema on the right side in a person who has probably suffered from tropical hepatitis, from simple or malignant ulcer of the stomach, or from other causes of subphrenic abscess, should always lead us to reflect upon the possible coexistence of this disease. The pus of subphrenic abscess and of the empyema is fetid. The abscess, even if there be no empyema, may burst into the lung, and lead to expectoration of most offensive pus. Whether there be an associated thoracic empyema or not makes little difference so far as the physical signs of a subphrenic abscess are concerned; for the empyema is local, enclosed in adhesions, and not nearly filling the pleural cavity. The signs are both abdominal and thoracic, sometimes more the one, sometimes the other. The abdominal signs are: (*a*) fulness and tightness in the hypochondrium; (*b*) the liver depressed, sometimes, but by no means always; moreover the liver is sometimes much depressed in uncomplicated thoracic empyema. The thoracic symptoms are (*a*) dulness to percussion and signs of pleural effusion at the base, whether there be a pleural effusion or not; in the latter case the diaphragm is much pushed upwards, and the lung proportionately collapsed; (*β*) the heart's apex-beat is sometimes displaced even in subphrenic abscess without empyema, but more often is not displaced. Some assistance may be afforded by a study of the position and excursions of the diaphragm shadow (see p. 544). Puncture, made as for pleural effusion, will probably reveal the presence of pus, but will not tell us whether the pus is above the diaphragm or below it. Uncomplicated subphrenic abscess may be mistaken for simple thoracic empyema, even after the abscess has been emptied of pus by aspiration; the needle having gone right through the diaphragm, which has been pushed much upwards, as high, it may be, as the third rib. Even resection of a portion of a rib, and exploration of the pus cavity by the finger, do not always enable us to say at first whether we have opened a cavity above or below the diaphragm; or, in the former case, whether the diaphragm be perforated or not.

Subphrenic abscess often contains gas derived from perforation of the alimentary canal or from decomposition. In this case the disease is apt to escape discovery by physical examination, because there is no dulness to percussion. Sometimes the percussion-note is clearer than natural; and sometimes the clear note is more extensive also, so that the liver dulness disappears. The resonance may possess amphoric quality. Auscultation usually detects one or more signs of a large cavity containing air; namely, amphoric hum (attending the sounds of breathing, speaking, and of the heart), metallic tinkle, bell sound, and succussion-

splash. If the diaphragm be perforated, the empyema will be a pyopneumothorax. (*Vide* also art. "Subphrenic Abscess," Vol. III. p. 1005.)

3. Of the frequent association of pericardial effusion with pleural effusion mention has already been made (p. 550). When a rib has been resected in the treatment of empyema the finger passed into the pleural cavity may possibly be able to feel a bulging pericardial sac.

4. The manner in which pulsating empyema counterfeits *aneurysm* has been already referred to (p. 565).

5. *An abscess in the thoracic walls* may be the only evidence of a small empyema (see p. 566) which has penetrated to an intercostal space. Even when the abscess has been opened it is not aways easy to say whether it communicates with the pleural cavity or not. It is possible that pleurisy may be the cause of abscess in the thoracic walls without actual perforation of the pleura. But more commonly parietal abscess (as distinguished from pointing empyema) is due to such causes as injury, pyaemia, periostitis of a rib, or necrosis of the same; and this "peri-pleuritis" may perhaps sometimes set up pleurisy. Lastly, in all cases of superficial abscess the question of actinomycosis must be pondered.

6. In rare cases of *primary malignant disease of the lung* the resemblance to empyema may be remarkably close. (*Vide* p. 511.)

Prognosis.—It seems unnecessary to reiterate many prognostics, which will be found in their appropriate places in the foregoing and following pages. As regards mortality in this disease an analysis of 499 cases treated in the medical wards of St. Bartholomew's Hospital during the twenty years 1884-1903 shews a death-rate of 22·2 per cent. There was practically no difference in the mortality during the first and the second decade of this period:—1884-1893, 216 cases with mortality 22·6 per cent; 1894-1903, 283 cases with a mortality of 21·9 per cent.

The nature of the infecting microbe has a distinct bearing upon prognosis. Netter's observation that there is a relative benignancy in the pneumococcal cases has been confirmed by most authorities. Empyemas due to mixed infections are often much delayed in recovery; the uncommon cases due entirely, or in part, to staphylococci, are perhaps the most troublesome of all. Streptococcal cases take an intermediate position between these two groups.

Unexpected and speedy death may occur in empyema as in serous effusion (p. 551), but the recorded cases have been fewer. One cause, which is peculiar to empyema, is the sudden rupture of the abscess (and it may be quite a small one) into the lung; this may choke the patient in a few minutes.

Treatment.—(I.) The exploring needle having determined that a pleural effusion is purulent, the pus must be removed as soon as possible. If it be bloody, or if the pleura contain air as well as pus, the same rule holds good. Free evacuation of pus may be expected to bring the patient's temperature down nearly or quite to the normal; if this be

not the result, we may assume that there is some retention of pus. Any subsequent rise of temperature, after a fall to the normal, will most likely be due to imperfect drainage. But perfect drainage cannot always be attained, especially when a small quantity of pus is secreted in an inaccessible cavity shut off from the rest; in cases of this kind time usually surmounts the difficulty, the retaining lymph breaking down under persistent drainage.

(i.) When the quantity of pus is not very large it is best to make a permanent opening and drain at once. In some cases thorough and speedy drainage cannot be obtained unless a large opening is made by excising a portion of one of the ribs; and, therefore, to avoid all doubt upon this point it is good practice to resect a rib in all cases.

(ii.) When the empyema fills the pleural cavity it is safer to remove as much of the pus as possible by paracentesis at first, and to make the incision a day or two afterwards. The sudden discharge of a very large quantity of pus from the chest causes a great shock to some patients, and previous paracentesis lessens the shock. Paracentesis, and sometimes even a single paracentesis, can cure empyema, even though the pus be fetid and quite considerable in amount. One of us (S. G.) has known paracentesis, which removed more than five pints of pus from the pleura, to be followed within a week or two by effusion of clear serum to the same amount in the same pleura. But cases of this sort are very uncommon, and incision and drainage are the proper treatment of empyema.

In order, then, that the drainage may be thorough it is best to remove a small portion of one of the ribs. Incision is made right down upon the rib, the periosteum is separated all round by an elevator, and the rib is divided in two places by cutting forceps, so that about an inch can be removed. It is not good practice to swill the empyematous cavity out; nothing is gained by removing false membranes in this way; a fetid empyema is soon deodorised by thorough drainage and careful antiseptic dressing, and even if not, washing out does not help. Moreover, injections are dangerous if there be an ulcerous opening through which they can enter the lung; the shock which immediately ensues upon such an entrance puts life in jeopardy. Even if there be no such ulcer, injections are dangerous. One of us (S. G.) has known a patient die very suddenly during injection, when but a very small quantity of a weak carbolic acid solution had been injected: no chloroform was given, and nothing could be found post-mortem to explain the death. Dr. Cayley reported a similar case, in which the injection consisted of a solution of iodine. But sudden syncope coming on in this way is not always fatal; a case has been recorded in which the right chambers of the heart were found post-mortem to be distended with gas. In most of the cases, however, nothing is discovered at the necropsy. Some light has been thrown upon the mechanism of this syncope by the recent experimental work of Capps and Lewis. These observers found that irrigation of the pleural cavity in dogs, in whom empyemas had been induced, led to pronounced depressor effects upon the arterial circulation. The best means of restoring blood-

pressure in the circumstances was found to be artificial respiration, which produced a more lasting effect than the administration of adrenalin intravenously. The syncope is sometimes followed by convulsions and coma; in this case death usually ensues within twenty-four hours. If the temperature rise much above 105° F. recovery is very unlikely. Yet recovery even after convulsions may occur; temporary palsy of a limb or of one side of the body has been noted upon cessation of the convulsions. In other cases the sudden syncope has been attended by palsy without convulsions, by spastic rigidity of a limb or of the jaw, or by aphasia; these symptoms commonly pass away in an hour or less. Convulsions and paralyses of this kind are probably epileptoid in nature and quite different from the paralyses which will be spoken of hereafter, and which are due to embolism.

If there be any probability of the coexistence of pulmonary tubercle the line of treatment is not so clear. To release the lung from compression may accelerate the infective and destructive changes going on therein; to say nothing of the debilitating effect of a free purulent discharge, which there is but small chance of stopping. In these circumstances it is best to resort to paracentesis several times at least, the result being watched before proceeding to drainage.

In dealing with a small deeply-seated empyema, such as that which so often leads to fetid expectoration, it is sometimes necessary to remove portions of two or three ribs, so that adhesions can be broken down and the cavity opened by the finger. To cut through the lung in such cases may cost the patient his life.

For a day or two after opening the chest the discharge will probably continue to be abundant. It will then, in most cases, gradually lessen until it ceases altogether in a few weeks, three or more. In proportion as the discharge becomes scantier the drainage-tube must be shortened so as to allow the sinus to heal from the bottom.

The temperature ought to fall almost or quite to the normal after the pus has been discharged. Should the temperature remain raised, there must be either retention of pus or some other concomitant disease. When, after the fever has ceased, the temperature rises again there is probably retention of pus, and should the temperature not fall again in a few days the sinus should be probed, and a longer piece of tube be inserted if necessary. But the temperature will often rise for a few days without obvious retention of pus, and will fall again without obvious increase in the amount of discharge.

When the sinus shews no tendency to close it is best to wait two or three months before undertaking any further operation. But when the discharge continues for a longer time (and these remarks apply also to cases of neglected empyema which has been allowed to open spontaneously), and it seems necessary that something else should be done (especially when the discharge remains abundant and the health of the patient suffers), a more extensive operation must be performed. Longer portions (two or three inches) of three, four, or more ribs in the neigh-

bourhood of the sinus must be resected, so as to allow the chest walls to fall in and meet the lung. The cases in which the discharge is not finally arrested by this operation are very few.

II. **Specific Inoculation.**—Of late years some degree of prominence has been given to the principle of specific inoculation in cases of pyogenetic infection (Wright). Experience shews that considerable benefit follows this mode of treatment in certain localised infective processes, and empyema sinus is one of these. After efficient drainage has been established, therefore, any delay in the progress of the case may be profitably met by the injection of one or two appropriate doses of the killed micro-organism isolated from the patient. Whatever benefit is to be obtained by this means will probably follow the first or second dose. In a case of pneumococcus empyema an initial dose of 50 million killed cocci may be given, followed in a week by a dose double this size. No ill-effects, local or constitutional, will ensue provided the technique be sound; experience teaches that with this additional aid to treatment a hastened recovery may be looked for.

III. **Dangers of Paracentesis.**—1. *Serous (albuminous) Expectoration.*—Out of the 42 cases recently collected by Dr. Horton-Smith Hartley 3 only are stated to have followed the removal of a purulent effusion. For details of this event see p. 559.

2. *Pneumothorax.*—(i.) As in serous effusion the lung may be injured (see p. 559). (ii.) There is sometimes a small ulcer on the surface of the lung existing before the operation. (iii.) The pus sometimes contains so much gas dissolved in it that in some cases this is a very probable cause of pneumothorax.

3. *Haemorrhage from the Pleura* (see p. 559).

4. *Fatal haemoptysis* has ensued upon evacuation of empyema in pulmonary tuberculosis which has gone on to the formation of a cavity containing a small aneurysm.

5. *Hemiplegia* due to cerebral embolism (see p. 569).

6. *Sudden death*, apart from that which may follow washing out the pleural cavity, may occur in rare cases (see pp. 559-560).

IV. The treatment of *fetid expectoration* from a deeply-seated empyema which cannot be laid open by an operation, is the same as that of a similar condition in bronchiectasis and in pulmonary tuberculosis. Here also specific inoculation may be given a good trial.

V. For the treatment of *subsequent deformity* see p. 560.

SAMUEL GEE, 1898.
THOMAS J. HORDER, 1909.

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PNEUMOTHORAX

By Prof. D. W. FINLAY, M.D., LL.D., F.R.C.P.

Definition.—By pneumothorax is meant the presence of air in the pleural sac. Generally speaking, the air or gas is accompanied by serous fluid or pus; hence the synonyms hydro- or pyo-pneumothorax to denote one or other of these composite conditions.

Etiology.—Although causes leading to the production of pneumothorax are fairly numerous, most of them, as detailed by various observers, are of remarkably infrequent occurrence; indeed the disease itself may be said to be rather uncommon.

The fullest and most complete statistical statement with which I am

acquainted is that of Biach, compiled from a thirty-eight years' record of three large Viennese hospitals. The total number of cases dealt with, 918, are tabulated as follows:—

Phthisis	715	Nematode worms in pleural cavity	2
Gangrene of lung	65	Rupture of an encapsuled peritoneal effusion	1
Empyema	45	Hydatid of lung	1
Injury	32	Caries of ribs	1
Bronchiectasis	10	Caries of sternum	1
Abscess of lung	10	Rupture of bronchial glands	1
Emphysema	7	Abscess of breast	1
Breaking down of a haemorrhagic infarct	4	Fistula between pleura and colon resulting from hydatids	1
Paracentesis thoracis	3	Uncertain causes	14
Perforation of oesophagus	2		
Perforation of stomach	2		

The causes in this list represented by single instances, and even the undetermined 14, must be of very great rarity in view of the large total of cases; and others might be added; thus, Dr. Champneys has pointed out that double, and therefore fatal, pneumothorax may follow the operation of tracheotomy, being associated with emphysema of the neck and of the mediastinal tissue, air passing down by way of the deep cervical fascia and causing rupture of the pleura. This has been found chiefly to occur in cases in which artificial respiration has been employed. Again, pneumothorax has been attributed by some authors to the production of gas by bacterial activity (*Bacillus aerogenes capsulatus, B. coli*) in empyemas, especially when secondary to appendicitis (Dieulafoy). This must be infinitely rare. I have never seen a case of it, and I think there is good reason to doubt whether it does occur. The explanation for its apparent occurrence, given by Dr. Fowler and Mr. Godlee, is probably the correct one, namely, that a perforation of the pleura had been present, but had become closed, leaving no sign. Emerson points out that it is significant that many of the recorded cases had been previously explored. It should be added that pneumothorax occasionally occurs in persons otherwise apparently healthy as a result of strain in severe muscular effort. As a curiosity, attention may be directed to recurring pneumothorax; these cases are accompanied by few symptoms, nearly always recover, and may therefore be due to rupture of emphysematous bullae. Extremely rare cases also are on record in which air and effused blood have been found in the pleura (haemopneumothorax), apart from injury, the causes of these effusions being altogether obscure. Two cases illustrative of this condition have been described by Dr. Rolleston and by Dr. Newton Pitt.

All the varieties of causes group themselves in two divisions, one containing those in which the condition producing pneumothorax results from injury or disease acting from within the thorax; the other including those which act from without. The former is, of course, much the more important. The outstanding point in the etiology is that pulmonary tuberculosis, producing perforation by ulceration of the visceral

pleura, is by far the most frequent cause of pneumothorax; and most observers place the proportion of such cases at about 90 per cent of the whole. Biach's table brings out the percentage at 77·8.

The relative frequency of the disease in cases of pulmonary tuberculosis is variously stated by different authorities as being from 1 (Biach) to 14 per cent (24). My own experience would suggest the smaller number as being nearer the general average. It was found present twice only in 60 post-mortem examinations made on cases of pulmonary tuberculosis at the Middlesex Hospital in the years 1877, 1878, and 1879. Probably from 5 to 7 per cent would not be far from correct; differences doubtless arise from the varied totals dealt with (11).

It should be added that men are more apt to be attacked by pneumothorax than women; among 10,212 cases of pulmonary tuberculosis there were 198 of pneumothorax (1·93 per cent), 158 in males and 40 in females (Drasche). Of James' 125 cases of pneumothorax, 103 were in males and 22 in females. It is a disease especially of the earlier periods of adult life; as might be expected from its connexion with pulmonary tuberculosis.

Pathology and Morbid Anatomy.—The mode in which air gains access to the pleura in such cases as those of external injury, or the bursting of an empyema, are so obvious as to require no explanation. With regard to the tuberculous cases, which, as we have seen, form an enormous majority of the whole, it is in the acute forms that pneumothorax is most apt to occur. Those in which the disease of the lung progresses slowly are comparatively little likely to perforate, owing to the formation of protecting adhesions between the visceral and parietal layers of the pleura. In the former class of cases tuberculous masses become softened, and break down close under the surface of the lung; necrosis of the overlying portion of the pleura takes place; and some effort, or an attack of coughing, is sufficient to determine a rupture, or it may occur without any apparent exciting cause.

In connexion with this portion of the subject it is interesting to note how the conservative processes of nature tend to the prevention of pneumothorax. In the more slowly progressive cases of pulmonary tuberculosis perforation of the pleura is anticipated by the formation of inflammatory adhesions—such inflammation being apparently set up by the commencing necrosis of the pleural tissue. Were it not for this, pneumothorax, instead of being a somewhat uncommon event, would be a very frequent if not an invariable incident in the course of caseous tubercle in the lungs.

In a few instances the perforation seems to take place by the extension towards the surface of a cavity itself, or by a sinus proceeding from the cavity. With very rare exceptions the disease is unilateral; and the left pleura is more frequently the seat of the lesion than the right Usually there is only one perforation, which may be found at almost any part of the lung. The common site, however, is the lower part of the upper lobe, or the upper part of the lower lobe; and the reason for this is

that the higher parts of the lung are usually the seat of pleural adhesions, which, as we have seen, prevent perforation.

The size of the perforation varies much, in great degree according to the length of time the patient survives. It may be large enough to admit the tip of the finger, or so small as to be discerned with difficulty; indeed, it is often not discovered at all, being overlaid with lymph which has become organised in the repair of the mischief. The opening may be direct or valvular; and these conditions have an important bearing on treatment and prognosis, as well as on the amount of suffering to which the occurrence of the lesion gives rise. When the perforation takes place, the elastic traction of the affected lung is neutralised, and the heart and mediastinum are displaced towards the sound side. If the opening be direct and free, air passes out of the pleural sac as well as into it, and there may be no intrapleural pressure; if, on the other hand, the opening be valvular, air enters the pleura during inspiration, and as the respiratory movement is reversed, the valve closes so that no air can escape: the consequence is that the pleura gradually becomes as full of air as bulging of the chest, shrinking of the lung on the affected side, depression of the diaphragm, and displacement of the mediastinum will permit. (*Vide* art. "Intrapleural Tension," p. 524.) The quantity of gas present depends on various circumstances—chiefly on the presence of serum or pus in the pleura, and the condition of the lungs themselves, especially of that which is perforated. Adhesions and consolidation tend to minimise the quantity, whilst the opposite conditions favour the largest possible accumulation.

The gas itself, as regards its chemical composition, very much resembles expired air; it consists of nitrogen with oxygen and carbonic acid, together with sulphuretted hydrogen in cases in which a fetid liquid is also present in the pleural cavity. The proportion of oxygen and carbonic acid may vary from time to time; but this matter, however interesting, is of no practical importance.

When a rupture of the pleura is due to one of the simpler causes—such as injury or the giving way of an emphysematous vesicle—the opening is soon closed, the air becomes absorbed, and the previous state is completely restored. But it is different with the tuberculous perforation: here, owing to the leakage of septic liquid from the pulmonary cavity into the pleura, acute inflammation of the pleural membrane is set up, which may be both intense and widespread. Following this comes more or less rapid effusion, which is most likely to be purulent.

On post-mortem examination the escape of pent-up air, when the cut is made through the chest wall for removal of the sternum and rib-cartilages, may bear witness to the intrapleural pressure which sometimes exists. The mediastinum and heart are displaced towards the sound side; and shrinking of the affected lung, much or little according to its condition as regards intrinsic disease or adhesions, will be observed. Where the pneumothorax has lasted for some time the pleural surfaces are covered with quantities of lymph (the result of the pleurisy), which,

as before mentioned, may render the discovery of the perforation difficult or even impossible. In ordinary cases the lung may be adherent in part to the chest wall at the apex, and may be the seat of cavities and of nodules of caseous tubercle. The opposite lung may shew a similar state; or, if the perforation have occurred early in the history of the tuberculous condition, it may be perfectly sound. The pleura contains serous fluid or pus, the quality of the liquid as well as its quantity depending to some extent upon the time which has elapsed since the occurrence of the perforation. Exceptions to this rule, however, may be found in cases which have proved rapidly fatal, as there may not have been time for an obvious effusion to take place.

Symptoms.—In the ordinary case the patient, perhaps during a fit of coughing, is attacked by agonising pain in the chest, and a feeling as of something having given way, together with great difficulty of breathing. Any of these symptoms, however, may be wanting; in some cases all of them may be comparatively inconspicuous. Nor will this appear strange when we consider that the accident, as it may be called, of pneumothorax often occurs in patients already acutely ill, with rapidly caseating or softening tubercle, probably confined to bed, and suffering from respiratory discomfort and thoracic pain. Pulse- and respiration-rate are both increased, the latter more so than the former; the patient is cyanosed, the expression anxious, the alae nasi working, the heart palpitating, the extremities cold, the voice weak, the temperature lowered, and the body bathed in cold sweat—in fact, as regards his general condition the patient is in a state of collapse. Dyspnoea, which is perhaps the most characteristic of the symptoms, is often extreme and distressing, the patient feeling as if he were about to be suffocated. It is most marked when the perforation through the pleura is valvular, because the condition producing dyspnoea is aggravated with every inspiration; and it may readily happen, especially if the function of the opposite lung be impaired by disease, that the case may speedily have a fatal issue. The decubitus of the patient varies a good deal in different cases. There may be orthopnoea, or he may lie half propped up on the back, or on either side. In a case under my care the position chosen was semi-prone towards the sound side, with the head low.

Physical signs are often more definite than the symptoms. The following points are to be noted:—

Inspection.—The shoulder of the affected side is elevated, the intercostal spaces partially or wholly obliterated, the side distended, and the movements of respiration diminished or altogether absent. The respiratory movements of the sound side are correspondingly exaggerated. The heart's maximum impulse may be seen displaced towards the sound side; although, owing to the rapid and disturbed respiratory movements together with the weakness of the heart's action, it may be difficult to make out.

Palpation.—This means may enable the last-named point to be more distinctly perceived; and by it we can also appreciate the diminution or

abolition of respiratory movements: tactile fremitus is also abolished. Displacement downwards of the liver or spleen may be observed according to the side affected; and the displacement may be very considerable in amount if the pleural cavity contain much air or liquid, or both. This change has an important bearing upon treatment, since downward displacement of the diaphragm forms such a large pocket for the accumulation of pus that its amount is very apt to be underestimated; thus steps for its prompt removal may not be taken.

Percussion.—The presence of air in the pleura gives rise to a marked change in the percussion resonance; the note is over-resonant, and may generally be described as tympanitic. When the tension of the walls, however, becomes very great, there is a change in the note, so that it is shorter and of higher pitch, and hence of a less tympanitic quality. The characteristic note may not be made out over the whole of the affected side; adhesions fixing a portion of lung to the thoracic wall may prevent it, and this condition is of course most frequently observed at the apex of the lung. Or the presence of an accumulation of liquid—purulent or otherwise—at the base of the pleural cavity will cause a dulness in the percussion-note over the area so occupied. In the latter case the dulness and tympanitic resonance may be made to alter their relative positions by changes in the position of the patient's chest.

The normal area of cardiac dulness is abolished in cases of left-sided pneumothorax; and in any case, owing to great displacement of the mediastinum, the tympanitic note often encroaches considerably on the sound side.

Lastly, there is what is known as the bell-sound, the "bruit d'airain" of Trousseau, an interesting phenomenon which may be said to belong partly to the domain of percussion and partly to that of auscultation. It is recognised when some part of the side which is distended with air is auscultated, while a coin placed on another part is struck with another coin or some similar hard substance, such as a key. The sound conveyed to the ear of the listener is of a ringing metallic quality often closely resembling the tinkling of a small bell. Anvil sound and coin sound are alternative names for this sign.

Auscultation.—When the opening is valvular, and the pleura has become as full of air as possible, no breath-sound may be audible, except perhaps along the spine where the compressed lung lies; but when the opening is patent, breathing of an amphoric quality is well heard, as a rule, both with inspiration and expiration.

It was formerly thought that there must be a passage of air through the perforation in order that breath-sounds may be heard, but this opinion is no longer held. If air enter and leave the lung at all, as it may do in parts where adhesions have prevented complete collapse, breath-sounds of the quality referred to, although distant and feebly conducted to the ear of the observer, may often be heard, even through the pneumothorax.

The amphoric breath-sound, when present, is most likely to be easily detected just over the site of perforation. Voice- and cough-sounds have

a metallic ring in cases in which the opening into the pleural cavity is free; and, in connexion with the cough especially, the phenomenon known by the name of "metallic tinkling" is often well heard. It is not due, as was thought by Laennec, to drops of fluid falling into the air-filled cavity; but it may be produced by various adventitious sounds having their origin in the lung. In a case seen by Sir Clifford Allbutt in a healthy, athletic young man of some twenty years of age, the air escaped into the pleural cavity with a succession of tinkles or clicks. These were audible in all parts of the large room, and continued until the family medical attendant arrived, probably two hours, so that he also heard them plainly. The sounds were thought to be due to a rupture of a tiny bubble at each issue of air. Their frequency varied, they came much faster at first and grew rarer. Inspiration, at any rate at first, increased the number and loudness of the tinkles. The rupture was brought about by an attempt to bend the body backwards so as, if possible, to touch the ground with the hands without removing the toes from a line. The patient, whose pneumothorax was considerable, soon recovered and has remained well.

Finally, there is the succussion-sound, often associated with the name of Hippocrates, because it was first described by him. To elicit it, the patient, preferably sitting up, is sharply jolted or shaken, while the observer has his ear applied to the chest; or, if not acutely ill, the patient may be made to shake himself so as to bring out the sound. It is caused by the splashing of the liquid effusion in the cavity containing also air, just as it would be produced in a cask having similar contents; and it is of the metallic ringing quality which characterises all the adventitious sounds of pneumothorax. The patient himself may be conscious of the presence of fluid in his chest, while under examination he may both hear and feel the splashing of the fluid. In cases of suspected left-sided pneumothorax care must be taken not to regard succussion produced in the stomach as evidence of air and fluid in the thorax.

Skiagraphy shews the affected side to be abnormally light (*vide* Figs. 30, 31, Vol. I. pp. 502, 503); the surface of the fluid in a pyopneumothorax may be seen to move, and the displacement of the diaphragm and the heart are very clearly shewn.

Diagnosis.—As many of the phenomena accompanying the majority of cases of pneumothorax are of a definite and striking character, the diagnosis, generally speaking, is not a matter of much difficulty. The essential points are: over-resonance; absence or great enfeeblement of breath-sounds (these, if present at all, being of amphoric quality); displacement of the heart, and the bell-sound. These are perhaps more than enough for diagnosis; and they are necessarily strengthened if we have a history of sudden attack of pain in the chest with dyspnoea. The only class of cases at all likely to give rise to doubt are those in which the pneumothorax is partial, and limited by old adhesions between the pleural layers.

From emphysema, which in some points may seem to resemble pneumothorax, the distinction is easily made by the rule that emphysema

is bilateral, and that in it there is no lateral displacement of the heart and no bell-sound; also, that the resonance of emphysematous lung is not so tympanitic as is usual in pneumothorax. It must be admitted, however, that rare instances occur in which the distinction is a fair point for discussion. I can recall two such cases.

From a large pulmonary vomica pneumothorax is distinguished by the absence of the bell-sound, a duller quality of resonance, even where the conditions of the cavity are most favourable for confusion of diagnosis, and the absence of displacement of the heart; or, at any rate, if the heart be displaced, it is towards the affected side, and is due to contraction of the lung. The side of the chest affected would also be rather retracted than distended. Metallic tinkling and amphoric breath-sounds may, of course, both be obtained in cases of cavity; and, indeed, even the succussion-sound, if the cavity be large and contain a quantity of liquid.

Cases of gaseous subphrenic abscess are often erroneously regarded as ordinary pneumothorax, but the converse mistake is rare. All the physical signs met with in pneumothorax may occur in a subphrenic pyopneumothorax, but in the latter the hyper-resonance never extends to the extreme apex of the lungs. Skiagraphy, by shewing the position of the diaphragm, depressed in pneumothorax or pushed up in a gaseous subphrenic abscess, gives valuable information. The diagnosis between these conditions is considered in detail in the article on "Gas-containing Subphrenic Abscess" in Vol. III. p. 1005.

Resonance and breath-sounds somewhat resembling those of pneumothorax are occasionally found at the apex of the lung in cases of pleural effusion; and sometimes over part of a lung consolidated by pneumonia. The site of the physical signs here, and a careful estimation of the condition generally, will probably prevent any mistake in such cases.

A few other rare conditions, such as hernia of a part of the stomach, or colon, through the diaphragm, have simulated pneumothorax: such an accident is usually the result of injury, and it can generally be distinguished without much trouble.

Should there be any difficulty in deciding on the causation of a case of pneumothorax, the withdrawal of a few drops of fluid from the pleural cavity, if such be present, and its examination for tubercle bacilli may be of material help. This was done in a case under my own care, and it furnished positive results (9). Careful attention to the physical signs and symptoms of the case will probably enable the physician to arrive at the correct conclusion as to the nature of the perforation in the lung, which is important from the point of view of treatment.

Prognosis.—The prospects in a case of pneumothorax depend chiefly on its cause. In the simple and traumatic class of cases the opening soon becomes sealed by inflammatory exudation and the air is absorbed. In all the other varieties prognosis must be guided practically by the underlying disease. The tuberculous cases, which, as we have seen, form a large majority, end for the most part unfavourably, and that at no distant

date. The shock and intensity of the early symptoms may even cut life short in a few hours. At the same time, much depends upon the condition of the opposite lung, as well as upon the presence of adhesions limiting the extent of the pneumothorax in that which has become perforated. Although it may seem paradoxical to say so, patients who, before the occurrence of the pneumothorax, had been in comparatively sound condition are, so far as the pneumothorax is concerned, in greater danger than those whose affected lung has been much crippled by disease; and this is chiefly due to the fact that in the latter case the system has gradually adapted itself so far to its changed conditions as to tolerate an amount of interference with normal function which would excite much greater disturbance if it fell upon the patient with all its force suddenly. The same thing is seen in cases of ordinary pleuritic effusion. If this occur very slowly, the physical signs may indicate that one side is practically full of fluid, and no respiratory distress, apart from exertion, may be complained of; whilst a second case in which half the quantity of fluid is present may be characterised by great dyspnoea if the accumulation have been rapid.

Both clinical and pathological experience go to shew that even in tuberculous cases of pneumothorax rare cures have taken place; but in the great majority the outlook is a very dismal and discouraging one. According to Dr. S. West (30), the general mortality is about 70 per cent.

Treatment.—In most cases this can only be palliative and symptomatic. So far as drugs are concerned, opiates and stimulants comprise practically all the medicines likely to be useful. Morphine, either by the mouth or subcutaneously, is perhaps the best of the former class; alcohol in some form of the latter, but its effects may be helped by ether and ammonia. The opiate acts beneficially by relieving pain, checking the cough, and diminishing the discomfort of the patient generally, especially that resulting from the dyspnoea; and the stimulants are called for both to counteract the collapse first occurring, and to help the heart to carry on its work in which it is handicapped both by the alteration in its position and the obstruction of the circulation through the compressed lung tissue. Some external applications are useful. Dry cupping may be recommended if the dyspnoea and cyanosis be great; and where pain, resulting from the accompanying pleurisy, is much complained of, the application of two or three leeches and hot fomentations are likely to give relief. Subsequently strapping the side may be thought of.

Sooner or later the question of paracentesis will, in most cases, have to be considered. If there be evidence that the pressure within the thorax is considerable, we have practically no choice; especially if, owing to the valvular character of the perforation, this pressure be increasing. A fine trocar should be used, but no aspiration. The danger, of course, is that the diminution of the intrathoracic pressure may encourage the reopening of the perforation which may have been closed by lymph, a condition on which our hopes for a cure of the pneumothorax depend; but it is better to run this risk than to allow the patient to die from asphyxia and

exhaustion. If the opening should not have closed, the passage of the trocar will at least do no harm, and it will enable the presence or absence of intrapleural pressure to be demonstrated. After puncture, strapping of the affected side, in order so far to prevent the recurrence of distension, may be employed in some cases with advantage. The only danger which attends puncture is that subcutaneous emphysema, partial or general, may spread from the seat of it; but this rarely happens, and all risk may be practically abolished by keeping up a little pressure on the wound after the puncturing instrument has been withdrawn.

In any case when there is evidence that the pleural cavity is partly occupied with liquid, it is wise to explore from time to time to ascertain the nature of the liquid. If serous, the general condition of the patient will be no worse than if air alone were present; probably indeed better, as the pressure exerted on the lung may tend to check the progress of disease in it, and will promote the effectual sealing up of the perforation. If the liquid be fetid pus, nothing but harm can come from letting it remain in the pleura, and it ought to be freely evacuated at once. But there is an intermediate class of cases in which the fluid is purulent, not fetid; and it is more difficult to decide what should be done here, and when. In such a case, if the pneumothorax have resulted from the rupture of an empyema into the lung, the chest should be freely opened and drained; and the same would hold good if the empyema had ruptured through the chest wall, the opening which nature makes not being, as a rule, sufficient for free drainage. And even in the case of pyopneumothorax of tuberculous origin, a consideration of general principles dictates the free evacuation of the pus, and resection of ribs if necessary, the case being thus converted into an empyema with some chance of the perforation in the lung being closed, followed by slight re-expansion of lung and possible obliteration of the pleural cavity. It is true that tuberculous patients in whom this is done rarely recover; this, however, is not because of the removal of the pus, but of the progress of the disease which produced it. On general grounds it is something of an opprobrium to allow a patient to die with a large quantity of pus in the chest.

The diet should be light and nutritious, and the bowels must not be allowed to become constipated. The treatment does not differ otherwise from that of uncomplicated pulmonary tuberculosis.

The question of *prophylaxis* is a more difficult one, and has reference, of course, almost solely to tuberculous cases. In them, as has been pointed out by the late Dr. H. Thompson, there may be a warning of coming danger. He believed that a hint of impending perforation may be found in a persistent and prolonged decubitus on one side, on account of pain and cough when lying on the other side is attempted; and that such a condition suggests the presence of cavities underneath a part of the pleura unprotected by adhesions; for with adhesions there would be no such severe and continuous pain. In such circumstances strapping of the side is more than ever advisable; medicines should be administered to keep down the cough, which in these cases is apt to be frequent and exhaust-

ing, as well as superfluous: this form of cough, says the author, "is imminently dangerous from the strain it puts upon the damaged lungs, and upon their frail investing membranes." Every physician must have seen cases which correspond exactly to his description.

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NEW GROWTHS OF THE PLEURA

By Frederick T. Roberts, M.D., F.R.C.P., and J. J. Perkins, M.B., F.R.C.P.

Non-malignant new growths of the pleura are very rare, and, since they do not give rise to definite clinical symptoms, are of pathological interest only.

Lipomas derived from the pleura have been met with, and are usually small; Fitz described an intrapleural lipoma the size of a new-born child's head, which arose from the mediastinum.

Malignant Disease.—**Morbid Anatomy and Histology.**—*Primary malignant disease* of the pleura is rare, *endothelioma*, believed to arise from the endothelium of the lymphatics, being the most common form; although the origin of primary malignant disease from the surface endothelium has generally been denied, its occurrence has been described (Coats, Benda). In a characteristic specimen (Bassoe, Dean) groups of polyhedral or cubical cells are seen under the microscope lying in spaces which are regarded as lymphatics. In longitudinal section these spaces with their living cells look like "cords"—a distinctive appearance of these growths. The cells vary greatly in form; in places they become cylindrical or columnar, and the lymph-channels then closely resemble gland tubules; giant cells are also very common. A characteristic feature of endothelioma is that the whole serous membrane is simultaneously implicated. In some instances the pleura is but little thickened, and the new growth forms a thin hard pellicle over the lung, more like chronic pleurisy than a tumour; the undulating or trabeculated surface thus produced recalls the inner wall of a hypertrophied bladder. In other cases there is an enormous fibrous thickening of the pleura from overgrowth of its original tissue; between the fibres are seen sparsely scattered the cord-like collections of the malignant cells. In a true endothelioma of the pleura the spread of the growth takes place by direct lymphatic extension, the bronchial glands, the serous coverings of the diaphragm, the capsule of the liver, the peritoneum and omentum being chiefly affected. Scagliosi has collected 14 cases of endothelioma of the pleura—11 in men, 3 in women. Of these, 10 occurred between the ages of forty and fifty, 1 between thirty and forty, 1 between fifty and sixty, and 2 between sixty and seventy. Distant metastases are rare. From what has been said it is evident that it may be difficult in a given case of pleural new growth to distinguish an endothelioma from a true *carcinoma*, which has also been described (Bloch), especially when the histological character of the growth is that of glandular tubes lined with columnar cells. A further difficulty lies in the uncertainty of the exact origin of endothelium itself. In consequence Benda has been able to describe a malignant growth arising from the surface of the pleura as a carcinoma.

Sarcoma is very rare as a primary growth of the pleura; it appears that 10 cases have been recorded (Robbins); round- and spindle-celled sarcoma, myxo- (Busse), chondromyxo- (Kidd), and fibromyxo-sarcoma (Mehrdorff) have all been met with. Endothelioma, on account of its characteristic giant-cells, has been mistaken for a myeloid tumour.

Secondary malignant disease of the pleura is much commoner than primary growths. It often appears late, namely, long after the removal of the primary growth and without any recurrence at the original site. The pleura may be the site of secondary growths in carcinoma of the mamma; the primary growth extends by permeating the lymphatics into the subserous lymphatic plexuses of the pleura; carcinomatous cells then escape into the pleura, and by becoming implanted on the surface of the serous membrane give rise to discrete growths (Handley). In rare instances secondary growths may form a continuous layer over the pleura. The pleura may, of course, become invaded by a primary growth of the lung, bronchi, or mediastinum.

Anatomical Characters.—Malignant growths involving the pleura, whether primary or secondary, assume different forms. There may be a *general uniform infiltration*, greatly increasing the thickness of the membrane, and affecting in some cases almost exclusively the parietal pleura, sparing the bones and muscles, but invading and thickening the mediastinal tissues with a hard growth. Another variety is the *tuberiform*, in which enormous masses project from the surface into the pleural sac, and may become so pedunculated as to lose all apparent connexion with the lung, hanging like grapes from the pleura, to which they may be attached by a narrow pedicle. In other instances scattered *nodules* are found on both the visceral and parietal membrane; or both nodules and infiltration may be present together. Cancer is described as usually in the form of small flattened or rounded elevations, rich in blood-vessels. Prolongations from the pleura into the interior of the lung may or may not take place. The growth is likely to extend into the interlobar pleura, binding the lobes of the lung together. The diaphragmatic pleura may be invaded, along with the costal. Pleural effusion is said to be common, and not infrequently haemorrhagic, or it may be purulent or putrid; but, on the other hand, the sac may be entirely obliterated by dense adhesions and thickening. In one of Harris's cases very great difficulty was experienced in removing the lung from the body, the growth having to be cut away from the chest wall, and the diaphragm removed with the lung and the growth. The organ was completely encapsuled by a mass of very firm, hard, white new growth, with trabeculae like bands of fibrous tissue, which varied in thickness from half an inch to two inches, being thickest over the diaphragm. The interlobar pleura was also invaded by the new growth and everywhere thickened. The pleural cavity was practically obliterated. The lung was compressed, but still contained air; and there was no infiltration or extension into the organ. The microscopical appearances were those of a primary cylindrical-celled endothelioma of the pleura. In Harris's second case the left pleural cavity was entirely

obliterated, and the lung firmly adherent. The pleura was found everywhere thickened by a fine white new growth, which not only encased the lung but also extended into that organ from the hilum along the bronchi, and by delicate bands from various parts over its surface. The lymphatic glands in the hilum and mediastinum were likewise involved. The thickening generally ranged from one-eighth to a quarter of an inch. The growth presented on microscopical examination all the features of a squamous-celled carcinoma.

A subpleural sarcoma may simply cause pressure effects, crushing the organs aside without invading them to any great extent. This is explained by the fact that it is prone to present itself as a single rounded mass, with a very considerable fibrous basis.

Clinical History and Diagnosis.—It is impossible to give a systematic account of the clinical features of malignant disease of the pleura, and it must suffice to draw attention to the more important practical points bearing upon the diagnosis of this condition. It may be stated generally that this is founded mainly on physical signs rather than symptoms; and when these indicate the existence of chronic pleuritic changes, the nature of which is not clear, it is always well to be alive to the possibility that the case is one of malignant disease of the pleura. Often there is nothing for a long while to distinguish malignant disease of the pleura from a simple or non-malignant pleurisy. Cachexia is not so frequent in thoracic new growths as in abdominal, and may be completely absent; there may be no pain. Malignant disease of the pleura has even been known to start, or rather make its presence known, abruptly by a chill; fever is not uncommon (Jackson). More frequently the onset is insidious, and attention is first called by the dyspnoea due to a large effusion. The fluid may be haemorrhagic, but again it may be clear, and suspicion is then only excited by its rapid reaccumulation after tapping, associated perhaps with disproportionate dyspnoea and increasing cachexia. Implication of the pleura by extension from the lung or mediastinum will probably give more pronounced and superficial signs of dense consolidation, with marked sense of resistance on pressure and percussion; and the growth may ultimately extend through the chest walls to the surface. When a malignant growth starts primarily in the pleura, it usually comes under observation as a case of chronic pleurisy, often with little or no effusion, or there may be an obvious collection of fluid, even displacing organs. At first, however, there may be no particular signs to attract attention. Severe superficial pain is one of the most suggestive symptoms, perhaps with tenderness; whilst the breathing tends to become more or less disturbed; and cough may supervene, either dry or without any characteristic expectoration. For a long time there is often little or no fever; and should an apyrexial condition be associated with progressive and rapid wasting and unaccountable weakness, in a case with prominent pleuritic signs, malignant disease should be suspected.

It is hardly necessary to describe in detail the physical signs which may be present. They are those characteristic of chronic pleuritic condi-

tions, often a combination of fluid, thick adhesions, and solid material; and it may be very difficult or impossible to differentiate them. In other cases there are no signs of effusion, and the prominent feature is loud, rough, and persistent friction-sound, perhaps accompanied with friction-fremitus. Unusual localisation and distribution of dulness may be suggestive; and a marked sense of firmness and resistance is decidedly helpful in diagnosis. Of course, the use of the exploring needle is in doubtful cases essential. The removal of haemorrhagic effusion, especially if deficient in fibrin, is in favour of cancer of the pleura; and microscopical examination of the cells (cyto-diagnosis) found in the fluid may be a great help in diagnosis, for in many cases, it is not too much to say, they are typically malignant. Characteristic points are the size, much larger than that of the endothelial cells of the pleura, and the irregularity in shape. The protoplasm contains many vacuoles and the curious cell-inclusions which have been called "cancer-bodies"; glycogen can also be demonstrated by staining with iodine. Especially striking is the immense nucleus which usually contains one or more nucleoli (Labbé, Delille, and Aquinet; Erben, Régis). On the other hand, should there be no effusion the needle is felt to be arrested by solid material, and this sensation gives valuable information. Possibly a portion of a growth might be brought away and utilised for examination. If removal of a considerable effusion gives no relief, this is another point in favour of malignant disease.

One of Harris's cases of malignant disease of the pleura illustrates a possible fallacy deserving of notice. In using an exploring syringe he happened to hit upon a very small cavity in the pleura, and withdrew a syringeful of perfectly clear pale-yellow fluid. He took the case to be one of chronic pleurisy with much effusion, but only about an ounce could subsequently be obtained, and the necropsy revealed that the pleural space was entirely obliterated except at the point where the needle was introduced.

In difficult and obscure cases of malignant disease of the pleura, the progress of events usually clears up the diagnosis sooner or later. Thus, there may be definite indications of implication of the lung or mediastinum; or of growth in remote structures. It is always important to watch for enlargement of glands, especially the tracheo-bronchial beneath the sternum, or in the interscapular region, and those in the supra-clavicular fossa.

Prognosis.—Malignant disease of the pleura is absolutely hopeless. The complaint is essentially chronic, but its duration varies according to circumstances, and no definite opinion should be offered on this point in any individual case.

Treatment.—Nothing can be done directly for any growth of a malignant nature invading the pleura, and any attempt at its removal by operative measures would be worse than useless. It is particularly necessary to warn against using strong and irritating applications to the chest, once the nature of the disease is recognised; or to carry out any other

method of treatment which can only cause suffering or annoyance to the patient. Paracentesis may certainly be useful when fluid collects in the pleura, and should be repeated for the purpose of prolonging life, or affording temporary relief. Reaccumulation of fluid, the frequent removal of which when rich in blood is a great drain on the patient's strength, has been prevented in several cases by the injection of sterilised air at the time of the tapping; the injection in a similar manner of a dram or so of a solution of adrenalin chloride (1 in 1000) has also been recommended for this purpose. Symptoms may require attention; the patient should be well fed and made as comfortable as possible; and the functions duly regulated.

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DISEASES OF THE MEDIASTINUM AND THYMUS

DISEASES OF THE MEDIASTINUM

MEDIASTINAL NEW GROWTHS

DISEASES OF THE THYMUS

DISEASES OF THE MEDIASTINUM

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General Anatomy.—It is desirable in the introduction to this article to refer briefly to the normal anatomical relations of the region known as the mediastinum. Under this name is included the median space within the thoracic cavity which lies between the lungs, and is bounded on each side by the reflexions of the pleurae passing from the front to the back of this cavity. It has been arbitrarily subdivided—usually into three portions, namely, *anterior*, in front of the pericardium; *middle*, which is occupied mainly by the heart enclosed in the pericardial sac; and *posterior*, limited by the posterior aspect of this sac and roots of the lungs anteriorly, and the spinal column behind. Some anatomists recognise further a *superior* division, extending from the upper opening of the chest to about the level of the upper end of the pericardium and the roots of the lungs. It is hardly necessary to describe in detail the several structures contained in each division of the mediastinum; it will suffice to state that, setting aside the heart and pericardium, the important contents of the space to be borne in mind from a pathological point of view are the thymus gland or its remains in the anterior division; the arch of the aorta and its descending portion, with the innominate and commencement of the left carotid and subclavian arteries; the superior vena cava, innominate, and azygos veins, and the termination of the inferior vena cava within the pericardium before it enters the right auricle; the pulmonary vessels; the trachea and its bifurcation, with the main bronchial divisions; the pneumogastric nerves, with the left recurrent laryngeal and cardiac branches, phrenic, and splanchnic nerves, and the cardiac plexuses; the roots of the lungs, including the pulmonary vessels and bronchi with their primary branches, and the anterior and posterior pulmonary plexuses; the oesophagus; the thoracic duct; and the lymphatic glands and vessels. The loose cellular tissue which is also present in the mediastinum must not be forgotten. With regard to nerves, although the sympathetic trunk is not exactly within the mediastinum, it certainly may be implicated in diseases of this region; and the same remark applies to the right recurrent laryngeal, which originates higher up than the left, about the level of the root of the neck. The lymphatic glands within the thorax have been differently

grouped, but the following arrangement answers well for practical purposes, namely :—(i.) *Anterior mediastinal* or *sternal*, lying in the loose cellular tissue between the sternum and pericardium ; (ii.) *Superior mediastinal* or *cardiac*, in front of the upper part of the pericardium, the arch of the aorta, and the left innominate vein ; (iii.) *Posterior mediastinal*, along the course of the aorta and oesophagus ; (iv.) *Bronchial*, which are situated in front of and behind the bifurcation of the trachea, along the main bronchi, and in the angles of their chief branches at the roots of the lungs.

It requires but little consideration to realise the difficulty of determining what should be included under diseases of the mediastinum, and any arrangement adopted must be a somewhat arbitrary one, modified by the views of the individual writer. The affections of the principal contents of this region just enumerated are discussed, in their appropriate connexions, in other parts of this work; and it is entirely beyond the province of the present article to deal with them, except incidentally.

Whilst thus avoiding, as far as possible, any trespass on the domain of other articles in this work, it must be clearly recognised that in a considerable proportion of the cases which come within the category of mediastinal diseases, the morbid conditions either originate in, or sooner or later (and often at an early period) implicate in some way one or more of the important structures already referred to. Further, such affections as aneurysm necessarily encroach in various degrees upon the mediastinum, and in a sense might fairly be included amongst its diseases, especially as they often lead to secondary morbid changes in this region ; but custom has established that they shall not be so included, and they will therefore only be incidentally alluded to in this article.

Clinical Investigation.—Seeing that the clinical phenomena, upon which our recognition of the presence and nature of morbid conditions of the mediastinum is founded, are to a large extent due to the effects of these conditions upon the contents of this region, upon adjacent intrathoracic structures, and upon the walls of the chest, it will materially help in their general study, as well as in their clinical investigation in individual cases, to start with a definite and comprehensive knowledge of what these effects might be in various circumstances. They are of different kinds, and may be summed up in the following way :—(i.) Mere general encroachment on the thoracic space, interfering with the breathing capacity more especially, but not obviously affecting any one particular structure more than another. (ii.) Mechanical effects on individual structures ; namely, diffused compression, especially affecting the lung or heart ; local direct pressure, causing obstruction of hollow tubes and vessels, or irritation followed by paralysis of nerves ; stretching or traction ; and displacement, as the result of pressure or dragging. (iii.) Inflammatory changes, due to irritation or pressure. (iv.) Implication or invasion of structures in connexion with particular morbid processes, such as acute inflammation, fibrotic changes, or growths. (v.) Atrophy, degeneration, or actual destruction of tissues, leading to perforation of tubes or vessels, ulceration or gangrene, erosion of bones and cartilages,

removal of soft tissues, division of nerves, and other more or less serious lesions.

Summary of Clinical Phenomena and Methods of Investigation.—It may be assumed that any one who is acquainted with the anatomy and physiology of the thoracic contents, and who has duly studied the clinical investigation of this region, will have acquired a comprehensive knowledge of the symptoms which may result from interference with the more important individual structures, and will fairly understand the nature of the phenomena which are likely to be produced by the disturbances just indicated. For this and other reasons it is not intended to discuss this part of the subject in detail; but it may afford a clearer perception of its general clinical aspects, and at the same time save unnecessary repetition, to present a preliminary summary of the phenomena which have to be borne in mind, and to point out the course of investigation which it may be requisite to follow in dealing with particular cases of mediastinal disease. In the normal state we have no subjective consciousness of the existence of any of the structures which occupy this region; nor, with the exception of the heart, do they give any external indication of their presence. Their morbid conditions may be revealed by one or more of the following groups of clinical signs, to which attention will now be briefly directed. They may be arranged under the heads of:—I. Symptoms of local origin; II. General symptoms; III. Physical and special signs; IV. External manifestations.

I. *Symptoms of Local Origin.*—Under this head come all phenomena usually classed as symptoms, as distinguished from physical signs, which are directly due to the effects of the mediastinal disease upon the thoracic structures; and they always need careful study, for they are of the greatest importance in diagnosis. These symptoms are usually both subjective and objective; and they include not only the local disturbances commonly associated with chest affections, but also certain phenomena which may be observed in more or less remote parts of the body.

(*a*) Painful and other Morbid Sensations.—Different kinds of pain are often complained of in connexion with mediastinal affections, and this symptom is not uncommonly very pronounced. There may, however, be rather a sense of uneasiness, discomfort, irritation, tightness or oppression, weight, and the like, or of subjective heat, than actual pain. A painful sensation may be part of the disease itself, but generally results more from its effects upon adjoining structures. Hence it varies much as regards its site, extent, intensity, characters, and other particulars. Further, it may be constant, or occasionally intermittent, or prone to exacerbations. The most important forms of pain to be borne in mind are those due to direct interference with nerves, causing neuralgia or neuritis, when it is of shooting or lancinating type; to inflammatory changes, especially pleurisy; or to erosion of bones, the pain being then heavy, grinding, gnawing, or boring in character. Probably it is occasionally due to muscular cramp. It may be distinctly localised in the chest walls, and shoot along the course of one or more of the intercostal

nerves, or run up the neck; or more or less of the brachial plexus may be involved; so that painful or other sensations, such as tingling and numbness, are referred to the upper extremity, even to the fingers. In exceptional instances pain is felt in the abdomen or back in connexion with mediastinal disease. Local tenderness over more or less of the chest is often noticed; and occasionally there is remarkable superficial hyperaesthesia.

(*b*) Disorders of Respiration.—As might be expected, breathing is extremely apt to be affected by morbid conditions of the mediastinum; and the disturbances thus produced always demand special study and consideration in individual instances. To sum up all such disturbances indiscriminately under the term "dyspnoea" is specially wrong and misleading in this class of cases, for they present great variety; and as different kinds of respiratory disorder are often present even in the same case, it is of essential importance to understand their significance. The factors which may lead to such disorders are many, and not uncommonly several of them act together. Without entering into details, it must suffice to state that these factors are chiefly direct interference with, or implication of one or both lungs, diminishing their breathing capacity or power; obstruction of the trachea or a main bronchus; bronchitis; pleural or occasionally pericardial effusion; obstruction of the pulmonary vessels, either preventing a due supply of blood to the lungs, or causing pulmonary congestion and oedema; compression, displacement, or other kind of embarrassment of the heart; and implication of the vagus or recurrent laryngeal nerves, the pulmonary plexuses, or the phrenic nerves. In exceptional cases the movements of breathing are directly prevented or diminished by physical changes involving the chest wall or diaphragm, or by muscular paralysis. It would not serve any useful purpose to describe at length the several respiratory disorders which may be associated with mediastinal diseases, for, as a matter of fact, all varieties and degrees of such disorders are met with, from mere shortness of breath, or somewhat hurried breathing, to the most urgent and terrible orthopnoea, or even fatal apnoea; and it will be more practical to discuss this part of the subject in relation to the particular affections of this region. It may be pointed out, however, that the dyspnoea is often definitely obstructive in character, due to pressure on the trachea or a main bronchus; or is associated with muscular laryngeal disorder affecting the glottis, and resulting from nerve disturbance within the thorax. The breathing is not uncommonly noisy and stridulous, or accompanied by audible wheezing, and the sounds thus heard during the act may be highly significant. In many instances also the respiratory disorder is more or less paroxysmal; and in certain circumstances it may assume the characters of "spasmodic asthma." The subjective sensations accompanying the disturbances of breathing are not uncommonly pronounced, and may be very distressing; while the aspect of the patient reveals the effects of the interference with the respiratory function. Hiccup, due to irritation of the phrenic nerves, may be a prominent symptom.

(*c*) Cough; Expectoration; Haemoptysis.—Cough is another very common symptom in mediastinal diseases, but varies much in its severity. It is only, however, when it assumes certain peculiar characters that it becomes significant. It may be irritable and teasing, almost constant or paroxysmal, and either quite dry or attended with slight and difficult mucous expectoration. Pressure upon the trachea renders the cough peculiarly stridulous; or it may have the spasmodic and clanging, hoarse, husky, or aphonic character associated with different degrees of interference with the laryngeal nerves. Bronchitis is a very frequent factor in the causation of cough in mediastinal diseases.

Expectoration, when present, as a rule gives no positive information in relation to affections of the mediastinum. In most cases it is simply bronchitic. Should an abscess in this region open into the air-passage, a quantity of pus would probably be expectorated; or exceptionally the sputum may be fetid or gangrenous. In certain circumstances very careful examination of materials thus discharged occasionally reveals the presence of portions of morbid growths or other admixtures, which might be of great diagnostic significance. Special kinds of expectoration have been described; but these will be more conveniently noted in connexion with the particular diseases to which they belong. Haemoptysis, in various degrees and of different kinds, is not uncommon in connexion with mediastinal complaints; and the intimate admixture of blood with the sputa may give rise to peculiar appearances. Haemorrhage may be the first symptom, or may be repeated; it is occasionally so grave as to prove directly fatal.

(*d*) Alterations in Voice.—These are also important phenomena to be watched for and studied, as indicating direct interference with the trachea, or revealing implication of the vagus or laryngeal nerves in different degrees. Thus, there may be a peculiar reedy quality of voice; a change in pitch; more or less huskiness or hoarseness; or weakness to absolute aphonia. These symptoms present considerable variety in different cases, and may also change in the same case from time to time; intermitting aphonia is sometimes observed. It may be noted that pressure on the recurrent laryngeal nerve may not only lead to muscular disturbance affecting the glottis, but may also set up chronic changes in the larynx itself, such as laryngitis or ulceration, which naturally tend to aggravate the symptoms.

(*e*) Cardiac and Arterial Symptoms.—As a consequence of embarrassment of the heart in various ways, or of disturbance set up through the vagi nerves or cardiac plexuses, the action of this organ is liable to be affected. Thus the patient may be conscious of cardiac disorder, and complain of palpitation; and such disorder may be evident at once to the clinical observer. It may be paroxysmal. Occasionally the heart may be markedly slowed or quickened. Should either of the main arterial branches be obstructed—innominate, left carotid, or left subclavian—there will be corresponding changes in the carotid or radial pulse, or both, on the affected side; as evidenced by diminution of its

strength and fulness, or, it may be, even complete obliteration of the pulse.

(*f*) Symptoms of Deficient Blood-aeration and Venous Obstruction.—These are amongst the most common and striking evidences of morbid conditions occupying the mediastinum, and the phenomena resulting from venous obstruction often afford much information as to its situation, and as to the vein which happens to be interfered with. The difficulty is usually associated either with the superior vena cava, one or other innominate, or the azygos vein; and it may not only be due to pressure, but also to blocking of the channel by thrombosis or a growth. Only in very exceptional circumstances is the inferior vena cava obstructed. The symptoms are both objective and subjective, and those due to imperfect aeration of blood may be added to those consequent upon local venous stasis.

The objective symptoms are merely those which ordinarily result from venous obstruction, and consequent mechanical congestion, namely:—more or less change of colour in the direction of lividity or cyanosis; swelling, chiefly from oedema, which may be soft, or of a firm and brawny character; increased visibility, dilatation, tortuosity, and varicosity of the superficial veins, venules, and capillaries; and possibly haemorrhage from rupture of vessels. Their significance lies in the localisation and distribution of the phenomena, and often in their intensity; though their absolute and relative degree is subject to much variety. They are also likely to be increased by any exertion, and in the stooping posture. When the superior vena cava is affected, the whole head, face, ears, neck, both arms, and the chest present these appearances, contrasting remarkably with the lower half of the body. The aspect of the patient is very striking, and the condition can hardly be mistaken for anything else. Not only are the features discoloured, bloated and swollen, but the eyes may be prominent and staring, as if starting from their sockets, and the conjunctivae injected, suffused, or oedematous; exceptionally distinct exophthalmos may be noticed. On examination it may be found that the tongue and throat are similarly affected. In well-marked cases there is a distressing appearance of semi-strangulation, with a very anxious expression. The neck is obviously enlarged and tumid-looking, and has in some instances a peculiar spongy or elastic feel. In certain cases the swelling may be partly due to dilatation of the subcutaneous veins above the clavicles. The vascular phenomena are chiefly seen over the thorax, involving especially the mammary and superior epigastric veins. The intercostal veins and the subcutaneous veins near the spine may also be dilated, which is suggestive of occlusion of the vena azygos. Those of the arms may be much enlarged. It is stated that enlargement of the superficial veins is sometimes obviated by the formation of deeper-seated anastomoses returning the blood by the iliac veins. When either innominate or one of the subclavian veins is implicated alone, the resulting phenomena are correspondingly limited and unilateral. Cases have been noted in which pressure on these veins by mediastinal conditions has

been followed by venous distension on the opposite side. In some instances the obstruction is at first unilateral, and afterwards becomes bilateral. The chief form of haemorrhage likely to occur is epistaxis; but it may also take place under the conjunctiva, or into the cerebral meninges. In the very exceptional cases in which obstruction of the inferior vena cava is caused by mediastinal disease, the chief consequences are oedema of the legs and abdominal walls, ascites, albuminuria, and enlargement of the superficial veins, especially over the abdomen.

The subjective symptoms to be noted in this connexion are chiefly associated with the brain, being indicative of cerebral congestion, namely:—headache, vertigo, tinnitus or deafness, visual disturbances, and somnolence, which sometimes passes into temporary attacks of stupor or unconsciousness; these may be brought on by exertion or stooping. Epileptiform seizures have been noted occasionally. It is believed that spinal symptoms may result from obstruction of the vena azygos, in the form of sensory and motor disturbances affecting the limbs and lower part of the body.

(*g*) Disorders of Deglutition.—More or less dysphagia is not uncommon in certain forms of mediastinal disease. It may be of different kinds, and attended with pain or other unpleasant sensations associated with the attempts at swallowing. It is sometimes influenced by posture. The difficulty of deglutition is naturally likely to be prominent when the disease starts in or implicates the oesophagus; but it may also result from pressure upon this tube, diffused or localised; or from nervous disturbance, being then of reflex origin, when the dysphagia is sometimes intermittent.

(*h*) Special Nerve-Symptoms.—Pressure upon the brachial plexus not only causes sensory disturbances in the arm, but may lead ultimately to paralysis and muscular atrophy. As the result of different degrees of interference with the sympathetic trunk, contraction of the pupil or, more rarely, dilatation is observed on the affected side; and the temperature and nutrition of the same side of the face and head are exceptionally affected, as results of vasomotor influence.

(*i*) Spinal Symptoms.—In extremely rare instances a morbid condition starting in the posterior mediastinum makes its way through the vertebral column, and affects the spinal meninges, or ultimately even the cord itself. The symptoms are first those of irritation of this structure, and of the spinal nerves corresponding to the seat of mischief; followed by evidences of inflammatory or destructive changes, which may end in complete paraplegia. I can vouch for the possibility of these occurrences.

(*k*) Subcutaneous Emphysema.—As a symptom, accumulation of air in the subcutaneous tissue of the neck and chest, or even spreading more widely, may be an indication of a similar condition in the mediastinal cellular tissue, as the result of some perforative lesion in this locality, injury, or other causes.

II. *General Symptoms.*—But little need be said under this head at present, as the general symptoms in mediastinal cases must necessarily

depend very much on the nature of the individual disease, and they can be more conveniently discussed in that relationship. They are referred to here mainly to emphasise the necessity of duly considering them in the investigation of these complaints. There is one symptom, however, belonging to this category which needs particular notice and attention, as it may be the direct result of certain mediastinal affections, and sometimes reaches an extreme degree, namely, wasting. This condition is especially likely to follow any oesophageal obstruction interfering with the taking of food. It is also believed to be produced by closure of the thoracic duct, preventing the passage of the chyle and lymph into the circulation; the supposition is a reasonable one, but a doubt has been expressed whether the connexion has ever been actually demonstrated. It may be noted as a remarkable fact that in some cases of grave mediastinal disease the general system suffers in but a very slight degree, and this fact may be of diagnostic significance.

III. *Physical and Special Signs.*—The systematic study of mediastinal disease by the ordinary methods of physical examination, and in other ways, is obviously of the highest importance in its clinical investigation, and, indeed, is indispensable in every case. In many instances the phenomena thus revealed are quite pathognomonic, and indicate at once the nature of the morbid condition. The fact must be recognised, however, that there is no class of chest cases which presents greater difficulties in their physical diagnosis, and the examination should therefore always be conducted with the utmost care and thoroughness. Indeed, it not uncommonly happens that the knowledge and skill of the most experienced clinical observers are severely taxed, and the aid of expert specialists is often essential for the complete clinical investigation of these cases.

The details of this part of the subject can only be satisfactorily discussed in relation to the several mediastinal diseases, and at present it will be sufficient to point out the general course of procedure which may be called for in different circumstances.

(*a*) Physical examination of the chest according to the usual methods naturally comes first, and often reveals all that it is necessary to know. The signs to be looked for in relation to mediastinal diseases are:—(i.) Those of the morbid condition itself, such as a solid growth. (ii.) Those of its effects upon neighbouring structures, the most important being displacement of organs, especially of the heart; and various degrees of collapse, distension, congestion and oedema, consolidation, or actual destruction of one or both lungs. (iii.) Those of serous effusion; pleural in the large majority of cases, rarely pericardial. These conditions are not uncommonly mixed up in various ways and degrees, and consequently the physical signs are sometimes exceedingly complicated and difficult to describe or explain.

(*b*) The sputum has already been referred to, as a mere symptom; but in the present connexion it is important to point out that a more thorough and systematic examination of any materials expectorated, by the aid of the microscope and the more modern scientific methods of investigation,

sometimes affords valuable help in the diagnosis of mediastinal diseases, and may give very definite information as to their nature.

(*c*) It is also worth while in certain cases to pay special attention to the arteries and veins which may be affected by morbid conditions in the mediastinum, and to study them by particular methods. Thus, the sphygmograph may be of service in the examination of the arteries; whilst the effects of cough and respiratory movements upon the veins may also be of much significance.

(*d*) The methodical examination of the main air-tube, especially with the aid of the laryngoscope, should always be carried out in cases of suspected mediastinal affections; and the signs thus recognised are in not a few cases most instructive. It may be necessary to investigate not only the larynx and vocal cords, but also the trachea, bronchi, and oesophagus (*vide* art. "Direct Laryngoscopy, Tracheoscopy, Bronchoscopy, Oesophagoscopy," Vol. IV. Part II. p. 299).

(*e*) For particular purposes, and especially in obscure and difficult cases, the use of the exploratory trocar or aspirator may be of conspicuous service in the diagnosis of mediastinal affections. At the same time, this method of investigation must not be adopted rashly or needlessly, but should always be carried out on rational and intelligent principles.

(*f*) Skiagraphy is of great use in the diagnosis of some cases of mediastinal disease (*vide* Vol. I. p. 509).

IV. *External Manifestations.*—Under this head it will suffice to state that certain morbid conditions starting in the mediastinum may make their way outwards through the chest wall, sometimes involving or even perforating the subcutaneous cellular tissue and skin; thus their nature may be clearly revealed to sight and touch. It should further be noted that the appearance of enlarged glands in the neck or axilla may be of special significance in the diagnosis of certain of these conditions.

Special Mediastinal Diseases

The preceding general discussion of the mediastinum and its clinical investigation will, it is hoped, have prepared the way for the consideration of the individual morbid conditions affecting this region; these will now be dealt with in the following order:—I. Abnormal mediastinal contents. II. Acute simple mediastinitis and oedema. III. Suppurative and gangrenous mediastinitis—Mediastinal abscess. IV. Chronic indurative mediastinitis. V. Tuberculous disease of the mediastinal lymphatic glands and of the thoracic duct. VI. Mediastinal emphysema. VII. Mediastinal new growths (p. 623).

I. Abnormal Mediastinal Contents.—There is a definite class of cases, of extremely exceptional occurrence, and as a rule most difficult to recognise clinically, which nevertheless demands brief notice, namely,

those in which certain structures, which ought not to be there, have gained access into the mediastinum. Such an event happens practically only in cases of diaphragmatic hernia, either congenital or acquired from injury or other causes, when one or more of the abdominal contents find their way into the chest, usually on the left side. The stomach is the organ most frequently thus displaced; then come in order the colon (almost as frequently), spleen, small intestines, liver, duodenum, pancreas, caecum, and extremely rarely the left kidney. Usually the hernia is into the left pleura, but it may occupy the anterior or posterior mediastinum (*vide* also Vol. III. p. 782). The left half of the chest has been found filled with coils of intestine as high as the second rib. The most prominent secondary effects of diaphragmatic hernia are displacement of the heart, and compression of the lung, but the oesophagus has also been seriously interfered with.

Clinical Signs and Diagnosis.—Congenital diaphragmatic hernia has usually been found on dissection of a fetus or stillborn child; or death occurs very soon after birth. Exceptionally life may be prolonged for some years; and it is affirmed that individuals born with this condition have lived even to old age. Cases have also been recorded in which a hernia into the thorax had not caused any symptoms to attract attention; but as a rule some disturbances are produced. In any circumstances the diagnosis must be extremely difficult and uncertain; and it is only practicable to point out generally the data upon which such a diagnosis might possibly be made. A knowledge or history of certain injuries, or a strain likely to affect the diaphragm, might be of some value. The actual occurrence of the hernia has sometimes caused almost immediate or very rapid death, from shock and compression of the lung; or has been attended with the phenomena of an acute internal strangulation. Usually there are more or less urgent or grave chest symptoms, especially dyspnoea; and among other symptoms which have been noted are a feeling as if something had given way, sudden pain, a sense of oppression, cough, cardiac disturbance, faintness or signs of shock, and inability to lie on the sound side. Therefore, when such symptoms occur suddenly, and cannot be explained, the possibility of diaphragmatic hernia should be borne in mind. The next group of phenomena deserving attention is that associated with the displaced organs, of which nausea and vomiting are often very pronounced; and enormous quantities of dark-coloured mucus or yeasty fetid fluid may be brought up. In the majority of chronic and established cases, in addition to more or less thoracic symptoms, those associated with the alimentary canal have been prominent; and they have usually been attributed to dyspepsia, including chiefly various painful or other sensations, aversion to food, thirst, flatulence, eructations, regurgitation of mucus, heartburn, colic, and obstinate constipation which may alternate with diarrhoea. The troubles are generally worse after meals and exertion; but in some instances a heavy meal has given relief. Exceptionally the patient has felt conscious that the food has not gone to the right place. More or less general

wasting is observed; and emaciation may be rapid and extreme. The symptoms may simulate those of cancer of the stomach, of which I have met with a striking example in an old woman. Death has occurred from compression of the oesophagus, and consequent complete dysphagia.

Physical examination may afford some aid in the diagnosis of the presence of abnormal contents in the mediastinum. The signs to be chiefly looked for are depression or hollowness of the abdomen, indicating displacement of some of its contents; fulness and impaired movement of the affected side of the chest, with abnormal percussion and auscultatory signs in connexion with the lung; tympanitic resonance or gurgling sounds over the same region, due to the stomach or intestines; and marked displacement of the heart towards the right. Such displacement has been mistaken for ectopia cordis. The *x*-rays help in the diagnosis (*vide* Vol. III. p. 784).

Treatment, in the large majority of cases of mediastinal hernia, must be mainly symptomatic, and no definite rules can be laid down. How far operative interference may be justified, and what particular procedure should be adopted, are questions which can only be decided in relation to individual cases, and they belong to the province of modern surgery.

II. Acute Simple Mediastinitis and Oedema. — It cannot be doubted that in certain circumstances an acute inflammatory process affecting the mediastinal cellular tissue occurs, which does not go on to suppuration, but either subsides and undergoes resolution without leaving any ill effects, or lays the foundation for permanent changes, such as will be described under chronic mediastinitis, by which the existence of the previous disease is revealed. Several supposed cases of this kind have been recorded from time to time, and attributed to injury and other very doubtful causes. From a practical point of view it is far more important to note that this condition is not infrequently associated with other acute intrathoracic inflammatory diseases, especially pericarditis and pleurisy, resulting either from the same cause or from extension; and the possible combination should be duly borne in mind. Local mediastinitis might also be produced by some neighbouring irritation; for example, in connexion with periostitis or bone disease, or a tumour.

Mediastinitis of the kind now under consideration would be characterised by increased vascularity, and by the presence of more or less serous fluid or fibrinous exudation in the cellular tissue. Probably the lymphatic glands are sometimes involved. Local mediastinal oedema may possibly occur apart from actual inflammation, or it may be a part of general dropsy. Should the lymph become organised, more or less thickening would remain, with adhesion of the pericardium or pleura to the chest wall and to each other. *Clinically* this complaint can only be recognised when it affects the anterior mediastinum, and even then a positive diagnosis can hardly be made with certainty. It might be suspected from the intensity and superficialness of post-sternal pain,

with tenderness; but the only positive sign is the presence of a "mediastinal crepitation," or a quasi-friction sound, elicited by deep respiration, or possibly of cardiac rhythm. I am convinced that such phenomena are sometimes the result of an acute mediastinitis. If the case is not fatal they subside after a time, and subsequently those indicative of chronic mediastinitis may supervene. No special *treatment* is required for this affection, which must be dealt with on general principles.

III. Suppurative and Gangrenous Mediastinitis—Mediastinal Abscess.—Suppuration and gangrene involving the mediastinal structures must be considered together, as in individual cases there is no definite line of demarcation between them. Mediastinal suppuration, usually terminating in an abscess, and occurring either as an acute or chronic condition, should not be forgotten in relation to chest affections, although it is very rare. Gangrene is extremely exceptional, and is only met with in special circumstances, being the result of an acute septic or putrid inflammation of some of the lymphatic glands, ending in sloughing, and involving the mediastinal cellular tissue in the destructive process. Suppuration also frequently starts in the glands; but it may begin in the cellular tissue; and abscesses originating in the thymus body may likewise become mediastinal. The suppurative and gangrenous changes are of course directly set up by the micro-organisms which usually originate these processes.

Etiology.—Mediastinal suppuration is on the whole most commonly associated with tuberculous disease of the lymphatic glands, which is separately considered (p. 617). Apart from this group of cases it may occur in the following circumstances:—(i.) From injury. Abscess in the mediastinum has been attributed to a blow on the chest; and suppuration may certainly result from wounds, though it appears to be exceptional as the result of gun-shot wounds. In this category may be included cases originating from injury by foreign bodies, such as artificial teeth and coins, producing ulceration of the oesophagus (*vide* art. "Foreign Bodies in the Air- and Upper Food-Passages," Vol. IV. Part II. p. 325); such injury generally leads to gangrene. (ii.) Secondary to disease of bone or periosteum, as caries of the sternum or spine, or post-sternal syphilitic nodes. (iii.) As the result of burrowing of pus from above. In this connexion mediastinal suppuration may be associated with a similar condition in the cellular tissue of the neck—"Angina Ludovici" (*vide* Vol. IV. Part II. p. 117); suppurating tuberculous glands; retro-pharyngeal abscess; and suppuration starting in the thyroid or thymus gland. Under this head it may also be mentioned that purulent mediastinitis has occasionally followed the operation of tracheotomy for certain conditions. (iv.) From general septic causes. Thus, mediastinal abscess may occur in cases of erysipelas, pyaemia, or even of enteric fever, measles, and other exanthems. (v.) By extension from pneumonia or pleurisy of low type. (vi.) Extremely rarely from suppuration of a hydatid cyst in the mediastinum, or of a

dermoid cyst. (vii.) As a consequence of "taking cold" or a chill, it is alleged; but although in exceptional cases no other cause can be suggested, this mode of origin is very doubtful.

Gangrenous mediastinitis may result from some of the causes just mentioned, especially extension from above. In the very large majority of cases, however,—indeed with rare exceptions,—it is directly due to ulceration and perforation of the oesophagus. In this way it has followed injury by a foreign body; sword-swallowing, or the unskilful passage of an oesophageal bougie; the effects of corrosive fluids; perforation in connexion with diseases of the oesophagus,—namely, various forms of inflammation, ulceration, stricture, malignant disease, dilatation, and diverticula; perforation of the tube from without, as a consequence of surrounding inflammation, or of degeneration and breaking-down of the mediastinal glands. Exceptional cases of mediastinal gangrene have been reported, associated with pulmonary gangrene, due to extension; gangrene of the larynx; and infective endocarditis. It is also stated that the glands have been found primarily affected. It is important to note that diseased lymphatic glands in the chest, which have been lying dormant for years, do very rarely become the seat of some fresh infection, which may lead to acute suppuration or gangrene.

With regard to disposing causes, mediastinal abscess appears to be far more frequent in men than women; and in comparatively early life—from twenty to thirty. Occupations involving pressure on the chest or liability to injury may possibly have some disposing influence.

Anatomical Characters.—When mediastinitis goes on to suppuration, the pus may infiltrate or be lodged in the meshes of newly-formed fibrous tissue, or be collected in one or more definite abscesses. Either the anterior or posterior mediastinum may be affected, or both; the pus passing from one division to the other. According to Hare's statistics, including all cases, abscess is far more common in the anterior mediastinum, even when of a tuberculous nature. The amount of pus varies considerably, and it is sometimes very large. As a result of extension, pleurisy, usually purulent, or acute interlobular suppurative pneumonia may be set up. A mediastinal abscess may make its way to the surface, or upwards towards the neck; or it may burst into the oesophagus, pericardium, pleura, lung, trachea, or a bronchus. It has been known to ulcerate into the arch of the aorta, causing fatal haemorrhage. Very exceptionally pus has burrowed from the posterior mediastinum downwards between the pillars of the diaphragm, and pointed in the iliac or femoral region.

The cavity caused by the sloughing of infected mediastinal glands is described as usually situated at the bifurcation of the trachea, behind and below the right bronchus. "It is rarely more than an inch or so in diameter, in one case only it measured $2\frac{1}{2}$ inches. Its walls are soft, dark, smooth, and regular, not sinuous like the walls of a gangrenous cavity in the lung; its contents are greyish, fetid, and may contain the remnants of a gland, or what remains of the gland may be found still adherent to

the walls of the cavity" (S. Paget). Gangrenous mediastinitis may lead secondarily to gangrenous pleurisy or pyo-pneumothorax; to putrid bronchitis or bronchopneumonia, from perforation of one or both bronchi; or to pulmonary gangrene, usually diffuse, sometimes superficial. Very rarely the great vessels give way; or the oesophagus may be perforated in a different place from that which caused the disease originally. Very large ichorous collections may result from perforation of traction-diverticula associated with this tube.

Symptoms and Signs.—Mediastinal suppuration may be almost latent from first to last; but, on the other hand, the clinical phenomena and course may be sufficiently definite for diagnostic purposes, or even quite characteristic. As regards local symptoms, in acute cases one of the most frequent and prominent is pain, though this varies a good deal in individual instances, according to the position of the abscess and other circumstances. In most cases it has been described as post-sternal, and accompanied with marked superficial tenderness; but it may be deep-seated between the shoulders, or pass from one point to the other. The pain generally corresponds to the region affected, but not uncommonly it seems to radiate through the entire chest, and may be centred in some part quite away from the actual seat of mischief. When the abscess is in the posterior mediastinum it is said that sometimes, owing to pressure on the nerves at their exit from the spine, the painful sensations are referred to their peripheral endings on the front of the chest, thus giving a wrong impression as to the seat of the disease. The pain as a rule increases steadily until suppuration takes place, and the pus finds an outlet in some direction. Occasionally it remits, or even assumes a paroxysmal character. Exceptionally it is accompanied by a feeling of pulsation.

A mediastinal abscess, when of considerable size, or so situated as to interfere with the structures in this space, gives rise to more or less of the symptoms of irritation or pressure. As a rule these are slight or moderate; but occasionally they are very pronounced, and may even mask the pain. The most common are some form of dyspnoea, wheezing respiration, and cough, either short and dry, or distinctly paroxysmal, and presenting laryngeal or tracheal characters, with mucous expectoration. The voice may be husky. Occasionally haemoptysis occurs. There is also not uncommonly a certain degree of venous obstruction, and now and then the signs of this difficulty are very obvious; there may even be arterial pressure also, with obliteration of the pulse on the affected side. Dysphagia is not common, but there may be some degree of pain and difficulty in swallowing. Owing to implication of the vagus nerves, disordered cardiac action and gastric symptoms, with vomiting, may supervene. Pain and numbness in one arm have also been noticed, due to nerve irritation or pressure. The patient may be unable to lie down on account of a feeling of suffocation, or for other reasons. In individual cases it has been noted that dyspnoea was induced by pressure on an external prominence formed by a mediastinal abscess; or that interruption of discharge

through a fistulous opening was followed by palpitation, faintness, and cough.

Acute suppurative inflammation in the mediastinum will be accompanied by more or less of the usual general symptoms, namely, chills or rigors, sometimes repeated; pyrexia, which tends to assume a hectic type; and sweating. Such symptoms, with local pain, may be present for some days before any definite indications of mediastinal abscess appear. Soon various degrees of wasting and weakness ensue, and in prolonged or chronic cases these symptoms, with anaemia, become prominent.

A definite mediastinal abscess is likely to give rise to *physical signs* more or less distinct and characteristic. The signs to be more particularly looked for at first are fulness or prominence over the upper sternal region, sometimes with superficial redness and slight oedema, and corresponding dulness. When the abscess is in the posterior mediastinum it is affirmed that one or two of the dorsal spines may project. Occasionally the tracheal sound is unduly conducted to the surface over the affected area. Should an abscess make its way to the surface and point, the fluctuation of pus will be felt; and it is said to be frequently noted at the borders of the sternum or at the suprasternal notch (Hare). An important point to be borne in mind is that a mediastinal abscess sometimes presents an obscure or even distinct pulsation, conducted from the aorta, and may thus simulate an aneurysm, for which indeed it has been actually mistaken. In a few instances the pus has partially detached the pleura from the costal cartilages, and presented externally as a round, soft, and fluctuating tumour.

Course and Terminations.—The progress and termination of a case of mediastinal suppuration depend very much on the course of certain events. An abscess may burst externally or be evacuated by operation; or it may lead to inflammation of the internal periosteum covering the sternum, and subsequent caries of the bone itself. Sometimes it gives way into the cellular tissue of the mediastinum, when death ensues. It is probable that a small collection of pus may be partially absorbed, the remains becoming caseous or calcified. As already mentioned a mediastinal abscess may make its way downwards, and come to the surface in the abdominal wall or thigh. Should it open into the trachea, either bronchus, or a lung, a quantity of matter is likely to be coughed up; or death may speedily follow from suffocation. When rupture takes place into the oesophagus, the pus may be discharged by vomiting, and subcutaneous emphysema may then supervene. Death from haemorrhage has resulted from a mediastinal abscess opening into the aorta. When it communicates with either of the serous cavities, or sets up inflammation in connexion with these structures, the effects will be evident, and they add seriously to the danger. Acute mediastinal abscess may run its course in a few days, or last two or three months or more. It may also end in the chronic variety, which, in whatsoever way it begins, may persist for years. Death sometimes occurs during a paroxysm of

dyspnoea; or it may result from exhaustion due to the disease itself, or to intercurrent complications.

The occurrence of gangrene in the mediastinum can only be revealed when a communication is established with the air-passages or lung. Then the breath or the gas driven out by the act of coughing emits a foul odour, and sloughing materials may possibly be expectorated. There is nothing, however, to distinguish such symptoms from those indicating pulmonary gangrene, and the two conditions may be associated. It is said that the breath sometimes becomes fetid very early in the course of gangrenous mediastinitis. As the result of extension or perforation grave accidents are likely to ensue; and the general symptoms will probably be of a well-marked septic type.

Diagnosis.—The recognition of the morbid conditions of the mediastinum now under discussion is in some cases impossible, and is often surrounded with great difficulties. An important factor in diagnosis is the discovery of some disease with which such conditions are likely to be associated, and in this connexion periosteal or bone disease, affecting the sternum or vertebrae, is worthy of special attention. So long as a mediastinal abscess does not come to the surface it might be confounded with a tumour in this region, but the general history and course of the case ought, as a rule, to clear up any obscurity or difficulty in this direction. Should the abscess approach the surface it may be recognised by the usual objective signs. The possibility of confounding such a condition with an aneurysm, when pulsation is present, must be particularly borne in mind; but there is rarely any great difficulty from this point of view. The fluctuation of an abscess may, it is affirmed, be simulated by that of a dermoid cyst. As already intimated, the diagnosis between mediastinal and pulmonary gangrene is practically impossible. The complications and untoward events which may supervene in cases of this class must be watched for from a diagnostic point of view, and they can generally be made out by their usual symptoms and physical signs.

Prognosis.—Mediastinal suppuration is obviously a very dangerous condition, and ends fatally, sooner or later, in a considerable proportion of cases. No definite rules for prognosis can be laid down, but each case must be dealt with on its own characters, and according to general principles. In individual instances there may be hopeful elements, and the modern advances in surgical treatment no doubt make the prognosis less grave at the present day than formerly. It is better when an abscess occupies the anterior mediastinum than when the posterior division is affected. In the latter case there is much less chance of the pus coming to the surface, definite treatment is often impossible, and serious complications are more likely to arise, owing to the matter burrowing into vital structures. Some of the untoward events which have already been mentioned are necessarily fatal, and the supervention of complications adds greatly to the danger. Mediastinal gangrene may be regarded as practically hopeless. On the other hand, the advance of an abscess to the surface is a favourable indication. It has occasionally happened also that

communication with a bronchus has ended in recovery, the pus being in course of time completely evacuated. Some remarkable instances have been recorded of very large collections of pus in the mediastinum, which were cured or greatly benefited by treatment, and in which the patients either lived for many years afterwards, or ultimately succumbed to other and independent diseases.

Treatment.—It is most important to prevent the occurrence of mediastinitis when a foreign body has become impacted in the oesophagus; the position of the foreign body can be determined and its removal effected by means of direct oesophagoscopy (*vide* Vol. IV. Part II. p. 314). In the early stages of acute mediastinitis, ending in suppuration, the treatment can only be conducted on the general principles applicable to inflammatory conditions. Of course the patient should be kept absolutely at rest in bed, and suitably dieted; nourishing articles of food being soon required, as well as alcoholic stimulants judiciously administered. Poultices or other applications may be useful to relieve pain; and particular symptoms must be attended to as they arise. Leeching and counter-irritation have been recommended, but it is doubtful whether they can be of any real service, and lowering measures may certainly be ultimately to the disadvantage of the patient, whose strength generally has to be sustained in every possible way. With regard to medicinal treatment there are no definite indications at first; but a saline mixture may be given, or perhaps antipyretic or cardiac drugs may be useful in some instances. Subsequently quinine and acids, or other tonics, are chiefly needed, or perhaps stimulant remedies; but no definite rules can be laid down. Of course the general functions must be attended to. In dealing with chronic mediastinal abscess a general tonic and nutrient plan of treatment is invariably indicated.

When suppuration in the mediastinum is definitely recognised, or even reasonably suspected, and especially if a localised abscess can be made out, surgical treatment is obviously called for, if it can be carried out; but the difficulties are often great, and may be insurmountable. It is quite beyond the province of this article to discuss in detail the surgical measures which may be required; and a few general remarks must suffice. Should an abscess come to the surface, and especially should symptoms be urgent, it must be evacuated as speedily as possible, by free opening and drainage, with the employment of antiseptic precautions and applications. Possibly the aspirator may be of service, especially when there is a large quantity of pus in the mediastinum, which it may not be desirable to draw off all at once, lest the sudden removal of pressure within the chest should lead to syncope. Before the abscess can be properly emptied, it might be necessary to remove one or more rib cartilages. Another operation which is practised in certain circumstances, and which in several cases has proved most successful, is trephining the sternum. This may be called for, even on suspicion of abscess in the anterior mediastinum, if there are alarming symptoms in the direction of cardiac failure or suffocation. When the suppuration is

associated with caries or necrosis of the sternum or spine, operative interference may aim at the removal of the diseased bone, as well as at the treatment of any abscesses or sinuses associated therewith. When the posterior mediastinum is the seat of a purulent collection, surgical measures are practically inadmissible, so far as I am aware; and the same remark applies to gangrenous mediastinitis. It may happen that the secondary results of either abscess or gangrene in connexion with the pleura may call for operative treatment, in the way of removing fluid or gas. Should a mediastinal abscess open into the air-passages, the discharge of the pus should be encouraged by the act of coughing, and antiseptic inhalations employed.

IV. Chronic Mediastinitis—Indurative or Callous Mediastino-Pericarditis.—Before considering the important group of cases in which chronic inflammation of the mediastinal tissues is a prominent feature, allusion may be made to its occurrence in other circumstances. There may be a localised change of this nature, associated with degeneration and pigmentation of the lymphatic glands in this region as life advances, especially in those who have lived in smoky cities or towns, or have worked at dusty trades. The glands become shrunken and tough, fibrous, or calcified, and may set up a chronic inflammatory process around, leading to fibrotic thickening and adhesion. It is only in exceptional cases that any ill effects ensue, from pressure on the trachea or a bronchus, the oesophagus, or one of the great vessels. In rare instances a fibrous growth of considerable thickness is thus produced. These changes may give rise to traction-diverticula of the oesophagus, by dragging on its walls. More or less extensive chronic mediastinitis is often associated with prolonged suppuration, tuberculous disease of the glands, or tumours of various kinds; but its effects are, as a rule, then of quite secondary importance, and are obscured by the primary affection. It may also possibly occur in connexion with actinomycosis.

The more pronounced forms of chronic mediastinitis are usually intimately connected with adherent pericardium, and are dealt with from this point of view in the article on "Diseases of the Pericardium" (Vol. VI.). The late Thomas Harris, in his monograph on *Indurative Mediastino-Pericarditis*, published in 1895, gave a tabular abstract of cases reported up to that time, as well as the details of others observed by himself, and discussed the subject generally. The complaint was thus named by Kussmaul, who first brought it into prominent notice in 1873. It was, however, known before that period, as I can testify from personal experience and observation at the Liverpool Northern Hospital; and Sir Samuel Wilks had drawn special attention to the subject in relation to pericardial adhesions in 1871. As a matter of fact chronic mediastinitis in its various degrees is much more common than is recognised in ordinary practice. The records of the subject, however, are almost entirely founded upon fatal cases in which a necropsy was made.

The particular conditions to be referred to in the present connexion

are:—(1) The rare variety which has been specially termed *chronic mediastinitis*, in which the morbid changes are entirely external to the pericardium, and confined to the mediastinum. (2) *Pericarditis externa et interna*, in which, although the pericardium is more or less adherent to the sternum, costal cartilages, and lungs, as well as internally, there is little or no general mediastinitis. (3) That form to which the term *indurative mediastino-pericarditis* more properly belongs, where, along with an adherent pericardium, there is extensive and marked increase of fibrous tissue in the mediastinum. Clinically, however, it is impossible to draw any definite line of demarcation between these several groups.

Etiology and Pathology.—The origin of the mediastinal changes associated with pericardial adhesion will be discussed in relation to that condition, to which reference may be made. In the present article it must suffice to offer a few remarks on the general bearings of the subject. A certain proportion of cases can be definitely traced to an acute chest affection, of which acute pericarditis formed a prominent feature; but it is highly probable that, in some instances at any rate, there has been at the same time an acute mediastinitis, or an adjacent pleurisy, which formed the starting-point of the subsequent mediastinal lesions. I have met with a few cases during their acute stage strongly supporting this view. Should those grave cases, in which the pleurae as well as the pericardium are extensively involved, end in recovery, mediastinal mischief is very likely to remain. Occasionally a history of an acute illness can be obtained, especially scarlet fever or measles, but without any record of disease in the chest; though no doubt in such instances pericarditis had occurred as a complication. In many cases no definite history of an acute origin can be obtained, but at the same time such an origin is revealed by the results of the necropsy. Another important point to be remembered is that should attacks of pericarditis be repeated, the probability of mediastinal implication is much increased. Of this course of events I have met with striking instances, and have watched their progress for some time.

Occasionally chronic mediastinitis follows injury of various kinds, and has even been attributed to prolonged pressure on the sternum in connexion with some handicraft; but I have never personally met with a case in which such a mode of origin could be possibly ascertained.

In some instances mediastinitis is chronic from the outset, being then almost always secondary to tuberculous disease, either affecting the glands or associated with pulmonary phthisis. Possibly it may arise in old cases of bronchitis and emphysema, especially when these conditions are engendered by the inhalation of irritating particles. It has also been attributed to syphilis and bone-disease. Once a chronic inflammation of the mediastinal tissues has started, I believe that it tends to advance; and thus what was originally a very limited and slight change may ultimately become pronounced and extensive.

Age and Sex.—Speaking of indurative mediastino-pericarditis Harris (9) writes:—"I think many physicians have an impression that the

affection occurs more commonly in children than in adults. Such an impression may be correct; but if so, a large number of cases in children must have escaped having been placed on record, or have not been followed by a post-mortem examination." Of the 22 cases included in his tables, verified after death, he observes that 9 occurred in persons under eighteen years of age, and 13 in persons over that age; only 2 patients were over thirty. He, therefore, concludes that "the affection would appear to be rather more common in adults than in children." On further analysing these tables, however, I note that the eldest of the patients under eighteen was really only sixteen; that 4 ranged from fourteen to twelve, and that the remainder were aged respectively ten, eight, 6¼, and two. Moreover, of the cases under thirty, no less than 8 ranged from nineteen to twenty-two; 2 others being twenty-four and twenty-six. These facts seem to bear out the view, which certainly accords with my own experience, that at any rate the foundation of indurative mediastino-pericarditis, as well as of *pericarditis externa et interna*, is generally laid in childhood or in early life, although their effects may not become evident until a later date. Simple chronic mediastinitis has quite a different history, for it occurs later in life, and this is easily explained. Of the 3 cases mentioned in Harris's tables the youngest was thirty-seven. As regards *sex*, all the varieties of chronic mediastinitis are decidedly more common in males than females. In Harris's tables 20 out of the 25 cases were males.

Anatomical Characters.—The essential and characteristic change in chronic mediastinitis of any kind is an increase, more or less pronounced, of fibrous tissue in the mediastinal space, which tends to promote adhesion or agglutination of the different intrathoracic structures to each other or to the chest wall, and to compress or contract certain of these structures, thus leading to secondary consequences, usually of a grave nature. This change is, as already stated, generally associated with pericardial adhesions, and we have, as a rule, to deal in individual cases with their combined pathological effects, which it may be impossible to differentiate. In some instances also one or both lungs are adherent to the chest wall, it may be extensively or universally. The mediastinal changes vary a good deal in situation, extent, and exact characters. In a fair proportion of cases they are limited to the anterior mediastinum, rarely to the posterior or middle, or to the lateral boundaries; but the entire space is not uncommonly involved. They may merely amount to adhesion of the pericardium to the sternum and rib-cartilages, or to one or both lungs at the same time, with little or no thickening. In other instances there is marked increase of the fibrous tissue, which sometimes attains a great thickness, or even forms definite masses. The material is firm and tough, and often very dense, indurated, or callous—hence the terms "indurative" or "callous" mediastino-pericarditis. There may be considerable fibrous mediastinitis, without any internal pericardial adhesions. In this condition the external adhesions of the pericardium are very dense and strong; and it may be impossible to separate the sac

from the chest wall or adjoining structures without forcibly tearing them asunder. In the midst of the fibrous material the remains of lymphatic glands are often found, usually caseous.

One of the most important pathological effects of chronic mediastinitis is that it often leads to compression of certain mediastinal structures, or to other kinds of physical interference. It is most likely to involve the large vessels, especially the veins. In several instances the superior vena cava has been implicated, and sometimes occluded. Many years ago a remarkable case came under my observation, with all the symptoms of complete closure of this vessel, in which the necropsy revealed nothing more than a limited mediastinal fibrous thickening surrounding the vein. Other intrathoracic veins may be implicated singly. The aorta has been found narrowed and twisted in some instances. The pulmonary vessels may also be compressed, and in all Kussmaul's cases haemorrhagic infarcts were found in the lungs, which probably were associated with this condition. In one of this observer's cases the ascending part of the arch of the aorta, the trunk of the pulmonary artery, and the superior vena cava were all compressed to a marked degree. Thrombosis may add to the difficulty in the circulation, helping to obstruct the vessels. Pressure upon the inferior vena cava may possibly aid in causing enlargement of the liver, and also dropsy. The main air-passages often escape altogether, and are seldom much narrowed, but may be somewhat compressed. The oesophagus, again, is rarely interfered with to any material degree, and as a rule escapes. In exceptional instances the left vagus or recurrent laryngeal nerve has been involved in mediastinal fibrous thickening.

Extreme cases are occasionally met with in which all the intrathoracic structures are matted together, as well as to the chest wall, by thick and dense adhesions,—pericardial, pleuritic, and mediastinal; so that at the necropsy the contents of the thorax have to be torn away and removed in a mass. Even after their removal it is very difficult, and may be impossible, to separate them or to dissect them out properly. On opening the chest these conditions sometimes give the impression at first sight of the presence of an intrathoracic tumour. In connexion with mediastino-pericarditis, should the pleurae be partially or entirely free from adhesion, effusion is often found on one or both sides. The lungs are congested or affected in other ways.

The remote effects of the morbid conditions now under consideration must be duly recognised. They are mainly those resulting from marked obstruction of the venous system, which, in the case of mediastino-pericarditis, are of general distribution, being then due chiefly to cardiac difficulty; but there may also be the local consequences of the mediastinal changes as affecting particular veins. From general venous obstruction the usual effects ensue, especially in connexion with the liver, spleen, and kidneys; in inveterate cases they become very pronounced. Chronic inflammation of the pleurae and peritoneum, multiple progressive hyalo-serositis (*vide* Vol. III. p. 946, and Vol. IV. Part I. p. 165), may also be

present, and in many of these cases the peritoneal changes are secondary to the chronic pericarditis.

Clinical History.—It will be readily understood that no definite or independent description can be given of the symptoms and physical signs of chronic mediastinitis. As a matter of fact, the condition frequently cannot be recognised during life; or its clinical phenomena are so intimately blended with those of pericardial agglutination and its consequences that they cannot be differentiated. Indeed, in cases of well-marked indurative mediastino-pericarditis the symptoms are practically of cardiac origin in the main; leading not only to certain forms of dyspnoea, disturbance of the heart's action, and other chest symptoms, but also to those of general venous obstruction, as evidenced by dropsy and other phenomena described in relation to adherent pericardium. When all the structures are matted together, it becomes still more difficult to make out what share each particular factor has in the causation of the symptoms. The explanation of the occurrence of ascites in some instances of mediastino-pericarditis, before the anasarca, or out of all proportion to it, is not always evident; but it has been attributed to a chronic peritonitis resulting from venous congestion. In one of the cases collected by Harris, it was found to be due to acute tuberculosis of the peritoneum. Personally, I have usually associated the ascites with hepatic changes, and Pick described pericarditic pseudo-cirrhosis of the liver, but its existence as a distinct disease has not been generally accepted (*vide* Vol. IV. Part I. p. 165). There may, of course, be an independent portal cirrhosis, but this is rare in adherent pericardium except in cases with calcified adherent pericardium in which cirrhosis is present in a high proportion (Diemar, Wells). Occasionally mere cardiac dilatation originates ascites without oedema of the legs. The urine is generally deficient in quantity and dark-coloured; it may be albuminous.

The symptoms more directly due to the chronic mediastinal changes, if any, result mainly from their effects upon the structures contained in the space. There may be pain behind the sternum, or a sense of oppression or dragging, and an inability to expand the chest in deep breathing. Signs of local venous obstruction are those most likely to occur, with enlargement of the superficial veins; and there may be the characteristic evidences of occlusion of the superior vena cava. Definite symptoms referable to the aorta, trachea, or oesophagus are rare. In one of Harris's cases there was limited oedema of the left arm; and paralysis of the left vocal cord, due to implication of the recurrent laryngeal nerve.

In a case of indurative mediastino-pericarditis observed by Jaccoud, the patient had to sit up in bed with the trunk markedly bent forward, because in the erect posture, and still more in the recumbent, the dyspnoea and intrathoracic pain became much worse. This posture, however, is by no means characteristic of the condition, and many exceptions are observed in both directions.

Physical Signs.—Here again it is impossible to give any description apart from the pericardial and cardiac conditions, discussed under adherent pericardium. In fact the signs are mainly associated with the heart; but others are often present at the same time, due to pleuritic and pulmonary complications. Possibly the anterior part of the chest may be somewhat depressed as the direct result of chronic mediastinitis; and it certainly interferes with respiratory movements. Further, a considerable mass of fibrous tissue, with enlarged glands, may undoubtedly add to the dulness over the upper part of the sternum, which is then likely to be very pronounced, and accompanied with much sense of resistance. The sign to which attention has been specially called by Dr. George Perez, of Orotava,—namely, a creaking or other sound audible on auscultation when the patient moves the arm,—is well worthy of attention, and may give definite evidence of the presence of chronic mediastinitis. The significance of the *pulsus paradoxus*, and of inspiratory swelling of the veins in the neck, in relation to the diagnosis of indurative mediastino-pericarditis, is fully discussed in the article on Pericardial Adhesions (Vol. VI.). Examination of the abdomen will reveal ascites or enlarged liver when present; but the spleen is usually small and contracted.

Chronic mediastinitis can sometimes be followed up from its acute origin; but as a rule it comes under observation for the first time as a chronic condition. Its duration varies considerably, even after the disease has been discovered. It may last from a few months to several years. Indurative mediastino-pericarditis generally tends to go from bad to worse, causing much suffering. Death usually results from progressive cardiac dilatation and failure. The fatal termination may be hastened by pulmonary, pleuritic, or other complications.

Treatment.—Unfortunately nothing can be done directly to influence the morbid conditions associated with chronic mediastinitis of any form. It is of no use whatever to go on applying iodine or such remedies to the chest indefinitely, or to carry out any other plan of treatment for the supposed purpose of promoting absorption of the fibrous tissue in the mediastinum. Various measures are often called for to relieve symptoms. The chief indication is to study the cardiac action, and to endeavour to assist it in such ways as may be requisite or practicable. Each case must be dealt with on its own merits, judiciously and rationally; and the treatment varied according to circumstances. The operation named "cardiolysis," described in relation to the pericardium, may possibly be admissible in exceptional suitable cases (*see* "Chronic Pericarditis," Vol. VI.). The dropsical conditions often require operative interference, and the fluid may have to be removed again and again, both from the subcutaneous tissue and serous cavities.

V. Tuberculous Disease of Mediastinal Lymphatic Glands and Thoracic Duct.—The lymphatic glands occupying the mediastinum are liable to different morbid changes, most of which are sufficiently noticed in other parts of this general article. At present attention will be briefly

directed to *tuberculous* disease of these structures. In the large majority of cases it is the bronchial glands which are mainly or entirely affected, especially those situated at the bifurcation of the trachea; but occasionally those more particularly termed mediastinal, it may be the anterior mediastinal, are chiefly or alone implicated, and they sometimes attain a very large size.

Etiology.—The intrathoracic glands are usually involved in tuberculosis by secondary infection from neighbouring structures, especially the lung or pleura; occasionally from bone. The disease may also extend directly from the glands of the neck, or from those in the abdomen, along the lymphatics through the diaphragm; or it may result from remote infection. Although this statement has been disputed, there can be no doubt that the glands in the chest are attacked primarily in a certain proportion of cases. Such a mode of origin is far more frequent in children than in adults; in the latter it is very exceptional. It also occurs more commonly in the acute than in the chronic form of tuberculosis. Implication of the thoracic duct is always a secondary event; tuberculous infection commonly spreads from the abdomen along the thoracic duct to the intrathoracic lymphatic glands. This path of infection is fully discussed on p. 305. With regard to primary tuberculous disease of the bronchial glands, it is by no means improbable that they may, when in a healthy state, be directly infected by the tubercle bacillus. They are far more likely to be attacked, however, when previously irritated or inflamed from any cause; especially if such disturbance should continue for some time, or if the inflammatory process should end in suppuration. Possibly a cold or some traumatic cause may be the starting-point of mediastinal tuberculosis.

Intrathoracic tuberculous disease of glands is, in my opinion, more likely to arise in those who present a marked hereditary tendency to tuberculosis; but in many of the patients no such tendency can be traced. The complaint is far more common in children and young subjects than in adults, but the relative proportion of cases at particular ages has been variously stated by different observers. No doubt conditions which impair the general health, such as want of proper food, unfavourable hygienic surroundings, and the like, may act as remote causes in children; as well as lowering illnesses. Tuberculosis of the bronchial glands sometimes follows an acute illness, or it may be a sequel of whooping-cough. The thoracic duct is but rarely definitely affected; but this may happen from extension, or in acute cases.

Anatomical Characters and Pathological Changes.—In the early stage, or when involved in acute tuberculosis, the intrathoracic glands in rare instances merely present discrete grey granulations. As a rule, however, the growth is infiltrated, there being a general inflammatory process which is of a tuberculous nature—*lymphadenitis tuberculosa*—as proved by the presence of abundant tubercle bacilli. The two conditions may be associated. The affected glands are swollen and enlarged, sometimes considerably, and by their aggregation they may form masses or

tumours of great size. They are of soft consistence, and may present a medullary appearance. In different parts they may be pale and opaque, or highly vascular. The usual tendency is for the tuberculous glands to undergo caseous degeneration, either in spots or extensively; and this change may take place very rapidly. On the other hand, a fibroid transformation sometimes takes place, but whether this is due partly to a direct change in the tuberculous granulomas or entirely to a secondary growth of connective tissue after caseation, is disputed. It is commonly accompanied with intense pigmentation; and the glands become firm and resistant, and may shrink in size. The bronchial glands are particularly liable to be thus affected.

A further change which is prone to take place in glands which have become caseous is that they break down, and pus is formed, this being the common origin of chronic abscess in the mediastinum. Such a collection of pus may open externally, or into the various structures already mentioned in relation to mediastinal abscess generally, especially the trachea or a main bronchus, or the oesophagus. It is important to bear in mind also that a tuberculous abscess may perforate the aorta or pulmonary artery, causing fatal haemorrhage. In one case the trachea, oesophagus, and pericardium were simultaneously perforated. Suppurating glands are occasionally embedded in the lung, and it may then be very difficult or impossible to distinguish them from pulmonary cavities. Ulceration associated with caseous glands may take place without actual suppuration, and this may also lead to perforation. Cases have been recorded in which a gland has ulcerated into the trachea, and then, becoming detached, has caused sudden death from suffocation by impaction in the rima glottidis. In the majority of cases the material resulting from caseation of the glands becomes inspissated, and being encapsuled by fibrous tissue, may remain inert for long periods. Such a condition, however, is always a source of danger as a centre of infection; or acute suppuration may be set up at any time. The final change which tuberculous glands in the mediastinum may undergo is calcification, encapsuled cretaceous material or calcareous masses remaining as the sole evidence of the previous existence of the disease.

With regard to the thoracic duct, it has been found in some cases, by Ponfick and others, to be the seat of extensive tuberculous infiltration, with ulceration; this condition being an obvious source of general infection. Perforation of the duct by a mediastinal gland has also been observed in rare instances.

Clinical History and Diagnosis.—The phenomena associated with tuberculous disease of the mediastinal glands present considerable variety in individual cases; and as the more characteristic of them are described in relation to other subjects in this article, of which such disease forms a part, it will only be necessary to deal here with the clinical history in general terms. It can be easily understood that the glands may not be sufficiently affected to give rise to any obvious or trustworthy symptoms, and in a fair proportion of cases no doubt this happens. Moreover, when

they become involved secondarily, in connexion with pulmonary tuberculosis, there are often no special indications of the event, or they are obscured by those of the lung trouble. Again, there may only be the usual chest symptoms, such as pain, disturbance of breathing, cough, and expectoration of no definite significance. When the bronchial glands are affected, and attain a sufficient size, the characters of the breathing and cough will reveal more or less obstruction of the main air-passages, or nerve irritation; and it is to the phenomena thus originated that special attention must be paid in early diagnosis, particularly in children. Any tendency to obstructive, noisy, or stridulous respiration, to attacks simulating spasmodic asthma, or to spasmodic cough of a "croupy" quality, or resembling that of whooping-cough, should always suggest mediastinal glandular disease as a possible cause. The voice may also be affected; and other pressure symptoms may be present. At the same time there may be signs on *physical examination* of deficient entrance of air into one or both lungs; changes in the normal percussion-sounds; tactile and auscultatory phenomena indicating unusual conduction of breath-sounds, and of vocal or tussive vibrations and sounds from the main air-tubes, especially in one or both interscapular regions, and the sounds often have peculiar characters. In short, there are the signs of the presence of some unusual solid collection in the mediastinum, which culminate in those of a distinct mediastinal tumour, in relation to which they will be more fully discussed. Extensive tuberculosis of the anterior mediastinal glands will give rise to marked dulness over the sternum. Dr. Eustace Smith has described in children a venous hum, audible at the root of the neck when the head is thrown back, which he attributes to pressure by enlarged glands on the venous trunks. The presence of enlarged glands can be determined by skiagraphy.

Another class of phenomena which may occur in connexion with tuberculous mediastinal glands is that due to the formation of an abscess, and its communication with the trachea or a bronchus. This event may be immediately followed by urgent symptoms; and if not fatal there will be expectoration of purulent or caseous material, accompanied with the development of signs of a cavity. On examination of the sputum tubercle bacilli will probably be detected in abundance. Haemoptysis may also occur. In old chronic cases calcareous particles may be expectorated. Should the abscess come to the surface there will be the usual objective evidences of this condition. It must be remembered that it may possibly open in other directions, and that fatal haemorrhage may happen from perforation of a great vessel.

Mediastinal tuberculous disease will be attended with the ordinary general symptoms of this complaint, and they are likely to be pronounced; namely, fever, wasting, anaemia, night-sweats, general debility, and loss of appetite. Occlusion of the thoracic duct may cause extreme emaciation, but it is impossible in these cases to recognise this condition definitely during life. The presence of pulmonary phthisis, or of tuberculous lesions in other parts of the body, will materially help in a

doubtful case in the diagnosis of the nature of a morbid condition giving rise to mediastinal symptoms or physical signs. The complaint sometimes runs an acute course, but is generally chronic. It is important to observe that the symptoms, after having been prominent, may gradually subside, and practical recovery ultimately ensue.

Treatment.—Mediastinal tuberculosis is in many cases so intimately associated with the same condition in the lungs or other parts, that any independent treatment is quite out of the question. Even when it exists alone, the indications to be carried out are merely those applicable to tuberculous disease in general. It is very doubtful whether any of the vaunted "specific" methods of treatment now in vogue can have any positive beneficial effect upon this complaint when it involves the mediastinal glands. Should an abscess form, and come to the surface, or open internally, it must be treated on ordinary principles. How far operative interference is practicable or permissible, and what measures should be carried out, must be determined by the circumstances of each individual case; and for guidance in relation to this part of the subject reference must be made to surgical works.

VI. Mediastinal Emphysema.—Accumulation of air in the mediastinal cellular tissue is of extremely rare occurrence, but it is nevertheless a definite morbid condition in connexion with this region, and must be briefly referred to in this article. In the large majority of cases it is of traumatic origin, or occurs during or after the performance of tracheotomy for different purposes. In this way it may be associated with diphtheria. The air then gains access into the anterior mediastinum beneath the deep cervical fascia. Very exceptionally mediastinal emphysema results from rupture or perforation of the trachea or a bronchus, or of the lung and pleura, in connexion with ulceration, abscess, gangrene, tuberculous disease, or extreme pulmonary emphysema, either vesicular or interstitial. The condition is said to have been produced by a violent paroxysm of whooping-cough. Gas may also find its way into the mediastinum as a consequence of perforation of the oesophagus. Moreover, it may be present from decomposition, occurring either during life or after death.

The amount, distribution, and characters of a gaseous accumulation in the mediastinum vary much under different circumstances. In certain conditions it has an offensive smell. When a persistent leakage of air takes place through an opening in an air-tube or in the pleura, it enters with each inspiration; but a valve-like action prevents its escape during expiration, so that the chest becomes rapidly more and more filled and distended, the lungs are compressed, and death speedily ensues. When an escape of gas occurs into any part of the mediastinal space, it is likely to find its way to the other divisions. A limited emphysema has been described, named *extra-pericardial*, in which the air accumulates around the pericardium, interfering with the cardiac movements.

Clinically mediastinal emphysema may be recognised in certain

circumstances, especially should it originate from injury or tracheotomy. Symptoms of interference with the intrathoracic structures would rapidly supervene; whilst the chest would become distended, and yield signs indicating that this distension was due to accumulation of gas. It might be difficult to determine the situation of the gas, especially as the mediastinal condition may be associated with pneumothorax; but the extensive distribution of hyper-resonance or tympanitic percussion-sound, or its presence over the front of the chest, would help the diagnosis. The air in the cellular tissue may give rise to a very peculiar and characteristic dry crackling sound, produced by deep respiration, or by moving the arms, and audible on auscultation. It might further make its way to the cellular tissue of the neck or front of the chest, or even more extensively, thus causing subcutaneous emphysema, which would be an additional help in diagnosis.

Treatment can only be conducted on general principles, especially to combat symptoms. Nothing definite can be done for the mediastinal emphysema itself as a rule; but possibly some kind of operative interference might be indicated in special circumstances. It is important to take due precautions to prevent the occurrence of this complication during or after the performance of tracheotomy.

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MEDIASTINAL NEW GROWTHS

By Frederick T. Roberts, M.D., F.R.C.P.

In the original article contributed to the first edition of this work intrathoracic growths were dealt with as a whole, including amongst them those originating in the lung and pleura. On the present occasion, however, it has been thought desirable by the editors to separate mediastinal new growths from malignant growths of the lung and pleura, and to discuss these morbid conditions in relation to the structures with which they are severally directly associated. It must be emphasised, however, that there is no positive line of demarcation between growths starting in the lung or pleura, and those occupying the mediastinal region; that the former are liable to encroach upon this region, giving rise to a mediastinal tumour and vice versa; and that they may all be affected together, either simultaneously or in succession. It will be impossible, therefore, when dealing with mediastinal new growths, to avoid referring to the connexion which exists between the different structures, in relation to certain points bearing upon their morbid anatomy and clinical history.

General Pathology.—There are certain preliminary matters calling for notice which may be conveniently considered under this comprehensive heading, and to these attention will now be directed.

Summary of Growths.—According to the usual classification mediastinal new growths are primarily divided into *malignant*, and *non-malignant* or *benign*; but this arrangement cannot be strictly carried out on an anatomical or histological basis, as certain of them, which appear to be structurally alike, may in different circumstances belong to either category. Without further comment they may, for practical purposes, be enumerated as follows:—(i.) *Carcinoma*, in its several varieties; these being all essentially malignant. (ii.) *Sarcoma*, in the form of round-celled, spindle-celled, small-celled, and mixed-celled sarcoma, *lympho-sarcoma*, and *endothelioma*. (iii.) *Lymphoma* and *lymphadenoma*. (iv.) *Fibroma*, *fibro-cellular* and *fibro-plastic* growths. (v.) *Dermoid cyst* and *teratoma*. (vi.) *Hydatids*. (vii.) *Syphilitic gumma*. Growths of this nature are exceptionally met with in the mediastinum, embedded in dense fibrous material. (viii.) *Tuberculous glands*, discussed on p. 617, which occasionally attain such a size as to form a mediastinal tumour of considerable dimensions. (ix.) A miscellaneous group, including *lipoma*; *chondroma* of soft parts, *osteochondroma*, or *enchondroma*; *myeloid* tumour; and *haematoma*. Mediastinal tumours occasionally present a mixed structure, but reference will be made later on to these combinations.

Most of the growths in the foregoing list are quite rare in the mediastinum, and the large majority of tumours occupying this region, which

are of practical importance, and which can be recognised during life, are either carcinomatous or sarcomatous. It is to these formations, therefore, that attention must be more especially directed.

Seat of Origin.—In the next place, it is desirable to get a general notion of the structures from which mediastinal growths may originate; though later on this question will have to be considered more particularly in relation to special morbid formations. Taking them as a whole, these growths may start from:—(*a*) Either lung, which is not very common. (*b*) The pleural or subpleural tissue, in comparatively few cases. (*c*) The thoracic wall,—a tumour growing inwards from the periosteum covering the sternum; or from the cartilaginous or bony framework of the chest. This seat of origin applies more particularly to osteochondroma or enchondroma, but sarcoma and osteosarcoma may arise from the sternal periosteum. (*d*) The lymphatic structures, especially the glands. A large proportion of mediastinal growths have their starting-point in these structures. Not only may the glands within the chest be thus primarily affected, but it is important to note that those at the base of the neck may be implicated first, the mischief extending thence directly into the thorax. The anterior mediastinal glands, and those associated with the trachea and main bronchi, are frequently involved; or the growth may begin in the lymphatic structures in the root of the lung. (*e*) The important tubes occupying the mediastinum. Thus tumours, which subsequently become mediastinal, may have their seat of origin in the oesophagus, the trachea, or a main bronchus. (*f*) The cellular tissue or fat of the mediastinum. A fatty tumour of sarcomatous type or "lipoma sarcomatodes" has been described as originating in the fatty tissues. (*g*) The pericardium or subpericardial tissue; or, very rarely, the adventitia of the large blood-vessels, or an endothelioma starting from the pulmonary vein (Sailer). (*h*) The thymus gland. It is now well recognised that a persistent thymus gland is not uncommonly the seat of origin of a tumour occupying the mediastinum, especially its anterior division (*vide* art. "Diseases of the Thymus," p. 674). (*i*) The thyroid gland. A growth starting in this structure may possibly extend into the chest, and become a mediastinal tumour.

General Grouping of Cases.—It is customary to divide cases of mediastinal new growths, as they come under observation in practice, into *primary* and *secondary*, these terms having the signification usually recognised in relation to morbid conditions of this nature. For practical purposes, however, it may be useful to make a further subdivision, and I venture to suggest the following as indicating the circumstances under which such growths may occur in the mediastinum:—

(i.) They may be strictly *primary*, starting from some definite intrathoracic structure. According to Kaulich, nearly half of all mediastinal tumours are primary. Growths thus originating may (*a*) remain throughout confined to the structure first attacked, which applies to many benign growths; (*b*) spread so as to implicate other structures within the chest, this being the usual course of events in the case of

malignant growths; (*c*) extend directly to the surface or into the abdominal cavity; or (*d*) give rise to secondary formations in more or less remote parts.

(ii.) As already stated, tumours beginning on the inner surface of the chest wall may grow inwards and encroach upon the mediastinal region, or even implicate some of its contents. But, further, a growth starting outside the chest, in the mammary gland for instance, occasionally penetrates the wall, so that ultimately it becomes intrathoracic also. Whether originating from within or from without, we now and then meet with cases in which all the structures seem to be involved in a common mass.

(iii.) Of the *secondary* group, the following subdivisions may be recognised:—(*a*) Primary malignant disease within the chest, not giving rise to any obvious disturbance, may be the source of infection, and originate a secondary growth forming a distinct tumour with all its consequences. A very interesting example of such a case came under my care at University Hospital, in which a mass of glands formed a tumour giving rise to very pronounced symptoms, the primary mischief having been a limited area of malignant disease near the lower end of the oesophagus, which during life had been entirely latent. (*b*) Direct extension from the abdomen into the chest takes place now and then, leading to secondary development in this region. Such extension is most likely to come from the peritoneum, very rarely from the stomach, liver, or kidney. (*c*) An independent secondary malignant tumour may grow in the mediastinum, in cases in which a primary disease of this nature exists in some other more or less distant part of the body. Such primary disease is generally quite obvious clinically, but not always, and it may not be discovered till after death. Instances occasionally come under observation in which, along with an intrathoracic tumour, many structures are involved, so that it is impossible to determine the original seat of the mischief. (*d*) An important group of secondary formations within the thorax is that in which a recurrence of malignant disease is thus revealed; as in cases in which one or more growths of this nature have been removed by operation from other parts of the body.

(iv.) It appears to me desirable to recognise separately a class of cases in which a mediastinal tumour is merely part of a general disease affecting the absorbent glands, and involving these structures in various parts of the body, it may be universally. This description fairly applies at any rate to lymphadenoma, which may start in some of the intrathoracic glands, or these may become involved by direct extension from the glands of the neck, or as a secondary event at a period more or less remote after the primary implication of distant glands. Tuberculous glands in the mediastinum might also in some instances be included in this category.

Special Growths.—With regard to the majority of new growths within the chest already enumerated, which may occur in the mediastinum, nothing more need be said, but there are a few the pathology of which, in relation to the structures occupying this region, demand further consideration, especially carcinoma and sarcoma.

1. *Carcinoma.*—There is a decided difference of opinion as to the real nature of the majority of mediastinal tumours, and especially as to the comparative frequency of primary carcinomatous and sarcomatous growths in this region. Most writers on this subject have regarded carcinoma as the least common of such tumours, and it has even been stated that as a primary growth it is almost unheard of. Sir R. Douglas Powell affirms that even secondary carcinoma is rare, except when it travels inwards from the breast. Lindsay Steven (whose recent death, in the prime of life, and the full vigour of his professional career, the editors and writer of this article, in common with the whole medical profession, so deeply regret and deplore) expressed his strong opinion that cancer is not anything like so frequently met with as sarcoma, especially lymphosarcoma. He wrote:—"Cancer is a disease which can only originate, except in very rare and exceptional circumstances indeed, in connexion with epithelial tissues, and more particularly in those epithelial tissues which are especially prone to injury or irritation. For this reason the most likely place for a primary carcinoma to develop within the chest is the posterior mediastinum, where we have the epithelial structures of the trachea, bronchi, and oesophagus to afford a starting-point for the disease." Steven, however, acknowledged the difficulties which arise from apparently cancerous tumours in the mediastinum originating in other than epithelial tissues, but he thought it not at all improbable that very often this appearance may be caused by a sarcoma forming a stroma for itself out of the loose connective tissue amongst which it has frequently to grow.

In opposition to the views just considered, some writers place cancer first, especially in relation to tumours occurring in the anterior mediastinum. Hare, founding his conclusions on the cases collected by him, strongly supports this opinion, both as regards primary and secondary mediastinal growths. Out of 520 cases he classes 134 as of this nature; and affirms that "the tissues in which cancer may arise in the mediastinum are exceedingly numerous; indeed, those which it does not attack can scarcely be mentioned."

Individual experience of mediastinal tumours is necessarily limited, and no positive opinion can be founded upon such experience as to the relative frequency of carcinoma in this region; but I have met with a sufficient number of cases to give me the impression that it is at any rate a less rare form of growth than is generally recognised, and the literature of the last ten years contains the records of not a few. At the same time, Hare's views as to the structures from which it may arise can hardly be maintained. Moreover, there can be no doubt, as has been often pointed out, that many tumours formerly described as carcinoma would now be removed from this category; and it is wise to admit only such as have been investigated in recent years. If this rule is followed, it will be found that the sarcomas, or lymphosarcomas, form the vast majority.

An interesting group of the primary carcinomas are those arising

from fetal tissues. These comprise a group of cutaneous tumours which take their origin in the same way as the "dermoid cysts," or teratomas, of the mediastinum, either from embryonic skin shut in at the time of the closure of the thorax, or from the ectoderm of branchial clefts which has been drawn down into the chest by the descent of the heart. In structure they are squamous-celled carcinomas in which cornification occurs. Branchial tumours exactly similar to those of the neck are found in the mediastinum, their position there again being due to the descent of the heart (branchiomes malins).

With regard to secondary mediastinal carcinoma, there is but little to be said. As an independent condition resulting from metastasis, and following carcinoma in some remote organ or structure, it is extremely rare. Of course the mediastinum is liable to be encroached upon by a cancerous growth starting from the lung or pleura, as well as from other adjacent structures. In the case of the lung, the bulk of extension of such a growth may be mediastinal. Other classes of cases of secondary cancer are those which either follow a similar disease in the breast, in its later stages offshoots passing directly through the chest wall and invading the mediastinum, or the complaint breaking out again after the removal of this organ by operation; or those which result from extension of the mischief, through the lymphatics of the diaphragm, from the abdomen. From a practical point of view, however, such modes of origin are mere pathological curiosities.

2. *Sarcoma.*—The chief forms met with are round-celled, small round-celled, spindle-celled, irregular-celled sarcoma, and lymphosarcoma; the last mentioned being of special consequence as a primary growth. A secondary sarcoma appears to be very unusual in the mediastinum, and, according to Hare, even where this growth is extensively distributed, the mediastinum appears to escape.

The mediastinum is the seat of origin of the large majority of primary sarcomas within the chest; and, as already mentioned, many eminent authorities regard lymphosarcoma as the most frequent primary mediastinal growth. Sir R. Douglas Powell goes so far as to say that a primary sarcoma in this region is almost invariably lymphomatous. It is a matter of general agreement that the glands are the usual starting-point for the growth, especially the anterior mediastinal or bronchial; but this is by no means invariably the case. The fact is fully recognised that it is often difficult at the necropsy to say precisely where a mediastinal tumour has originated; but its situation and characters (even when there are large nodulated masses), as well as its histological structure, are very suggestive of glandular origin. Writing on this point, Steven considered the name lymphosarcoma to indicate "that variety of sarcoma which both by its naked-eye appearances and its histological characters is to be looked upon as originating in connexion with the lymphatic glands—that is, a sarcoma of the lymphatic glands. . . . A lymphosarcoma may originate in one gland, or in a part of one gland, and in its growth may surround and involve neighbouring glands, which

may be quite recognisable in the midst of the tumour tissue." This authority strongly argued against any relationship between mediastinal lymphosarcoma and lymphadenoma, even though certain other glands should become affected; and with this view I fully agree. Lymphosarcoma in the mediastinum may be associated with a similar condition in the neck: or there may be an independent mass in the lung.

Cases are on record of sarcomatous growth arising from the sternal periosteum, and also from the remains of the thymus body. Hare affirms that in nearly every case of secondary mediastinal sarcoma it has been primary in the pleura. Several cases have been reported in which this kind of tumour had arisen from the subpleural tissue, and afterwards encroached upon the mediastinum. Such mediastinal tumours seem to be not uncommon in very young children. This writer further states that next to the pleura come the abdominal viscera as the primary seat; and that the secondary tumour may arise either from direct extension through the diaphragm along the oesophagus, or from metastasis. Steven thought it not at all unlikely that if a secondary sarcomatous mass does fill the mediastinum, it has spread from the lung. It may, however, follow a similar disease in the arm or leg, or in any part of the body; and may occur after amputation for sarcoma of bone, of which I have met with some interesting and striking examples. Hare observes that "where the disease is primary in an arm, the secondary growth not infrequently occurs in the mediastinum, comparatively speaking, while sarcoma in the leg, as a general rule, attacks secondarily the abdominal viscera rather than the tissues above the diaphragm." I am not aware whether this statement holds good generally, but certainly, according to my experience, there are remarkable exceptions. Primary mediastinal sarcoma, especially lymphosarcoma, is apt to be followed by secondary metastatic nodules in distant organs, as the liver, spleen, and kidneys, so that a case may ultimately become more or less complicated. The tumour in the mediastinum secondary to sarcoma in remote parts, generally belongs to the round-celled or spindle-celled varieties of this growth; but it may be osteoid or enchondromatous.

Miscellaneous Growths.—It is necessary to offer a few general remarks, from a pathological point of view, about some of the other kinds of tumour mentioned in the list previously given, but which are of exceptional occurrence. With regard to *lymphoma* and *lymphadenoma*, Hare gives a table of 21 cases of mediastinal growths which he includes under these names; but Steven was decidedly of opinion that a number of these cases might with perfect accuracy have been relegated to the table of lymphosarcoma. It is quite possible, I think, that from local causes a group of lymphatic glands in the chest may become so enlarged as to constitute a tumour; and, of course, as already stated, these glands may be involved either primarily or secondarily in cases of generalised lymphadenoma.

Fibroma is a definite variety of tumour to be borne in mind in relation to the mediastinum, though it is very rare. It may start from

the sternum or the cellular tissue. Mediastinal fibroma is solitary, and seldom reaches any large size, but may do so. It is of very slow growth. The structure may be fibro-cellular or fibro-fatty, but is generally dense and fibrous. *Fibrosarcoma* has also been described. Steven gave an account of a case which he regarded as a fibrous-tissue tumour of the mediastinum, and which he names "malignant fibrosis," associated with pronounced rheumatic manifestations; and he believed the growth to be of rheumatic origin.

Dermoid cyst and *teratoma* are other varieties of mediastinal tumour which, though of very infrequent occurrence, must not be forgotten. Hare states that the mediastinum occupies the fourth position as the site of dermoid cysts. Out of 42 cases of mediastinal growth, collected by Rumpf in 1894, 5 were of this nature. The cyst originates as an embryonal development during fetal life, either from dipping in of the skin of the neck, or out of remnants of germinal folds. It does not, however, give any clinical indications of its presence until long after birth. In Christian's list of 40 cases the age at the time of operation or death was in 21 from 20 to 35; in 19 from 20 to 30. Symptoms had, however, existed long before.

As regards its structure, speaking generally, a dermoid cyst may be unilocular or multilocular, and besides fluid of different kinds, may contain such substances as cholesterin and oil globules, sebaceous glands and solid sebaceous material, sweat-glands, hair, teeth, fragments of bone sometimes closely resembling the superior maxilla, pieces of cartilage, and exceptionally structures suggesting spinal ganglia, or fetal lung and intestine.

Christian classified the cases as follows:—(1) Those of slight complexity, which are essentially dermoid cysts of ectodermal origin; (2) those of great complexity, which contain derivatives from all three germ layers, with the formation of rudimentary organs, and which may be regarded as teratomas; (3) tumours of the first and second class, which in some part of their structure are malignant, and form metastases in other organs. Of 60 cases collected and analysed by this observer in 1907, 7 belonged to the teratoma group; and he gives details of 3 cases, in one of which there was marked malignancy, in the sense of metastasis. He regards them as constituting a fairly definite group of mediastinal teratomas. "All occurred in young adults, and made their presence manifest by symptoms developing in the period following shortly after puberty. Duration of symptoms was relatively short as compared with most teratoid tumours of this region. The tumour grew from the mediastinum, but largely occupied the pleural cavity in each case. The bulk of the tumours consisted of a solid mass of tissue containing many small cysts. The cysts were lined by a variety of epithelium, and between the cysts was a stroma composed of unstriated muscle, fat, cartilage, bone, fibrous tissue, and neuroglia; the tumours thus made up are of great complexity of structure, and resemble in this aspect tumours which are far more common in ovary and testicle, and for which the name embryomata has been suggested."

Hydatids, syphilitic gumma, and *tuberculous glands* in the mediastinum have to be remembered as possible varieties of tumours in this region, but their nature and origin are well understood, and they do not call for any description here. Syphilitic growths may certainly originate in the bony structures and extend inwards; and cases are on record of gummatous tumours arising in the glands of the mediastinum (Wall). Whilst tuberculous glands are very common in the chest, it is only in exceptional cases that they attain such a size as to be regarded as tumours. Most of the others mentioned in the preliminary list are mere pathological curiosities. *Chondroma* of the soft parts is almost unknown, except when associated with sarcoma or other growth. *Osteochondroma* or *enchondroma* may grow inwards from the cartilaginous or bony structures forming the thoracic walls.

Etiology.—Several of the more important questions relating to the causation of mediastinal growths have been discussed in the preceding section, and it will only be necessary to draw attention here to a few additional points. It must be acknowledged that the precise etiology of primary growths in this region is very obscure; and in a large proportion of cases no definite or even probable existing cause can be suggested. Hereditary proclivity may account partly for some malignant tumours; or they may fairly be looked upon in many instances as manifestations of a general diathesis, favoured by local circumstances. Syphilitic and tuberculous formations in the mediastinum are of course mere local developments of these conditions; and, as already stated, fibroma was regarded by Steven as a rheumatic manifestation. The growth last mentioned may, however, be associated with caries of the sternum or vertebrae; and in some instances it can only be regarded as an exaggerated local result of chronic mediastinitis. Individual cases of tumour in the chest have been attributed to prolonged pressure in connexion with occupation, a blow or other injury, or the effects of cold; but the real influence of such antecedents is very difficult to estimate. It is quite possible that in some instances local irritation or injury of different kinds, which is not evident, may have some effect in starting a growth in favouring circumstances. Hare thinks that "sarcoma is much more frequently produced by pressure on the chest by foreign bodies, or like causes, than is cancer, probably owing to the fact that the tissues particularly favourable to sarcoma are the ones most generally affected by such causes."

The influence of *age* and *sex* in relation to intrathoracic growths, especially those of a cancerous or sarcomatous nature, demands brief notice, but there are marked discrepancies between the conclusions of different observers. With regard to *age*, it may be affirmed that no age is exempt, even from early childhood—though very exceptionally—to advanced life,—70 years or more. Among Hare's cases one is mentioned of encephaloid in the mediastinum in a patient only 4 years old; and a case was reported by the late Dr. Angel Money in an infant 18 months old. Taking all mediastinal tumours together, of 55 cases collected by Eger, 67 per cent were under 40. Sir R. Douglas

Powell states that true cancer in this region rarely occurs before middle life. Hare concludes that most mediastinal growths occur in adults. Hertz says that they are chiefly met with in the young and middle-aged, from 20 to 40; most cases from 20 to 30. It is generally agreed that lymphosarcoma and other sarcomatous growths occur at an earlier period of life than carcinoma; and the largest number of cases of this kind are met with in the decade from 20 to 30.

With regard to *sex*, taking all mediastinal growths together, the general conclusion is that there is a large preponderance among males; and this conclusion is supported by the cases collected by Hare, both as regards cancer and sarcoma, the proportion being more than two to one; it applies also to the other tumours in this region. Sir R. Douglas Powell, however, states that sarcoma is more frequent in females, cancer rather more prevalent in males.

MORBID ANATOMY. — It is a difficult matter to determine how far it is desirable to enter here into the consideration of the morbid anatomy of mediastinal growths; obviously the limits of this article forbid much detailed description of the several varieties, or of their histological structure; and it will only be necessary under this heading to deal specially with carcinoma and sarcoma, sufficient account having already been given of the characters of such of the exceptional kinds of tumour as seemed to require more than mere enumeration.

The first point to be noticed in relation to the morbid anatomy of mediastinal growths is their situation, in respect of the divisions of the space in which they are found. According to some writers, primary cancer is most frequent in the posterior mediastinum; and Steven properly pointed out that, considering the origin of cancer in epithelial tissues, this is the most likely place for a primary carcinoma to develop within the chest. Hare, however, maintains from his statistics that all primary growths are far more frequent in the anterior division than in other parts of the mediastinum. The late Dr. Wilson Fox stated that primary tumours occur nearly twice as often in the anterior as the posterior mediastinum. The latter division comes next in order; or there may be independent growths in both parts. The middle mediastinum is very rarely affected alone. Extension from one division to another is not uncommon, and occasionally the entire space is ultimately involved by carcinoma or sarcoma. In exceptional cases the growth may be fairly described as occupying the superior mediastinum. When sarcoma is secondary, it appears to affect most frequently the posterior or middle division.

The size, extent, shape, and rapidity of growth, as well as the characters of mediastinal growths, vary considerably according to their nature. In general terms they may be classified as solitary tumours of different sizes; multiple small or large tumours united into one mass, usually irregular or lobulated; and diffuse infiltrations. Haemorrhage into their substance, or degenerative changes, with softening, may alter materially their original characters. The softer growths are likely to

make rapid progress; and those which begin in the glands, once they break through their capsules, tend speedily to infiltrate the mediastinal space generally. A tumour starting in the mediastinum may grow upwards into the neck, or downwards into the abdomen.

While it is not practicable to give any definite general description of mediastinal tumours, it appears desirable to point out the chief characters of lymphosarcomatous growths in this region. They usually give rise to an irregularly lobulated tumour, evidently composed of agglomerated glands, often of considerable size, superficially firm to the touch, and sometimes surrounded entirely or partially by a dense fibrous tissue or capsule. The growth may, however, be remarkably adherent to surrounding structures. On section it is generally white or yellowish-white, but may be very vascular, or even exhibit minute haemorrhages scattered through its substance. Its consistence is usually soft and friable, and a white creamy juice sometimes escapes on section. A lymphosarcoma may, however, be hard and cartilaginous, as in a case of Dr. Mott's. Microscopical examination shews small round or oval-shaped cells, with a delicate connective-tissue stroma.

Effects of Mediastinal Growths upon Adjacent Structures. — In the introductory remarks to the article on diseases of the mediastinum a summary is given of the different ways in which the neighbouring structures may be affected. The effects thus produced assume a peculiar importance in relation to growths or tumours originating in or encroaching upon this region, and therefore call for somewhat detailed consideration in the present connexion. It will be readily understood that these effects differ widely according to the situation, anatomical relations, and dimensions of a growth; whilst there may be more than one tumour. Moreover, they vary materially with the nature of the growth, and before dealing with individual structures it is desirable to offer a few general remarks on this point. Localised non-malignant tumours merely lead to such physical consequences as are liable to happen from their situation, as the result of pressure or irritation; and they do not tend in any way to implicate adjacent structures. "Malignant growths, be their variety what it may, have certain peculiarities as to their development when in the mediastinum which they do not possess elsewhere, at least to so marked a degree. For example, mediastinal cancer does not confine itself as a general rule to any one or two tissues, but makes its onward march, involving whatever may come in its path" (Hare). When of a hard scirrhous nature, however, it tends to remain circumscribed; encephaloid, on the other hand, spreads rapidly and over a considerable area, usually soon attacking different structures in its progress. Steven correctly stated that carcinoma, as a rule, does not become so bulky as a sarcoma; whilst in its growth it steadily infiltrates, and causes ulceration of everything coming into contact with it. This may occur, moreover, with a minimum of growth of the tumour as regards its bulk. Hence it happens that cancer not only invades, but causes ulceration and perforation of tubes or vessels, severs nerves,

erodes bones, and produces other destructive effects. In his very instructive and interesting discussion of the local relationships of mediastinal sarcoma, this writer brought into prominence certain important peculiarities. He first mentions that the effects of a sarcomatous tumour may vary a good deal according to the form which is present. Mediastinal lymphosarcoma exhibits well-marked local malignancy, which plays an important part in determining the relationship of the tumour. One of the features of these growths, which Steven regarded as perhaps the most characteristic, is the manner in which they mould themselves round the great tubular and vascular structures of the upper portion of the thoracic cavity, without actually implicating them. He describes the aorta and its large branches as often completely buried in the midst of the tumour; but, as a general rule, by careful dissection the morbid tissues can be pretty completely separated from the arterial wall. The veins suffer much more severely than the arteries, and may present well-marked intravenous growths of the morbid tissue. Steven describes changes in the bronchi which will be more conveniently referred to later on. The relationship of a lymphosarcomatous growth to the nerve-trunks within the thorax which it happens to implicate is of a similar nature. They are often found to pass into and to become buried in the midst of the tumour, but they are merely surrounded, and perhaps flattened but not destroyed, so that they can be dissected out.

Another peculiarity of lymphosarcomatous tumours of the mediastinum, upon which Steven laid stress, is their tendency to grow in the direction of least resistance. He called attention to the manner in which, though bulky and lobulated as most of them are, they insinuate themselves in and out between the different structures in their neighbourhood, and do not simply crush the organs aside, or actually incorporate the surrounded structures and tissues into their substance, at least in the first instance. My experience agrees with his, that sarcoma occupying this region never causes erosion of bone.

It will now be convenient to indicate the possible effects of mediastinal growths upon the more important thoracic structures, so far as these have a practical bearing upon the clinical history and progress of individual cases.

Apart from tumours originating in the respiratory apparatus itself, and setting aside functional disorders which may arise from interference with nerves, this system is very liable to be directly affected in some part or other by mediastinal growths. The trachea is often compressed, and may be so narrowed as to leave only a small fissure; or it is surrounded by lymphosarcomatous tissue which can be separated from the tube. It may, however, become itself involved by a cancerous growth, but is very rarely perforated. Obstruction may occur at the bifurcation of the trachea. A main bronchus is often interfered with by pressure, being flattened, and its channel becoming much narrowed or even obliterated; or it is directly implicated in a growth at the root of the lung, which may penetrate it, or even extend along its divisions into the substance

of the organ. Moreover, independent small tumours may develop in connexion with these tubes, projecting into their interior. With regard to lymphosarcoma Steven writes: "The bronchi very frequently suffer severely from the local malignancy of lymphosarcomatous mediastinal tumours. The whole normal histological structure of the bronchial wall may entirely disappear, nothing being left but a channel, more or less narrowed, through the tumour tissue. . . . It is not at all unlikely that in many cases the bronchial tubes may be very considerably dilated, the bronchiectasis being partly due to the local action of the tumour on the bronchial wall, and partly to paralytic conditions induced by pressure on nerves and plexuses."

The conditions which may be produced in the lung itself by mediastinal tumours, besides its secondary implication, demand special attention. They vary a good deal under different circumstances. Either organ may be merely compressed, sometimes so completely as to become practically airless. More or less collapse also usually results from obstruction of a main bronchus. On the other hand, distension of the air-vesicles occurs from the slighter degrees of pressure; or there may be a combination of collapse and distension in different parts of the same lung; whilst if one organ is compressed or collapsed, the opposite one will probably undergo compensatory enlargement. Bronchiectasis may follow compression of the bronchi. In rare instances interlobular and subpleural emphysema has been observed. Another group of pulmonary conditions which may be associated with a mediastinal tumour are congestion, oedema, and sometimes haemorrhage. Congestion may arise merely from grave interference with the respiratory function; or it may be hypostatic in patients confined to bed. Oedema and haemorrhage have been attributed in most cases to pressure on and obstruction of the pulmonary veins. The haemorrhage may be in the form of partially decolorised infarcts, or it may consolidate the greater part of a lung. Thrombosis of the branches of the pulmonary artery occasionally occurs, or this vessel may be invaded by a growth.

Lesions of an inflammatory nature not uncommonly involve one or both lungs in cases of mediastinal tumour; and destructive changes may take place, occasionally ending in gangrene. As the result of obstruction of the air-tubes, bronchitis with excessive secretion is very common, and the secretion may be extremely dense and adhesive. Purulent material may collect in bronchi or dilated bronchi, giving rise to the appearance of scattered puriform spots, general purulent infiltration, abscesses, or cavities. Pneumonia, with red or grey hepatisation, is sometimes produced, and catarrhal pneumonia may follow collapse. Destructive and gangrenous lesions have been attributed to various causes, including chiefly obstruction of the bronchial arteries; compression or invasion of the pneumogastric nerve, or of the pulmonary plexus at the root of the lung; direct pressure on the pulmonary tissue; implication of the pulmonary arteries; and accumulation of retained secretions in the bronchi. The last mentioned was believed by Wilson Fox to be the

most probable cause in the majority of cases. With regard to the mode in which interference with nerves is supposed to produce its effects on the lungs, they have been referred to direct nutritive disturbances (Budd); paralysis of the bronchial tubes (Gull); or the passage of food or saliva into the larynx, as the result of paralysis, these materials thus gaining access into the bronchial tubes. The last seems to be the most probable explanation as a rule. The various infective micro-organisms which are known to produce the changes in the lung now under consideration, will of course have ample scope for their action in many cases of mediastinal tumour, and it is to these organisms that the lesions just mentioned must be directly attributed.

The pleura must always be borne in mind in relation to mediastinal tumour, altogether apart from its primary or secondary implication by a morbid growth, or the projection of such a growth into the pleural space. Effusion into this cavity is common, and in a certain proportion of cases it is sero-sanguinolent or actually haemorrhagic; but too much reliance must not be placed on this latter point from a clinical aspect, for the fluid is in most cases perfectly clear. In very rare instances the effusion is bilateral. Pleural effusion may result either from pressure on the pulmonary veins or vena azygos, or from inflammation. All malignant tumours in the mediastinum have a great tendency to excite inflammation of the serous membranes with which they come immediately into contact; and it appears to be usually of a very acute and intense character, the fibrinous exudation being often very abundant. Empyema is extremely rare, but may occur; and pneumothorax has been recorded.

The structures next to be mentioned in relation to the effects of mediastinal growths are the pericardium, heart, and great vessels. The implication of the pericardium is considered in the article on "Diseases of the Pericardium" (Vol. VI.). Pericardial effusion is not uncommon; and acute pericarditis of a severe type may supervene, sometimes haemorrhagic, very rarely purulent. The cardiac walls may be invaded from the pericardium; or direct extension of a growth has been known to take place from the superior vena cava into the right auricle, or from the pulmonary vein into the left auricle. The heart is often displaced in various directions by a mediastinal tumour, sometimes considerably; and the organ may be thus much embarrassed. Occasionally it appears to be compressed by an enveloping growth.

The aorta and its branches are much less frequently and severely interfered with than the veins, but one or more of these vessels may be compressed or even obliterated. The aorta has even been perforated by a cancerous growth, leading to fatal haemorrhage. Allusion has already been made to Steven's description of this vessel and its branches being buried in lymphosarcomatous tissue, which can be completely separated by careful dissection.

The large intrathoracic veins are very liable to suffer from the effects of mediastinal tumours, being often compressed or obliterated, or sometimes directly invaded. Steven observed in some of his specimens that

lymphosarcoma exhibited well-marked intravenous growths. The superior vena cava or either of its larger branches may be implicated, and very rarely the inferior vena cava. The vena azygos is occasionally affected; but this vessel may also be greatly dilated as the result of an impediment in the superior vena cava.

With regard to the nerves, the pneumogastric or recurrent laryngeal are much the most commonly affected. Some years ago I met with two cases, in one of which the right, and in the other the left recurrent nerve was involved in a tumour. The phrenic is very rarely implicated. In most cases the nerves are merely flattened out by pressure; but when they pass through a growth all traces of them may be lost. The pneumogastric has been found, however, to traverse a tumour unchanged. Infiltration of cancer cells between the nerve fibres and other structural changes have been described. The pulmonary plexus may be interfered with. No doubt the sympathetic trunk may be implicated; and also some of the nerves forming the brachial plexus.

The oesophagus is not only the starting-point for not a few cases of mediastinal tumour, but is also liable to be compressed, and its calibre thus seriously narrowed. The tube is seldom penetrated, but this event may happen. In lymphosarcomatous cases, although surrounded by the growth, it may not be materially interfered with. Compression or implication of the thoracic duct occasionally occurs; and it is said that when this duct is obliterated chylous ascites may follow.

The invasion of the chest wall by mediastinal tumours has been previously referred to. The sternum and ribs seem to be usually only pushed forward; erosion and destruction of bone or cartilage may result from pressure, chiefly in cases of cancer. Very exceptionally a tumour encroaches upon the vertebral canal, and affects the spinal cord or its membranes. The diaphragm is not uncommonly implicated during the progress of a mediastinal growth, and may be extensively infiltrated.

Clinical History.—The preceding discussion of the morbid anatomy of mediastinal growths, and of the diverse effects which they may produce in connexion with the several adjacent structures, will have made it at once evident that it is by no means an easy matter to give any comprehensive description of their clinical history, or of the phenomena by which their presence is revealed in individual cases. These phenomena are met with in the most varied combinations, and it is hardly possible to find any two cases exactly alike. They naturally come under the usual broad divisions of symptoms; and physical or other signs revealed by different methods of skilled examination. In the following discussion it will be convenient to recognise this distinction; whilst the plan of clinical investigation outlined in the introductory remarks to the article on "Diseases of the Mediastinum," p. 597, will form a practical basis for their systematic consideration. In this way it will be possible at any rate to present a fairly intelligible account of the phenomena which may be met with in different circumstances; and at

the same time an opportunity will be afforded of emphasising those which are of most frequent occurrence, and most important from a diagnostic point of view; and of explaining when necessary their immediate causation and significance.

Taking a comprehensive survey of cases of mediastinal growth or tumour as they come before us in practice, they may be primarily arranged under certain groups, to which attention will be directed before considering the symptoms and physical or special signs in detail.

(1) In the first place, it is important to note that growths sometimes develop in the mediastinum, which are either entirely latent, or occasion such slight disturbance that they do not attract sufficient attention to lead to examination of the chest; or if such examination be made, it reveals nothing at all, or perhaps only signs so indefinite as to appear to be of little or no consequence. Thus it may happen that a mediastinal tumour, of small dimensions, or so situated as not to interfere with the functions of any important structure, may altogether escape recognition during life. Even a growth of some size in this region, especially in the anterior mediastinum, has thus remained undetected in circumstances in which other conditions giving rise to prominent or grave symptoms have obscured its presence.

(2) Occasionally it happens that a mediastinal growth of small dimensions, it may be a mere nodule, from its situation originates pronounced symptoms, thus simulating one of considerable size; whilst physical examination yields no results, or none of a definite or trustworthy character. Cases beginning in this way are likely, however, after a time to present more or less characteristic physical signs, either associated with the tumour itself, or due to its effects on some of the thoracic contents.

(3) There is an important class of cases in which a mediastinal tumour comes under clinical observation under the aspect of a chronic pleurisy with more or less effusion. In these circumstances the real nature of the disease is liable to be altogether overlooked or misunderstood, unless the concomitant circumstances of the case or the general symptoms excite suspicions which may ultimately lead to the correct diagnosis.

(4) The last group to be mentioned consists of those which present themselves as obvious cases of mediastinal tumour, both as regards symptoms and physical signs; though these phenomena present great variety as to their exact nature, mode of onset and progress, degree, and combinations. Whether the growth has started in the mediastinum or has encroached upon this region from other structures, the clinical signs are more or less of a similar kind; and, as a rule, in the group of cases now under consideration, they are at any rate sufficiently characteristic to point to the conclusion that the mediastinal space is occupied by some abnormal mass or infiltration. Of course a mediastinal tumour may have existed for some time before its presence is thus revealed clinically; or it may have been preceded by phenomena merely indicating

pulmonary or pleuritic disease, the case sooner or later assuming a mediastinal character.

Symptoms.—Having thus attempted to give a comprehensive summary of the chief aspects under which mediastinal growths present themselves clinically, my next object is to endeavour to discuss from a practical standpoint the symptoms which have to be studied in connexion with these morbid conditions.

A. *Symptoms of Local Origin.*—The phenomena coming under this category will now be considered according to the arrangement adopted in the introductory summary in the article on "Diseases of the Mediastinum," p. 597.

(*a*) Painful and other Morbid Sensations.—Pain is usually regarded as a frequent symptom in connexion with mediastinal tumour, and may be the earliest or even the only one; a number of cases have, however, been observed in which well-marked pain was quite exceptional, or came on late in the course of a particular case; so that it is by no means essential. It may be due to various causes, and different kinds of pain may be met with in the same case. It varies in its site according to circumstances. When a growth occupies the anterior mediastinum, and presses upon the sternum, the pain will be post-sternal; in other cases it is referred to a greater or less area on one side, or to the back of the chest. It is frequently of a darting or lancinating character, shooting in different directions, as up the neck, towards the abdomen or loin, or to the opposite side of the thorax. In some instances it has been described as of a pressing or grinding character. Pain in the head is not uncommon. When the brachial plexus is involved, painful sensations are experienced in the shoulder or arm, on one or both sides, even down to the hands or fingers, it may be. Pain is sometimes intermittent or paroxysmal. It varies greatly in degree, and is occasionally very severe, or even agonising. As a result of implication of the intercostal nerves intense pain over one side of the chest has been observed, with corresponding sweating and herpetic eruption. More or less local tenderness on pressure or forcible percussion may be present; and occasionally there is very well-marked superficial hyperaesthesia or hyperalgesia. Pain associated with mediastinal tumour is sometimes increased at first by bodily exertion.

In some instances the subjective sensations hardly amount to pain, but are described rather as a feeling of uneasiness or discomfort in the chest, oppression, pressure, fulness, constriction, and the like. Numbness, tingling, or other paraesthesiae are sometimes felt in the upper extremity, as the result of pressure upon the brachial plexus. Abnormal sensations may also be referred to the throat, as of a foreign body; or there may be pain on swallowing.

(*b*) Disorders of Respiration.—The phenomena coming under this head are amongst the most common and prominent symptoms in cases of mediastinal tumour. Not infrequently some form of dyspnoea first attracts attention; whilst its undue proportion to other symptoms and physical signs may be of considerable diagnostic importance, or it may

even be practically the only symptom for long periods or throughout. The disturbances of breathing may result from any of the factors associated with mediastinal diseases, which often act in various combinations. They demand in every instance particularly careful and systematic investigation; for when properly studied and understood the phenomena observed are often highly significant, or even quite characteristic.

The disturbance of respiration generally comes on in an insidious and progressive manner, until it ultimately may become very severe, and assume grave characters. Not uncommonly it is at first paroxysmal, occurring only at intervals, which may be prolonged; and, even when constant dyspnoea is established, it may present paroxysmal exacerbations from different causes, sometimes amounting to partial suffocation. Occasionally the presence of a tumour in the mediastinum is revealed by an acute or sudden onset of dyspnoea. The respiratory disorder differs much in its characters in different cases, as well as in its severity, and it usually changes in these respects during the progress of a particular case. It may only amount to more or less shortness of breath, or breathlessness on exertion; and in any circumstances this is usually one of its prominent features. In advanced cases the least movement or effort causes great distress. The frequency of respiration, when the patient is quiet, differs a good deal in individual instances, and is not uncommonly quite normal; so that no particular importance can be attached to this point. The breathing may, however, be persistently quickened. In some instances it is obviously laboured; whilst in others distinct asthmatic attacks occur, one of which may end fatally. These paroxysms of dyspnoea may be associated with enlarged mediastinal glands in children, as pointed out by Dr. Goodhart, who attributes them to a spasm of the whole lung due to interference with the mediastinal nerves. Similar attacks may certainly be met with in cases of other kinds of mediastinal tumour; and they may occur in the course of malignant growths.

The most significant respiratory disorders associated with mediastinal growths, which are to be specially watched for, are those indicating definite tracheal or bronchial obstruction, or implication of the vagus or inferior laryngeal nerves. In the former case there will be an obvious and constant obstructive difficulty, varying in degrees, attended probably with noisy or stridulous breathing, or with wheezing or whistling sounds of various kinds; the phenomena being often highly characteristic. Interference with nerves affects the respiration in different ways, but it must be particularly noted that dyspnoea may thus arise due to muscular disturbance, whether spasmodic or paralytic, affecting the glottis; being then likely to assume a paroxysmal character, though in certain circumstances it may be always present more or less. When the phrenic nerve is involved the diaphragm will be affected, but the difficulty in breathing induced in this way could only be made out by investigating the diaphragmatic movements. Possibly in these circumstances hiccup might be a prominent symptom.

The subjective sensations associated with the respiratory difficulties in cases of mediastinal tumour are often very pronounced, giving rise to much evident suffering and distress. The patient also frequently presents a more or less cyanotic aspect, which may be entirely due to such difficulties, along with cardiac embarrassment; but this condition is generally associated with and aggravated by the effects of venous obstruction. In a considerable proportion of cases orthopnoea is established sooner or later, any attempt at the recumbent posture causing urgent and intense fits of dyspnoea. Some patients are ultimately obliged to sit up in a chair constantly, never daring to go to bed, and at the best only having fitful snatches of slumber. They may instinctively and habitually, even during sleep, lean forwards or sidewards, in order to relieve the pressure on the main air-tube.

(*c*) Cough; Expectoration; Haemoptysis.—Cough is another symptom which is almost always present during some part of the course of a case of mediastinal growth, and it comes on not uncommonly at a very early period. It is, however, not absolutely essential, and may hardly amount to more than a voluntary attempt on the part of the patient to get rid of some persistent feeling of obstruction or accumulation of mucus. When present, cough differs much in severity in mediastinal tumour, but tends to increase, and to become more and more troublesome as the case progresses. It is often of a teasing and irritable character, giving the impression of being due to irritation of the main air-passage or bronchi. The more significant kinds of cough are the stridulous or wheezy variety, indicative of pressure on the trachea or a main bronchus; or the paroxysmal and spasmodic type, associated with laryngeal muscular disorder or organic changes, and of croupy or clanging quality, or accompanied with various degrees of huskiness or hoarseness, in some instances being almost entirely aphonic. The different sounds produced during the act of coughing in cases of mediastinal tumour are highly suggestive to the educated and accustomed ear. The paroxysms are in some instances very distressing, and attended with grave disturbance of breathing.

Not uncommonly cough associated with mediastinal growth is practically dry; and this may be a suggestive point in diagnosis, when the cough is irritable or paroxysmal. Even when expectoration is present, in the very large majority of cases ordinary examination of the sputum does not afford any reliable information. Often only a small quantity of viscid, tenacious mucus is discharged; or the expectoration is simply bronchitic, muco-purulent, or bronchorrhoeal, the last being probably the result of a pulmonary congestive condition.

When a dermoid cyst communicates with the main air-passages, hairs or other characteristic structures may be discharged with the expectoration.

Haemoptysis only calls for brief notice. The expectoration is frequently streaked with blood, but this is of no special significance when associated with violent cough. My experience agrees with that of Sir R. Douglas Powell that haemoptysis is not an important sign of

mediastinal tumour; but sanguineous expectoration may be observed should the growth invade the lung, and sometimes profuse haemoptysis then occurs, which may be followed by considerable though temporary amelioration of symptoms. In only a few of the cases collected by Dr. Vincent Harris was the sputum tinged with blood. It is important to note, however, that when a mediastinal growth perforates the trachea it may bleed into its interior, and thus give rise to definite haemoptysis; as happened in a case which came under my observation.

(*d*) Alterations in Voice.—A mediastinal tumour is likely to originate symptoms coming under this category, but their frequency varies considerably. An intermittent aphonia has been observed amongst the earliest phenomena, sometimes along with paroxysmal dyspnoea. A change in the quality and pitch of the voice, as well as more or less hoarseness, may certainly result from direct pressure on the trachea, or invasion of its channel. By far the most frequent and important symptoms of this kind, however, are those due to implication of one of the vagus nerves or its inferior laryngeal branch. A certain degree of hoarseness may be present without any obvious paralysis of the vocal cords, being then probably due to irritation or spasm. Pronounced hoarseness and weakness of the voice, culminating in aphonia, are chiefly associated with paralysis of the cords. In some instances actual morbid changes in the larynx give rise to alterations in the voice. Thus the laryngeal muscles occasionally become atrophied; or laryngitis, oedema of the glottis, or ulceration of the larynx may be set up; or there may be independent malignant disease of the larynx.

(*e*) Cardiac and Arterial Symptoms.—Palpitation and obvious cardiac disorder are not uncommon in cases of mediastinal tumour, owing to displacement or embarrassment of the organ; implication of its substance along with the pericardium; pericardial effusion; interference with the pulmonary circulation; or nerve disturbance due to the vagus trunk or cardiac plexus being involved. The condition last mentioned may also cause either tachycardia or bradycardia; and these disorders may occur at intervals. Different kinds of irregular cardiac action are observed in some cases. Anginal attacks, or a tendency to syncope, have also been noted. The pulse is in most cases increased in frequency. Should a mediastinal growth interfere with either of the main branches of the arch of the aorta, the corresponding pulses will be affected—carotid, radial, or both—in the way of retardation, or of more or less feebleness, to complete extinction. Inequality of the radial pulses may disappear, owing to the pressure becoming equalised during the growth of the tumour. It must not be forgotten that in exceptional cases a growth makes its way into the aorta, and fatal haemorrhage occurs. It is a question whether arterial obstruction may help in causing oedema of one arm, but when this condition is present the veins are generally implicated also. Gangrene of the legs has been noted in a case in which the descending aorta and inferior vena cava were both pressed upon by a mediastinal tumour. The *pulsus paradoxus* has been observed in some cases.

(*f*) Symptoms of Deficient Blood-aeration and Venous Obstruction.—As already stated, more or less cyanosis may result in cases of mediastinal tumour from interference with the respiratory functions. This condition may, however, give rise to definite signs of local venous obstruction, without any evidence of deficient blood-aeration. Most commonly the objective and subjective phenomena coming under this category are the outcome of the combination of both these causes. These phenomena were described in detail in the introductory remarks on the clinical investigation of "Diseases of the Mediastinum," p. 600; and it will suffice here to offer a few remarks bearing upon their relation to tumours in this region. They are of much importance in this class of cases, and often afford valuable information as to the presence and situation of a mediastinal growth. The evidences of venous obstruction may appear a considerable time before any other symptoms; especially swelling of the neck and face, which sometimes comes on suddenly, and is usually bilateral, but occasionally unilateral. Not uncommonly the patient has first noticed that he cannot button his shirt on account of enlargement of the neck; or puffiness of the eyelids has attracted attention at the outset. Sometimes the swelling has started in one arm. In other instances lividity of the face is the earliest indication of venous engorgement. Sooner or later, in a considerable proportion of cases of mediastinal tumour all the signs of this condition become prominent, as indicated by the cyanotic colour, oedematous swelling, distension and tortuosity of superficial veins, and so on. They are usually bilateral, and give rise to a highly characteristic appearance. Sir R. Douglas Powell describes a slightly staring, suffused, and anxious expression of countenance as most common; but in marked cases there is an aspect of semi-strangulation most painful to witness. The changes may be unilateral or localised, and the jugular vein on the compressed side may remain distended during inspiration, while that on the opposite side becomes emptied. Any of the consequences of cerebral congestion are apt to arise; and epistaxis or other haemorrhages may occur. Exceptionally exophthalmos has been noticed in mediastinal tumour in association with enlarged thyroid, or with malignant growths around this organ. Signs of obstruction of the inferior vena cava are extremely rare in cases of this nature, but they do occur. A mediastinal growth may interfere with the vena azygos, and originate corresponding symptoms.

(*g*) Disorders of Deglutition.—Dysphagia is an important symptom of mediastinal tumour, not only when it starts in the oesophagus, but also when this tube is compressed by or involved in a growth. This symptom may be amongst the earliest, and is sometimes very prominent for a considerable time, as I can testify from personal observation. The difficulty is occasionally influenced by posture, and may be intermittent when of reflex nervous origin. Deglutition may be painful, or attended with other unpleasant or even distressing subjective sensations. Ultimately the oesophagus may become the seat of complete obstruction or stricture, and a pouch-like dilatation may form above the tumour. In

the very exceptional cases, in which the tube is perforated by a growth, vomiting of blood may possibly occur.

(*h*) Special Nerve Symptoms.—As a result of pressure by a tumour upon the brachial plexus, not only may sensation in the arm be affected, but in exceptional cases muscular paralysis and wasting are produced. Vomiting has occasionally been attributed to interference with the vagus nerve. Owing to pressure on the sympathetic trunk, contraction of the pupil, generally on one side, has been observed, which may be associated with ptosis; occasionally, on the contrary, there is dilatation. Possibly unilateral vasomotor disorders may be noticed in the face and head. All these phenomena, however, are extremely rare in connexion with mediastinal tumour.

(*i*) Spinal Symptoms.—It is believed that numbness and paraesthesiae in the legs may result from congestion of the spinal cord, due to interference with the vena azygos by a mediastinal tumour. What is more important, however, is that in rare instances the cord and its membranes become themselves involved during its progress, giving rise to spinal pain, and eventually to paraplegia or other phenomena, of which I have met with a very striking example. Growths in connexion with the cord may, however, be primary, being followed by secondary development in the mediastinum, and then the spinal symptoms occur at an early period.

Having thus attempted to give a comprehensive account of the local symptoms which may be associated with mediastinal growths, it must again be emphasised that in individual instances they present great differences as regards their time and mode of onset and succession, degree, exact characters, combinations, and progress. Signs of pressure or irritation may develop early, and at first in an irregular or intermitting manner; or they may not come on until a late period. Sometimes they occur in distinct groups; but often they seem to be capriciously associated. Pressure-symptoms are, as a rule, insidious in cases of mediastinal growth, but more persistent and less variable than those of aneurysm. They may, however, come on very rapidly or almost suddenly. The practical point to be insisted upon is, that the clinical observer must regard and study every case separately and individually, and, taking an intelligent grasp of the phenomena presented for his consideration, endeavour to understand them, and to interpret their significance—by no means always an easy task. It may be stated generally that the more pronounced symptoms when the tumour occupies the anterior mediastinum are those of venous obstruction and interference with the arterial circulation; whilst in the case of posterior mediastinal growths the air-passages, oesophagus, and nerves are more affected.

B. *General and Remote Symptoms.*—Under this head it will be convenient to mention not only the symptoms which are more strictly general, but certain others, not immediately associated with the chest, affecting particular organs or systems. Here again remarkable differences are observed in different cases. The general system may not be materially affected even when there is a large mediastinal tumour; whilst,

on the other hand, when the local evidences of intrathoracic disease are indefinite or absent, constitutional symptoms may be very prominent. In some forms of growth there is no reason why such symptoms should be produced, but as a rule they are likely to be more or less marked, either on account of the nature of the tumour itself, the changes it undergoes, or its effects upon vital structures. They are both subjective and objective, but of no specially defined character. The subjective feelings of the patient must not be overlooked, and sometimes a sense of fatigue and weariness, aching in the limbs, or indisposition for exertion have been among the first symptoms complained of. More or less weakness, culminating in exhaustion or prostration, is likely to be associated with the objective general symptoms now to be described. Amongst them wasting is very common, and should be particularly watched for. In some cases wasting is not sufficiently marked to attract attention, but probably there is always more or less loss of weight in connexion with a definite mediastinal growth. Sometimes emaciation is remarkably rapid; in other instances it is more slowly progressive, but ultimately reaching a marked or extreme degree. It is when the oesophagus is obstructed that wasting is most pronounced; and emaciation has also been specially attributed to pressure on the thoracic duct. A gradual and increasing deterioration of the blood, leading to marked anaemia, is one of the most prominent phenomena in many instances, and this symptom may appear at an early period. Exceptionally a leukaemic condition is met with. In the great majority of cases there are no indications of the so-called "cancerous cachexia," even though the disease be malignant. Sometimes the finger-ends are clubbed. With regard to pyrexia, it is as a rule practically absent; and, indeed, in connexion with cancerous and sarcomatous growths the temperature is often below the normal. During the progress of rapid malignant disease, however, fever is likely to occur, and in the last stages it may be of a hectic type. When lymphadenomatous growths develop within the chest in connexion with Hodgkin's disease, there may also be considerable pyrexia, with a peculiar range of temperature. Fever may, moreover, be associated with tuberculous formations, or even with a dermoid cyst. When the temperature is raised, it seldom follows any particular type; and, apart from complications, the elevation is only slight or moderate as a rule. Night-sweats are sometimes troublesome. Impairment or loss of appetite, dyspeptic symptoms, insomnia, or other disturbances not uncommonly add to the patient's troubles in cases of mediastinal growth, and contribute to the general wasting and weakness. Diarrhoea is present occasionally. Free diuresis has been observed in the early stages of mediastinal tumour; and albuminuria may result from obstruction of the inferior vena cava.

C. *Physical and Special Signs.*—The phenomena coming under this category are obviously of essential importance in the recognition of mediastinal growths; but their study in this class of cases often taxes to the utmost the practical knowledge and skill of the clinical investigator, both in carrying out the several methods of examination, and in duly

estimating the value and teaching of the signs which they reveal. Hence it is particularly necessary to understand clearly at the outset the course of procedure to be followed, and to adopt it systematically in each individual case, so far as may be required. Of course cases do occur in which, even when symptoms are prominent, or, it may be, characteristic, physical or other special modes of examination give little or no help; whilst, on the other hand, the signs thus elicited may at once reveal the presence and situation of a mediastinal growth or tumour, which does not give rise to any appreciable symptoms, or, at any rate, to none of diagnostic significance. In most instances they afford valuable corroborative evidence in relation to diagnosis; or they clear up various points which cannot be otherwise demonstrated.

I. Physical Examination of the Chest. — The examination of the thorax by the usual methods will, as a matter of course, first receive attention in any case of suspected mediastinal tumour; yet it may not reveal anything when a growth is of small size, or is so situated as not to affect the normal physical signs of this region. Any one who has had much experience in these cases, and who is aware of the almost endless diversity in the combinations of physical conditions within the chest which they present in different circumstances, cannot fail to realise the difficulty of attempting anything like a systematic and comprehensive description of the abnormal signs which may be met with. Personally I am deeply conscious of this difficulty, and it will be impossible within the limits of this article to do more than to give a general summary or outline of the phenomena to be looked for in connexion with mediastinal growths, and to explain, so far as is practicable, their relation to these growths, or to their associated secondary effects. It is most important at the outset to understand clearly what these associated conditions may be, and to be prepared to recognise them in individual cases. In the discussion of physical signs I propose to follow the plan which I am accustomed to adopt in recording thoracic physical signs.

(1) Superficial Structures.—(*a*) The chief phenomena to be noted under this heading are those indicating venous obstruction within the thorax. They have already been referred to under Symptoms, but it must be remembered that as physical signs they not uncommonly require more or less careful investigation in cases of mediastinal tumour, and this applies particularly to dilated superficial veins, which by their situation and distribution often reveal clearly, not only that one or more of the intrathoracic veins are obstructed, but also which of them it happens to be. In this investigation attention must of course be paid to the parts above the limits of the thorax and to the arms, as well as to any enlarged veins over the abdominal surface. In order to determine the degree of venous difficulty, and how far the signs depend on interference with the respiratory functions, it may be desirable to observe the effects on the distended veins of deep breathing and vigorous cough.

(*b*) It will be convenient here to draw attention to the great importance of carefully looking and feeling for implication of the superficial

lymphatic glands in relation to mediastinal growths, and of noting their characters should they be found enlarged. Those to be more particularly studied are the supraclavicular, the infraclavicular, and the axillary glands. The cervical glands are said to be specially liable to be affected in cases of lymphosarcomatous growths, but they may also be involved in those of a cancerous or tuberculous nature.

(*c*) The third point to be noted in relation to the superficial thoracic structures is whether they are themselves involved in any morbid growth? A mediastinal tumour may follow primary malignant disease of the breast, or vice versa, and the two conditions may thus be met with together. It is extremely rare for centrifugal perforation of the chest wall to take place, even when it is much pushed out by a growth; but this event does occur exceptionally, its structures becoming implicated, though practically only in carcinoma. A growth of this nature may involve the sterno-clavicular joint, or the intercostal spaces; or may even penetrate the sternum. I have met with two or three remarkable cases in which the thoracic walls have been extensively infiltrated, along with intrathoracic growths; or in which disseminated sarcomatous collections have appeared in the superficial tissues in similar cases. These external manifestations are recognised by inspection and palpation; and it must be remembered that not only are they important in diagnosis, but they may also materially modify the signs elicited by other methods of examination.

In addition to the special points referred to in the investigation of the superficial structures, it must be noted that these structures are in many instances much wasted, as a part of the general emaciation.

(2) Shape and Size of Chest.—Mediastinal growths are very apt to affect the shape and size of the chest in different ways, though there may be no obvious change in these respects, even when other signs of tumour are well marked. As the outcome of the study of cases which have come under my personal observation, I submit the following summary of the deviations from the normal which may be met with; premising, however, that they present numerous diversities in detail in individual instances. In order to obtain more definite and correct records of dimensions and conformation, it may be desirable to take measurements of the chest, or to make cyrtometric tracings.

(*a*) The thorax is sometimes generally enlarged, though the two sides are seldom quite symmetrical. This may happen when a growth interferes with the trachea only to such a degree as to cause accumulation of air and consequent distension of both lungs; or when there is a large tumour occupying one side of the chest, with compensatory enlargement of the opposite lung. A similar condition of things might result from a large pleural effusion associated with a morbid growth. Pericardial effusion or displacement of the heart might also help in making enlargement of the thorax more general in cases of tumour on the left side.

(*b*) Unilateral enlargement of the thorax, affecting practically the whole side, though not necessarily to the same degree in all parts, is

quite exceptional in cases of mediastinal growths, but it may be observed when it is accompanied with a large pleuritic effusion, while the opposite lung remains of its normal size. I have, moreover, known the side to be practically distended throughout in connexion with a very large mediastinal tumour, or with one interfering in a minor degree with the main bronchus, thus causing accumulation of air in the lung. When the enlargement is due to a solid growth, the intercostal spaces are not prominent, though the normal depressions may be more or less obliterated, so that the surface feels unusually smooth.

(*c*) The opposite condition of unilateral retraction of the thorax associated with mediastinal tumour is only observed when a main bronchus is so obstructed by a growth as to lead to a collapse of the lung. Pleuritic adhesions may help to cause retraction; but it must be borne in mind that there may even be some fluid in the pleura, and yet the side be smaller than normal.

(*d*) A local prominence or definite bulging of some part of the thorax is one of the signs to be specially looked for in connexion with a circumscribed mediastinal tumour coming to the surface. Its situation and extent will necessarily vary; but it is most often noticed in front, at the upper part, and involving the sternum more or less. Bulging may, however, be observed laterally or posteriorly. The intercostal spaces will be affected in the same way as when a solid growth produces a more general enlargement. It may also be mentioned here that a mediastinal tumour sometimes extends upwards towards the neck, giving rise to a prominence in this direction.

(3) Movements of Respiration.—It may be stated generally that the effect of a growth in the mediastinum is to interfere more or less, and often to a marked degree, with the respiratory movements, which always demand careful investigation in a particular case, in order to determine the actual nature and significance of the disorder, and the conditions upon which it depends. A large mediastinal tumour will probably directly prevent pulmonary expansion. Other factors to be specially borne in mind are spasmodic laryngeal disorders; various degrees of obstruction of the trachea or a main bronchus; secondary effects involving the lungs; pleuritic conditions; and interference with the movements of the chest wall or diaphragm. As a rule, the most striking disorder of breathing, as determined by physical examination, is deficiency or abolition of inspiratory expansion of the chest, elevation being often at the same time excessive. This is occasionally general, but usually unilateral or local. When one lung is embarrassed, the opposite one may act excessively, so that the contrast between the movements on the two sides becomes very pronounced. Sometimes retraction of the lower part of the chest is observed during deep inspiration, this being as a rule unilateral; but it may be bilateral when the main air-tube is interfered with. In connexion with laryngeal or tracheal obstruction I have seen the lower part of the sternum and the contiguous rib-cartilages on both sides fall in markedly with each inspiration, even in adults. Depression of the supra-

sternal, supra- and infra-clavicular, and epigastric regions is occasionally observed. In some instances the breathing is entirely abdominal. In connexion with an emphysematous condition of the lungs expiratory retraction may be affected more than inspiratory expansion. In cases attended with unilateral bulging the corresponding intercostal spaces are practically motionless. The frequency and rhythm of respiration are often affected in connexion with mediastinal tumour, but these deviations present no common or regular type.

(4) Tactile Sensations.—The feeling on digital palpation over a tumour within the chest which reaches the surface is generally that of abnormal firmness and resistance, and this may be very pronounced. Exceptionally a sensation of indistinct fluctuation is noticed.

As regards vocal fremitus in cases of mediastinal tumour, it may be stated generally that such a growth always tends to impair or totally abolish this tactile sensation over the area which it occupies, but it may be increased at its confines, owing to condensed lung. Pleuritic conditions and emphysema must always be remembered as modifying the vocal fremitus. Tussive fremitus is affected in the same manner as that associated with the voice. Rhonchal fremitus, due to conditions of the bronchi, and often resulting indirectly from obstruction of the trachea or a main bronchus, is not uncommonly met with in cases of mediastinal tumour; and when unilateral or localised it may be of considerable diagnostic significance. In exceptional instances a more or less distinct pulsation is felt over a mediastinal tumour, possibly simulating that of an aneurysm. The movement is transmitted from the heart or aorta. A double impulse has been noticed, which may be felt by observer and patient as a sort of inward succussion (Walshe). The pulsation conducted from the aorta has been described as of a "knocking" character, and is, as a rule, essentially different from that of an aneurysm.

(5) Percussion Signs.—It is highly important in relation to mediastinal tumours to bear in mind when carrying out the method of percussion, not only the sounds which are thus elicited, but also the sensations which are felt by the fingers during the act. Not uncommonly the latter afford most useful information.

The *percussion-sounds* demand the first consideration, but the abnormal signs coming under this category vary a good deal in different circumstances. Mediastinal tumours, when of small size or occupying certain situations, may not affect the percussion-sound in the least, either in themselves, or by their effects upon the air-tubes or lungs.

The changes in the percussion-sound which are chiefly met with in cases of mediastinal growth may be indicated as follows:—

(*a*) In some instances the striking change in the percussion-sound is an increase in the extent of the pulmonary resonance, with hyper-resonance or possibly a tympanitic note; either generally distributed over the chest, or unilateral. Such a change indicates distension, either of both lungs, from a certain degree of obstruction of the trachea by a mediastinal tumour, or of one lung from similar obstruction of a bronchus.

In these circumstances a tumour, even of some considerable size, may be entirely obscured as regards its own percussion-signs.

(*b*) The percussion-sound to be more particularly looked for as evidence of the existence of a mediastinal growth is more or less pronounced dulness or flatness; and when such a growth comes to the surface the dulness is of the most marked and absolute kind. Obviously its situation and extent will vary in different cases. In some instances the whole of one side of the chest is completely dull, flat, and toneless, and this change may be conspicuous at the first examination. In other cases it increases progressively while under observation. This extensive dulness may be due to the coexistence of a pulmonary with a mediastinal growth, completely filling one side of the chest. Implication of the pleura, whether primary or secondary, is likely also to be attended with widespread dulness; and the possible effect of pleural effusion upon the percussion-sound must always be borne in mind, even in cases of limited tumour, which it may completely mask. As subsidiary causes of extensive unilateral dulness in some instances, associated with a mediastinal tumour, must be mentioned pulmonary collapse, or secondary consolidation of the lung due to inflammatory changes. The sound elicited over the corresponding regions of the thorax would, however, probably not be so absolutely dull as over the tumour itself, though it might be very difficult to distinguish between them. Pericardial effusion, if present, would also add to the dulness. When the superficial structures of the chest are involved in a growth, this condition will certainly contribute to the impairment of resonance, sometimes to a considerable degree.

In the large majority of cases of mediastinal growth the dulness is limited in its area, varying in its locality according to the situation of the disease. The following points are worthy of special attention in cases of this nature. As a rule the dulness, which is absolute, is observed in the upper and anterior region. It is then often mainly post-sternal, and in all cases crosses the middle line, though it encroaches more towards one side than the other, so that it is asymmetrical. The dulness varies much in extent, but may be noted over a considerable superficial area. Its shape is irregular, and it may present a distinctly sinuous border. On careful percussion towards the lung the circumference of the area of dulness is found to be bounded by the pulmonary note, which is considered very characteristic of mediastinal tumour as distinguished from primary lung disease. In some instances the dulness is not observed in front, but posteriorly; and occasionally it is limited to the interscapular region. I have met with cases of lymphosarcoma in which the upper part of the chest, both front and back, was extensively dull.

With regard to the heart and liver, it may be impossible to draw any line of demarcation between the dulness due to a mediastinal tumour and that associated with these organs; but such distinction can sometimes be made out by careful percussion, or possibly by auscultatory

percussion. It may be stated generally that dulness due to a mediastinal growth is in no way affected by change of posture. When the heart is displaced, this organ will also add to the dulness in the situation to which it happens to correspond.

(*c*) In exceptional cases the percussion-sound elicited over a localised mediastinal tumour is peculiar. Thus it may be of high-pitched, tubular, or amphoric quality, owing to conduction of the sound from the trachea or a main bronchus.

(*d*) Lastly, it is always necessary, in studying the percussion-sounds associated with mediastinal tumours, to be prepared to recognise different modifications over different regions. Thus there may be marked dulness in one part, while in other parts, or even over the rest of the side, the note is hyper-resonant, tympanitic, or amphoric. In rare instances a cracked-pot sound may be elicited over some portion of the thorax.

The *sensation* felt on percussion over a tumour or growth in the mediastinum which reaches the surface is usually one of remarkable hardness and resistance. This will vary in its extent according to the area occupied by the growth ; and when the whole side is dull the feeling conveyed to the fingers is often of great service in revealing that we have to deal with a dense solid mass, and in distinguishing it from the dulness due to fluid effusion.

(6) Auscultatory Signs.—Under this heading it is only intended to discuss the auscultatory signs connected with the respiratory apparatus. These also present much variety in different cases ; not only individually and in their combinations, but also over different parts of the chest. In many instances, however, they afford most valuable information, especially when studied in their association with other physical signs.

(*a*) Respiratory Sounds.—These are not necessarily affected in cases of mediastinal growth ; even when the existence of such a growth is revealed by other definite signs. The following are the chief alterations which may be met with. When both lungs are distended from obstruction of the main air-tube, the breath-sounds will probably be weak all over the chest, but may be accompanied with stridor. A similar condition affecting one lung may cause high-pitched, harsh, or stridulous respiration on the corresponding side ; but, as the obstruction of the bronchus increases, the tendency is towards weakening and finally abolition of the sounds, until they become entirely inaudible over the area of lung corresponding to the distribution of the obstructed tube. These changes may be noted successively during the progress of a case under observation, and when associated with normal, increased, or high-pitched resonance are very significant.

The respiratory sounds over a mediastinal tumour, when of not too large a size, and situated in the upper sternal region or in the posterior division, are likely to be bronchial or tubular, and may be intensely so. I have known the breathing in a case of tumour even of considerable size assume a distinctly amphoric quality, audible practically over the upper half of the posterior aspect of the chest on one side. When

it attains large dimensions and involves the lung, the respiratory sounds are generally suppressed over a corresponding area, and should the lower lobe be at the same time collapsed they will be inaudible over the whole side.

(*b*) Adventitious Sounds. — Mediastinal growths seldom give rise directly to any signs coming under this category, unless they should happen to break down and form abscesses or cavities, with which bronchi communicate. In these circumstances various rales might be heard, more or less moist, and perhaps having a hollow quality. As the result of pressure on the main air-passages, different kinds of rhonchi, sonorous and sibilant, are often audible, and when accompanied with stridulous breathing are very suggestive, especially if of unilateral distribution. These sounds, as well as mucous rales, may indicate definite bronchitis. Pleuritic friction-sound may be audible from time to time in some cases. Possibly a mediastinal adventitious sound might be elicited by movement of the arms in connexion with certain tumours occupying this region.

(*c*) Vocal Resonance.—It is desirable to study the voice, as well as the cough and whisper, in relation to growths in the chest; but the signs coming under this category present many varieties, and their indications must be determined on general principles. In connexion with a definite tumour, conducting the vibrations from the main air-passages, the vocal resonance may be very intense, and sometimes of aegophonic or amphoric quality. It is a striking fact that the vocal resonance may be thus exaggerated when the fremitus is greatly impaired, or even altogether absent. Occasionally distinct whispering pectoriloquy can be heard over a tumour. In the upper part of the chest and interscapular region collapse of the lung may help to intensify the vocal resonance; but in the lower region this condition would tend to diminish or annul it. Over a cavity pectoriloquy and whispering pectoriloquy would probably be heard, and the voice might have peculiar characters. Intensification of the vocal resonance above, or even pectoriloquy, and its absence below, may be associated with a tumour in the upper part of the chest, and condensed lung lower down. When, however, a tumour attains a very large size, the vocal vibrations may in time become entirely suppressed throughout. Pleuritic thickening or effusion will necessarily produce their usual effects in the way of impairing or abolishing the vocal resonance. The study of this sign is of little or no use when there is pulmonary distension, though this condition tends to weaken it. The tussive resonance may not only present similar changes to those of the voice, but sometimes cough is useful in bringing out or modifying adventitious sounds associated with the air-tubes or lungs.

(7) Cardiovascular Signs.—Examination of the heart sometimes affords useful signs in cases of mediastinal tumour, and always demands attention. The impulse is often indistinct and the apex-beat indefinite, because the heart is covered by distended lung, or by a growth which pushes it towards the back of the chest. A mediastinal tumour not

uncommonly causes more or less lateral displacement. More important, however, from a diagnostic point of view, is the fact that the heart is often pushed downwards or towards the ensiform cartilage. Pleuritic effusion will tend to cause the usual displacement, but this may be prevented by cancerous growths involving the base of the heart. Collapse of the lung may lead to elevation of the apex-beat, but not necessarily, even in extreme cases. The organ is occasionally dragged over towards the side of the disease in cases of retraction, but usually it is pushed in the opposite direction by the tumour. Murmurs, generally systolic, have been described in several instances over a mediastinal growth, or along the course of the aorta or pulmonary artery. A systolic murmur, audible in the back, was noted by Kaulich, associated with a dilatation of the aorta on the cardiac side; the vessel being compressed and narrowed beyond this. Pressure on this artery does not, however, necessarily give rise to a murmur. Double murmurs are of very uncommon occurrence (Walshe). In exceptional instances a pericardial friction-sound is heard. Of course it is always necessary to be on the lookout for signs indicating pericardial effusion, or implication of the pericardium or of the heart itself in a growth; though the latter condition would be very difficult to demonstrate positively.

With regard to the arteries, any disorders of the circulation associated with these vessels can usually be easily recognised by inspection and digital examination. Possibly the sphygmograph or other apparatus in modern use, might be of service in some cases. The veins must receive due attention, but this point has already been sufficiently considered in connexion with the superficial structures (p. 642).

II. *Special Examination.*—Having thus far considered the signs to be studied by the ordinary methods of physical examination in relation to mediastinal growths, it will now be convenient under this general heading to indicate the phenomena which may be revealed by special modes of investigation, which are only called for in particular circumstances.

(1) Examination of the Sputum.—In addition to the general examination of the sputum already referred to, it is important in certain cases to subject any materials expectorated to careful investigation with the microscope, and the help of an expert pathologist may be required. This may reveal not only the presence of the distinctive elements of malignant growths, associated it may be with definite fragments, but also of blood-corpuscles when blood is not otherwise evident. Examination of the sputum is, however, much more likely to give useful information in the case of growths involving the lung itself, than in those limited to the mediastinal region.

(2) An exploratory puncture of the chest, by means of a fine trocar or exploring needle, is called for in certain circumstances, and may yield valuable information. In the first place it may reveal at once that we have to deal with a solid mass, and not with a collection of fluid. The needle may be felt to penetrate and to be fixed in solid tissue. If no

fluid is obtained, the needle-point should be carefully examined, in case a small fragment of growth may be found sticking to it. If only a few drops of blood come away, and the needle does not seem to move freely in a cavity, the fear of malignant disease is heightened (Stephen Paget). Of course fluid may be obtained in quantity from the pleural cavity in not a few cases of mediastinal growth, especially when of a malignant nature; and in some instances the tumour may afterwards be more readily recognised. If the fluid thus withdrawn be haemorrhagic, this is regarded as an important diagnostic point in favour of malignant tumour, but it must be remembered that in a considerable proportion of such cases it is quite clear, and resembles an ordinary effusion. In rare instances it presents a chylous appearance, and possibly this may result from obliteration of the thoracic duct. The cytodiagnosis of fluid removed from the pleural cavity in cases in which malignant disease implicates the pleural membranes has been discussed on p. 589.

(3) Laryngoscopic examination is in some cases of the greatest value in the clinical investigation of mediastinal tumour. It may disclose—(*a*) Motor disorders affecting the vocal cords, due to nerve-implication, which may be present without any prominent symptoms. (*b*) Organic changes in the larynx, resulting indirectly from the tumour, not forgetting wasting of the muscles, or local malignant disease associated with a similar growth in the chest. (*c*) Morbid conditions of the trachea. In exceptional instances tracheal stenosis has been seen with the laryngoscope. In a case under my care at University College Hospital many years ago, Mr. Herbert Tilley was able to demonstrate during life, by the aid of this instrument, that a growth had penetrated the trachea; the autopsy proved that his observation was perfectly correct. In exceptional conditions bronchoscopy may help (*vide* Vol. IV. Part II. p. 310). Oesophagoscopy may also be demanded in suitable circumstances.

(4) Examination of the chest by the *x*-rays, with the fluorescent screen, is now generally regarded as a valuable aid in the diagnosis of mediastinal tumour, but in my personal experience it has on more than one occasion been of no help in really difficult cases, or even actually misleading. It is stated that such a tumour gives a denser and darker shadow than pulmonary or pleuritic morbid conditions with a more distinct outline. No clue is afforded by the *x*-rays as to the nature of a growth. An aneurysm is distinguished as a rule by its pulsation, and to some extent by its position and shape. A growth, however, may receive communicated pulsation from the heart or aorta, and this has led to error in more than one case on examination by *x*-rays

(5) Abdominal Examination.—It is desirable to draw special attention to the necessity for examining the abdomen in relation to mediastinal growths. A tumour in this region occasionally extends towards the epigastrium in such a way as to give rise to a prominence in this region. More frequently there may be evidence of displacement of organs downwards, especially the liver, stomach, or spleen. The liver may also be

enlarged from congestion. In exceptional instances ascites may be associated indirectly with obstruction of the inferior vena cava; and any fluid removed from the peritoneum may possibly be chylous in appearance, in consequence of obstruction of the thoracic duct. An important object of abdominal examination, especially in doubtful cases, is to look for malignant disease in this region, either primary or secondary; and in such examination the more obscure organs must not be forgotten, as well as the absorbent glands. In females it may be desirable to make a special investigation directed to the generative organs.

Course, Duration, and Terminations.—The preceding discussion of the clinical history of mediastinal growths will have made it clear that individual cases present great variety in their course and mode of progress, and it is impossible to make any absolute statements on this subject. As a rule the onset of symptoms is more or less gradual, but which first attract attention, and in what combinations they appear, depend on the nature and situation of the tumour, its associated morbid changes, and other circumstances. It may happen that extensive malignant disease in the mediastinum is first discovered on physical examination, the mischief having progressed for a considerable time in a latent manner. The course is generally chronic but progressive, though marked differences in the symptoms are often observed in individual cases as they advance: fresh incidents may arise, and pronounced exacerbations may occur from time to time; or, on the other hand, striking intermissions, especially as regards the respiratory disorders, may last for weeks. The physical signs also frequently undergo remarkable changes. The *duration* of cases of mediastinal tumour varies a good deal within certain limits. No trustworthy general conclusions can be formed on this point, and each case must be studied individually in relation to this point. Of 42 cases collected by Eger, the duration in 32 was from under two months to twelve months, and the extreme limit was seven years. There is no reason why non-malignant growths may not continue for many years, provided they do not seriously interfere with the functions of vital structures. In malignant cases of any kind the duration would be much influenced by the existence of growths elsewhere.

Whilst the large majority of cases of mediastinal growth run a more or less chronic course, it is important to bear in mind that occasionally the progress of events is acute from first to last, and that the existence of a tumour, which may perhaps have been present for a considerable time previously, is now and then revealed by some sudden grave symptom or symptoms, the subsequent progress being very rapid. Cases known to be chronic may also terminate with some acute or sudden development. Jaccoud has recorded a remarkable case of mediastinal tumour in which death occurred on the ninth day from the first onset of dyspnoea, but the tumour had probably existed for some time. I believe I have seen a case of a similar kind, but a necropsy could not be obtained. Recently a case of lymphosarcoma has come under my notice in which the duration was only two months from first to last.

The *termination* in cases of mediastinal growth, with rare exceptions, must inevitably be fatal, sooner or later; and this applies with special force to all forms of malignant disease, though in some instances, especially when tumours are of an osteoid or fibro-plastic nature, and of secondary origin, they do not appear materially to hasten the fatal result, death being due to the primary disease. Mediastinal tumour may end gradually from apnoea and venous stasis, progressive weakness and exhaustion, inanition from oesophageal obstruction, cardiac failure, or other causes; and these causes of death may be variously combined. The chief events which lead to sudden or very speedy death are haemorrhage, either taking place internally or revealed by haemoptysis, which is very rare; an asthmatic or suffocative paroxysm; asphyxia, due to an abscess opening into the bronchi, and choking the tubes in the opposite lung; cardiac paralysis with consequent syncope, attributable in different instances to direct implication of the heart and pericardium, thrombosis of the pulmonary artery, or compression of the pneumogastric nerve; and cerebral vascular lesions. It may happen that no definite cause can be found. Death may be hastened by different complications, or by operations performed for the relief of urgent symptoms or other purposes. Of course in some cases the fatal result is not due directly to the morbid conditions in the mediastinum, but to disease elsewhere.

Diagnosis.—It is generally understood and insisted upon by most writers on the subject that the diagnosis of mediastinal growths presents many and multifarious difficulties, and that in some instances these are practically insuperable. If there be no definite symptoms or physical signs to draw attention to the presence of such a growth, it would probably never be suspected; whilst in cases in which the clinical phenomena and course resemble those of some of the more common pulmonary diseases, mistakes might easily be made; in such circumstances the most experienced and accomplished physicians and clinical observers have fallen into error. At the same time, the tendency is to exaggerate these difficulties; and in a considerable proportion of cases of this kind a definite diagnosis can be made, sufficient for all practical purposes, granted adequate knowledge and skill in the investigation, and that such investigation be carried out intelligently and methodically. Sir R. Douglas Powell affirms that when attention is seriously drawn to the case by the symptoms, the diagnosis, as a rule, is not difficult. Moreover, not uncommonly cases which at first excite no suspicion, or are more or less obscure, become quite characteristic during their subsequent progress. There are certain distinct questions to be briefly discussed in relation to the diagnosis of tumours in the mediastinum. It may be affirmed generally that an important factor in the recognition of these morbid conditions is that the practitioner should never forget the possibility of their occurrence in any chest case, and should particularly bear them in mind when thoracic symptoms or physical signs are observed which are of an unusual character.

(1) The first question for consideration is, What are the data upon

which a positive diagnosis of mediastinal growth can be made? In not a few cases the fact that the patient has malignant disease elsewhere, or has previously been operated upon for such disease, is of much importance; and when any chest symptoms supervene under such circumstances, the development of secondary mischief in this region should be particularly watched for. Even the occurrence of pain, especially if localised or lancinating and of a severe character, should always be regarded with suspicion, and frequent examinations made. The danger of regarding such pain as simply neuralgic or neurotic, because no physical changes can be detected, must be carefully guarded against. In doubtful cases very minute search should be made for unsuspected primary growth. When symptoms or physical signs, or both, are suggestive, or, it may be, more or less characteristic of tumour within the chest, the point now under consideration is of great value in corroboration of the diagnosis. The same remark applies to the development of lymphadenomatous growths in the thorax in connexion with obvious Hodgkin's disease. Again, the extension of a tumour towards the neck, implication of glands in this region or of the superficial structures, or the occurrence of secondary malignant disease in other parts of the body, are important factors in arriving at a positive diagnosis. Secondary nodules of carcinoma or sarcoma may appear in different parts of the body, over bones, or in the subcutaneous tissue, as well as in organs; and these appearances are highly significant; though in my experience they have not appeared until a late period, when the diagnosis was but too evident.

When a tumour occupies or encroaches upon the mediastinum its positive diagnosis is founded, as a rule, upon the abnormal physical signs which it originates either directly or indirectly; associated with the local symptoms resulting from its mechanical or pathological effects upon adjoining structures. It would involve needless repetition to refer to these again in any detail; and it will suffice to state that the chief symptoms to be looked for are the more characteristic disorders of breathing; the peculiar kinds of cough; the changes in the voice; the phenomena indicating venous or arterial obstruction; dysphagia; and special nerve-symptoms. It is in the investigation of the diverse combinations of symptoms and physical signs met with in this class of cases that individual experience and skill in clinical observation are of such great advantage. Occasionally it happens that a fairly confident diagnosis may be founded on the symptoms alone, if aneurysm can be excluded. It must be borne in mind that the positive diagnosis should aim not only at the recognition of a tumour in the mediastinal region, but also as far as possible of the secondary morbid conditions implicating the thoracic structures to which it may have given rise.

In some instances the general symptoms may be of more or less value in the diagnosis of mediastinal growth, but often they are of little or no positive significance. Fever and cachexia are much more common in connexion with a tumour in the posterior than in the anterior

mediastinum. Occasionally one or other of the special methods of investigation already described afford most useful information, and clear up any previous difficulty in arriving at a definite opinion. Cases which are obscure at first may, when properly watched during their progress, reveal phenomena which become more and more characteristic, until at last the diagnosis is quite easy. This fact is well exemplified by cases of growth beginning in the lung, and afterwards extending into the mediastinum. The appearance of a tumour through the chest wall is of course pathognomonic; but this is an event which very rarely happens, and as a rule only in cases previously obvious enough.

(2) Assuming a positive diagnosis of mediastinal tumour to have been made, it is desirable to endeavour to determine within due limits the situation which it occupies, and the structures which it involves. If a tumour is limited either to the anterior or posterior and middle mediastinum, the localisation of the physical signs, and the differences in the symptoms due to its effects will probably make this fact clear. Growths confined respectively to these regions have been called the "growth of physical signs," and the "growth of symptoms"; but this distinction does not altogether hold good. Pain is deep-seated, if present, when the posterior mediastinum is involved, and radiating neuralgic pains are said to be rare. When a mediastinal growth has attained a large size, and has implicated various structures, it is often very difficult to ascertain the exact state of things with any approach to certainty; in such circumstances, however, it is not a matter of much practical moment. It must be remembered that there may be more than one tumour in the same case; the phenomena may then be very complicated, and, unless this possibility is borne in mind, are more difficult to understand clearly.

(3) One of the most important questions to be considered is the differential diagnosis between mediastinal growth and other morbid conditions affecting the intrathoracic structures. This matter not uncommonly presents considerable difficulties when symptoms and physical signs of different kinds are associated with this region; and unless particular care is exercised mistakes may readily be made. In dealing with this aspect of the subject it will be convenient to consider separately the more important diseases and conditions in relation to which the differential diagnosis is likely to give trouble.

(*a*) *Lung Affections.*—The ordinary diseases of the lungs do not, unless under certain exceptional circumstances, give rise to pressure-symptoms; and this applies also, as a rule, to growths confined to these organs. The presence of any such symptoms constitutes therefore, speaking generally, a broad distinction between these affections and a mediastinal tumour. It must always be borne in mind, however, that the various pulmonary morbid conditions already described may be secondary to a growth in this region; and their true interpretation may, without due care, be then easily overlooked. The chief danger of error arises when definite pressure-signs are absent or not prominent, even though a tumour exists

in the mediastinum; and it is most important that the clinical observer should be constantly on the lookout for phenomena of this nature, which, even when slight, may be of the greatest value in diagnosis. The following are the principal pulmonary conditions in which difficulties may possibly arise, though it must be understood that they are of quite exceptional occurrence.

Emphysema and chronic bronchitis, both individually and in combination, demand special attention in relation to the diagnosis of growths in the mediastinum. Cases in which these conditions exist are usually dealt with in such an off-hand and casual manner that, when they are associated with other more serious diseases, their significance is very apt to be misunderstood; and I have known very grave errors in diagnosis result therefrom. True vesicular emphysema may exist before and along with a tumour; but it must be always borne in mind that a condition of so-called "emphysema," which is really due to distension of one or both lungs, owing to pressure on the main air-tube, may be the result of such a tumour, and one of the evidences of its presence. Bronchitis may be similarly produced. Without due attention and consideration the underlying causative conditions may easily be overlooked; especially as their more characteristic physical signs may be completely obscured by the emphysema and bronchitis. Should these affections be unilateral or localised, one of the causes to be particularly looked for is interference with the corresponding main bronchus or some of its divisions; and amongst them a tumour must not be forgotten. It may happen that, on careful examination, signs of a growth may be detected even when the lungs are much distended. It is, moreover, very important to be on the alert to note even slight audible peculiarities in the breathing, cough, or voice, suggestive of pressure on one or other of the large air-passages. In very obscure cases of this kind the presence of excessive dyspnoea or cyanosis should lead to the suspicion of growth; as well as repeated haemoptysis, and absence of fever with marked bronchitis. The diagnosis is rendered more probable if no other cause of this complaint can be discovered; and if there is no cardiac disease.

When pulmonary collapse affects one lung extensively, it may be difficult to determine whether it be due to a tumour obstructing a main bronchus, or to some other cause. The diagnosis must then be founded on due consideration of the case in all its aspects, including the past history, as well as the present state; and it seldom happens that a fairly definite opinion cannot then be arrived at, especially after watching the progress of events for a while.

A difficulty in diagnosis between chronic pulmonary tuberculosis and intrathoracic growth is by far most likely to occur when such a growth is associated with the lungs, and the question is more fully dealt with in that connexion (*vide* p. 510). Steven, however, recorded a case of a primary cancer of the mediastinum originating in the tissue of the right bronchus, which simulated pulmonary phthisis, and was thus diagnosed. On the other hand, old chronic tuberculous disease occasionally presents

certain phenomena which may be very suggestive of mediastinal growth, such as laryngeal symptoms, due to implication of one of the inferior laryngeal nerves. The possibility of the association of mediastinal tumour with chronic pulmonary tuberculosis must be borne in mind from a diagnostic point of view.

(*b*) *Pleuritic Conditions.*—Difficulties in diagnosis between mediastinal growths and morbid conditions of the pleura present themselves from different aspects, and it must always be borne in mind that they are not uncommonly associated in the same case; whilst the pleura may also itself be involved in a growth, either primarily or secondarily. Speaking generally, it may be stated that pleuritic changes rarely give rise to any evidence of centripetal pressure, and this is often an important point in diagnosis in doubtful cases. A difficulty might possibly arise in making a diagnosis between an adherent and much thickened pleura, with compression of the lung and retracted side, and the effects of a tumour; but due consideration of the history of the case, and of the existing symptoms and physical signs, ought to leave little room for doubt. There is an important group of cases in which an extensive intrathoracic growth, occupying the whole of one side, is liable to be mistaken for a chronic pleuritic effusion or empyema. As this difficulty is, however, chiefly met with when the growth is of pulmonary or pleural origin, the differential diagnosis is more conveniently discussed in relation to the lungs (*vide* p. 511). When a mediastinal tumour is associated with a pleuritic effusion, if there are no obvious pressure-signs, the diagnosis is likely to be extremely difficult, and may be impossible. The question as to the significance of haemorrhagic effusion in relation to malignant disease has already been discussed; and it must suffice to state that should such an effusion, in a marked degree, be obtained by paracentesis in a middle-aged or elderly patient, cardiac disease being excluded, it should excite grave suspicion. Adequate microscopical examination of any fluid removed might possibly reveal the presence of cellular elements of a malignant nature. Its rapid reaccumulation is in favour of cancer; but this may also be a prominent feature in tuberculous pleurisy. Want of relief of dyspnoea after the removal of the effusion may point to the existence of malignant disease. Physical examination after evacuation of the fluid sometimes affords positive evidence of the presence of a tumour. An important sign is the persistence of dulness over the upper part of the chest, especially if it extends beyond the middle line in front; phthisis and pneumonia being excluded. The results of paracentesis are not uncommonly, however, far from conclusive in helping to arrive at a positive diagnosis. It may be noted that the dulness of a mediastinal tumour has been simulated by an encysted empyema situated between the anterior edge of the lung and the pericardium, or passing round the root of the lung. A difficulty in diagnosis might possibly thus arise. It has been affirmed that the condition of lung resulting from compression of a bronchus by a mediastinal growth has simulated pneumothorax, but I have never personally met with any difficulty of this kind.

(*c*) *Pericardial Conditions.*—In ordinary circumstances it seems hardly possible that a pericardial effusion could be confounded with a mediastinal tumour. Exceptional cases have, however, occurred in which a cancerous tumour has been mistaken for such effusion, and unsuccessful attempts at paracentesis have been made. A case is reported in which repeated tapping of a supposed cyst in the chest was performed, which, at the post-mortem examination, proved to be a chronic pericardial effusion. One of the difficulties which may be met with arises from the fact that this condition sometimes causes symptoms of pressure. Moreover, it may be associated with a tumour, and such a combination might be very puzzling. As regards physical signs, the diagnosis between pericardial effusion and a mediastinal growth is chiefly founded on the situation, shape, and outline of the dulness; the position of the impulse of the heart; and the effects of change of posture upon these signs. When the two conditions exist together it is said that the diagnosis may be aided by the observation that the cardiac sounds are better heard at a distance from, than immediately over the heart. A haemorrhagic character of any fluid removed by paracentesis would be very suggestive of malignant disease. The possible implication of the pericardium and heart in a mediastinal growth must be borne in mind, but its diagnosis would be extremely difficult. Skiagraphy might afford some assistance.

(*d*) *Mediastinal Conditions.* — Another condition in which the pericardium is involved, where a difficulty might certainly arise in the diagnosis from mediastinal tumour, is indurative mediastino-pericarditis. It is impossible to lay down any definite distinctions, and the diagnosis can only be made from a comprehensive and intelligent consideration of all the circumstances relating to the particular case. Skiagraphy might possibly help in the diagnosis of difficult cases.

Other mediastinal affections must be borne in mind as possibly simulating tumour, especially abscess giving rise to pressure-symptoms. The history of the case, perhaps of injury; the characters of the pain, with tenderness; evidences of local inflammation or suppuration; general symptoms indicative of pyrexia, it may be of a hectic type; and the progress of events would probably enable a satisfactory diagnosis to be arrived at. A growth, however, might be complicated by infective inflammation and abscess. In this connexion may also be noticed certain conditions of some of the mediastinal contents, and of the thoracic walls. An enlarged and persistent thymus may give rise to marked phenomena of a tumour in the anterior mediastinum. Syphilitic disease may also simulate this condition. Thus a post-sternal node sometimes originates pronounced pressure-symptoms, at the same time causing dulness. Syphilitic ulceration and stricture of the lower end of the trachea or a main bronchus is another aspect of this disease which may present difficulty in diagnosis, especially when accompanied with enlarged glands, of which I have met with more than one striking instance. The distinction between such a condition of things and a small mediastinal tumour merely interfering with one or both of these tubes, and not

giving rise to any physical signs, has until now been almost impossible. By the use of the bronchoscope we may hope for better success. A history of syphilitic infection, and the effects of treatment, might help the diagnosis materially. When dysphagia is a prominent symptom, associated with an evident growth, it may be a question whether it is oesophageal in origin, or an independent mediastinal growth causing pressure on the tube. The former is the more probable; but experience has taught me that it may be impossible to come to any positive and certain conclusion on the point, especially when oesophageal cancer gives rise to pressure-symptoms; this, however, is not a question of great moment. Cautious examination with a bougie, or the use of the oesophagoscope, might perhaps afford some help. It will suffice to mention caries and malignant disease of the spinal column as possible conditions which may resemble mediastinal tumour in some respects.

(*e*) *Aortic Aneurysm.*—I have left to the last one of the most important diseases which embarrass the diagnosis of mediastinal growth. A difficulty in distinguishing between these two conditions arises chiefly in the following circumstances:—There may be definite indications of direct pressure on the trachea, but no signs to explain whether the cause of the pressure be an aneurysm or a solid tumour; but the probability is, as a rule, in favour of the former, so far as my experience goes. In another class of cases the question arises as to the nature of a pulsating tumour. I have known pulsation associated with a large aneurysm to be so diffused and indistinct, and accompanied with such extensive dulness, that it was supposed to be a transmitted movement from the aorta through a growth. On the other hand, such a growth may actually conduct an aortic pulsation to the surface, and there may even be a murmur, an aneurysm being thus simulated. Very rarely, also, a communication forms between the aorta and a cystic tumour within the chest; or a pulsating malignant growth is met with. In my experience the difficulties encountered in this direction have, as a matter of fact, been extremely exceptional, due attention being paid to the points of distinction usually recognised; but they do occur, and must not be ignored. Another condition which I have known to cause error in diagnosis is where an aneurysm has undergone a curative process, and become practically a solid mass. Such a condition might easily be mistaken for a growth, if the practitioner were unacquainted with the history of the case.

The discussion of this aspect of the subject would not be complete without a general summary of the points to be more particularly attended to in making a diagnosis between a mediastinal growth and an aneurysm within the chest, especially in doubtful cases.

(i.) Among general matters *age* and *sex* are worthy of note. The fact that the patient is a female and under twenty-five years of age is in favour of a growth; whilst in a male adult aneurysm would rather be thought of. In old persons carcinoma would be the more probable. This point, however, must not be pushed too far. Hereditary tendency to malignant disease, a history of a previous tumour in the patient, or still

more the presence of one or more growths in some other part of the body, or evidence of implication of glands, would of course afford strong indications in this direction. Occupations or violent forms of exertion favouring aneurysm, either past or present, would point to this complaint; and a history of syphilis might also be suggestive, as well as the condition of the arteries generally. (ii.) Symptoms always demand due consideration, particularly pressure phenomena. Severe pain, especially in the back, or radiating to the neck or arms, is most common in aneurysm, and has been regarded as much more characteristic of this complaint; whilst the reflected pain is of the aortic distribution. Characteristic anginal pains may occur. The peculiar pain due to erosion of bone is more frequent in aneurysm. Frequent haemoptysis, with prune-juice or red-currant jelly expectoration, points rather to tumour. Sir R. Douglas Powell insists that pressure-symptoms are insidious in cases of tumour, but more persistent and less variable than those of aneurysm. Thus dyspnoea tends to increase more gradually; whilst paroxysmal dyspnoea is less common, perhaps, except in the later stages of the disease. In discussing this question in relation to diagnosis, Steven emphasised the importance of distinguishing between pressure effects pure and simple, and pressure effects accompanied by structural alterations in the neighbouring tissues set up by the vital action of the tumour. Aneurysm and benign growths give rise to the former group; whilst the latter are associated with malignant tumours, in connexion with which the signs of pressure are therefore relatively more numerous and more frequent than with aneurysm. He stated: "In aneurysm we can often demonstrate only one pressure effect—for example, recurrent-nerve pressure—whereas in solid growths we often have a large number—for example, localised oedema, varicosity, dyspnoea, obstructed bronchi, hoarseness, etc., in one and the same case." It is generally agreed that the effects of pressure upon the larger intrathoracic veins are much more common and more pronounced in connexion with solid tumour than aneurysm. To quote Steven: "Varicosity of veins and localised oedema are relatively rare in cases of aneurysm, because the veins, though pressed upon and dislocated, are not very likely to be crushed against resistant points, and so the blood still circulates through them." On the other hand, arterial obstruction suggests aneurysm. Interference with the air-passages is most frequently observed in connexion with tumours. Steven insisted upon the fact of spasmodic asthma—that is, spasm of the whole bronchi rather than of the vocal cords—being a symptom very specially indicative of the presence of a malignant growth within the chest. He also concluded that, in our ordinary clinical experience, irritative and paralytic nervous symptoms are perhaps not so frequently associated with solid as with aneurysmal tumours. Oesophageal obstruction, with consequent dysphagia, is generally regarded as a much more common and persistent symptom of tumour than aneurysm, but the opposite statement has been made. My personal experience has convinced me that we must be careful not to rely too implicitly on the supposed distinctions between the pressure-symptoms of aneurysm and a solid

tumour respectively; though in not a few instances they certainly do afford useful indications. Among general symptoms, irregular pyrexia, anaemia, and marked constitutional disturbance are in favour of growth: and the very aspect of the patient may be quite pathognomonic of mediastinal tumour as distinguished from aneurysm. (iii.) Physical and other special signs obviously require intelligent and careful study in doubtful cases. As a rule the differences are obvious enough. It is when a pulsatile movement is associated with a mediastinal growth that the chief difficulty arises. This pulsation, however, is not expansile or heaving; and the site of its maximum intensity does not correspond so closely as in aneurysm with that of the most marked dulness. The gradual approach of a pulsation towards the surface is very suggestive of the latter disease. Great superficial area of dulness, altogether out of proportion to the amount of impulse, is in favour of tumour; but I have known this sign to mislead. The outline of the dulness may be irregular in the case of a growth. Other data pointing to aneurysm are limitation of the signs to the region of the arch of the aorta; marked local bulging; the presence of thrill; a distinct diastolic shock; accentuation of the second sound over the prominence of the tumour, or a diastolic murmur; cardiac hypertrophy; marked retardation in the pulsation of the distant arteries, or inequality on the two sides; and tracheal tugging. In exceptional cases examination of the sputum, or of the main air-tube by means of the laryngoscope, might help the diagnosis. The development of pleuritic and pericardial effusion would be in favour of malignant growth. The *x*-rays may assist in the diagnosis between aneurysm and a solid tumour within the chest, as already indicated. In a doubtful case the progress and duration will probably clear up any difficulty. A growth is much more likely to advance rapidly than an aneurysm, and its duration is as a rule much shorter.

(4) Supposing the diagnosis of the presence of a mediastinal tumour to have been made, and aneurysm excluded, the next procedure is to attempt to determine its nature, and this may be fairly easy. When a growth is secondary, it may be concluded that this is similar to the primary disease, if its nature is known. The association of a tumour within the chest with obvious tuberculous or syphilitic disease, or with diffused lymphadenoma, would suggest like conditions. In primary cases the main point is to determine whether a tumour is benign or malignant, and this is, as a rule, not a difficult matter if due consideration be given to all the data. Benign growths usually only give rise to pressure effects pure and simple. From their greater frequency, one would always be inclined towards the diagnosis either of carcinoma or some kind of lymphosarcoma. In elderly subjects, and if a growth in the mediastinum could be traced originally to the lung or pleura, the former would be more especially indicated. As regards primary tumours in this region, the diagnosis of their nature may be quite easy or very difficult in different cases, and much will depend upon individual experience and acumen. The comparative frequency of cancer and lymphosarcoma cannot be relied

upon. Lymphosarcoma must always be borne in mind, particularly in young subjects. The appearance of fulness and nodular or glandular projections beneath the clavicle and in the neck is, according to Steven, especially characteristic of this variety of growth. Speaking of the differential diagnosis between sarcomatous and cancerous tumours of the mediastinum, this writer remarked: "As a general rule lymphosarcomatous growths are bulky tumours, often giving rise to very definite physical signs, and causing multiple pressure-effects, which there is usually very little difficulty in recognising. Such tumours also very readily grow towards the front of the chest. Primary cancers of the mediastinum, on the other hand, are usually smaller and more limited tumours, and in respect of their general size or bulk are often incapable of giving rise to physical signs capable of detection." Should such a growth break down and communicate with the air-passages, its nature might be revealed by examination of the sputum. The secondary development of growths in other parts of the body might clear up any obscurity in the diagnosis in doubtful cases; as well as the progress of the general symptoms.

The special diagnosis of exceptional tumours in the mediastinum can only be made by exclusion of the more common varieties, and by detailed consideration of the clinical and pathological features of each individual case, but it is often impossible. The presence of a pronounced rheumatic diathesis, and the discovery of subcutaneous nodules, might suggest fibroma. This variety grows very slowly, and, even when it originates marked pressure-symptoms, years often elapse before it causes death, the surrounding tissues accommodating themselves to existing conditions. Dermoid cyst and teratoma must be remembered as possible conditions, but they present no pathognomonic symptoms or signs, unless a communication should form with a cyst, and hairs or other characteristic objects be discharged either externally or with expectoration. Hydatid tumour of the mediastinum must not be forgotten, but is extremely rare.

(5) The last point to be mentioned in relation to the diagnosis of intrathoracic tumours is that the practitioner must be prepared for the possibility of cases coming before him, of which he knows nothing, under an acute or sudden aspect, owing to the effects of such a tumour upon the contents of the thorax, rapidly and unexpectedly produced. In such circumstances it would probably be impossible to come to any definite or positive conclusion as to the actual state of things.

Prognosis.—Unfortunately but little can be said under this head, and that of a very unfavourable nature. The prognosis is always very grave in relation to mediastinal growths, and as a rule practically hopeless, especially if the disease is malignant. The probability also is that the patient will pass through much suffering during the progress of the growth. The question of duration must depend upon the nature of the tumour, its situation, effects and symptoms, rapidity and mode of development, and other circumstances; and it is generally quite impossible to give any definite opinion on this point. Benign growths may last for a very long time. The prognosis is obviously more hopeful in

such tumours as may be amenable to treatment under favourable conditions, such as those of a syphilitic or tuberculous nature, a dermoid cyst, or a sarcoma conveniently situated for operative interference. Possibly complete recovery may be brought about in some of these cases, but at the best the outlook is always serious, and in any circumstances a very cautious opinion should be given as to promising an ultimate cure.

Treatment.—It will only be practicable to indicate the general principles upon which the treatment of mediastinal growths must be founded, and to mention some of the more important measures which may be called for. Obviously remedial methods of any kind can only be palliative in the large majority of instances, and each case must be dealt with on its own merits. The desire to afford relief will often tax the therapeutic knowledge and resources of the practitioner to the utmost, and his efforts will but too frequently end in disappointment. The first principle to be enforced is that, considering the conditions with which we have to deal, it will be for the welfare of the patient that we should not be too active in treatment, or employ irritating applications and the like energetically or for a prolonged period without any definite purpose; and that we should not resort to the more powerful palliative measures at our command at too early a stage, but reserve them until the urgency of the symptoms call for their rational employment.

Any hope of curative treatment by medicinal methods can only be entertained in the case of tuberculous or syphilitic morbid conditions; or possibly of fibroma associated with the rheumatic diathesis. A tumour due to tuberculous glands must be dealt with according to the usual principles applicable to tuberculosis. Syphilitic conditions would be the most hopeful from a curative point of view; and the free administration of iodide of potassium and of mercurials has in some few recorded cases proved highly beneficial. The notion of absorbing lymphosarcomatous or cancerous tumours occupying the mediastinum by any of the vaunted therapeutic agents advanced from time to time, in whatever way administered, has, in my opinion, absolutely no foundation.

Nor can a much more hopeful view be taken of any operative measures for the removal or cure of mediastinal tumours. Those ordinarily met with are practically beyond the reach of any operation, especially considering their relation to the vital structures with which they are more or less intimately associated. How far the more heroic modern surgeons would be inclined to interfere in particular instances must be left to their individual judgment and skill. The only conditions which, as a rule, might rationally call for operative treatment are tuberculous disease forming an abscess approaching the surface; teratoma or dermoid cyst; possibly hydatids occupying the anterior mediastinum; osteochondroma or enchondroma growing from the sternum; or a sarcoma of not too large a size and favourably situated. In the treatment of dermoid cyst the sternum has been trephined, and the cyst punctured and injected with iodine. Christian has collected 8 cases of

operation with a cure in 2 (by drainage in one, partial excision in the other), improvement in 4, and 2 deaths.

In a few cases encouraging results in the elimination of the growth and relief of pressure have followed treatment by the *x*-rays. I have recently had the opportunity of examining the patient treated by *x*-rays, whose case was brought before the Clinical Society by Dr. Zum Busch in 1906. The result has really been most remarkable. The history pointed to the existence of a very considerable sarcomatous growth in the mediastinum, and the symptoms were evidently of a serious nature. They have entirely disappeared, and absolutely no signs of such a growth can be now detected. What radium can do remains to be seen.

In the large majority of cases of mediastinal growths, the only definite treatment that can be adopted is of a palliative kind, intended for the relief of symptoms, and for dealing with the secondary morbid conditions or complications to which they may give rise. The chief symptoms which may demand attention are pain, dyspnoea of various kinds, cough, haemoptysis, cardiac disorder, restlessness, and insomnia. These must be treated on general principles, but, sooner or later, they often baffle us completely. Rest and posture are frequently important factors in treatment, and should always be intelligently considered in individual cases. Among the agents and methods which may be particularly helpful in affording relief may be mentioned the internal administration of opium or morphine, or hypodermic injection of morphine, with or without atropine; hydrate of chloral; ether internally or by inhalation; possibly nitrite of amyl; dry-cupping; application of leeches to the chest, or even venesection if there be much venous obstruction and cyanosis; and inhalation of oxygen. Certain medicines may be helpful for bronchitic conditions. Poultices or irritant applications to the chest may be of service, or the ice-bag externally, but they must be employed rationally and judiciously. It is often not desirable to attempt to check haemoptysis, even if it were possible. Dysphagia must be dealt with on general principles, but should it be a prominent symptom it is practically beyond the reach of treatment. Oedema of the arms may be relieved in some cases by the very careful and accurate application of a soft flannel bandage from the fingers to the shoulders, as advised by Steven. Puncturing the skin, or the introduction of Southey's tubes, must only be resorted to as a last resource, and when absolutely needed.

There are two points in treatment which must be referred to separately, as they may demand special consideration in particular cases. The first is the performance of tracheotomy for the relief of urgent or paroxysmal dyspnoea. This operation can only be of service when the paroxysms depend chiefly on laryngeal spasm from nerve irritation. Unfortunately, however, there is usually at the same time direct pressure on the trachea or main bronchi, so that tracheotomy gives no relief. At the best the operation will probably be very difficult to perform, on account of the conditions present. For paroxysmal dyspnoea inhalations of chloroform are of far more service and often of great benefit. The

other point is the mode of dealing with pleural effusion, and possibly with pericardial effusion also. In my opinion it is not desirable to remove pleuritic effusion as a matter of course in cases of this nature; and Sir R. Douglas Powell expresses the opinion that it should not be interfered with unless it is definitely increasing the dyspnoea, its tendency being to retard the progress of the growth. On the other hand, there should be no hesitation about taking more or less of the fluid away if it is obviously adding to the difficulty of breathing or other ills; and this procedure may afford the greatest relief, as in a case of the late Sir William Broadbent's, in which two quarts of blood-stained fluid were removed. The fluid should be taken away slowly, and it is not necessary to withdraw the whole of it; but as much as six or seven pints have been removed. There may be danger of haemorrhage from the growth or its adhesions. As a rule the effusion returns speedily, and frequent repetitions of paracentesis may become necessary, sometimes at very short intervals. In exceptional cases profuse serous expectoration has followed the operation (*vide* p. 559). Should the fluid become purulent or semi-purulent, incision and drainage may be called for. Paracentesis of the pericardium may possibly be demanded for urgent symptoms, but this can only afford temporary relief. It has happened in some instances of mediastinal malignant disease that the fibrinous element has so predominated in pleuritic and pericardial effusion that tapping was of little or no service. Secondary cancerous nodules have sometimes been observed at the site of paracentesis.

The general condition and the remoter symptoms or complications occurring in the course of cases of mediastinal malignant growth must be dealt with on ordinary principles. The patient must take as nourishing a diet as possible; the appetite should be maintained; and the functions of the alimentary canal duly regulated. Stimulants may be given as required. The general surroundings should be made as comfortable and cheerful as circumstances permit; and everything done that can alleviate the sufferings of the patient, which often become very distressing before death closes the scene.

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FREDERICK T. ROBERTS.

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DISEASES OF THE THYMUS

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General Considerations.—In spite of the attention paid in recent years to the thymus in respect both to its structure and functions and to its pathological relations, there is still much obscurity about this ductless gland. It originates from the third branchial clefts, as a pair of hollow outgrowths which branch and divide, and at an early period of intrauterine life become associated with a mass of tissue apparently lymphoid in nature. Stohr, however, denies the lymphoid nature of the small round cells in question, and believes them to be embryonic epithelial elements. This view is of interest in connexion both with the question of an internal secretion of the gland and with the new growths which arise from it. It is not definitely proved that extracts derived from the thymus possess any physiological action; Svehla found that injection of such extracts into dogs produced a fall of blood-pressure and acceleration of the pulse, the animals ultimately dying with symptoms of suffocation;

but other observers have not obtained these results, and it must be borne in mind that extracts of many organs may cause a fall of blood-pressure (Batty Shaw). Minkowski, after thymus-feeding, found a special acid (urotinic) in the urine, and Cohn similarly found allantoin. Jones states that the thymus contains a special ferment that breaks up nucleo-proteins with the formation of phosphoric acid and xanthine bases. Attempts have been made experimentally to produce a thymotoxic serum, but so far with no definite result (W. T. Ritchie).

Removal of the thymus in animals has been practised, but here again the results obtained are discordant. Friedleben (1858) found that dogs thus mutilated ate ravenously, but being unable to assimilate their nourishment became thin; the blood was watery, and the urine was scanty but contained an increased amount of urea. Abelous and Billard, experimenting on frogs, observed weakness, oedema, and loss of pigment in the skin. Basch finds that in young animals (dogs) the bones become weak and flexible, and that fractures do not unite so readily as in normal conditions. Herbivorous animals do not suffer in the same way. In a boy, aged nine years, a patient of Koenig's, in whom the thymus was removed for suffocative symptoms, rickets subsequently supervened, but passed off again. Paton and Goodall deny that thymectomy influences growth or the formation of the erythrocytes (Ghika), but they found a diminished number of leucocytes and impaired leucocytic reaction to infections. It appears to be proved that in castrated animals the involution of the thymus is delayed. It has also been stated that if the thymus is removed, the testicles become hypertrophied (Paton, Soli).

Therapeutic administration of thymus extract has been tried in a considerable number of diseases. In Graves' disease it was employed by Owen, Mikulicz, and others, who formed a favourable opinion of its value. Dr. Hector Mackenzie, however, after trial in 20 cases, concluded that it was of little or no service (*vide* Vol. IV. Part I. p. 381). It has also been used in goitre (Mikulicz, Reinbach), in cretinism (Thomson, Bramwell), in infantile marasmus (Stoppato), and in pseudo-hypertrophic muscular paralysis (Macalister). Mendel thought that benefit accrued in rickety children from the administration of the substance of the gland, given in doses of as many grams as the children were months old. In spite of the favourable reports given by these writers the use of the remedy has not commended itself for general adoption. Ruhräh found it quite useless in infantile atrophy.

Persistent Thymus.—The thymus is usually stated to be present only during early life. Its weight at birth is very differently estimated by various authors, the figures ranging from 5 grams (Testut) to 30 grams (Osler). Perhaps 7-10 grams may be taken as an average weight (Dudgeon), but the gland varies to some extent with the weight of the infant. It increases in size up to the age of two years, when it reaches its maturity; remains more or less perfect until eight to twelve years of age, and then undergoes rapid wasting, accompanied by fatty change, shrivelling up so that at the age of twenty no trace of it, or but an

insignificant vestige, can be discovered by the naked eye. Waldeyer and others, however, maintain that traces of it can be found microscopically up to extreme old age, amidst the mass of fat by which it is then represented. Occasionally a well-defined thymus is persistent without any obvious reason, and it has been found of some size as late as ninety-four years of age (Claude). Goodall assigns the delayed involution of the gland to retardation of the normal process by which Hassall's corpuscles are invaded and absorbed by leucocytes. In an ordinary way the condition now under notice does not give rise to any symptoms or signs, and it may be found accidentally at a necropsy. The cases in which it is associated with conditions of disease may most conveniently be considered in the next section, as it is difficult to draw a line between a hypertrophied thymus and one that persists when it should have disappeared.

Enlargement or Hypertrophy.—This morbid condition of the thymus is extremely important, as it may occasion very definite and even grave symptoms; numerous examples of this association have now been observed and reported. It may occur during childhood and also in later life when the organ is persistent. The increase in size is not due, in the cases which we are considering, to any new growth, but is entirely or in the main a hypertrophy or hyperplasia of the gland-structures. The gland has been found in individual cases to weigh as much as 620 grains in a boy aged fourteen; 380 grains at twenty-five; and 356 at twenty years of age. Putnam records a case in a child (age not stated) in which the gland weighed 6 oz.; and in another case, a boy aged six years, the thymus and trachea weighed 11 oz. (Rolleston, (43)).

An enlarged thymus has frequently been found in association with certain diseases. Of these the most important is perhaps *exophthalmic goitre*. The association of an enlarged thymus with Graves' disease was considered by Dr. Hector Mackenzie to be too frequent to be accidental (*vide* Vol. IV. Part I. p. 362). On the other hand a similar hypertrophy has been met with in infantile myxoedema. The sudden death which occasionally takes place in cases of Graves' disease has been assigned to the effects of an enlarged thymus.

Lochte has recorded 2 cases of *acute leukaemia* in which there was great enlargement of the thymus. The first was that of a young man, aged twenty-one, who died with symptoms of severe purpura haemorrhagica, and the second that of a girl of eighteen, who suffered from ulcerative tonsillitis and enlargement of lymphatic glands; there were fever and leucocytosis, and after death, besides enlargement of the thymus and of the spleen, there were found petechial haemorrhages in the pleurae, pericardium, retinae, and kidneys. The thymus microscopically consisted of closely packed epithelioid cells in a reticulum of connective tissue, with but scanty remains of lymphoid tissue. In lymphatic leukaemia the thymus is usually enlarged (Muir), but the question of the connexion of enlargement of the thymus with leukaemia is complicated by the habit of certain writers of describing as leukaemia the condition of leucocytosis

encountered in some cases of tumours affecting the thymus. Fischer found the gland enlarged in a case of pseudo-leukaemia (Hodgkin's disease).

A causal connexion between disease of the thymus and the condition known as *myasthenia gravis* has been rendered somewhat probable by recent researches. Mandlebaum and Celler, who have collected the recorded observations, find that in 11 instances, or about 20 per cent of those examined after death, some affection of the thymus has existed. Lymphosarcoma was found by Oppenheim, Laquer and Weigert, and Hun; enlargement of the gland by Link, Hodlmoser, Burr, and Buzzard; a cystic condition of the gland by Buzzard; whilst Mandlebaum and Celler's case proved to be an endothelioma of the thymus. In a case reported by Goldflam in which no necropsy was obtained, a diagnosis of mediastinal tumour was made.

Allen Smith found thymic hypertrophy in a case of *amyotonia congenita*; the lymphoid tissue of the gland was largely replaced by epithelioid cells. Baudouin noted fibrosis of the thymus in other cases of this disease, but in a case recorded by Spiller the gland appeared normal to the naked eye. Marie states that the thymus is constantly enlarged in *acromegaly*, but this association is denied by others. Persistence or enlargement of the gland has often been found in epileptics, and less frequently in *Addison's disease*.

A peculiar *thinness of the coats* (*hypoplasia*) *of the aorta* has been noted in association with persistence of the thymus. Thus, in a boy of nine, who died after ether-anaesthesia, Richardson found the aorta of "paper-like thinness." Kohn records the case of a child of seven months, who suffered from dilatation of the heart and an aneurysmal condition of the first part of the aorta, due to pressure of an enlarged thymus, weighing 40 grams. A somewhat similar case was that of a boy of fifteen years, brought into Charing Cross Hospital dead. At the necropsy there was found an aneurysm of the ascending aorta, which had ruptured, the coats of the vessel being very thin and apparently fatty. The aorta beyond the dilatation was much reduced in calibre, and the thymus was persistent and large. Whether the stenosis of the aorta was due to past pressure of this gland could not be determined: at the time of death there was no evidence that injurious pressure had been exerted.

The peculiar condition called *status lymphaticus*, *status thymicus*, or *lymphatism*, in which sudden death occurs from some slight accident, shock or operation, or even without obvious cause, is constantly associated with enlargement of the thymus, and is described elsewhere (see Vol. IV. Part I. p. 482). It is difficult to draw any sharp distinction between cases of this affection and others in which the enlargement of the thymus is a direct cause of injurious symptoms by reason of the pressure caused upon surrounding parts. In the latter cases, the sufferers are invariably infants. Respiratory disturbance, in the form of attacks of obstructive dyspnoea, with stridulous breathing, cyanosis, and convulsions, is the most frequent of such symptoms. The dyspnoea is known variously as thymic asthma or Kopp's or Millar's asthma. There may be stridulous

cough, and swelling of the veins of the neck, with visible fulness of the throat. The attacks are prone to recur in some patients at irregular intervals, and death is likely to ensue in one of them at an early age. In other instances which are difficult to separate from the status lymphaticus, the first attack is fatal. Examination of the infant may reveal an area of dulness over the manubrium sterni; it is stated that this can be best elicited if percussion is made while the child is held face-downwards (Jacobi). That an enlarged thymus may in young infants exert direct pressure on the trachea is evident when it is borne in mind that the upper opening of the thorax at birth is only 2·5-3 cm. in diameter. To explain the recurring attacks it has been supposed that the thymus acts to some extent as a valve, causing obstruction when the infant throws its head back and so draws the gland into the neck. Definite signs of pressure on the trachea have been found in a certain proportion of these cases (Rehn, Beneke, Flügge), and illustrations shewing the relations of the parts in a case of greatly enlarged thymus are given by Tada. The cases which most closely resemble, if indeed they do not merge into, those classed as status lymphaticus are, however, those in which a large thymus has been supposed to exert its injurious pressure upon the nerves lying at the root of the neck, as well as possibly upon the great veins, and even on the heart itself. Pressure upon the recurrent laryngeal nerve has been invoked to explain the attacks of stridulous breathing which occur in some instances, closely resembling laryngismus stridulus; and sudden death without definite dyspnoea or cyanosis has been referred to embarrassment of the heart.

A special connexion between the thymus and chloroform poisoning has been asserted to exist by Barbarossa: the gland is said to become hyperaemic, and subsequently to undergo regressive changes as a result of inhalation of chloroform; animals deprived of the thymus shew a greater tolerance of this drug than do normal animals; whereas injection of extract of thymus reduces this tolerance. These results need confirmation.

Diagnosis of an enlarged thymus may be possible in some instances, the characteristic attacks of dyspnoea being associated with recognisable dulness on percussion over the manubrium sterni. Opinions differ as to the possibility of ascertaining its existence by *x*-ray examination; Warthin (49) gives a skiagram shewing a very definite shadow due to an enlarged thymus in a child with stridor. Hotz records a case in which symptoms resembling those of an enlarged thymus were caused by a prevertebral abscess.

Treatment of cases of enlarged thymus with respiratory embarrassment, in children, by surgical measures has been practised successfully by Koenig, Rehn, and Ehrhardt. The thymus may be entirely removed, or may be drawn upwards and fixed to the fascia of the neck. A case in which cure followed application of the *x*-rays to the throat is recorded by Friedlander. Warthin suggests the employment of antisyphilitic remedies.

Atrophy and Fibrosis.—Atrophy of the thymus gland is commonly met with in wasting diseases in children, and it has been supposed that in

primary atrophy or athrepsia the condition of the gland is the cause of the malady, some internal secretion being presumably lacking (Stokes, Ruhräh, and Rohrer). Dr. Fortescue-Brickdale states that the atrophy of the thymus in these cases is accompanied by fibrosis, and that the degree of wasting is greater than in secondary marasmus. The atrophic thymus is described by Mr. Dudgeon as soft, white, and oedematous. *Congenital absence* of the thymus was found in an infant which died with oedema of the extremities and haemorrhagic ecchymoses in the supraclavicular fossae (Clark).

Inflammation.—In rare instances the thymus becomes the seat of acute inflammation, which may terminate in foci of suppuration or in the formation of a definite abscess. In a case recorded by Mr. Dudgeon the suppuration was caused by pneumococci. The abscess has been known to burst into the trachea, and the pus to be thus evacuated; or it may extend more deeply and give rise to a mediastinal abscess. It is practically impossible to recognise these changes clinically, but it is conceivable that a thymic abscess might be attended by local pain and tenderness, some degree of pressure-symptoms, limited dulness, and more or less fever. Biedert has described acute inflammatory swelling of the thymus with sudden death in an infant of ten months.

Tuberculosis most often occurs as miliary nodules, and is almost invariably a manifestation of generalised infection. Demme has described a primary tuberculosis of the thymus. In rare instances the gland may be converted into a fibro-caseous mass (Dudgeon), or multiple tuberculous abscesses may exist (Helm).

Congenital syphilis is stated to affect the thymus, both in the form of interstitial fibrosis and as localised gummas. A peculiar condition, in which hollow spaces filled with puriform fluid occur in the thymus (Dubois' abscesses), has been looked upon as characteristic of syphilis, but Mr. Dudgeon regards it as due to post-mortem change, finding that similar cavities appear in any thymus which is exposed to the air. Puriform fluid, containing chiefly lymphocytes, can be squeezed from a fresh gland.

Haemorrhage.—Petechial haemorrhages are not infrequent in the thymus. Mendelsohn collected 6 cases of extensive haemorrhage in infants, and added one of his own, the oldest case being nine months of age. In 4 cases the children were syphilitic, and in most instances there were petechiae elsewhere. In one instance the blood escaped from the thymus into the pleura (Raudnitz).

Focal necroses have been found in the thymus in diphtheria; and **concretions** and **calculi** have also been discovered in the gland. It is natural to suggest that these last arise from Hassall's corpuscles, which frequently undergo calcification.

New Growths.—*Non-malignant tumours* of the thymus, apart from simple hyperplasia, are rare. Letulle states that lymphadenoma is a common form of enlargement, but Dr. Rolleston (71) suggests that the cases referred to were probably mere hypertrophy. Leukaemia has already

been alluded to. Soupault described a unique case of adenoma, consisting of tubules lined with columnar epithelium, in a girl who died from exophthalmic goitre : this was probably a developmental defect. A growth described as a myxoma was found by Winogradow in a male child aged one month, and Becchia and Visetti found a tumour consisting of spaces lined with columnar epithelium and filled with gelatinous contents. Lange records the occurrence of a fibroma in a boy of eleven years, but it is difficult to feel sure that the case was one of true neoplasm, as there were fever and definite infection with pyogenetic bacteria, along with the fibrous overgrowth in the thymus.

Malignant tumours are met with in the form of both carcinoma and sarcoma ; the former tends to occur late in life, the latter at a comparatively early age, and even in children. The irregular nature of the cells found in some tumours has been looked upon as pointing to mixed sarcomatous and carcinomatous growth, and the name thymoma has been coined to indicate malignant tumours of a special nature arising from this gland.

Carcinoma may take several forms. In spheroidal-celled cancer the cells are large and resemble those of the Malpighian layer of the skin. "In other cases of carcinoma epithelial pearls may be present, thus plainly indicating that the growth, like the normal concentric bodies of Hassall, is derived from the primitive thymus diverticulum from the foregut. The combination of polyhedral cells and squamous cells in the same tumour has also been observed" (Rolleston (71)). A form in which the cells are spheroidal and small, somewhat resembling those seen in sarcoma, has been described by Paviot and Gerest ; such a growth is of interest in connexion with Stohr's views as to the structure of the gland (2). French observers have noted as characteristic of thymus-growths the occurrence of "globes épidermiques inversés," that is, concentric bodies in which there are large cells in the centre, surrounded by flattened cells. Portions of the tissue of the thymus may be enclosed within the thyroid body, and give rise to tumours (*épitheliome thymique intrathyroïdien*, Achard and Paisseau).

Sarcoma is considerably commoner as a primary tumour of the thymus than is carcinoma. Growths consisting of small round cells, resembling the lymphocytes of the thymus, are most often encountered. They are very vascular, and are described by some writers as "haemorrhagic round-celled sarcoma." In some of these growths there is a delicate reticulum of fibrous tissue, resembling that of a lymphatic gland ; to these the name lymphosarcoma is rightly applied. The round-celled sarcomas grow rapidly, infiltrating the mediastinum, and forming metastases in distant organs (kidneys, liver). In a case recorded by Göppert the first signs of the disease consisted in swelling of the abdomen and wasting : large symmetrical tumours were palpable in the right and left hypochondria, which proved after death to be the kidneys, infiltrated with secondary growths. Spindle-celled sarcoma is less common : it may take the form of a tough, rather slow-growing fibrosarcoma, or of a soft,

rapidly-spreading tumour, with large succulent cells. Alveolar sarcoma of the thymus is recorded by Dr. Hawthorne; and the growth already alluded to, found by Mandlebaum and Celler in a case of myasthenia, was an endothelioma, growing from the lining cells of the perivascular lymphatics. Dr. Rolleston (70) has recorded a case in which there was found a mixed tumour, somewhat resembling those characteristic of the parotid gland, in which cartilage was present (adeno-chondrosarcoma). He regarded the cartilage as derived from an aberrant bronchial rudiment. Dansac described in a tumour of the thymus the occurrence of large cells ("voluminous cells"), which he suggested might have arisen from remains of ectoderm.

The proportion of all cases of mediastinal tumours which have their origin in the thymus is difficult to estimate. Dreschfeld, who examined over 20 cases of mediastinal lymphosarcoma, believed that the great majority arose in the lymphatic glands and very few in the thymus. Wilson Fox found that lymphosarcoma arose nearly twice as frequently in the anterior mediastinum as in the posterior, which he noted as remarkable, in view of the deep situation of the bronchial glands.

Tumours arising in the thymus give rise to the symptoms common to all mediastinal growths (see p. 638). Thus we find recorded:—cyanosis and oedema of the face, exophthalmos, and orthopnoea. Pressure on the recurrent laryngeal nerve may cause alteration of the voice ("voix bitonale") and stridulous cough. Tachycardia may result from disturbance of the vagi or of the sympathetic chain, and pleural effusion from secondary growths in the pleura or possibly from pressure on venous trunks. In one case chyliform fluid was found (Letulle). The tumour may project through one of the intercostal spaces, and if it be very vascular, may pulsate and closely simulate an aneurysm. In Achard and Paisseau's case suppuration occurred in the growth, and an abscess was opened in the neck. Lymphosarcoma may become generalised (sarcomatosis), and is then accompanied by marked lymphocytosis.

The diagnosis of mediastinal growths is dealt with elsewhere (*vide* p. 655). After death the thymic origin of a tumour may be recognised by its position, corresponding with that of the gland; by its shape which may be roughly that of the thymus; by its tendency to spread over the pericardium; and microscopically by the presence of concentric bodies. The absence of these last does not, however, negative an origin in the thymus.

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DISORDERS OF THE BLOOD

CHLOROSIS[1]

SYN.—Latin, *Morbus virgineus* (Lange, A.D. 1520); German, *Bleichsucht*; French, *Pâles couleurs*; English, *Green Sickness.*

By Sir CLIFFORD ALLBUTT, K.C.B., M.D., F.R.S.

Introductory.—The diagnosis, prognosis, and treatment of anaemia depend upon the nature of the primary malady of which it is a symptom; whether of chlorosis, syphilis, tuberculosis, plumbism, malaria, sapraemia, Addison's disease, and so forth. Indeed that in the course of many diseases the blood should vary in composition, chiefly in the direction of impoverishment, is to be expected. It may thus vary in one quality or more; it may vary in mass, in plasmatic value, in corpuscular value. In pining, for example, we note loss of water, loss of plasma, and loss of red corpuscles; as proteins fail the water, which is retained more or less loosely by them, escapes; then the corpuscles lose their vigour and the activity of their growth.

At the time of the last edition of this article, although it seemed certain that the blood does vary in mass, sometimes in the direction of excess, more frequently in that of defect, we had no means of measuring the fluctuations of the mass of the blood with any approach to accuracy. Recently, however, the method of Dr. Haldane and Prof. Lorrain Smith has afforded us valuable information in this respect. Volume of arterial pulse is no guide; the artery under observation may so contract upon its contents as to produce a relative anaemia of its particular area; or a general arterial anaemia may coexist with a venous plethora, the mass of the blood not being diminished, possibly increased. In some diseases, such as cancer or exhausting discharges, and in old age, the mass of the blood is probably diminished; the arteries are unfilled, yet there may be no sign in any area of venous repletion. In the transient anaemia of young persons the mass of the blood appears to decrease; in chlorosis, however, we now know, as Rubenstein and James suspected, that the total amount of plasma is in excess. Dr. Haldane has found the total plasma to be even doubled, although, as Dr. Lloyd Jones had pointed out, the specific gravity is not diminished, and may be even increased.

[1] Professor Stockman tells me that the name Chlorosis was given to this disease by Jean Vavandal in A.D. 1620.

Concerning the variations in the composition of the plasma and in corpusculation we are enabled, by methods described in the article on "The Clinical Examination of the Blood and its Significance" (Vol. I. p. 640), to submit these constituents to direct estimation. Moreover, seeing that anaemia is a factor in many diseases, the reader is referred to other articles of this work, in which certain deteriorations of the nutritive fluid are particularly described: such as those on pernicious anaemia, splenic anaemias, leukaemia, syphilis, wherein blood changes are eminent; and on pulmonary tuberculosis, chronic dyspepsia, or diarrhoea, wherein the anaemia is rather a secondary event. Apart, however, from the graver maladies, we are all of us familiar with states of debility and lack of colour and condition which, at whatsoever time of life they may come on, we attribute, and often with reason, to a temporary impoverishment of the blood; for instance in boys and girls in whom the demands of growth and development are extraordinary. In advancing years, again, when we are on the alert lest we see in the change a herald of organic disease, we may be happily deceived, for old persons too may fail in the common task of keeping the blood up to its proper standard; though in them this failure is nearly always of more serious meaning than it is in the young. Furthermore, the blood may be sufficient in mass, and yet deficient either in nutritive value, or in oxidising power; or indeed in both these qualities together. For these various states sundry and somewhat uncouth names have been provided, names not perhaps without some convenience, such as hypalbuminosis, oligocythaemia, and so on; whilst defect in the mass of the blood has been named oligaemia. We also hear of hydraemia as a name for a state of the blood in which the fluid is said to be unduly diluted with water, and thus, if not diminished in bulk, defective in protein matter. It is said that the blood of anaemic young men is not deficient in haemoglobin, and they are not very pallid; it may be the quantity of arterial blood, or at any rate of the plasma, in the vessels which is under the standard: the blood does not spring from a puncture as it does in the chlorotic girl. In young men's anaemia, therefore, the specific gravity of the whole blood may rise above the normal mean (Lloyd Jones). Again, in its salts the blood may be defective; or, on the other hand, unduly abundant. These variations are less important, as they are probably integral parts of the former changes: for instance, the salts probably depend directly upon the quantities of the albuminous elements of the blood; the water likewise may rise and fall in part with the albuminous elements with which it is more or less loosely combined: moreover it is dependent upon the relative saline density of the blood. Intimately speaking, therefore, whilst the causes of anaemia may be infinite, the number of anaemic permutations may be comparatively few (35).

Anaemias, then, may be divided into (*a*) those in which consumption of the blood is accelerated; (*b*) those in which renewal of the blood is slow, either by insufficient nutritive supply or by some defect of blood-forming machinery; (*c*) those in which some haemolytic ingredient is at work;

and (*d*) those in which modes of failure are multiple. Of the first, fever may be taken as an instance; of the second, inanition from whatever cause; of the third, pernicious anaemia, renal disease, or malaria; and in pulmonary tuberculosis, if both appetite and digestion be poor, we shall recognise the mode in which undue rapidity of consumption may conspire with imperfect renewal, and probably with some haemolysis also.

It need not be stated at large that such conditions as these merge by insensible gradations into health. For example, in growing youth rapid use of the blood may not be made up even by good food and digestion; in old age, although the use of the blood may be slow, appetite and assimilation may be slower still. Again, in direct loss of blood, or in an infection of it, recovery of health is often to be anticipated. Some persons are anaemic, or have a bent to anaemia, all their lives long; but, apart from toxins, simple anaemia is less apt to occur in the decades between thirty and fifty, for at these ages nutrition is more steadfast. Some persons again seem to have a richer blood store than others; they resist deprivation or the incursions of injurious agents more successfully, and recover more quickly from their consequences.

The symptoms of chlorosis, to which these considerations are but introductory, are not merely those of an anaemia; we have then to ascertain how far the phenomena of chlorosis are peculiar to this state, and how far they are common to it with other anaemias. We shall find that chlorosis consists in a series of symptoms observing a fairly uniform course and relations. The pulse, which in anaemias of failing quantity is not only quickened but also feeble and empty, in chlorosis is full and of good or perchance somewhat increased pressure. The heart, which in anaemias secondary to serious disease may be feeble and almost impalpable, in chlorosis is often irritable, sometimes obtrusive or laboured. Fatty and kindred changes in the heart are common in their degrees to all such impairment of nutrition. In chlorosis the anaemia tells rather on the respiration and on the steadiness of the heart; in other anaemias, or in many of them, the effect is marked rather by slackness of the cerebral circulation and syncope. Wasting, generally speaking, is not a notable symptom in anaemias, and in uncomplicated chlorosis rarely occurs.

Definition.—Chlorosis is a malady of women, and primarily of young women, at or about the age of puberty; it presents a peculiar series of symptoms; and pathologically a defect of the red corpuscles of the blood, partly in number, in which the relative defect is large, and may often be positive, chiefly in haemoglobin: the plasma is increased, often largely increased, in quantity; in quality it remains constant, or may be enriched.

Under one name or another chlorosis has attracted the attention of physicians, as for instance, of Sydenham, from early times; yet it was not until the clinical studies of Hoffmann and of Duncan gave accuracy to the description of the malady that it took a definite place in nosology. Vaguely apprehended or alluded to by ancient authors, chlorosis was gradually distinguished as something more than a symptomatic anaemia during the fifteenth and sixteenth centuries. The leading early description

of it, under the title *De morbo virgineo*, is to be found in the 21st Epistle of that able physician of the sixteenth century, Johann Lang, of Lemberg (45). Lang is surprised that physicians did not recognise the disease, name or no name; for he says there is on our lists many a disease lacking a name which does not lack a cure. After quoting the usual inconclusive paragraphs of Hippocrates and Galen, he himself describes the pallid cheeks and lips, the palpitation, the throbbing vessels, the tremor, the dyspepsia, the dislike of meat, the dyspnoea, and the anasarca. His prescription was marriage and conception. Baillou, who also gave a clear account of the malady, might perhaps have divided with Lang the honour of a first publication; but his works did not see the light until they appeared posthumously about the middle of the seventeenth century. Hayem was the first to place the disease on a firm pathological basis.

Causation.—It would serve little good purpose to dwell on the fanciful views of the causes and characters of chlorosis which have prevailed among physicians and poets—views adumbrated by the use of such names as *febris amatoria* (Hübner, 1688), *icterus amantium*, *icterus albus*, and so forth. We shall see hereafter that the attribution of chlorosis to perverted or thwarted sexual impulses is mistaken, except in so far as an emotional disturbance of whatever origin may contribute to the causes of a particular case. On the other hand, although we may have cleared our minds of certain false preconceptions, we cannot yet pretend to be in possession of a full knowledge of the nature of chlorosis. Many and various are the conjectures, of which we must give some account; but a theory of chlorosis cannot yet be formulated.

Heredity.—That chlorosis is in no small measure hereditary seems to be believed by most close observers of the disease, and certainly accords with common experience. In family after family in my later life I see the daughters, one after another, as they arrive at puberty, coming for aid in the disorder for which I had formerly treated their mothers. It may be replied that as chlorosis is so common a malady it will naturally appear in most or all families, as the girls grow up. Still, making all allowance for this fortuity, and for similarity of conditions, I agree with those who say that chlorosis, in its more strongly marked forms, tells especially upon certain families; and that in these families the girls are hit harder and resist treatment more obstinately than in others. Whether the bent to the disorder may run in a latent channel through the fathers, I cannot say; it seems rather as I have just said to run through the mothers. Dr. Lloyd Jones has published certain opinions on the heredity of chlorosis which I shall more conveniently discuss in the next paragraph.

Sex.—Between the extreme opinions of Dr. Lloyd Jones and those of Simon, the one holding that chlorosis is wholly and peculiarly a disease of women, or possibly also of a few male adolescents of feminine character, the other that chlorosis is little more than an anaemia of ill-thriven young people, there is a great interval. Dr. Hale White says: "Chlorosis is a disease which is confined to women." Dr. Gulland says: "So far as

is known chlorosis occurs only in the female sex." Krehl (1907), summing up the evidence, says "largely predominating in, if not exclusively confined to young women" (ganzvorwiegend, vielleicht ausschliesslich etc.). Dr. Lloyd Jones, in a series of papers remarkable not only for speculative ability, but also for industrious investigation of the phenomena of chlorosis, both clinically and in the Cambridge laboratories, expresses opinions which are briefly as follow:—In chlorotic women the specific gravity of the blood may fall: on further inquiry, however, it seems that this fall is due to defect in the corpuscular element; when the plasma is tested separately it is found that although, in contrast to other anaemias, its volume is in excess, yet the specific gravity is not only up to the normal standard, but may exceed that of other kinds. In this important respect the blood of chlorosis differs from that of other kinds of anaemia, in which the specific gravity of the blood may rise while that of the plasma alone falls. The chlorotic form of anaemia is peculiar to women in the child-bearing period of life, and in the cure of it iron has a high and specific value.

Dr. Jones goes on to say that the anaemia marked by abundant plasma and deficient haemoglobin-content—that of chlorosis—a kind of anaemia peculiar to women, is found moreover in women who come of large families, in women who have many brothers and sisters. Since his observations were published I have questioned my own experience, and, so far as impressions go, they are in accordance with this opinion. Dr. Jones indeed goes one step farther, and asserts that in large families the blood of the sons as well as of the daughters has the chlorotic bent, its plasma being abundant and of good specific gravity. From these and such facts he infers that this kind of blood is the blood of fertility; and that chlorosis is the exaggeration of a fertile blood, of blood, that is, which has for its end the storage of nutritive material for the fetus during pregnancy. If so, such a leaning in the blood of women at puberty becomes comprehensible. I consider that these opinions, which are based on a large number of observations, both clinical and pathological, hold the field at present, as a working hypothesis; one which has this in its favour, that, to close observers, perhaps every girl in her progress from youth to maturity may seem to pass, as it were, through the outer court of chlorosis. One other point seems to me to be in its favour, namely, that the causation of chlorosis is probably simple; as the symptoms are uniform, and are general in their incidence on one sex, it is probably due to some widely acting antecedents of a kind not very subject to contingencies. Dr. Lloyd Jones suggests that the immediate cause may be a profusion of an internal secretion from the sexual organs. Whether this conjecture be true or not, we are probably near the discovery of some such cause of general operation, deflected but little by contingent causes. The probability of plethora, in several conditions, is freely admitted by the leading pathologists (Krehl, Bollinger (8), Parkes Weber, Geisböck). I think, therefore, that the conceptions of causes of multiform or incidental activity, which we shall presently consider, are

less likely to be true. Some of Dr. Jones's results, such as the increase of the volume of the plasma, have been corroborated by Rubenstein, and by Dr. Haldane and Prof. Lorrain Smith; the maintenance of its specific gravity has been verified by Hammerschlag and others. Dr. C. F. Martin says that if a relative fall in haemoglobin be taken as a test, chlorosis occurs in men also, and gives four cases, estimated by Fleischl's method (duly controlled), in which with corpuscles from 4,800,000 to 5,300,000 the haemoglobin fell to 68, 72, 77, 77 respectively: he does not state whether these men were members of large families. However, as we have seen, a fall in haemoglobin is no criterion, it is but one term of the series; my own experience is that the occurrence of chlorosis in men if not unknown is very rare; certainly no records to the contrary can be accepted unless, with a full clinical history, they contain a careful examination of the blood in all its features.

Race and Climate.—We find an illustration of the independence of contingency in that chlorosis obeys no climate, no latitude, no altitude. Hirsch tells us that it is found in Asia Minor, in Algeria, in the West Indies (Creoles), and so forth. I have seen it abundantly in South European races, such as the Italian; and in women of all builds and of all breeding; but it must be admitted that, without examination of the blood, observations of this kind have but an approximate value. It is said that anaemia is commonest in blondes; and Dr. Lloyd Jones adds that blondes are more fertile. This assertion is open to the criticism that in the blonde chlorosis is more conspicuous; indeed the peculiarities of the district with which the observer is conversant must control his experience. Rörig of Wildungen, in an interesting pamphlet of statistics in my possession, concludes that chlorosis is more active in summer than in autumn and winter.

Age.—Chlorosis is a malady of puberty; if it occur in later life, as no doubt it often does, the attack is to be regarded as a relapse. All authors agree that a first attack is rarely postponed after the age of twenty-four. Professor Stockman gives twenty-three as the highest age of his series; and in a series of 63 cases, found that no fewer than 41 lay between the ages of fifteen and twenty (80). Now in this respect it is remarkable that in the age-period of women from eighteen to twenty-five Leichtenstern found the haemoglobin to be ordinarily about 8 per cent less than in the period from twenty-five to forty-five years of age. Sörensen substantially corroborates this statement, and attributes this diminution of red corpuscles directly to menstruation. Prof. Stockman attributes it to the demands of puberty in a more general sense; digestion and appetite being, moreover, often impaired at the time when menstruation is being established.

Conditions of Life.—Almost every fault in the circumstances of life has been regarded as a direct cause of chlorosis; that such faults continually intensify the disease is generally admitted. To work in a badly ventilated room will keep up chlorosis, or anaemia at any rate, in spite of remedies. Some overwrought and underfed women only keep

going by taking iron, from time to time, for the best part of a lifetime. Still, a contributory or accelerating cause is not necessarily the specific cause. Mental strain, again, is rather a favouring condition than a specific cause. Dyspepsia, with malnutrition, takes an important place among the contributing causes. In about one-half of Professor Stockman's cases disorders of digestion were present; although the primary cause may not lie in the stomach, malassimilation must be a favouring condition. Simon also lays great stress on this element in chlorosis; he tells us how capricious the appetite becomes in young girls, nay even depraved; such stuff as slate pencil and the like being devoured. There is, indeed, an especial proneness in chlorosis to atonic and perverted gastric functions, if not to atonic dilatation of the stomach. Many young women, as their frames develop, fall into a panic fear of obesity, and not only cut down their food, but swallow vinegar and other alleged antidotes to fatness. Nearly all chlorotic girls are disposed to shirk meat and to feed on pastry and sweets; and of the meat which is eaten, browned and burnt fragments form no inconsiderable part. If these ingesta do no direct harm, at any rate they conceal a process of inanition, and a fall in red corpuscles. These losses the full-grown woman may recover from readily; the growing and developing girl cannot so easily make up the multiplying arrears. Yet, after all, as such careful observers as Prof. Stockman record that only about 50 per cent of chlorotic women are dyspeptic, we cannot regard dyspepsia as a necessary antecedent; the specific cause lies deeper. We have only to look at the peasant girls who come with chlorosis to our rural hospitals, and again at the young maid-servants in good families, to see at once that chlorosis is in its essence independent of food caprices, city life, hard conditions, and indigestion. The weathered country girls may exhibit less of the malady; or it may fall on them with less intensity the better their conditions of life; still chlorosis does not pass them by. Niemeyer testifies to the number of robust peasant women from the surrounding villages who were wont to present themselves before him with chlorosis. Meinert presses this kind of explanation in a special argument: he attributes chlorosis to tight lacing, or to the belts worn by women; practices which, as he alleges, lead in a considerable percentage of women to splanchnoptosis; he records gastroptosis in most of his patients who suffered from the malady, and in 15 per cent he reported movable kidney. Surely, of movable kidney, at any rate, this is an exaggerated proportion; it is opposed to the reckonings of other physicians who have studied these dislocations. Eichhorst, for instance, has tested these statements in the Zurich clinic, and finds them to be much exaggerated. As regards the stomach, after reading Prof. Meinert's tract with the respect due to the author, I must surmise that in some cases he has taken toneless, inflated stomachs for dislocated stomachs; no reports on this subject are worth much unless at least the line of the smaller curvature be plotted out. In his view chlorosis is "no malady *sui generis*; it is a secondary anaemia due to a drag upon the spleen ('a

blood-forming organ') and the abdominal sympathetic." It is true, of course, that any embarrassment of the respiration lessens the intake of oxygen, but my experience does not accord with these anatomical assumptions. I would urge that the tendency of modern medicine to attenuate and disperse standard clinical concepts in an atmosphere of immature pathological notions is to be regretted.

Estimates of the hydrochloric acid present in the stomach in cases of chlorosis have been made by many investigators: in some this acid was found in excess, in some in defect; in others, again, it proved to be normal in amount. Similarly discordant results would probably be obtained in any group of sickly young persons of capricious appetites.

It is a common experience then that many girls otherwise healthy, normal, and living under the best conditions of life become chlorotic: perhaps no girl escapes it altogether; some, however, shew it but little, and recover rapidly. The secret does not lie in inanition, or dyspepsia, or in dislocation of organs.

A more potent cause, perhaps, is emotion; either emotion of a wearing and long-continued kind—such as love sickness, home sickness, and the like, or shocks of a more sudden onset. A remarkable case of this kind came under my notice some years ago. A young lady became very chlorotic, and her cure was not so easy as usual; however, after a little patience she was apparently cured, and the treatment was continued until fear of relapse had abated. Then, on a certain evening, the other members of her family having gone out till a late hour, she went to bed alone. At midnight she was awakened by a sense of some presence in the room, and on opening her eyes she saw a figure in white moving across it. She lay speechless with terror until the apparition, after some pacings, passed out of the room again. As it issued from the room she became aware that the ghost was the butler in his night-shirt; and she sprang out of bed to bolt the door after him. As she did so, he returned towards the door, and, thrusting against it, tried to re-enter the room. With strength renewed by fear she thrust against him and, after some effort, secured the door. For some time the man hung about the landing, and she sat on her bed in an agony of apprehension until her parents' return home, about four o'clock in the morning. It turned out afterwards that the poor man was a sleep-walker, and his promenades were innocent enough. On the next day, however, she was in a worse plight than before; the chlorosis was profound. I was assured by the girl's mother that when they left the patient on the evening of the alarm she was to all appearance well; by daylight next morning she was seen to be as I saw her. Other cases of the same kind are on record; still, such a mode of causation is uncommon, and probably depends upon a strong proclivity to the disease.

Generative Organs.—The fashion of attributing chlorosis to sexual perturbations, of which the patient may or may not be conscious, is passing away. The final extinction of this hypothesis we owe to Rokitansky and Virchow, who proved by necropsies that no uniform morbid condition of

the organs of generation is found in these cases: the parts may be normal; or this or that abnormality, such as hypoplasia, may be discovered: but all or any are of an incidental kind, and present no common factor. At the same time, if epithelial debris be found repeatedly in the urine, masturbation must not be forgotten, and corroborative evidence of the habit may be obtained.

Mesoblastic Hypoplasia.—Morgagni, Meckel, Rokitansky, and, still more definitely, Virchow have drawn attention to a peculiar arrest of development of the arterial system found after death in certain cases of chlorosis. (*Vide* art. "Diseases of Arteries," Vol. VI.) Apposite necropsies are few, for it is only by rare accident that cases of chlorosis come to the post-mortem table. In the cases mentioned, however, a strange state of things is revealed. The aorta may scarcely admit the little finger, and the abdominal portion of the vessel may be no bigger than the ordinary iliac or femoral artery. This remarkable arrest of development is but a part of a general arrest throughout the whole arterial system, and is supposed to indicate a like hypoplasia of the mesoblastic layer throughout, including the blood-forming organs; hence, it is said, the peculiar anaemia. Chronic renal disease is prone to supervene. As an explanation of chlorosis this is a hypothesis rather of the dead-house than of the bedside. That a disorder so common, and for the most part so curable, should depend upon a malformation so grave and so incurable as this aortic and general vascular hypoplasia is on the face of it improbable. Again, so far as our evidence goes, this kind of arrest occurs in either sex indifferently (Hayem). It is said, indeed, that Virchow was not always careful to exclude the cases of congenital or gradual heart defect with which a hypoplasia of this kind may be bound up (Pye-Smith). Krehl pronounces decisively against the hypoplastic hypothesis.

Haemorrhage.—Loss of blood is a common and direct cause of anaemia, and has been assumed to be an important cause of chlorosis. It is said that in many cases haemorrhage, whether in the form of menorrhagia, epistaxis, haemorrhoids, haematemesis, or otherwise, is or has been obvious enough. And it is urged, if haemorrhage be a *vera causa*, and in a considerable number of cases an immediate factor, may not haemorrhage be a universal antecedent—haemorrhage which, if it issue by some passage unobserved, or in recurrent quantities too minute to catch the eye, may often be overlooked? Such imperceptible oozings have been supposed to flow into the stomach, for example.

Now we have seen that the anaemia which results directly from haemorrhage is not identical with that of chlorosis. Besides, there can be no doubt that cases of chlorosis occur daily in which, after the closest inquiry, no haemorrhage can be seen or heard of: and in respect of the alleged persistent oozing of blood from mucous surfaces the contents of the stomach and bowels have been repeatedly tested without the discovery of any reactions due to blood or sanguineous effusion. That menstruation or other blood loss, even if moderate, may aggravate chlorosis is certain, and amenorrhoea, therefore, may be a protective condition; but on the

other hand chlorosis, as we all know, may occur in girls before the appearance of menstruation.

The insistence of v. Noorden and his school on a radical defect of blood formation in chlorosis seems, in the light of Drs. Haldane and Lorrain Smith's results, to be scarcely justified. Although the defect of haemoglobin and of red cells may be absolute, yet the chief feature is the dilution of the cells by a large bulk of plasma.

Bunge's Hypothesis.—An explanation of chlorosis, and of the behaviour of iron in the cure of it, has been proposed by Bunge. I will set forth the hypothesis in the lucid sentences of Prof. Stockman:—"Bunge holds that the ordinary preparations of iron, including the so-called albuminates and peptonates, cannot be absorbed from the alimentary canal. He points out that ordinarily the iron of the red corpuscles is formed from the organically combined iron in the food, which is something like haemoglobin in constitution, and can be readily absorbed and readily converted into haemoglobin. From milk and yolk he isolated such an organic combination. But he admits that inorganic iron preparations are capable of curing chlorosis, and explains this as follows. In chlorosis digestion is disturbed, with formation of sulphuretted hydrogen and alkaline sulphides in the bowel. These combine with and separate out the organic iron of the food, and sulphide is formed, an inorganic compound which, according to Bunge, cannot be absorbed; hence the blood loses its necessary supply of iron, and chlorosis results. When inorganic iron is given, however, it combines with and neutralises the sulphuretted hydrogen, and thus protects the organic iron of the food, which, therefore, becomes absorbed, and goes to form haemoglobin. In support of this view he adduces the received opinion that large doses of iron are necessary for the cure of chlorosis, and this he says is because large amounts are necessary to neutralise all the sulphuretted hydrogen in the bowel. Further, he states on the authority of Zander that hydrochloric acid cures anaemia more satisfactorily than iron does, because it is antiseptic, and prevents formation of sulphuretted hydrogen in the bowel." Now, as Prof. Stockman adds, "the presence of iron in our food, in the tissues and excretions of the body, its constant ingestion and excretion, and the small quantities with which we have to deal, apparently place a complete barrier in the way of rigidly proving by chemical methods that it is or is not absorbed."

Prof. Stockman met these difficulties by other expedients. First, in certain well-marked cases he removed the problem from the sphere of the bowel, and endeavoured to bring about the cure of chlorosis by injecting iron subcutaneously. Secondly, he administered sulphide of iron by the mouth, a preparation which cannot take up more sulphur, and, being non-astringent, cannot be credited with any tonic effect on the bowel such as might promote its absorptive activities. Thirdly, he administered bismuth, manganese, and other drugs which have a like power of neutralising sulphuretted hydrogen, and which should therefore have a like curative power in chlorosis. The results of these observations were

as follows: both in his own cases, and in the cases of others who had given iron subcutaneously for other reasons, iron thus administered did subcutaneously cure chlorosis, though the method is one which has its drawbacks; Warfvinge of Stockholm cured a series of cases by subcutaneous injection of iron, and found that thus used one-fifth of the ordinary doses of the metal sufficed: the cure of chlorosis seems then to be by absorption. This administration *per rectum* if it acts more slowly, answers fairly well. Secondly, sulphide of iron proved a satisfactory means of cure. Prof. Stockman also emphasises, what many of us had noted, that reduced iron cures chlorosis in doses too small to have any substantial effect in neutralising sulphuretted hydrogen. I may add that patients have complained to me that reduced iron seems, indeed, to have the unpleasant property of disengaging sulphuretted hydrogen in the bowel, so that the drug is quietly shirked by some of them. Thirdly, Prof. Stockman found that bismuth, which would absorb even more sulphuretted hydrogen than iron, is nevertheless quite inefficacious in the treatment of chlorosis. Kletzinsky speaks, therefore, in paradox when he says that "from all the hundredweights of iron given to anaemics during centuries not a single blood-corpuscle has been formed." Stockman thinks that iron is absorbed as other salts are, the ferric salts being reduced in the intestine to ferrous; and that the building of it into organic combinations, which are of various degrees of intimacy, is done in the liver. Mackay, at the Toronto Congress in 1897, stated that iron is absorbed by the epithelial cells of the villi, the iron of haemoglobin being taken up as haematin. He adds that the metal is passed inwards by the leucocytes. Binz has stated, I think, that an early effect of iron in chlorosis is a multiplication of leucocytes. That they are increased in total number rather than drawn from their hiding-places would be difficult to prove; but at any rate they may be more busily employed. That "inorganic iron" given as a remedy does no more than stimulate the atonic intestine to absorb the iron (Kobert) seems improbable. Bunge's ingenious suggestion seems, then, to be without foundation.

The appearance of an anaemia in pulmonary tuberculosis, emphasised by Trousseau, and called by him chlorosis, has since his day attracted some attention. It is not, however, a "*pre*tuberculous anaemia," but an accompaniment of the process itself. As Lloyd Jones and others have shewn, it is characterised by a diminution of the bulk of the blood and a fall of the specific gravity of the plasma. Thus in respect of the blood alone it is different from chlorosis, although similar to it in the apparent reduction of red cells and haemoglobin. Drs. Bardswell and Chapman have shewn that tuberculous anaemia is greatly ameliorated by sanatorium methods. It is an instance of our confused way of thinking in medicine, that a recent observer, having occupied himself at some length with proofs of the distinction between chlorosis and this anaemia, concluded by naming it "tuberculous chlorosis"!

Toxic Causes.—That chlorosis is an haemolysis, due to the influence of some toxin in the system, is a speculation which no doubt has presented

itself to many minds; not a few pathologists have busied themselves with hypotheses of this kind, from the inevitable microbe to the mere absorption of faecal juices from the constipated bowel, or the presence of uric acid in the blood (Haig). Bunge's hypothesis, indeed, rests upon some such postulates in respect of toxic agents, though in his view the toxins in the bowel act indirectly and within the canal. The toxic hypotheses of chlorosis depend for their proof on the discovery of such injurious agents in the blood or excretions. The simplest of them is that popularised by Andrew Clark, who earnestly contended that the impoverishment of the blood in this malady is directly due to constipation of the bowels; this, he said, brings about an accumulation of the products of decomposition in the alimentary canal which, passing thence into the blood, poison it either in its prime or at its sources. Stockman, Simon, and other observers who have tabulated cases with this problem in view, point out that, in the first place, only about half of the cases of chlorosis present constipation; on the other hand, constipated people who do not suffer from chlorosis are common in both sexes. After Clark published his paper I paid close attention to this point, and accepted no mere routine reply to my inquiries into the state of the intestinal functions; and I too found reason to believe that, when the cases are excluded in which constipation is attributable to the iron administered, chlorotic women are not more constipated than other women. No one has succeeded in shewing that chlorosis is to be cured by purgatives alone; yet almost all writers on chlorosis yield a little to the temptation to presume on a toxic cause in the blood in one direction or another. Even Dr. Lloyd Jones, believing as he does that chlorosis is but an abnormal activity of a normal storage process, yet fortifies himself with an argument out of the same quiver; he suspects, as do some other pathologists, that chlorosis is due to a toxic excess of an internal secretion from the parts of generation, a secretion which in normal quantity fulfils a natural purpose. However, he found no effect on the blood by the administration of ovary, tube, and uterus from healthy animals; though large quantities of uterine extract did excite profuse secretion of milk in the male! In the chlorotic such an internal secretion may be perverted. Von Noorden (59), and Arcangeli likewise, are disposed to assume some perversion, absence, or excess of an ovarian internal secretion as a factor in chlorosis.

Chvostek reported that in 21 cases out of 56 he found the spleen enlarged; thirteen times it was palpable: thus he is led to support the alleged kinship between chlorosis and splenic anaemia. Clement, if I understand him aright, looks for the infective agent outside the body; and, partly on analogy, considers that chlorosis should be classed with the infectious diseases. He tells the story of an epidemic which occurred in a small village; during its course eight young girls were attacked with febrile symptoms and enlargement of the spleen; phlegmasia alba, dry pericarditis, and pleurisy were among the complications. Anaemic these patients were no doubt, but few readers will be convinced that the

malady under which they suffered was chlorosis. Against these allegations of enlarged spleen I may say that Simon and Schrott, both of whom had their attention directed to this point, found this enlargement in two cases only (*vide* "Spleen in Anaemia," Vol. IV. Part I. p. 440; and art. "Splenic Anaemias," p. 757 of this volume). Splenic enlargement is no part of chlorosis.

Pick finds the source of the blood-poison in another place, namely, in a dilated stomach. His cure for chlorosis is lavage. Now, no doubt there are haemolytic poisons in plenty; such poisons as lead, arsenic, syphilis, those of rheumatic fever, Bright's disease, pernicious anaemia, and so forth; but it is a superficial way of looking at things to say that anaemia here and anaemia there must be due to kindred causes. Before we can listen to comparisons of this sort we must have many rules observed; we must know in all the cases the specific gravity of the blood-serum, if, that is, the blood plasma is up to the standard of health, or even above it; and in research cases we must have some appreciation of the mass of the blood. Lloyd Jones, Hayem, Stockman, indeed all careful students, tell us that in experiments and observations on this subject regard must be had not only to haemoglobin and apparent paucity of reds but also to other changes in the blood. For, as Immermann well says, "Chlorosis maintains its individuality in the teeth of all the attempts that have been made to merge it in the great ocean of anaemia."

Again, in anaemia there is ordinarily no evidence of poison in other parts or excretions of the body. For example, Simon (77) says that indican is not found in the urine of the chlorotic; and Rethers, by a series of important investigations, seems to have shaken the foundations of the toxic hypothesis by shewing that in 9 out of 18 cases of ordinary and severe chlorosis the ethereal sulphates were absent; and that in the remainder there was no uniform or considerable appearance of them. Von Noorden, who (*l.c.*, p. 347) discusses this point clearly, quotes Hennige and Heinemann to the same effect; and Prof. Stockman adds the testimony of Mörner. The secret of the causation of chlorosis does not seem to lie, then, in an haemolysis, either from a foul state of the intestine or by the absorption of some poison. The very poorness of the urine in many cases of definite chlorosis, its deficiency in colouring matter, suggests that, instead of an excessive breaking down of blood-corpuscles, such as results from the absorption of poisons of the kind under consideration, the life of the red cells appears, on the contrary, to be prolonged.

There seems to be a certain, though not very intimate association between chlorosis and Graves' disease. Chvostek gives 7 cases of chlorosis associated with Graves' disease. Dr. Lloyd Jones and others also note some fulness of the thyroid in many cases. I have described the same coincidence; but, without a standard calculation of the frequency of some fulness of the thyroid in healthy young women, in whom I think it is in some excess, it is not easy to express an opinion on the point. Dr. A. F. Martin has examined 49 consecutive cases of chlorotic girls from this point of view. Of them

18 shewed an enlargement of the thyroid, which he considered to be far in excess of this incident in health. No parallel was observed, however, between degrees of this enlargement and degrees of chlorosis. In uncomplicated cases I hear no murmurs in the gland; and I regard the increase as due only to plethora of a highly vascular part. The administration of thyroid extract in chlorosis has not proved to be of any service.

Prof. Stockman supposes that chlorosis depends mainly upon two causes; namely, on insufficient food at the age of development—especially in respect of iron (p. 699), in which conclusion he is supported by Simon,—and on the persistent effects of incidental haemorrhages, menstrual and other, which may be positively excessive, or relatively excessive in the individual case. When, however, we regard the many contingencies to which the operation of these several causes are open, the partiality of their incidence, and the many cases in which these factors produce disorders other than chlorosis—such as mere emaciation and debility, with a fall in the protein value of the blood,—I repeat that, in my opinion, we have to look for a more uniform cause, one more independent of contingencies; such a general cause as that proposed, rightly or wrongly, by Dr. Lloyd Jones.

I fear Dr. Haig's uric acid hypothesis has little to support it; against it we find on all hands that the excretion of nitrogen in chlorosis is rather diminished than increased. Grüber, moreover, found the apparent alkalinity of the blood up to the normal standard, and even above it; and von Noorden tells us that Peiper, Kraus, Rumpf, and Dronin corroborate this statement.

Pathology.—On pricking the finger of a chlorotic patient, bloodless as she may appear, the blood springs forth freely, more freely than in anaemias of other kinds; the colour also is different; the red corpuscles being fewer, the blood transmits light more readily and the colour is brighter; it is bright red or even borders on orange. The specific gravity of the blood is easily tested by Roy's method, but that of the plasma less readily; for this a centrifuge is required. The specific gravity of the blood is reduced; that of the plasma is steady, or occasionally somewhat raised. Dr. Lloyd Jones tells us that in both sexes alike the mean specific gravity of the whole blood rises till puberty; at this period, however, that of the man goes on rising, whilst that of the woman falls. Taking the blood of childhood (two to three years) at 1050, that of a young man of seventeen may be 1058; of a young woman, 1055·6. These observations were made, of course, under dietetic and other controls. From the age of seventeen, then, Dr. Lloyd Jones finds that the mean specific gravity in man still rises; in woman it remains low till twenty-five, after which age it rises to 1055 or 1056. Coincidently with these changes in the blood general metabolism is lessened, for the excretion of carbonic acid and of urea also falls (Landois and Stirling). In the Charts herewith, which I am enabled by the kindness of Dr. Lloyd Jones to publish, these changes are well exhibited. Whether the haemoglobin be increased, unaffected, or decreased during or by

menstruation seems as yet undetermined. I may repeat that Dr. Jones says, speaking generally, the specific gravity of the whole blood stands at a lower mean in women who have many brothers and sisters; that indeed the specific gravity may be taken, approximately, as a gauge of fertility,[1] the change in the blood in chlorosis being an extreme fluctuation of a physiological quality of the child-bearing period of life. Indeed it is said that the blood of a pregnant woman presents similar features in a high degree. Every girl, then, may be regarded as potentially chlorotic, and perhaps none passes through young womanhood without some phase of the disorder. The boundary between the physiological and the pathological states, if Lloyd Jones's conclusions are to be accepted, is an arbitrary one.

The specific gravity of the serum differs little, if at all, from that of health; if anything, it tends to rise. That of the blood as a whole falls by the diminution of the volume of the red corpuscles or of their haemoglobin, usually of both; changes which are commonly recognised in chlorosis. In twenty-six cases tabulated by Lloyd Jones (p. 22) the fall of the number of red corpuscles per cubic unit (and probably also absolutely) comes out strongly, so strongly as to teach us that this fall, taken together with a like fall in haemoglobin value, while at the same time the protein value of the blood keeps steady, is more characteristic of chlorosis than we are wont to suppose. The apparent alkalinity of the blood, especially of the plasma, as here said, is usually increased. Besides all this we must have regard to the terms of the morbid series taken as a whole.

In turning to the remarkable confirmation of Lloyd Jones's opinions by the researches of Haldane and Lorrain Smith, who have revealed in chlorosis enormous increases in the bulk of the plasma, I append a table by Prof. Lorrain Smith, in which these results are exhibited and compared with those of Addison's anaemia:—

Name.	Vol. of CO absorbed in c.c.	Saturation of the blood by CO.	Total capacity of the blood for oxygen.	Percentage oxygen capacity of the blood.	Total vol. of blood in c.c.	Red corpuscles in millions.	Body weight in kilos.	Ratio of vol. of blood to weight.	Ratio of oxygen capacity to weight.
Case of Chlorosis—									
C. H., age 18 .	33·4	8 %	418	6·6	6181	2·110	44·5	$\frac{1}{7·2}$	$\frac{1}{106·4}$
Case of Pernicious Anaemia—									
J. C., age 41 .	37	18·96 %	195	3	6500	·6520	58	$\frac{1}{8·9}$	$\frac{1}{297·4}$

Von Noorden has remarked that enrichment of the blood plasma (in potential mothers) finds an analogy in the suckling woman, in whom

[1] He thinks that the relation between the condition of the blood and fertility holds good for mammals and birds; but I cannot now pursue this line of inquiry.

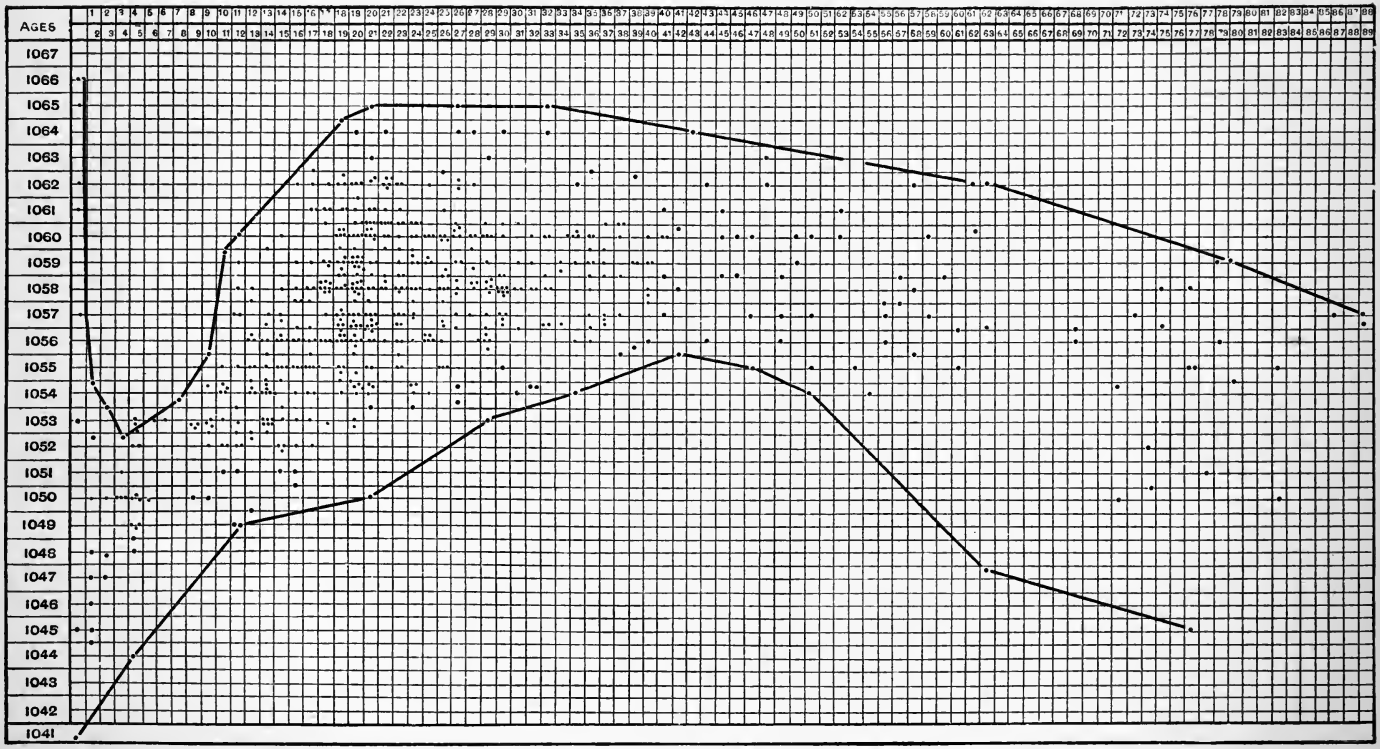

CHART 6.—Shewing the results of observations on the specific gravity of the blood of healthy males of different ages, and the upper and lower limits of variations consistent with health. (Lloyd Jones.)

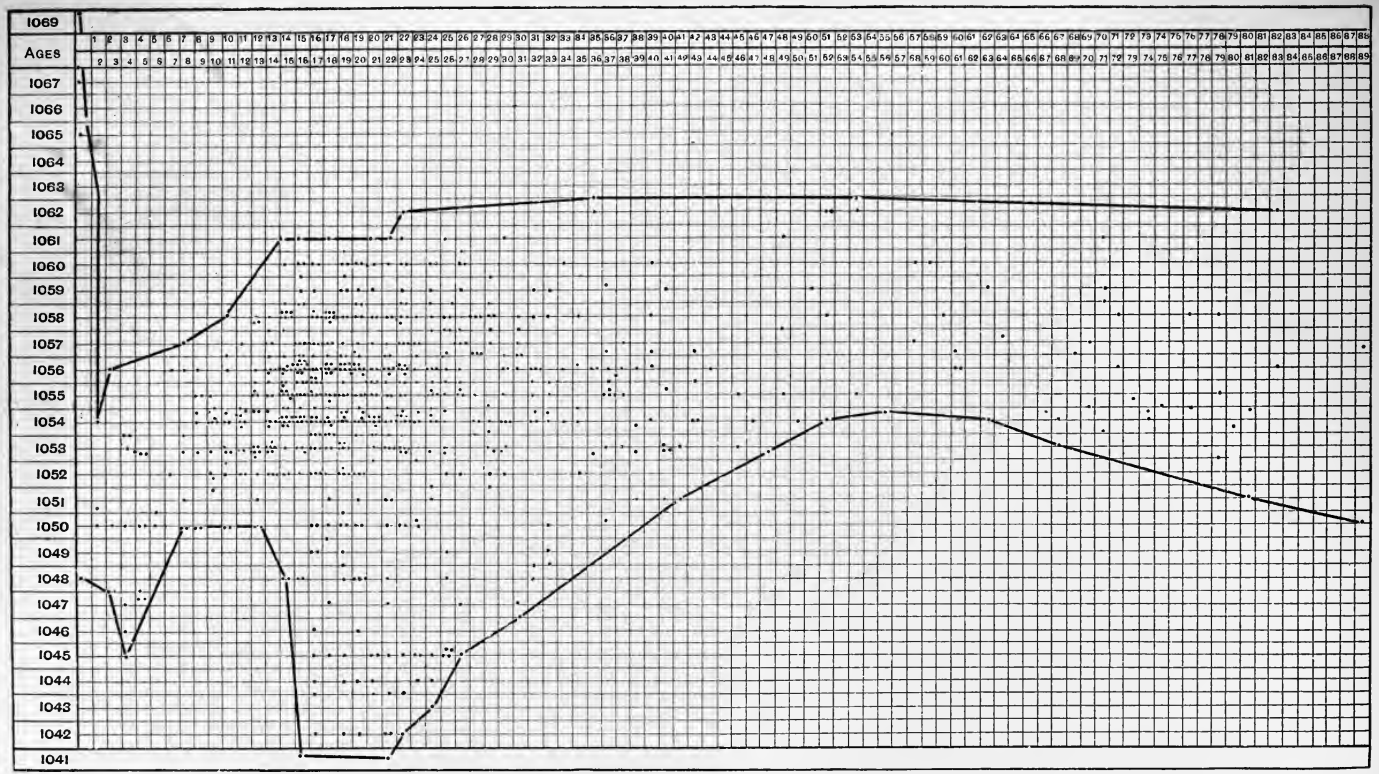

CHART 7.—Shewing the results of observations on the specific gravity of the blood of healthy females of different ages, and the upper and lower limits of variation consistent with health. (Lloyd Jones.) The two charts represent observations on 1400 individuals.

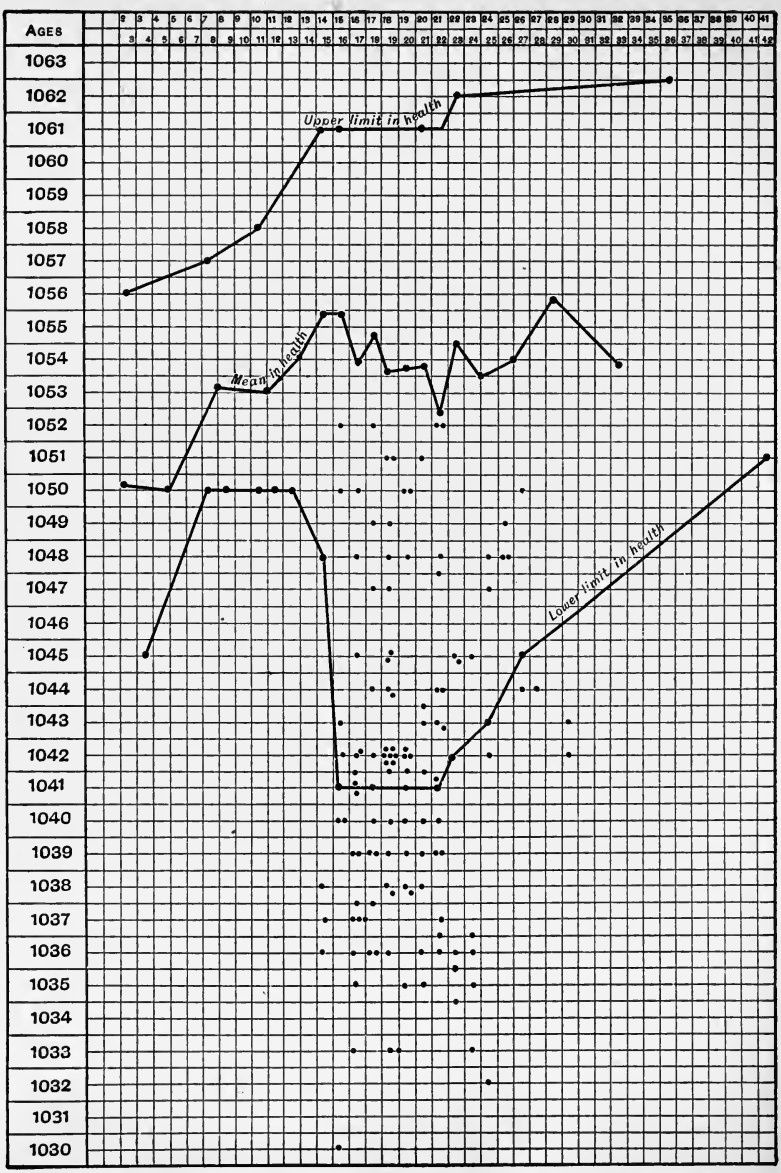

Chart 8.—Shewing the variations in the specific gravity of the blood in healthy females, from 2 to 42 years of age, and the results of observations upon 120 young women with chlorosis. (Lloyd Jones.

lactosuria may appear not because the lactose is made in overwhelming quantity, but because by natural providence the cells of the body refuse a material suitable for the nutrition of an infant.

Prof. Stockman has estimated the bearing of diet on chlorosis. That the iron needed for the blood is absorbed from the food seems probable, nay, it is proved. It is certain that the chick gets iron from the yolk, and the suckling from the milk. Stockman has estimated our sources of this metal. Taking the issue of iron daily as $\frac{1}{10}$ of a grain, he found that the daily food of fifteen healthy persons contained iron at the rate of $\frac{1}{10}$ to $\frac{1}{6}$ of a grain; thus the supply is equal to the demand: moreover, detained in the liver, there is a store of disengaged iron, the precipitate of defunct corpuscles, which acts as a reserve; in healthy livers Prof. Stockman found from $2\frac{7}{10}$ to $4\frac{3}{5}$ grains of it. Now if we compare this estimate with the state of chlorosis we find a derangement of these relations. Although in women, owing to menstruation and so forth, the reserve iron in the liver is less than in men, yet their food is apt to contain a smaller supply of the metal. In the habitual diets of four chlorotic women Prof. Stockman found iron in the respective quantities of $\frac{1}{50}$ to $\frac{1}{20}$ of a grain a day; so that if iron be escaping at a rate of $\frac{1}{10}$ of a grain daily, the red corpuscles may well starve. Coppola and other observers fed animals (cocks and dogs) on food from which all iron had previously been removed; the haemoglobin value of the corpuscles soon fell, but it was readily supplied on the administration of inorganic iron. It was found that on a non-ferruginous diet the haemoglobin fell 35 per cent. It is to be remembered that in the articles of diet the iron is held in various degrees of intimacy; in some organic molecules, as, for example, in the protoplasm of cells and nuclei, the combination may be so intimate that ordinary tests fail to detect it; the metal has to be recovered by incineration (Zaleski, Vay). In ordinary anaemia of an accidental kind—as, for instance, after an occasional haemorrhage—the iron of the food commonly proves to be sufficient for the restoration of health; although, if 20 grains of iron be lost, the food alone may be long in making it up. We have seen that the defect of the blood in chlorosis probably extends to the total number of red corpuscles as well as to the haemoglobin content per cell, or other volume unit. How far, in particular cases, in the presence of an increased blood mass, the reds are absolutely reduced in number we cannot be sure; but it is not so large as necessarily to throw us back upon a failure of the proliferation of the marrow. Both Prof. Stockman and Dr. Lloyd Jones insist on this defect; Stockman, in his cases, reports a "striking deficiency of red corpuscles as well as of haemoglobin," but, as the increase of the plasma was not then verified, the deficiency may have been only apparent. A deficiency down even to two millions on our ordinary method of counting may be observed, but it rarely falls lower. Prof. Stockman's highest figure was 66 per cent, his lowest 20 per cent. In four days after beginning ferruginous remedies the red corpuscles go up with a bound, and in 10 or 14 days reach the normal standard; iron has no

such potency as this in other anaemias. The haemoglobin rises much more slowly, and two months after the beginning of treatment may still be defective. What happens to the plasma we do not yet know.

Deformity of the red corpuscles is not a feature of chlorosis as it is of pernicious anaemia, though a certain number of them may be undersized, even when full allowance is made for the presence of microcytes; and their vitality is said to be low, that is, their histo-chemical properties fall; they fade before doing full work and the rouleaux are defective. Nucleated reds are occasionally recorded, in severe cases; and a few of the so-called megaloblasts. There is no leucocytosis, and the several kinds of leucocytes are in normal proportion; but blood-platelets are numerous. The fatty elements of the blood are said to be markedly increased, but the lecithin is diminished (v. Erben). The evidence that the defect lies on the formative and not on the destructive side is fairly complete. The signs, indeed, point to a diminished destruction; the hydrobilirubins in the urine and stools are less, not more.

The relations of water and of salts to the serum of the blood are less easy to discuss; the steady specific gravity of the proteins in the plasma indicates no tendency to hydraemia. It seems probable that the amount of water stands in some definite relation to the protein constituents, as its presence is not a mere dilution, but a combination with these substances: in like manner the salts are related to the state of the proteins and to the cell-osmotic activities. Von Erben reports that the sodium, potassium, iron, and phosphoric acid are diminished, and the calcium and magnesium increased. For the present, however, it does not seem that these are points of cardinal importance in chlorosis.

Coagulation is slower in chlorotic blood, outside the body, notwithstanding the tendency to thrombosis within it; the clots are scanty, and the fibrinogen is less, facts which are not easy to reconcile with that accident. A slow venous blood-stream may account for the tendency to thrombosis; but on this point we are really quite ignorant.

Until Haldane and Lorrain Smith's method can be adapted to clinical purposes,[1] the physician can only guess at the *mass of the blood*; in many anaemias we have seen that the mass of the blood seems to be diminished, and the blood issues slowly from a puncture; in chlorosis the increase of the blood mass is recognisable in a general fulness of the vessels—the *plethora serosa* of old writers. That the whole mass of the blood may be increased, even enormously, is admitted by modern pathologists as distinguished as v. Recklinghausen, Bollinger, and Krehl. Geisböck brings evidence to the same effect, as does also Dr. Parkes Weber (in a case of polycythaemia). Dr. Lloyd Jones thinks that the dyspepsia of chlorosis is due to an accumulation of blood in the splanchnic area, the dilatation of which he attributes to some influence on the splanchnic nerves. In dogs he found that, by section of the splanchnic and injection of saline solution, enormous additions to the blood volume could be made;

[1] According to Oerum ("Quantitative Blutuntersuchun," *Deutsches Arch. f. klin. Med.*, Leipzig, 1908, xciii. 356), such methods are finding their way into the wards.

finally the gastric mucosa became of a deep chocolate hue and haematemesis occurred. Meinert also (p. 687) insists on some interference with this area. If there be mesoblastic hypoplasia, the plethora may be relative. In some cases of prolonged chlorosis there may possibly be some mesoblastic hypoplasia, but not such as to forbid some further evolution; and the capacity of the arterial tree may grow with its nutrition and its contents. In ordinary cases, however, the vessels and plasmatic elements of the blood seem to be sufficient for vegetative growth; chlorotic girls do not lack size, nor do they fall away from the main lines of development.

On the other hand, in most of the organs there are signs of an oxygen famine; consequently the heart and vessels are subject to a deterioration which in its extremer degrees may attain somewhat serious proportions. The arteries, and especially the aorta, near the origin of its ascending portions, may present on the inner coat dull yellow spots and striae; indeed, superficial erosions of some extent may be detected. The striae may also be seen in the descending portion on its posterior inner aspect, between the intercostal and lumbar arteries (Virchow). These patches and streaks, when examined microscopically, are found to consist of minute dots, each, according to Virchow, being a fatty connective-tissue corpuscle. The heart is often of normal size, or but moderately dilated. Increased as the bulk of the blood may be, if the rate of the heart be accelerated the output per beat need not be enlarged. Speaking generally, however, the heart is usually rather dilated both to left and to right, for a larger output of the left ventricle, as the periphery is freely open, means a corresponding pulmonary delivery. Valvular disease is rare; but some deterioration of the myocardium is a feature of chlorosis as of all anaemias. The Leipzig pathologists especially have demonstrated that patches of such myocardial lesion, even to the degree of valvular incompetence, occur, and are recovered from, far more frequently than we have been wont to suppose. The change is primary, and is best seen in the papillary muscles, especially of the left ventricle, as spots and striae; healthy fibrils are mixed with others within which fatty granules have accumulated. Virchow describes a similar impairment in the capillaries also.

The renal, hepatic, and gastric cells are affected likewise, and all the organs are pale. The atonic stomach may be dilated (see, however, p. 704; and art. "Dilatation of the Stomach," Vol. III. p. 529). The spleen, marrow, and lymphatic glands are not usually described as abnormal. Grawitz found the marrow of the tibia normal in the only case which he examined.

Symptoms.—The chlorotic girl is well known in every consulting-room, public or private. The disease is no respecter of race,[1] rank, or

[1] If races differ, it may be that chlorosis is more frequent in the more prolific races. Dr. Lloyd Jones finds that the blood of the Red Indian, not a prolific race, is of much higher specific gravity than of that very prolific race, the Negro. He thinks the "Iberians" are bloodless, do not blush, and are not prolific.

fortune. Whether her aspect at first sight be indicative of the disease or not, her characteristic complaint is dyspnoea. Dyspnoea, due probably to incessant stimulation of the bulb by suboxidised blood, is more persistent and incapacitating in chlorosis than in any other functional disorder. Many of these patients bear in their features the classical sign of their malady, but not so all of them; not a few of them carry colour (Chlorosis florida or rubra); but in my experience all suffer from dyspnoea, and, however insidiously it creep on—for the disease may attack acutely or insidiously—the patient is never unaware of it. If she be asked whether she can trip upstairs as she was wont to do a few months previously, her answer will bring the physician near to his diagnosis. I have said that many chlorotic girls carry some colour, indeed a high colour, but the carmine is apt to be a little dusky or even plum-coloured. In past years this bloom was a little puzzling to me, as no doubt to others also; but we have now learned to look below the surface, and I see that Prof. Stockman, Dr. Lloyd Jones, and many others deal with this aberrancy, and point out why red cheeks may be as compatible with chlorosis as pallor with no lack of haemoglobin. In a certain very pallid girl Prof. Osler reported over 5,000,000 reds to the cubic millimetre, whilst in a florid patient they amounted to no more than 2,000,000. In this patient, he adds, pallor did not appear till the reds had fallen to 1,200,000. Chlorotic girls blush readily enough; and even in the height of an attack some of them never lose a vivid tint on the malar eminences. It is said that the conspicuous chlorotic is a blonde; but many blondes, in spite of an assured chlorosis, have no little carmine in their cheeks; and many brunettes are pale enough and green enough to reveal their disorder at once. Exposure to weather affects the more stable colour of the complexion, but not the fleeting tints of capillary distribution. A fair and clear skin takes the alabaster or old wax colour; a brown, muddy or thick skin does not. We have blondes with bad complexions and brunettes with transparent complexions. Transparent skins are often seen in the dark women of the so-called Iberians among ourselves, and chlorosis, when it occurs, is manifest enough in them; conversely, many blondes do not present the standard tint of chlorosis when suffering from it in no slight measure; in such persons a thick complexion, "cheeks of sorry grain," conceal or modify the characteristic tints; greyness or sallowness takes the place of marble or alabaster, and chloasmic tints may be seen here and there, as on the temples and about the knuckles and other joints. Such women do not flush readily or deeply, and their limbs, often rough and hairy, do not offer a good surface for the display of the tides of the blood. The upper part of the chest, bared for the stethoscope, may, however, manifest the peculiar hue; a pallor may be usually, but by no means always, detected also in the lacrymal caruncle, on the under side of the conjunctiva, and the mucous membrane of the mouth; the sclerotics may be blue, the pupils dilated, and the ear—that useful signal of variations in the colour of the blood—may be white. The nails, also, and the large blue veins on the skin

may have their story to tell.[1] If the pupils are dilated the eye brightens, though the face otherwise may be inanimate and puffy. If chlorosis be a disease in which the proteins of the blood are not wanting, and the mass of the blood is enlarged, the face may retain its ordinary contours and yet seem puffed, by contrast with other signs suggestive of serious ill-health. Epistaxis, due perhaps to vascular plethora, is not uncommon in chlorosis, and I think especially in florid cases; it is preceded by a sense of fulness and discomfort and followed by a sense of relief. In the secondary anaemias of malaria, plumbism, or cancer, as the vessels are more empty the face is more shrunken. Another sign may be seen in the face. If a healthy person be asked suddenly to look up at the ceiling without moving the head, the eyebrows are raised and the forehead is thrown into horizontal folds by a contraction of the anterior portion of the occipito-frontal muscle; but, says Dr. Lloyd Jones, in many chlorotic women this associated movement of the occipito-frontal muscle is wanting, as Joffroy pointed out in Graves' disease: yet they can contract this muscle if they try to do so. Dr. Jones attributes this lagging to a lessened irritability of the skeletal muscles, due to lack of haemoglobin; and thus it is that the face appears inanimate or even apathetic, the languid, listless look of chlorotic patients being due partly to this lack of facial expression, partly to languor of the limbs (Hayem). Sydenham writes of the "crurum tensiva lassitudo" of these patients. Yawning betrays a like muscular affection, and is often a vexatious symptom. The hands and feet are cold; and giddiness, tinnitus, faintness, may emphasise the defect of the blood or the instability of the circulation.

Digestive System.—The tongue is pale, moist, indented, but often clean: at other times it presents on its coated surface some evidence of disorder of the stomach or associated organs. The breath likewise in some patients is heavy in odour. These patients are often constipated, but great constipation is consistent with a clean tongue. That constipation, however frequent, is not by any means a constant symptom, I have already stated. It seems to be noted in about one-half of the tabulated cases, and probably depends upon torpor of the abdominal and intestinal muscles.

[1] For the following ingenious method of measuring the oxidising activity of the blood in chlorosis I can say nothing of my own experience: I therefore put it into a note. The passage is translated and a little abbreviated from Henocque, "L'hématoscope," *Gaz. hebd.*, Oct. 23, 1886, and April 1, 1887. It is quoted by Gilbert.

The reduction of oxyhaemoglobin into haemoglobin in the tissues can be determined by spectroscopic examination of the blood through the thumb-nail. Thus, the first band characteristic of oxyhaemoglobin may be seen, sometimes the second also. If a ligature be tied round the phalanx the bands disappear, the yellow on the level of the line D reappears, which was concealed, and then the bands vanish. The ligature isolates in the thumb a certain quantity of oxygenated blood, which for a certain time exhibits the bands of oxyhaemoglobin; the latter gives off its oxygen to the tissues, is reduced, and the absorption band is no longer intense enough to traverse the nail. In the normal state this process occupies 70 seconds, and the quantity of oxyhaemoglobin thus reduced is 0·20 per second. This is taken as the unit of reduction. In chlorosis the oxidising activity falls to 0·65-0·19 of this unit, the mean fall being 0·44.

The stomach is often the seat of some morbid changes; it may be permanently dilated (*vide* Meinert, p. 687), but dilatation, in the formal sense of the term, is not so common in chlorosis as to make it a part of our ordinary conception of the malady (Vol. III. p. 529); nor do I regard it as a very common complication; were it so, the cure of chlorosis would be a matter of more serious difficulty than it is. Dyspepsia of the sub-acute or chronic catarrhal kind, or that of flatulence and atony, sometimes stops the way, but rarely defies the usual means of treatment. Pain referred to the stomach is a common complaint. If ulcer be absent, the pain is usually no more than the epigastric burden of retarded digestion; as, however, ulcer of the stomach is no infrequent accompaniment of chlorosis, the reader is referred for the differential diagnosis of this disease from the mere dyspepsia of chlorosis to the article on Gastric Ulcer (Vol. III. p. 479). Dyspepsia is certainly characteristic of chlorosis; moreover, it is true that ulcer is very apt to be stealthy in its manifestations; notwithstanding, we must not assume the presence of ulcers in dyspeptic chlorosis. We shall note the behaviour of the pain, its constancy or its caprice, its relation to meals or other times of the day or night, and so on. That the pain of ulcer "goes through to the back" whilst that of chlorotic dyspepsia is felt only in the epigastrium is, I fear, a fallible axiom. The appetite may give us more trouble, as it is often marked by caprices and perversions which put serious obstacles in the way of nutrition; still these symptoms are often characteristic rather of the kind of patient than of the kind of disease. In neurasthenia this anorexia or parorexia leads to emaciation; in chlorosis this is not generally the case. In anorexia nervosa the wasting is extreme; the chlorotic woman eats better; her blood is also richer in proteins, and being relatively short of oxygen permits the deposit of fat. The causal relations of chlorosis to ulcer of the stomach are dealt with in the article on this subject (Vol. III. p. 462). Dr. E. C. Hort thinks that "gastrostaxis and ulceration are due to the presence in the blood of toxins cytolytic to vascular and mucous epithelium," and suggests that the impairment of the blood may be due to the same cause. But for the present we may be content to suppose that in chlorosis any breach of internal surface heals badly. There is no reason to assume hyperchlorhydria to be characteristic of this malady; rather the contrary. Diarrhœa is an exceptional and incidental occurrence.

Hysterical chlorosis is more compacted of fantasy, bizarrerie, and caprice than the common and uncomplicated form of the disease; tears and melancholy may alternate with fretfulness and self-importance. "Hysterical or barking cough" is a trying feature of some of these cases; indeed, it is no infrequent feature of chlorosis not otherwise marked by hysteria or neurosis. Such a cough may be interpreted by an examination of the blood, and cured by iron; indeed, it is rather chlorotic than hysterical in nature (cf. Vol. IV. Part II. p. 269).

Circulatory System.—Sydenham describes "pulsus febrilis" as a symptom of chlorosis; and later authors, relying on the thermometer, describe a

"febrile chlorosis." Were not such observers as Prof. Osler in their ranks I should say that fever is significant of some complication. The use of such a name by less experienced physicians might, for instance, lead to confusion between chlorosis and pernicious or syphilitic anaemia, or some other anaemia due to a toxic agent. I should be content to say that the temperature in chlorosis is not subnormal, as it is in anorexia nervosa, for instance; but that under the influence of occasional disturbances it may be too mobile. The patients complain of chilliness. Prof. Stockman and Dr. Jones tell me that all bloodless people are liable to slight febrile attacks, and the causes of this instability are discussed by Grüber and others. The pulse, as Sydenham said, is generally quickened more or less, and is very susceptible to change of posture or emotion. I can scarcely admit with Immermann that in chlorosis the arterial blood-pressure generally ranges above the normal, though no doubt such a rise may be observed occasionally; as the mass of blood is usually increased, the artery is well filled, so that the total pressure on the finger being more, the observer may be deceived. In extreme cases perhaps bulbar anaemia may induce a compensatory vaso-constriction with a rise of arterial pressure, especially if the O_2 tension falls more quickly than the system is prepared for. Bihler, who has gone over the ground carefully, concludes that there is no rise of blood-pressure, but the output of the left ventricle, at least normal in amount, is probably often excessive. The dizzy or syncopic attacks may indicate that the blood-pressure, if sustained as a mean, is subject to extreme fluctuations; but some of such attacks belong to Sir William Gowers' "vaso-vagal" class. The arteries often throb; the vessels, though full, are slackened in tone: dilatation of the aorta is often conspicuous by its dimensions and by throbbing in the epigastrium and in the episternal notch, and both first and second sounds are very loud in the carotids. The second sound is often louder at the apex than at the aortic cartilage. V. Leube has paid close attention to pulsation of the veins of the neck in chlorosis, which may be pathological in degree and increased by pressure on the liver and abdomen. Pressure on the jugular vein arrests it peripherally, not centrally. The rising wave is dicrotic and the vein collapses in cardiac diastole. The phenomenon is attributed by him to a temporary tricuspid regurgitation; but the corresponding murmur may be absent. It is to be seen in other anaemias also, and disappears on convalescence. If mitral regurgitation sets in, the orifices yield in a common atony, the tricuspid orifice giving way sympathetically with the mitral, not as a consequence of it; or the mitral insufficiency may be the result of a local myocardial lesion. Dr. Mackenzie finds that the venous pulsation in chlorosis is auricular in time. (*Vide* art. "Physics of Circulation," Vol. VI. Fig. 2.)

The heart also is irritable; it often palpitates, it may be to the great distress of the patient. The palpitation makes itself felt on exertion—on the least exertion; a perturbation due to the call of the anaemic tissues, probably the muscles, for more blood, that is for more oxygen;

their supply of material being probably sufficient. The heart itself varies a good deal. Its beat is often throbbing or laboured, sometimes feeble and ill-defined. After effort the rate does not readily subside to the normal. That the heart is dilated is the assertion of many observers; but the conditions of physical diagnosis are too inconstant for very accurate appraisements. For instance, in this and other such ailments (57), the mean volume of the lungs may be reduced (cf. Vol. III. p. 543). The respiration in chlorosis is obviously shallow; and, although to tight lacing is attributed every mischief which may befall a woman, it is probable that the fashion of feminine garments does prevent the full excursion of the diaphragm; thus in chlorosis the heart more or less denuded or tilted may offer a larger front to the auscultator. In cases of alleged cure of dilatation of the heart we may have but the contrary phase; the lungs may expand under this measure or that, and the heart be enveloped over a larger part of its surface than before; or in lanky girls the diaphragm may sink and the heart thus recede from the mammary area: thus it is very difficult, without the *x*-ray screen, to infer confidently, in the one case or the other, the precise dimensions of the heart. Barié has recently gone over this ground again very carefully, and, in respect of physical signs, very critically. He concludes that the volume of the heart in chlorosis is variable. If in some cases it is increased, in others it is diminished; and when increased this may be in variable directions, but is generally on the right side. In all ordinary cases of increase it is moderate and temporary. The volume is small in ill-developed or not fully grown young women; some of these, he suspects, are the hypoplastic cases of Virchow. In anaemia, no doubt, dilatation of the heart, as of the stomach, is prone to occur from loss of tone; in chlorosis, moreover, to accommodate the excess of blood and to obtain sufficient oxygen by passing more of it through the lungs, the heart does probably undergo some enlargement both in substance and in capacity; and frequently the impulse is a little outside its normal seat. Over-exertion under such conditions may set up "irritable heart" or "weak heart"—symptoms often very difficult to get rid of, although due for the most part to vasomotor instability.

Venous Murmurs.—The murmurs heard in the heart and veins in chlorosis have been studied with an interest enhanced by the obscurity of their causation. The phenomena are very common, they are demonstrated to every student in the out-patient room, and the problem of their generation is a fascinating puzzle for ingenious clinicians. And whoso cannot himself explain may select his explanation from many teachers.

The venous hums, which, although they may occur in any anaemia, in Graves' disease, and occasionally even in normal persons, are very characteristic of chlorosis, may be considered first. These murmurs—known as *bruit de diable* by the French, as *Nonnengeräusch* or *Venensausen* by the Germans—the two former names being taken from the humming-top—are most conveniently heard in the jugular vein. As the venous current is continuous the hum is persistent; it was likened by Sansom to the

shell sound which Landor has made his own, by Watson to the hum of a gnat, or of the wind sighing through a crevice. When this hum is loud it can be felt; if the left hand be laid on the neck, grasping it lightly so as to let the thumb rest upon the right jugular, a vibration in the walls of the vein is perceptible to the touch; and by such pressure as to stop the venous current the hum is made to cease. Being favoured by gravitation, it is heard best, or may be heard only, in the standing position, and during inspiration. The stethoscope must lie without pressure upon the insertions of the sterno-mastoid muscle. If the patient be directed to inspire, or to rise from a recumbent to an upright position, the venous current is accelerated and the hum is intensified. The sound is usually louder in the right jugular, because this vessel, by way of the innominate vein, enters the vena cava almost in a right line, whereas the left cervical veins collect and fall into this channel at a considerable angle. In these and other circumstances the pitch and intensity of the murmur vary; it is sometimes louder during the cardiac diastole, but never simulates the rhythm of a carotid murmur. If the stethoscope be very lightly pressed on the vessel the murmur may be increased; and to turn the head to the opposite side, which by muscular contraction compresses the vein, may have a like effect; but the sound is a capricious one, and that disposition which on one day or in one person seems to intensify it, on another day or in another person may extinguish it; often indeed it varies during continuous observation. The explanation of the hum generally given is that the vibration of the walls of the vein is due to partial changes in the calibre of the vein, the lower portion being of a constant or almost constant calibre, secured by the adhesion of the coats to the cervical fascia. But we shall ask why it occurs in some anaemias and not in others? And why it is more frequent in chlorosis than in other anaemias? It is not usual to get the venous hum in plumbism, in malaria, in cancer, and so forth; it may be there, but it is not to be foretold; in chlorosis, however, to foretell it is a fairly safe prophecy. Now if it be true that in chlorosis the vessels are fuller than they are in other anaemias, while at the same time the tone of the walls of the vessels is low, we may have a combination of conditions favourable to the hums. The larger bulk of the blood may compass an adaptive relaxation of all peripheral areas and, as with corpuscular rarefaction viscosity falls, we may suppose that in chlorosis velocity is increased. Potain arranged a tube in connexion with a reservoir so that at one time serum should run down the tube, at another defibrinated blood containing the normal number of red corpuscles; on the use of the stethoscope the murmur was heard to fall in intensity when corpusculated blood was substituted for the serum. The hum may be heard in other large veins, as for instance in the crural. Many years ago in a foreign hospital I was told to hearken for the murmur on placing the stethoscope on the eyeball of a chlorotic patient; by this manœuvre, which I have often repeated since, the hum, fainter than in the jugular, can be heard; but before we can say that it is generated in the cerebral sinuses we must be

sure that it is not transmitted from the jugular through the bones of the face. Prof. Stockman tells me it may be heard sometimes over the torcular Herophili. It is scarcely necessary to say that no murmur about the base of the heart is to be accepted as cardiac without comparison of the venous areas. There is no doubt that some of the alleged functional diastolic murmurs on record were of venous origin.

Cardio-arterial Murmurs.—That in healthy persons a systolic murmur is not infrequently heard over the subclavian artery, especially on the left side and towards the outer third of the clavicle, is an old observation which has interested both the experienced physicians who have found food for speculation as to its causes, and younger practitioners who have been alarmed by what they regarded as a sign of aneurysm. This murmur was carefully studied by the late Sir Benjamin Richardson, who named it the "carpenter's murmur," as in these and other labourers it is more frequent. To pursue this side of the subject would lead us into digression; but in chlorosis and other anaemias such systolic murmurs are to be heard in more than one artery. It is a matter of doubt, indeed, whether the systolic murmurs of obscure causation heard about the base of the heart in chlorosis are formed in the heart proper, or more or less in the large vessels of the same region. Sansom suggested that under nervous (vasomotor) disturbance the arteries may be unequally affected in their calibre, some lengths being contracted, others of normal size or dilated; so that the blood would pass from narrower to wider channels. If this be so, we are in possession of a *vera causa*, whether it be the efficient cause or not. Richardson attributed the murmur in the subclavian, increased by manual labour, to the constricting pressure of voluminous muscles on the vessel; but as it may be heard in anaemic persons whose muscles are far from voluminous, we may find in Sansom's hypothesis an essentially similar explanation. For in anaemia, not in chlorosis only, the murmur is to be heard in vessels, such as the carotids, which are not mechanically constricted from without, as in muscular men the subclavian may be. The sound may be generated also in Graves' disease. Sansom quotes from Roger a case in which this murmur was musical, audible at a distance from the body, and in every accessible artery of the body. No pressure of the stethoscope was needed to bring it out, and the persistent noise was a torment to the patient. These sounds then, like the venous hum, are due to vibrations of the walls of vessels, possibly set up by local constrictions; but as they are only clinical curiosities we may not spend any more time upon them.

The humming-top sounds are also little more than curiosities, and cannot be relied upon for diagnosis; the heart murmurs, if such they be, have a more important signification. Physicians of the authority of George Balfour do not hesitate to say that some at least of the murmurs heard about the heart in chlorosis are mitral in origin, and significant of atony of the cardiac muscle. It seems clear, however, that more than one kind of murmur is to be heard in or about the chlorotic heart; and, if possible, these are to be distinguished, for some of them may be of graver meaning

than others (*vide* p. 705). By the kindness of the late Dr. Sansom I was enabled to reproduce the diagrams from his valuable work on the *Diagnosis of Diseases of the Heart*, wherein these problems are carefully discussed. The diversity of explanations of the cardiac murmurs of chlorosis makes it difficult to treat of the matter except from a phenomenal point of view; when we pass from phenomena to explanation we find ourselves in the midst of conflicting hypotheses without any clue to a decision.

A precise appreciation of the phenomena is, then, our first duty. The murmurs to be heard in or about the heart are as follows:—(i.) First in frequency are the murmurs to be heard in the region of the pulmonary artery and conus (Sansom's diagram, Fig. 22). In my student days all murmurs of chlorosis heard about the upper chest were indiscriminately referred to the aorta; to Walshe, I think, we owed the closer description of these sounds with which we afterwards became familiar. All recent observers are agreed that the murmur now under consideration occupies the area delineated by Sansom; and Sansom, with whom later observers are in agreement, says that it is "greatly influenced" by the posture of the body, being louder as the patient returns to the recumbent attitude. This reinforcement may be due in part to the retardation of the pulse-rate. In this quality it is to be distinguished from the static systolic murmurs, most of which are less influenced by this change. Sansom quoted Dr. Handford to the effect that this murmur again increases as the patient turns over to the right, and wanes as she turns prone. It varies with respiration, but in no constant way. It is to be remarked that in these cases pulsation is often to be felt about the parts occupied by basic murmurs, namely, in the second and third intercostal spaces, or even lower, and in the episternal notch. This we have all often observed and demonstrated at the bedside. Now in respect of these pulsations we shall remember that in Graves' disease, where they are very evident, we also hear these basic or "pulmonary" murmurs, although the blood may present no change either in the number or colour of the red corpuscles. Sansom says that of twenty-nine of his own cases murmurs over some part of the cardiac region were heard in sixteen; and in eleven they were in the pulmonary area. There is a large amount of evidence that similar murmurs may be produced by displacements of the normal heart; one such case I remember well in which, after death, the absence of all cardiac mischief was verified. Also, while listening to murmurs such as these, the warning may be given not to forget to direct the patient to hold his breath, lest we be deceived by a souffle of pulmonary origin.

Arguments of weight seem to prove that these murmurs about the pulmonary area are not due to mitral regurgitation, if any, nor to pressure of a dilated auricle on the pulmonary artery (Russell, Handford), nor of a distended conus or of anything else. Sansom suggested that the murmur is due to want of apposition of the mitral flaps on account of an enfeeblement of the muscular apparatus of the left ventricle; a modification of Balfour's surmise. I think the solution will be found in some

altered relation between the blood, the cavities and the walls of the vessels, in this case of the pulmonary artery and conus arteriosus, so

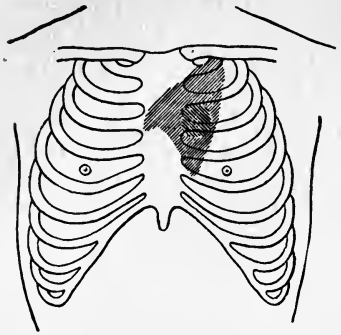

FIG. 22.—Area of pulmonary artery and conus, 59 per cent of cases. (After Sansom.)

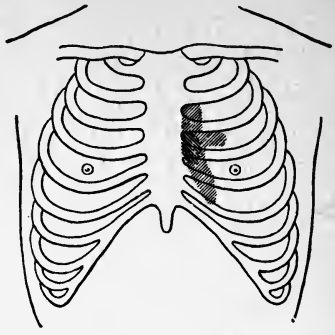

FIG. 23.—Area of right ventricle and conus, 11 per cent of cases. (After Sansom.)

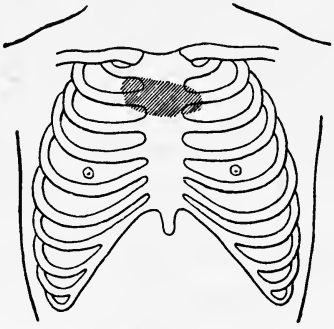

FIG. 24.—Area of aorta, 11 per cent of cases. (After Sansom.)

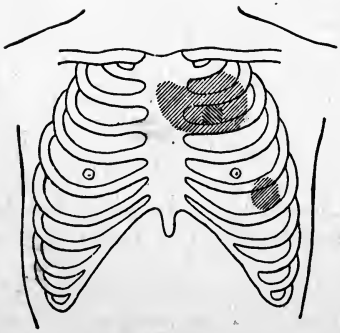

FIG. 25.—Systolic murmurs in pulmonary artery and at apex coexisting, 9 per cent of cases. (After Sansom.)

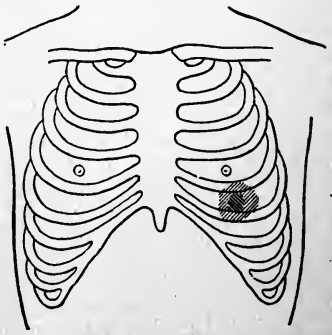

FIG. 26.—Systolic apex murmur only, 7 per cent of cases. (After Sansom.)

that vibration of the walls is excessive. If this be so, the "cardiac" murmurs, or some of them, will fall into line with the arterial vibrations

of the same disease (p. 708), and with the venous hums. In Graves' disease this vibratile state of the slackened great vessels is apparent enough.

It is stated that in some of these cases an enlargement of the conus arteriosus can be mapped out, about the second and third left intercostal space; and Dr. Stacey Wilson and Dr. Foxwell have made certain observations and experiments which may throw some light upon the question of anaemic murmurs. Dr. Wilson says (and he produces casts of such hearts) that dilatation of the right ventricle in children and young adults is not, as in older persons, to the right, but upwards to the left; so that the conus arteriosus is pushed upwards and the pulmonary artery is shortened and somewhat twisted: consequently the stream of blood is no longer axial in direction, but strikes against the anterior wall of the conus which is, moreover, considerably dilated. The pulmonary valve may thus be lifted to the second cartilage; and eddies are formed whereby murmurs and thrills are engendered. Even if we hesitate to admit that dilatation in children and adolescents is notable to the right of the sternum, it may well be that such an upward and leftward dilatation is apt to occur at an age when the parts are capable of large elastic extension. In my experience such dilatations are frequently notable; the argument is certainly an interesting one.

(ii.) The murmur the site of which is indicated in Sansom's Fig. 23 need not detain us long. No doubt it is substantially the same murmur as the last mentioned, diverted a little in its area by incidental circumstances which may be guessed at rather than appreciated. Sansom found it in 11 per cent of his cases.

(iii.) Next come murmurs heard about the aortic region; that is, at the manubrium and second right intercostal cartilage (Fig. 24). These murmurs are soft and diffuse, not leading in any certain direction. Seeing that we were formerly taught to regard a murmur at the aortic base as a common feature of chlorosis, it is curious that in Sansom's series this was the rarest of the chlorotic murmurs. A murmur may be heard occasionally in this area, as distinguished from that of the pulmonary region; the two, indeed, may coexist, and their maximum areas may be distinguished. The history and other features of the case, as a rule, will prevent any confusion between this murmur and a murmur of organic disease. Functional systolic murmurs at the base are not uncommon in healthy persons (*vide* art. "Functional Diseases of the Heart," Vol. VI.). They are usually intensified by deep expiration.

(iv.) The apex murmur in the region indicated in Figs. 25 and 26 was found by Sansom in 16 per cent of his cases, and is a more serious matter, for it may indicate mitral regurgitation; though in the cases we are considering the disorder is usually of a temporary nature. There is no common experience to which we may look back with more satisfaction than to systolic apex murmurs, which in their characters, as, for instance, in extension to the angle of the scapula and so forth, seemed to signify permanent organic disease, but disappeared entirely

nevertheless. Loud or harsh murmurs in this place are not so common, if I may speak for my own experience, as the softer murmurs; still, soft or harsh, they usually clear away altogether on appropriate treatment. Similar murmurs, indicative of mitral regurgitation as they probably are, I have occasionally heard for a few months in middle-aged men who have indulged too freely in the pleasures of the table; men who shew perhaps a little sugar in the urine for a time, or other such sign of ill-health, and probably suffer from a temporary myocardial lesion. The like murmur arises in Graves' disease, in pernicious anaemia, after haemorrhage in childbed, and so forth. Sir Donald MacAlister wrote in 1882, "If an animal be bled till it is feeble a murmur indicative of regurgitation from the ventricle is heard with the heart-sounds. You may inject proper salt solution to make up the normal quantity of circulating fluid, but still the regurgitation occurs. As the animal makes blood again, so that its muscles are properly nourished, the murmur disappears." Thus he demonstrated, what is better known now than at the date of his lecture, the large part taken by the auriculo-ventricular muscular structures in closing this orifice during the systole. Some remarkable cases were recorded by Sansom, which progressed to dropsical and other systemic changes and yet ended in recovery. If the relaxed or damaged muscle fails to do its share of the work, the valve cannot quite make up for the defect. The papillary muscles are among the first to suffer in impoverishment of the blood, and in less benign anaemias and in toxaemias, which bring the patient to the post-mortem table, degenerative lesions of these structures are often found (p. 701). In chlorosis such a murmur may not appear till the second or third attack, when the patient is further reduced, and these portions of the myocardium more gravely affected.

(v.) Finally, v. Leube has reported in chlorosis 7 cases of temporary tricuspid insufficiency with or without definite murmur; in 3 of which there was a positive centrifugal wave in the jugular, due to tricuspid regurgitation which arose not consecutively but instantaneously with a murmur of mitral regurgitation (*vide* p. 711).

The coexistence of chlorosis and mitral stenosis is considered in the article in Vol. VI. As both of these diseases prevail in women, a large proportion of fortuitous coincidence must be allowed for. The gallop rhythm, prone to appear in any severe anaemia, and probably significant of defective contractility, must not be confounded with the reduplicated second sound ("canter") of mitral stenosis. It may be, as to one element, protosystolic; or the ventricles under different pressures, or of unequal energy at common pressures, may lose their synchronism.

Potain endeavours with much ingenuity to prove that the murmurs of anaemia, or the chief of them, are of pulmonary origin. It is impossible to do justice to Potain's views in this place, and the advanced student is referred to his well-known memoir. Sewall asserts that all "non-organic" murmurs at the base of the heart can be stopped by pressure with the stethoscope.

Oedema of the ankles and feet is often very considerable in chlorosis, and occurs earlier than in other anaemias; as, for instance, in pulmonary tuberculosis or cancer, when it is a sign of dissolution. In chlorosis it seems to bear little relation to the apex murmur, which may be present or absent. Indeed the oedema, the smooth face, and the general "plumpness" of many chlorotics suggests a fulness of the lymphatic vessels and spaces. Salt excretion is said in chlorosis to be normal (v. Erben). Although, as I have said, recovery may be anticipated with some confidence from these conditions, even when attended by murmurs and further evidence of cardiac failure, it is often, nevertheless, a matter of critical judgment to decide when the murmurs and other symptoms indicate something more than a dynamic change—when the heart disorder may have undergone a static alteration. The hope of complete recovery need not vanish on the appearance of a mitral regurgitant murmur and dropsy; that in many cases all such symptoms pass away entirely rests on a consensus of opinion among those who have studied the subject. I remember having a serious difference of opinion with a physician whom, unfortunately, I had no opportunity of meeting personally, in respect of a case of chlorosis in a young lady in whom a mitral murmur was audible at the apex and in the axillary and subscapular regions. He had assured the parents that the chlorosis was but a subordinate matter, and a permanent heart disease the principal evil. For this alleged disease she was put under conditions which were not in all respects good for the anaemia, besides the mental anxiety and apprehension thus entailed on the patient and her friends. I did my best to root out this disheartening prepossession, but with little immediate success. However, a year or so later I heard, not from my professional correspondent, that the subject of incurable heart disease was playing lawn tennis vigorously at all the parties in her neighbourhood. Yet to lead the unwary reader to mistake, let us say, the anaemia of insidious rheumatism with heart lesion, for chlorosis with but a temporary relaxation or malnutrition of the structures about the orifice, would be a grievous error.

Hypoplasia of the blood-vessels has been discussed already, and for a fuller account of these phenomena the reader is referred to the article on "Diseases of the Arteries" in Vol. VI.

Thrombosis.—A terrible event in some rare cases of chlorosis, is venous thrombosis. Trousseau called attention to this peril, and many cases have been placed on record since. In the Nuremberg hospital, v. Erben found in 431 cases of chlorosis 6 (1·4 per cent) of venous thrombosis; but hospital statistics would consist on the whole of severer cases. It may be due to accumulation of blood-platelets; Lee Dickinson attributed it to excess of carbonic acid in the blood; others have attributed it to fatty degeneration of the venous endothelium, and a few writers, among them the late Prof. Birch-Hirschfeld, believe the coagulability of the blood to be raised in chlorosis. Thrombosis is most frequent in the femoral vein; or in the longitudinal or other cerebral sinus, and may be both extensive and recurrent; or it may occur in an artery. Prof. Osler quotes a case in

which chlorotic thrombosis occurred in the axillary artery, with the consequent loss of the thumb and parts of the fingers. The symptoms of thrombosis of the cerebral sinuses are dulness, stupor, vomiting, dilated pupils, delirium, proptosis, and double choked disks. Dr. Hawthorne has reported a case of subclavian, and 4 cases of retinal thrombosis in chlorotic women. In a case reported by Bristowe, tenderness and swelling of the right internal jugular vein appeared, which were followed by thrombosis in the right leg; the patient ultimately recovered. I have a vivid recollection of a fatal cerebral sinus case in the Leeds Infirmary, in a servant girl of some twenty years of age; and another in a young chlorotic lady in a great Yorkshire household who was carried off in an awfully swift and sudden death by the same process. Unhappily in this case I had regarded the initial symptoms as "hysterical." In other cases, of which I also remember one, hemiplegia may occur; cases of this accident in chlorosis have been published by many observers, and, as illustrated by Dr. M'Kechnie's remarkable case, may sometimes be due to cerebral haemorrhage—in this case attributed to thrombosis of the veins of Galen. In thrombosis of the sinuses alone there is no palsy. These thromboses do not occur in pernicious anaemia. Reference to cases of this kind will be found in the list at the end of this article, and in the article on "Thrombosis" in Vol. VI. It is a distressing thing to hear of the sudden death from such an accident of a young woman in whom, but a day or two before, a ready recovery may have been confidently predicted.

Phlebitis in the legs is not so rare an event in chlorotic women; it is said to be often bilateral in them, supervening in the second limb eight or ten days later (9, 62, 64, 66). A few cases are recorded in which the process extended to the iliac veins, and even to the vena cava. It occurs in the graver cases of chlorosis, and has been attributed to fatigue or chill. Its progress is usually rapid, but, accidents apart, the prognosis is favourable. In these cases there is some fever. In more than one case the thrombus has been examined with due precautions, and proved to have been sterile. These clots seem more prone to resolution, and even to reopening of the vein, than the infective varieties. In a case of chlorotic thrombosis of the left subclavian vein reported by E. A. Rogers, in which the arm was much swollen, the veins enlarged over the pectoral region and shoulder, the oedema wholly subsided in eight days; the parts completely recovered their normal condition, and the patient was restored to health.

Genito-Urinary System.—In some cases of chlorosis the pelvic organs, like the arterial, are ill-developed—the uterine hypoplasia of Virchow. It is difficult to believe that such imperfections are ever cured by medical means, or by any means. They find their way into the museums of pathology. Amenorrhoea is naturally a feature of them.

Amenorrhoea is also usual in ordinary chlorosis, though as it is far from invariable, we can hardly say that the two events are closely related. In some cases, indeed, the menses continue, even regularly, but are brief, painful, and pale and slimy. No definite success in treatment

has followed the administration of ovarian extract; nor does chlorosis result from extirpation of the ovaries. Moreover, the rule seems to be (p. 685) that chlorotic women are fertile. Amenorrhoea is not only the ordinary condition, but indeed may be called a protective side of the process. If I may speak from a few examinations, I would say that in the cases of chlorosis in which the red corpuscles are numerically much diminished (say to 3,000,000 or under) menorrhagia or even menstruation in normal quantity (which in such persons is a relative menorrhagia) is or recently has been present. I find that Sir W. Gowers has observed falls of 10 to 20 per cent in the number of the red corpuscles after a menstrual period. These cases are less easy to cure. I need not say that many chlorotic girls are brought to us in order that the menses may be recalled; and we have to explain to the friends that if, by local and specific means, such an achievement were possible, the step would be rather a bane than a blessing. As an old medical friend of mine used to say to troublesome mothers, "Madam, when the works are put in order the clock will strike." In chlorosis a very slight loss of blood intensifies the impoverishment of the blood beyond expectation.

Before menstruation has shewn itself chlorosis may appear, and such cases are said to be of greater severity. Prof. Stockman in 63 cases found menstruation scanty or irregular in 29, absent in 12, normal in 4, profuse in 10. Three girls (aged thirteen, fifteen, and nineteen) had never menstruated; in 5 no note had been made. Leucorrhoea is not infrequently present, and may be betrayed by the *point de côté*. It is usually cured by the iron, but careful inquiry should be made about this, as day by day we are learning more and more about the risks of auto-infection from such discharges. Of the urine I have already spoken; it is as a rule poor in solids rather than loaded by products of waste, whether normal or abnormal. It does not suggest, therefore, that blood destruction is of the essence of the disease. The absence of such elements as indican and the conjugate sulphates seems to negative perverted putrefaction in the intestines.

Neuro-Muscular System.—Girls and young men alike, as they are adolescent, often go through phases of temper which are a source of anxiety to their friends; more new impressions, more new desires crowd in upon them than they can understand, or set in due order. It will not do, then, to put down the caprices, passions, perversities, and apathies of this season of life to any one of its disorders. They may occur even in the healthiest of both sexes; and with a little patience and protection from folly will "defecate to a pure transparency." Yet chlorosis has, no doubt, some fretfulness of its own; lassitude, torpor, and irritability meet together, and are due to want of direct and inhibitory vigour in the nervous system. There is no staying power; for, although proteins are abundant, oxidation is tardy. Fatigue products also accumulate unoxidised in the muscles. Sansom was disposed to attribute the fatty and other atrophic changes in the heart to the nervous centres; at any rate we see irritability and loss of control (inhibition) in those higher centres which are the last

to develop and the first to feel the lack of good blood. With these perturbations neuralgias are common, especially the neuralgias of the face, and headaches—frontal, temporal, or vertical. Gastralgia and pain under the left breast are common troubles of the chlorotic; this pain often coexists with leucorrhoea and disorderly heart, and with hysteria. It was on account of this pain the older authors insisted that in chlorosis the spleen was generally affected. And no doubt they confused certain splenic anaemias with chlorosis. Dr. Head has shewn that all referred pains, with their accompanying tenderness, are apt to spread widely under the influence of anaemia; and thus widespread "neuralgic" pain and superficial tenderness may, in anaemia, be due to some simple cause. In the same way the headaches so common in anaemia are, in the majority of cases, a true referred pain, accompanied by tenderness, and correlated with pain and tenderness of a like nature on the chest or abdomen; according to the laws Head and Mackenzie have laid down. In a certain number of cases, for instance, the headache and neuralgia represent a pain referred from some organ of the head, such as the eye or the teeth. In extremely few cases of chlorosis is the headache due only to the anaemia; though its wide distribution from the focus, and its prominence as a symptom, are due to this condition. Certain kinds of palsy have been noted under the circulatory system.

Optic neuritis, or even neuro-retinitis, is discovered occasionally in chlorosis; a considerable number of definite instances (Hirschberg, Gowers, Saundby) are now on record, but the nature of the association is undetermined. Sometimes it appears rapidly as a papillitis, as in many cases of tumour. In many, perhaps in most cases, it would be overlooked but for the routine use of the ophthalmoscope. The prognosis is probably favourable: I had never come across an instance of permanent injury to vision in this kind, but, since the first issue of this essay, Dr. Hawthorne, in a description of 3 cases, has stated that unless treatment by large doses of iron be instituted at an early stage, sight may be considerably and even permanently impaired. In his later papers Dr. Hawthorne holds most decisively that in these cases thrombosis was concerned. Sir William Gowers, however, in the absence of proptosis and some other symptoms, does not admit thrombosis, and the complete recovery of most of the patients under the use of iron seems contrary to a cerebral thrombosis. Moreover, the published cases of chlorosis with cerebral thrombosis and optic neuritis have for the most part ended fatally. In a very grave case of chlorosis, however, with optic neuritis and severe cerebral symptoms, published by Dr. Hichens, complete recovery ensued; after, by the way, a subsequent episode of thrombosis in one leg during convalescence. The sign may, however, embarrass the diagnosis, especially if headache be present; and the occurrence of optic neuritis must be regarded as an ominous event. The spinal degenerations met with in some cases of anaemia, cases in which the two effects probably have a common toxic origin, fortunately do not arise in chlorosis. Occasionally a disappearance of knee-jerk has been said to indicate a peripheral neuritis; but, as

we shall see under Diagnosis, such cases are probably of a compound nature.

Diagnosis.—The chief difficulty in the diagnosis is to distinguish chlorosis from other anaemias, simple or toxic. Gilbert lays much stress upon the doctrine that upon chlorosis another anaemia may be superposed; or that, from the first, in one person two kinds of anaemia may be associated. Dr. Lloyd Jones discusses the same problem. In such a case the diagnosis may be no easy matter until the method of Haldane and Lorrain Smith can be simplified for practical purposes. For instance, menstruation, unfavourable conditions of life or work, or lactation may "superpose" a simple anaemia on the chlorotic (chloro-anaemia). Such may be the compound causation of cases of chlorosis in which the number of red corpuscles is very deficient (3,000,000 and under). A further difficulty, and a far more important one, lies in the possible confusion between chlorosis and the toxic anaemias—plumbism, rheumatism, chronic Bright's disease, pernicious anaemia, syphilis, arsenic poisoning, and so forth. Of such puzzles we see striking examples. One young lady, with a green pale face and menorrhagia, presented on closer examination a blue line on the gums; in the drinking water lead was found in considerable quantities. In another such case, one which resisted all treatment, after a protracted search for some external cause we discovered arsenic in large quantity in the green unsized wall-distemper (not a paper) of her own sitting-room. On the removal of this distemper the symptoms gradually subsided. In a third, a diagnosis of pernicious anaemia in a somewhat elderly case of chlorosis was on more careful blood examination corrected, and the patient cured by iron in a few weeks. Syphilitic anaemia does not give us so much trouble in women as in men, but it is not to be forgotten; if there be no other criterion, the quick effects of specific remedies may place the diagnosis beyond doubt. The syphilitic, however, superficially resembles Addison's anaemia; it is more apt to be sub-febrile, and Wassermann's test may give a positive reaction. For the distinction of syphilitic, tuberculous, and other such anaemias a practicable blood-volume test would be very valuable. Rheumatism, a potent cause of anaemia, is often perilously insidious in young people. To the anaemia of malignant disease I need do no more than refer; I do not remember this difficulty in such cases; but in chronic Bright's disease in young persons there may be a moment of indecision. The touch of the pulse will in all probability put the observer on the right line, and an examination of the retina and of the urine should be decisive.

The anaemia which precedes an outbreak of pulmonary phthisis or tuberculosis elsewhere may create embarrassment in some cases; the absence of murmurs may guide us more or less, and the thermometer will come to our assistance. Dyspepsia may accompany any anaemia; there is nothing characteristic in the dyspepsia of chlorosis and, if a murmur be also present, we may find it impossible to arrive at a certain diagnosis without delay. Fagge published a case from the records of Guy's Hospital,

in a girl of eighteen, in whose case a diagnosis of chlorosis was upset on the post-mortem table; a large caseous mass of tubercle was dislodged from the cerebellum, and a few scattered tubercles were found also in the lungs. The blood was not systematically examined in those days (1861).

For the diagnosis between chlorosis and splenic anaemia, the blood of which is of the "chlorotic type," the reader is referred to the article on the subject (p. 775). The relation of chlorosis to ulcer of the stomach has been already alluded to. On suspicion of ulcer occult blood must be sought for in the faeces.

Dyspnoea with a systolic murmur at the apex, and even behind, may suggest permanent disease; a difficulty we have discussed already. In a few cases it may be necessary to suspend judgment for a while.

Ankylostomiasis produces a state resembling chlorosis in many respects, especially as regards the low colour-index; but the leucocytes are generally in some excess, say 12-14,000 per c.mm., and eosinophilia, both relative and absolute, is present (Haldane), (*vide* also Vol. II. Part II. p. 902). Pernicious anaemia is readily to be distinguished by the blood, with the aid of the thermometer, and of an examination of the urine (*vide* art. "Pernicious Anaemia," p. 748).

Addison's disease may give us pause for a while. I remember one such doubtful case in a young woman; but, even in the absence of pigmentation, a careful survey of the symptoms and history of the case should preserve us from error.

Prognosis.—Chlorosis has never seemed to me to be the obstinate disease that it is for some writers. In a large hospital and private experience I recall few cases which seriously resisted treatment. The vexation is that the disorder relapses again and again. How this is to be prevented we shall consider presently.

Prof. Stockman tells us that of his 63 cases 27 were in the first attack, 11 in the second; 22 had suffered from more than two attacks. Many of these, he adds, did not persist in the remedies ordered for them, and became chronically anaemic. Some patients relapse in spite of all care; their blood is perpetually biassed, and iron is a necessary aid even in middle and later life. Prof. Stockman estimates the time of apparent recovery at four to six weeks. This period will be considered more fully under the head of Treatment.

An opinion was prevalent, and still has some vogue, that phthisis is to be feared as a sequel of chlorosis. A patient weakened by chlorosis, or by any other malady, may become more susceptible to tubercle; yet in my experience this sequel is far from being a common result. No doubt the "prephthisical anaemia" (p. 691) is occasionally mistaken for chlorosis. Gastric ulcer is far more to be feared. Thromboses of veins or sinuses are happily events too rare to enter into ordinary forecasts. No careful prognosis can be given without repeated examinations of the blood. Many cases of chlorosis recorded as aberrant or peculiar were not cases of chlorosis at all. It is in accordance with the supposed sexual nature of chlorosis that, as Johann Lang perceived, it disappears after marriage.

Dr. Lloyd Jones says that in twenty years he has seen only two married chlorotics. Both were in service, and neither had borne children. Marriage, therefore, under reasonable precautions, is not to be forbidden. Finally, we must never quite forget that amenorrhoea may be due to concealed pregnancy.

Treatment.—The curious reader may remember the story of Melampus, who is said to have made Iphiclus a father by administering to him for ten days the rust from an old knife; but the practical man may be content to hear that Sydenham was perhaps the first physician to lay stress on the effects of iron in chlorosis. "We give mars," he says, "in the pale colours . . . the pallor disappears, and once again the face is rosy and ruddy." Willis gives the same advice. Indeed, I may paraphrase the words of Prof. Osler, spoken in respect of quinine and malarial fever: "The physician who cannot treat chlorosis successfully with iron should abandon the practice of medicine." The physician who must turn restlessly from one preparation of iron to another, and from one drug to another, to find a cure for unmanageable chlorosis, must meet with peculiar cases. I cannot readily recollect cases of chlorosis in persons of common sense and reasonable obedience in which iron failed to effect a cure; on the contrary, I have seen many cases regarded as intractable in which there was no great difficulty in compassing the cure. How are we to explain the failures? The chief reasons are three: first, that iron failed of success because given in insufficient quantity; secondly, that the treatment was not continued long enough to counteract the strong bent to relapse which is seen in all cases more or less, and in some most doggedly; thirdly, that anaemias in which the blood presents a chlorotic form, such as those of tuberculosis and syphilis, are mistaken for chlorosis, a disease which does not consist only in a certain aspect of the blood. It is well never to undertake a case of chlorosis without telling the patient that even the first course of medicine will extend to no less than three months; and that for a year thereafter she must be re-examined, and in all probability submitted to further courses of iron, as the signs may indicate. The blood should be examined from time to time, a process which has the incidental advantage of keeping the importance of the business before the patient's eyes. During the first two or three weeks of ferruginous treatment the red corpuscles will rise quickly to the normal standard in number; though probably not in size, colour, or vitality.

It has been said of late that the first change to be seen is an increase of white corpuscles, and that these bodies act in some way as carriers of iron to the red. The manifold conditions on which the increased apparition, if not the increased generation, of white corpuscles depends are so little understood that we cannot always discriminate between a local afflux and a multiplication of them.

The numerical increase of red corpuscles gives rise to a sense of relief often so rapid and so great that the unwarned patient jumps to the conclusion that she is "all right again"; and is too ready to throw

physic to the dogs. If she does, the case may well be an "incurable" one. The increase of haemoglobin, and the attainment of full growth by the corpuscles—which are the essential elements in recovery, as are the reverse processes in falling ill,—take place much more slowly. It is no uncommon thing to find that a return of haemoglobin to the normal standard needs as long as three months; and it is for this reason that three months should be enjoined as the shortest time in which a cure is to be completed. And even then relapse is more common than not. When I began practice, iron was given in doses too small to effect a satisfactory amendment; gradually it became apparent that larger doses are required. Now there is a reaction, and physicians are saying that smaller doses suffice. My own opinion is that in cases of any severity, if recovery is to be ensured, iron must be given with a liberal hand; the quantity of the metal is more important than the particular preparation. Without returning to what has been said concerning the mode of operation of iron in chlorosis, I may repeat that, although in anaemia of simpler kind, as for instance after a haemorrhage, the "food iron" may be adequate for repair, the iron given in medicinal doses in chlorosis must certainly have some further effect than the mere supply of that required to rebuild the haemoglobin; it must have some chemical or "specific" action which conspires to the same end. A few grains of the ammonio-citrate of iron is not a dose to cure chlorosis of any severity; far more than this may be needed. It is my custom to use the sulphate of iron, alone or with aloes, in the form of pill. The addition of a little alkali to the iron pill is scarcely worth the trouble, and by making the pills more bulky is inconvenient. I generally administer 1 grain of the dried sulphate thrice daily after meals for the first week, 2 grains in the second week, 3 grains in the third; it is rarely necessary to go beyond this, though some patients do not respond till 5-grain doses are reached. When the dose of 3 grains is reached, I direct that this quantity—9 grains daily—shall be continued for two months; the dose is then reduced by a grain, and thus administered for a fortnight; then 1-grain doses are ordered for a month. During this time the pulse is probably settling to the normal rate, and if for a month before the end of this course the haemoglobin has been constant at a fair standard a relapse is less likely to occur; though of course the disorder may reappear after a time from the original causes. Vesicles or lozenges containing iron "*in statu nascendi*" are successful; partly no doubt because, being convenient and palatable, and arousing no fears of injury to the teeth, they are taken regularly; partly because they are freely soluble. One often suspects that incurable chlorosis means insoluble pills; pills made up, for instance, with gum tragacanth and the like become as hard as pebbles, and about as useful to the patient. Occasionally the sulphate of iron causes some gastric irritation, which the more refined preparations do not seem to do. For the flushed chlorotic patients (p. 702) the laxative iron mixtures often answer better; such as the combinations of tincture of the perchloride

with sulphate of magnesium; or of equal parts of Griffith's mixture and compound decoction of aloes, a most efficacious medicine, and not so nasty to the palate as to the eye.

It was an imposing lesson of our youth that iron is not to be given till the patient is "prepared" for it; and to this end bottlefuls of soda and gentian, and so forth, were prescribed; far be it from me to encourage a careless mode of administering any drug, yet nevertheless I think this so-called preparation was often otiose, and even mischievous in so far as it wasted time. Such preparatory courses are, it is true, appropriate in some cases, and even necessary. If the tongue be white and sticky and the bowels constipated, let a blue pill and a dose of salts be given, followed by gentle laxatives with bitters for a few days; this done, begin with the iron, and watch the remainder of the tongue-cleaning process going on fast enough under this tonic. The dyspepsia being in many instances the consequence of the deprivation of oxygen, the assimilative changes will improve, without any direct attention, as the haemoglobin is restored. In exceptional cases, no doubt, more precautions will be required; of these the physician will judge in the particular instances.

I have tried all or most of the so-called preparations of "organic iron" produced for us by our allies the manufacturing druggists, but have not discovered in them the peculiar advantages which are attributed to them. One must presume they would be converted by the stomach into the chloride. They are prescribed, however, on authority so high that in obstinate cases they ought to be tried. I have certainly found that an old-fashioned French solution of malate of iron is often successful in patients with queasy stomachs, by whom ordinary ferruginous drugs are ill tolerated, or for some reason inappropriate. Gilbert has found the protoxalate very useful; it is said to be soluble in the gastric juice. Prof. Stockman's opinion is that "inorganic iron" is more rapidly effective than "organic iron." The combination of glycero-phosphates with albumin, as in the preparation known as sanatogen, proves a useful addition in some cases. Bone-marrow is ordered by some physicians, but is probably useful only by virtue of the iron which it contains.

Of "adjuvants" many are recommended; ether, liquor ammonii acetatis, nux vomica, and so forth: but I cannot say that I have found in any of them more advantage than such as may flow in the individual case from the ordinary properties of these accessories; they may be needed or they may not—usually not. It is well, however, to add some cordial such as chloric ether or sal volatile to all steel mixtures. In some cases associated with morning headache, cold extremities, or chilblains, calcium salts, on Sir A. Wright's hypothesis, may prove to be a valuable ally. Nickel, cobalt, manganese, even when their absorption into the system is verified, have no effect on chlorosis.

On pathological grounds much has been made of late of an antiseptic treatment. Dr. P. W. Latham has laid stress on the value of the liquor of the perchloride of iron, because it contains much free chlorine. Dr. Latham's claims on behalf of the antiseptic salt are in accord with

other observations of the kind. It may be suggested that a hypochlorhydria is thus mitigated, but on the other hand this very astringent preparation is apt to disagree with the stomach. Townsend thus tabulated the results of antiseptic drugs in 87 cases:—

	Hgbn. incr.
β-naphthol (30 cases)	1·85 per cent.
Blaud's pills (31 cases)	5·07 ,,
Naphthol first and afterwards Blaud's pills (12 cases)	6·70 ,,
Blaud's pills alone (19 cases)	4·50 ,,

This table shews an advantage in favour of the use of β-naphthol before the pills; and in another such series, of 28 cases, the Hgbn. increase was 7·9 per cent. In the Boston Medical Society, to which body this paper was read, it was generally agreed that intestinal antisepsis combined with iron gives better results than iron alone.

I remember in a few cases, when for some reason the iron did not take good hold at first, the drug seemed to get a start on the addition of arsenic or phosphide of zinc; ordinarily to treat chlorosis with these drugs is a waste of time. It is conjectured that the arsenic, by an action on the bone-marrow, promotes rather the number of the cells, and the iron the increase of the haemoglobin; if so the addition of arsenic would be proper when the count of cells was especially low. I should say that by many physicians arsenic is regarded as a very valuable remedy in this disease.

In the belief that in chlorosis the volume of the serum is increased (serous plethora), bleeding and diaphoresis have been recommended as means of cure. Many of the older physicians testified in favour of venesection, at any rate as a preliminary measure. It is not apparent how an operation which reduces the number of the red corpuscles can be otherwise than injurious; but it is alleged that the operation stimulates blood formation. However this may be, Schmidt treated and tabulated the following 8 cases (a "bleeding" was 80 c.c.):—

	Average incr. Hbgn. per cent.	Weekly incr. of weight in kilos.
i. One bleeding and iron	6·20	0·73
ii. Iron alone	6·18	0·48
iii. One bleeding	2·50	0·92
iv. Several bleedings	0·59	0·51
v. Sweating cure	0·39	0·44
vi. Bleeding and sweating	0·36	0·46
vii. Several bleedings, sweating, and iron	0·02	0·04
viii. Several bleedings and sweatings; no iron	0·56	0·19

The good effect in the first case was due, no doubt, entirely to the iron. Senator and some of his pupils have recommended treatment by a series of hot baths. The first two baths seem to aggravate the

lassitude, but after that they are said to prove restorative. About eight to twelve baths are required, at a temperature of 103° F. The patient with a cold-water cloth on her head lies in the first bath for about a quarter of an hour, in the later ones for half an hour.

If there be jugular pulsation, mitral murmurs, or other well-marked evidence of cardiac defect, digitalis may be a useful adjunct to the ferruginous salts, especially in cases of palpitation.

While prescribing pharmaceutical remedies the physician will not forget to rectify such disadvantages of life as he may be able to ascertain and control. Over-pressure at school, unwholesome conditions of work or amusement, late hours, love affairs, social fag, worry, tight-lacing are points to which his attention will be directed; yet while relaxing overwork, if any, he will be no less alive to the evil of idleness or desultoriness. Some course of study should be ordained which, without fatigue, may interest and discipline the mind and temper. It is useless to increase the haemoglobin if meanwhile by pulmonary inaction it is insufficiently exposed to the air. And the patient lies in the vicious circle of a reduced activity of the respiratory centre, due to the anaemia it should help to dispel. As much time as possible should be spent in the open air, at rest or in such gentle exercise as the strength and respiratory functions will permit. Quiet horse-exercise or slow cycling may be encouraged in cases of no great severity. Gentle respiratory gymnastics may be advised in some cases of bad functional habit or deformity of frame. The patient should sleep with the bedroom window open; chlorotics are, however, liable to neuralgia in hard weather, and may need not only a hot bottle and warm bedclothing but also some protection, such as a Shetland shawl, for the head and face. A cold bath will probably prove more than the deficient heat-production can support, but the rapid application of the wet sheet can usually be prescribed with advantage; this is better done in the forenoon two hours after breakfast, and, during the colder months, in a room with a fire. Excessive cold, as we see in haemoglobinuria, seems to impair the red corpuscles.

As the deficient powers of heat-production often forbid too bracing a line of treatment, such as cold bathing, so in a severe case of chlorosis, or one in which iron is not telling at once, the dissipation of heat and the expense of muscular activity must be husbanded by a week or a fortnight in bed. Such a measure often gives an impulse to the curative movement, and proves in the end to be an economy of time. The facial, gastric, and other neuralgias are usually relieved also by this simple means. Dr. George Oliver says the calibre of the arteries is thus enlarged, so that residual blood in the ventricles is reduced, and dilatation of the heart is prevented or relieved. This may be true; though the cardiac dilatation, if really present, is probably due rather to anaemic atony of the myocardium than to overloading. Massage is often recommended, but the degree of its usefulness in chlorosis has yet to be estimated. As soon as the appetite improves, and the other graver symptoms begin to give way, change to the seaside or to the hills may be advised; but cold, I repeat,

is injurious in anaemias; for this reason, and because at considerable altitudes the deficiency of oxygen would be more and more sensibly felt, high mountain resorts are not usually to be recommended. Mild or convalescent cases, however, often derive great benefit from the place and the waters of such highlands as St. Moritz. The iron springs of the close warm valleys of Central Europe are, on account of the climate, to be avoided, at any rate in summer. Harrogate and other upland spas are preferable. But the chief disadvantage of recommending baths and water, except during convalescence, is that the cure of chlorosis being by a definite "specific," spa treatment is too dilute, and the case drags on till more active medication is brought to bear.

It only remains now to say the few words which are necessary on the diet of chlorosis. It is of the first importance to overcome the common distaste for meat. Girls will say that the entry of a dish of hot meat into the room makes them feel sick; kindly and gradually this aversion must be overcome, and meat must take its due place in the diet. Eggs and milk, so far as well digested, will be included; and sweets and other kickshaws discouraged. It is not usually necessary to increase the fatty elements of the food. Green vegetables are said to be useful for their chlorophyl; at any rate they avert constipation. It is desirable, if a fair meal be taken, that nothing be offered between meals. We are pointedly asked in these cases of chlorosis whether alcohol in any form is to be prescribed. Of itself I believe that alcohol is of no direct service. Now and then a bad appetite may be coaxed into more activity by a glass of stout, or of red wine and water; if so, the use of these aids is justified. Some young persons dislike mere water; indeed, if their blood be excessive in mass their instinct may be justifiable; at any rate it is not well for them to drink much with meals: half a tumbler of milk may be the table drink, and three hours after meals a glass of hot water will act beneficially, both on the stomach and on the secretions. Careful mastication of the food is of great importance. On this account, and for the removal of the septic influences, the teeth should be kept scrupulously clean and in repair.

In conclusion, I would repeat that we must be guided continuously not only by the number of red corpuscles and their haemoglobin value, but also by their approximation to full-size and equality; a lowered pulse-rate, however, is a sign of amendment, as is re-acceleration of impending relapse. We shall not forget that colour generally returns to the face, and steadiness to the breathing, long before the cure is established.

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C. A.

PERNICIOUS ANAEMIA

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Synonyms.—*Idiopathic Anaemia; Essential Anaemia; Myelogenic Anaemia; Progressive Pernicious Anaemia; Ganglionic Anaemia; Addison's Anaemia.*

Introduction and Definition. — Many cases of severe anaemia are apparently causeless—"idiopathic," "essential," or "primary"—that is to say, not the result of any obvious lesion, such as carcinoma of the stomach. In many of these cases the anaemia arises insidiously, and passes more or less rapidly to a fatal termination, the downward progress being sometimes interrupted by periods of improvement due to treatment. The adjective "pernicious" might be applied to all of these, but by general consent it has been restricted to one particular form, in which the patient not only has anaemia, which is progressive, severe, ultimately fatal, and apparently causeless, but also at some period of the disease presents certain characteristic blood changes, namely, great diminution in the number of red corpuscles (oligocythaemia), with a less diminution in the haemoglobin, so that the colour-index is high; absence of leucocytosis; and considerable variations in the sizes and shapes of the red corpuscles, large ones (megalocytes) being numerous. When the patient is severely ill there is usually a lemon- or primrose-yellow colour of the skin; and when death results, the liver, and to a less extent the spleen and kidneys, give a marked Prussian-blue reaction with the potassium ferrocyanide test for iron (Perl's test). It will be seen presently that whilst a certain number of cases of grave anaemia, bearing some resemblance to pernicious anaemia, are left without a distinctive name when these somewhat arbitrary restrictions are made, the cases which are thus brought together bear such a close resemblance to one another that they merit a distinctive title. This title is "Pernicious Anaemia," which may be shortly defined as a severe, progressive, and ultimately fatal anaemia, apparently without cause, in which at one time or another the blood exhibits oligocythaemia with a high colour-index and no leucocytosis; whilst the liver after death gives a marked Prussian-blue reaction when tested by the ferrocyanide process for iron.

History.—Thomas Addison gave the first clear account of pernicious anaemia, or "idiopathic anaemia" as he called it, in his monograph *On the Constitutional and Local Effects of Disease of the Supra-renal Capsules*, published in 1855, which represented what he had been teaching for several years (*vide* Vol. IV. Part I. p. 395). It was when investigating the morbid anatomy of these cases of severe anaemia that he discovered that there were two groups, those with healthy and

those with diseased suprarenals. Addison's anaemia and Addison's disease were the names used to distinguish the two; the latter is still called by its original name, whilst "Addison's Anaemia" has been renamed "pernicious anaemia."

Lépine and Dr. Pye-Smith, in their historical summaries of the subject, shew that isolated examples of the disease were recorded prior to Addison's succinct description. Thus Combe (1823), Andral (1823), Marshall Hall (1837), Piorry (1841), Pearce (1845), each describe one case, and Barclay (1851) two. Some of the cases given by Channing of Boston (Mass.), in a paper written in 1842, dealing with anaemia in relation to the puerperal state and uterine disorders, probably belong to the same class. Comparatively little attention, however, was paid to the subject for several years after Addison wrote, except amongst those who were familiar with his personal teaching. Thus Sir Samuel Wilks in 1857 referred to fatty degeneration as a characteristic morbid change in idiopathic anaemia; and cases were recorded by S. O. Habershon and others of the Guy's school.

The writings of Gusserow and Biermer of Zürich, especially the memoir in which the latter first uses the phrase progressive pernicious anaemia (1871-72), did much to awaken interest in the subject; Biermer claimed and abroad was given the credit of describing for the first time the characters of a condition not hitherto recognised. It is clear, however, that he had been anticipated by Addison; it is also probable that the cases of anaemia amongst pregnant women, to which Gusserow drew attention, were of the same nature as those indicated by Channing thirty years previously. Nevertheless, the service rendered by Biermer was considerable, both from the clinical and pathological standpoint; and his choice of the name "pernicious" directed attention to the fatal character of the disease. We must recognise, however, that many cases included by Addison as "idiopathic" or by Biermer as "pernicious" would now be placed amongst the secondary anaemias. Not only have definite causes, such as ankylostomiasis, been discovered to account for some of the anaemias which Addison and Biermer would have termed primary, but definite pathological differences have been shewn to exist between pernicious anaemia proper and certain other cases which a few years ago were regarded as examples of pernicious anaemia. This is not a mere question of nomenclature; it concerns the true interpretation of the pathology of the disease before us, and will be referred to again in the discussion of this part of the subject. We must bear in mind, therefore, that some of the cases on record are not strictly to be ranked in the category of "pernicious anaemia" properly so called.

It is not possible in such an article as this to review all that has been written since 1873 upon the subject. The Guy's Hospital Reports contain contributions by Drs. Pye-Smith, F. Taylor, and Hale White. Sir Stephen Mackenzie in 1878 did much to invite attention to the subject to which he reverted in his Lettsomian Lectures in 1891. Dr. Byrom Bramwell published a full account of pernicious anaemia in 1877, and

discovered the value of arsenic in its treatment. Dr. W. Hunter's researches upon the iron in the liver and other organs form the basis upon which the haemolytic conception of the disease is based. Other labourers in the same field have been W. Russell, Brakenridge, G. A. Gibson, Stockman, Fraser, and Gulland of Edinburgh; Finny, Purser, and Craig of Dublin; Mott, Risien Russell, and James Taylor of London. The disease was studied at an early date in America, the contributions of Osler, Gardner, and Howard of Montreal being amongst the first. Prof. Osler has also published numerous subsequent observations. W. Pepper of Philadelphia in 1872 discovered the changes in the marrow of the bones, which were speedily confirmed by others. Musser, Henry, Kinnicutt, Wood, and Cabot have contributed to the subject in the United States. Numerous essays and monographs have appeared in the Continental schools by Eichhorst, Quincke, Müller, Neumann, Immermann, Lépine, Hayem, Laache, Litten, Michaelis, Faber, Bloch, Boekelman, Sabrazès, and others.

Etiology.—Pernicious anaemia is not a very common affection, but between the years 1890 and 1907 there were 58 cases admitted to Guy's Hospital. The condition is diagnosed with greater certainty now than formerly, chiefly owing to greater precision in examinations of the blood; cases which formerly remained obscure are with increasing frequency recognised for what they really are.

It is distinctly a disease of adult life. Cases have been recorded in patients as young as seven, eleven, and twelve years, but these are very exceptional; infants and children are subject to obscure and severe anaemias, but these very rarely have all the characteristics of pernicious anaemia. The great majority of the patients are of the cancer-age, that is to say, between thirty and sixty; and the two sexes are about equally affected. Amongst 58 consecutive cases at Guy's Hospital there were 32 males and 26 females, and the age-incidence was as follows:—

10 years of age	1 case
Between 20 and 30 years of age . . .	2 cases
„ 30 „ 40 „ . . .	13 „
„ 40 „ 50 „ . . .	21 „
„ 50 „ 60 „ . . .	16 „
„ 60 „ 70 „ . . .	5 „

The average age of the 26 females was forty-three years, the minimum being ten and the maximum fifty-seven. The average age of the 32 males was forty-nine, the minimum being twenty-two and the maximum sixty-seven. The average age of the total 58 cases was just over forty-six years.

The disease is not hereditary, and it does not appear to have any relation to occupation. It often comes on in those who hitherto have been in robust health. It is not restricted to the poorer classes, nor to any particular nationality. Certain writers have laid stress upon uterine disorders as an etiological factor, but there is reason to believe that many

of the cases attributed to this were not really examples of pernicious anaemia. The same applies to the severe illness that may follow repeated loss of blood from haematemesis, menorrhagia, piles, and so forth. Haemorrhages are not uncommon in pernicious anaemia, but for the most part they occur during the illness, and not as its precursor.

Swiss authors have thought that the disease is more likely to occur in one locality than in another, but there is no clear evidence of this. Some epidemics of what has at first seemed to be pernicious anaemia have been recorded, but these have usually turned out to be due to ankylostomiasis or some similar affection; pernicious anaemia is not known to be epidemic.

Gastro-intestinal symptoms are not uncommon in connexion with the illness; and the patients not infrequently have carious teeth or pyorrhoea alveolaris; the relation of these to pernicious anaemia will be discussed in connexion with the pathology of the disease (pp. 738-739).

Sometimes the patients attribute their illness to bad smells, bad drains, chills, mental worry, biliousness, or something equally indefinite. When the disease is already incipient, any factor which causes the patient to run down may be the first to make the condition noticeable. Even allowing for this, however, more than half the patients are unable to assign any cause for their insidious illness. Apart from the influence of age and probably of gastro-intestinal disorders, the etiology of pernicious anaemia is unknown. This is well expressed in Addison's words: "I had from time to time met with a very remarkable form of general anaemia, occurring without any discoverable cause whatever—cases in which there had been no previous loss of blood, no exhaustive diarrhoea, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, or malignant disease. Accordingly, in speaking of this form in clinical lecture, I perhaps with little propriety applied to it the term 'idiopathic' to distinguish it from cases in which there existed more or less evidence of some of the usual causes or concomitants of the anaemic state."

Morbid Anatomy.—In the majority of cases the body appears fairly well nourished. The pallor of the surface is striking; petechiae may be distributed over the lower extremities, and there may be some oedema about the ankles. The panniculus adiposus is of a bright yellow colour, and the dark brown-red tint of the muscular layers attracts attention by its contrast. Slight excess of fluid is usually found in the peritoneal and other serous sacs. The blood is thin and its specific gravity is diminished; it may be 1028, for example, instead of 1056. Its microscopical characters are described on p. 742. It coagulates fairly well, though the clots in the cardiac cavities are small and pale. The *heart* is generally well covered by epicardial fat, and sometimes petechiae may be seen on both surfaces of the pericardium, beneath the endocardium, and even in the myocardium. The muscular substance is soft, flaccid, and of a tawny, brownish tint, sometimes compared to that of a faded leaf. The musculi papillares, especially of the left ventricle, are nearly always variegated by wavy whitish streaks—the "tabby-cat striation"

Fig. 1.

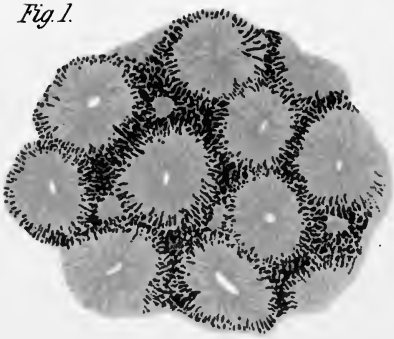

Fig. 2.

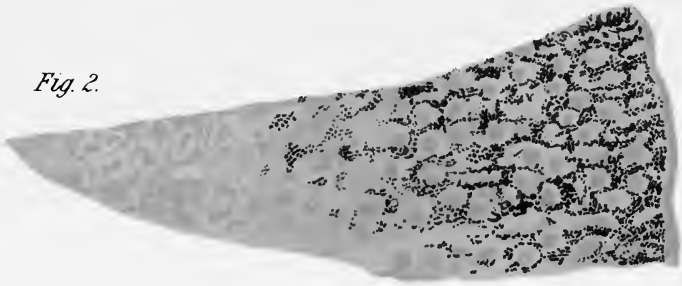

FIG. 1.—Section of Liver, treated in bulk with dilute hydrochloric acid and ferrocyanide of potassium and stained with carmine after cutting. Shews the presence of iron in the peripheral zone of the lobules."

FIG. 2.—Low-power drawing of kidney, stained in the same way, shewing the cortical distribution of the iron.

After Hopkins, *Guy's Hospital Reports*, Vol. L.

of Quain, or the "throstle's breast markings" of some other observers. The cavities, especially those of the right side, shew moderate dilatation, with little or no hypertrophy. The weight of the heart is usually below normal. Microscopically the fibres are found to be in various stages of fatty and pigmentary change, some wholly converted into fatty, granular, and oily detritus, others with accumulated fat and pigment granules around the muscle nuclei. The valves are normal, but small areas of opaque white fatty deposit may stud the intima of the aorta. Similar fatty change has been found in the arterioles and capillaries. The lungs do not shew any notable lesion, except that, like all the viscera, they are very pale. The lower lobes present some oedema, and there may be petechiae beneath the pleura. Some old caseous or cretified tubercle may be found in the lung, and occasionally an intercurrent pneumonia terminates life, but neither the old nor the recent changes are characteristic. The teeth may be carious, loose, and surrounded by suppuration, but in some cases there is nothing wrong with the teeth at all. The stomach exhibits a striking pallor of its mucous membrane, and, according to some (Faber, Bloch, W. Fenwick), atrophy of the glands, with or without thickening of the submucosa.

The *liver* is nearly always slightly enlarged, and shews fatty change. Its colour differs from that of an ordinary fatty liver in that it has a *café au lait* rather than a yellow tint. The most conclusive post-mortem evidence that a case is one of pernicious anaemia is afforded by the ferrocyanide reaction in this organ. If a thin slice of the liver be immersed for five minutes in a 5 per cent solution of potassium ferrocyanide, and thence transferred to a 1 per cent solution of hydrochloric acid, a Prussian-blue colour begins to appear in about two minutes and goes on deepening for half an hour or more. The reaction, also spoken of as Perl's test, depends not only upon the presence of an excess of iron, but also upon that iron being in a sufficiently simple combination to respond to this ordinary chemical test. A normal liver, or a liver from a patient who has died from some disease other than pernicious anaemia, turns pale green or even a greenish-blue when tested in this way, whilst in pernicious anaemia the Prussian-blue is unmistakable (Plate I.). On closer inspection it is seen that the deepest blue is around the periphery of each lobule, and microscopical sections of the organ shew that the cells at the periphery of the lobules contain innumerable fine particles of an iron compound called haemosiderin, in addition to the fat-globules of all sizes which are present in all the hepatic cells. Particles of haemosiderin may also be seen in the capillaries outside them and in the portal canals. Two other viscera, the spleen and the kidneys, give a similar Prussian-blue reaction, though less constantly than does the liver; in the spleen the reaction is usually diffuse, whilst in the kidney the blue is deposited as streaks in the cortex corresponding to the convoluted tubules. Excess of iron is found constantly in the liver, and very commonly in the spleen and the kidneys. It is difficult to give absolute figures, because in the hands of different observers the degree to which

the blood is washed out of the vessels previous to analysis is variable. If, however, the same chemist analyses the organs from a case of pernicious anaemia and from a case of some other disease as a control, the percentage of iron in the liver, spleen, and kidneys is greater in the former than in the latter. The following figures are characteristic of the percentages of iron found in the dried residues of the three organs:—

	Normal.	Pernicious Anaemia.
Liver	0·09	0·53
Spleen	0·18	0·32
Kidneys	0·01	0·09

There appears to be no similar excess of iron in the other viscera, nor in the connective tissues.

The gall-bladder contains dark bile.

The *spleen* is often slightly enlarged, but it may be quite small. One or more thrombotic infarcts are occasionally present. The organ is usually pale. Its consistence is very variable. Granules of ferruginous pigment may be seen in the pulp in microscopical sections, but seldom to the same extent as in the liver. The pancreas and suprarenals shew no decided changes. The intestinal plexuses of nerves and the great abdominal ganglia have been found to exhibit evidence of degeneration. The mesenteric and other *lymphatic glands* are not as a rule affected macroscopically, but Warthin lays particular stress upon the changes which may be observed in the haemolymph glands in the abdomen. These changes consist in dilatation of their blood sinuses, together with evidence of increased haemolysis, as shewn by the increased number of phagocytes in them containing disintegrating red cells and blood pigment. In some of Warthin's cases these changes were accompanied by great increase in size and apparent increase in number of the haemolymph glands; in other cases there was no hyperplasia, the only evidence of the changes present being that obtained by microscopic examination. The changes found cannot be regarded as specific for pernicious anaemia, since there is evidence that they may be produced by other infectious or toxic processes characterised by great haemolysis. The *stomach*, *small intestine*, and *colon* are pallid and sometimes oedematous; the mucosa is shrunken, but there is seldom macroscopical evidence of inflammation or ulceration unless such as may be due to arsenic. Microscopically, there is some atrophy of the mucous glands, and occasionally some small round-celled infiltration of the tissues between and beneath these glands, but neither of these changes is by any means distinctive of pernicious anaemia. The *kidneys* are smooth and pale; pigment granules have been found in the cells of the cortical tubules, and not infrequently there are minute droplets of fat in the epithelium. As regards the nervous system, there may be capillary haemorrhages in the meninges. The *brain* is strikingly exsanguine. Sinus thrombosis does not appear to have been recorded in pernicious anaemia. Cerebral haemorrhage, however, may be present either in the form of scattered petechiae, or more rarely as a large and

fatal extravasation. The *spinal cord*, even in cases which have not presented any symptoms of such disease during life, often exhibits a variable amount of sclerosis in the posterior, lateral, or anterior columns; the nerve-roots and the grey matter are generally intact. Miliary sclerosis or minute haemorrhagic foci are sometimes found scattered irregularly throughout the substance of the cord. Some fibres of the peripheral nerves may shew degenerative changes, the result of a neuritis. The *retinae* often contain macroscopic haemorrhages, and there may be a few degenerated fibres in the optic nerve. In the skeletal *muscles* there is shrinkage of the individual fibres, but their striations are still well-marked, and fatty change is not a prominent feature here as it is in the heart muscle. *Thrombosis* of veins is not common, but occasionally it has occurred in one or other leg. Notable changes have been found in the *marrow* of the long bones. Macroscopically this is red instead of yellow. Microscopically, nucleated red corpuscles abound, the megaloblastic type predominating, and there are also large numbers of colourless cells of the myelocyte type. The characters may be summarised as being a reversion to the fetal condition of red marrow, and it is very possible that they indicate an increase of the haemogenetic function. When first met with, they were thought to be distinctive, but they have been found in several other conditions. Whether or not it is possible for a case of pernicious anaemia to exhibit no reaction in the marrow of the long bones leading to a return to the red embryonic type, is a question the answer to which involves a very wide issue. Some observers speak of an aplastic type of pernicious anaemia in which the marrow of the long bones is found to be pale, the erythroblastic elements in it being no more numerous than they are in the marrow of the long bones of healthy persons. Analysis of cases of this so-called aplastic anaemia shews, however, that the patients are mostly quite young, with a preponderance of females, and that the blood picture differs very materially from that of pernicious anaemia, particularly in the fact that the colour-index is hardly ever greater than 1, whilst it is sometimes as low as 0·4. I do not see any reason for including such cases under the heading of pernicious or Addisonian anaemia, and regard them rather as some other form of very grave anaemia that has yet to be named.

Metabolism in Pernicious Anaemia.—A great deal of work has been done in connexion with metabolism in cases of pernicious anaemia, but it is not yet possible to make many dogmatic statements as to the interpretation of the results.

Little is known as to the condition of the saliva, the pancreatic juice, the bile, or the succus entericus. The gastric juice is not necessarily abnormal, but in many patients it shews a tendency to subacidity and to deficiency in pepsin. Analyses in 20 cases gave the following results:—Normal or increased acidity in 7 cases, subacidity in 11 cases, absence of free hydrochloric acid in 2 cases. Nevertheless, apart from excessive diarrhoea or vomiting, the absorption of nitrogenous compounds, of fats, and carbohydrates is good; the faeces contain no excess of them. The

patient may be unable to eat heartily, but what is taken is well absorbed.

The metabolism of protein, carbohydrate, and of fat within the body is also fairly natural, and this notwithstanding the low oxygen-capacity of the blood. Since Dr. Haldane and Professor Lorrain Smith have shewn, by their carbon monoxide method, that the total volume of blood in the body does not present any very definite departure from the normal, the diminution in the haemoglobin is real and not merely apparent. Professor Lorrain Smith shewed that, whereas the oxygen-capacity of the blood, in cubic centimetres per 100 grams of body weight, is 0·83 in normal persons, and 0·79 in severe chlorosis, in pernicious anaemia cases with 25 per cent of haemoglobin it is only 0·40. It might therefore have been expected that notable abnormalities of metabolism would result. Serious errors of nutrition there are, and doubtless the fatty changes in the liver and in the heart and the sclerosis in the spinal cord are largely due to the deficient oxygen-capacity of the blood. Serious errors of ultimate metabolism, however, have not been established, except in the case of iron. There is no abnormal tendency to the passage of sugar, acetone, diacetic or fatty acids in the urine. The excretion of uric acid is variable both in different patients and in the same patient at different times, but upon the whole it is not abnormal. The same is true of the purine bases, both exogenous and endogenous. Hippuric acid is often more abundant than normal, but the significance of this is not known. The ammonia in the urine lies, as a rule, within the limits of health. The excretion of urea is proportional to the amount of protein food taken. Occasionally the urea nitrogen is as low as 69 per cent of the total nitrogen in the urine, but more commonly it is between 89 and 94 per cent. It may be noted, however, that tyrosine has been found in the spontaneous deposit in the urine of some cases of pernicious anaemia, a point of considerable interest in connexion with the changes in the liver. The presence of tyrosine in the urine suggests that conditions are sometimes present which interfere with the transformation of the amino compounds into urea in pernicious anaemia, just as is the case in acute yellow atrophy of the liver (*vide* Vol. IV. Part I. p. 126). The toxicity of the urine is if anything less than normal. The gaseous exchange in the lungs is apparently abnormal in one respect only, namely, that there is a total diminution in the CO_2 given out and in the O_2 absorbed. This is what would be expected in persons whose bodily activities are much curtailed. As regards the metabolism of inorganic substances, that of chlorides, phosphates, and sulphates is not obviously abnormal. Not only do the total sulphates in the urine bear the same relation to those in the food that they do in health, but also the relative proportions of preformed sulphates, of ethereal sulphates, and of neutral sulphur are within the normal limits. This is of interest because it does not lend any support to the statement that there is undue putrefaction in the alimentary canal in pernicious anaemia. The amount of indican is sometimes a little above the normal, but as often as not it is not increased,

though much stress has sometimes been laid both upon it and upon such other substances as putrescine in the urine in these cases.

The metabolism of iron is distinctly abnormal. Whereas in chlorosis the average amount of iron in the urine is 7 to 9 milligrams, in pernicious anaemia it reaches 22 and even 52 milligrams per diem. Kraus points out that the little that is known concerning the metabolism of iron is not opposed to the conclusion that deficient formation of haemoglobin is at the root of chlorosis, and that increased destruction of haemoglobin is at the root of pernicious anaemia. The quantities of urobilin in the urine and faeces point to the same conclusion. Whereas in severe chlorosis the amount of urobilin in the urine varies from 0·03 to 0·124 gram per diem, and in the faeces from 0·021 to 0·029 gram, in pernicious anaemia the corresponding figures are 0·153 gram in the urine and 0·92 gram in the faeces.

Pathology.—The attempt to afford a rational explanation of the clinical, anatomical, and chemical data of pernicious anaemia has led to much speculation and to extensive investigation. The most satisfactory exposition is that given by Dr. William Hunter, although in some respects it may be necessary to admit certain modifications in his argument. His conclusion that pernicious anaemia is a specific disorder consisting in haemolysis, affords so far a satisfactory explanation of the phenomena, but his further contention that the cause of the haemolysis is a specific toxin absorbed from the alimentary canal may or may not be true.

The problem may be discussed under the following headings:—(i.) Is pernicious anaemia a specific disease? (ii.) Which of the anatomical changes are of primary and which of secondary importance? (iii.) What evidence is there that haemolysis is a feature of the disease? (iv.) What is the significance of the changes in the bone-marrow? (v.) What is the evidence that a toxin is the cause of the disease? (vi.) What is the evidence that the toxin is derived from the alimentary canal?

(i.) *Is Pernicious Anaemia a Specific Disease?*—Theoretically, it is better to try to amalgamate diseases into broad groups rather than to differentiate them into smaller ones, but in practice the converse is true. The great advantages that clinicians have gained from the differentiation of enteric fever from typhus, and of gonorrhoeal arthritis from other forms of rheumatism, are instances in point. The same holds true of those diseases which, grouped together broadly as "idiopathic anaemias," are very confusing, but which, differentiated into varieties, are becoming better understood every year. The less that was known about the different patients whose main symptom was a severe and progressive anaemia, the greater was the inclination to regard them as similar in kind though differing in degree. The more the matter is looked into, the greater is the number of cases, at first sight similar to one another, which can be given definite but different labels upon a pathological basis. For instance, anaemias due to *Bothriocephalus latus* or to ankylostomiasis have now been removed from the nondescript group of "idiopathic anaemias"

and given definite and distinct names. There are, it is true, many obscure conditions in which severe anaemia is the main symptom, to which no name can yet be given if the title of pernicious anaemia is restricted to a limited group of them, but the fact that the restriction of the term pernicious anaemia to one particular group leaves other cases nameless is no good ground for not restricting the term in this way. The removal of pernicious anaemia cases from the general mass of apparently causeless anaemias should make it easier to deal with those which remain unnamed. The chief misfortune is the adjective "pernicious." Strictly speaking, many different anaemias may be pernicious—for example, ankylostomiasis, or the grave aplastic anaemia mentioned on p. 733. There is much in favour of Dr. Hunter's plea that the title should be changed back from "pernicious" to "Addisonian" anaemia. An anaemia must be more than merely pernicious to merit the name pernicious anaemia as it is at present used. One case of "pernicious" or "Addisonian" anaemia is so like another, each runs such a definite course, with such a marked similarity in the tendency to temporary recovery under arsenic, the clinical picture is so different from that of other obscure anaemias, the blood changes are so distinctive, particularly the high colour-index at some stage of the illness, and there is such certainty that the living case will give a Prussian-blue reaction in the liver at the necropsy, whereas no such reaction will be given by the liver in other cases, that there can be little hesitation in allowing that, of all the obscure anaemias, pernicious or Addisonian anaemia deserves a special name to itself.

(ii.) *Which of the Anatomical Facts are of Primary Importance and which of them are Secondary?*—It is probable that the fatty changes in the heart, the fatty changes in the liver, the retinal and other haemorrhages, the sclerosis in the spinal cord, the changes in the mesenteric and other sympathetic nerve plexuses, and those in the peripheral nerves, are all secondary; they may all be found in other kinds of profound anaemia.

The lesions which occupy the front rank in pernicious anaemia from the pathological point of view are: the iron in the liver, spleen, kidneys, and urine, the changes in the bone-marrow, those in the blood itself, and possibly those in the teeth and gums, the stomach, and the intestines.

(iii.) *What is the Evidence to shew that Haemolysis is a Feature of the Disease?*—It cannot be said that pernicious anaemia has yet been experimentally reproduced, but the nearest approaches to such an artificial production of the disease have been by the use of various haemolytic substances. Dr. Hunter employed toluylenediamine, Bunting and others used ricin, saponin, pyridine, and pyrogallol. Not only the blood picture of pernicious anaemia, but also the accumulation of haemosiderin in the spleen, liver, and kidneys, and the megaloblastic changes in the bone-marrow, have been brought about by these substances. The rabbit reacts with machine-like regularity to such haemolysis, the blood rapidly assuming the characters of pernicious anaemia: normoblasts and megaloblasts appear, the non-nucleated red corpuscles develop variations in size, with a predominance of those above the average, poikilocytosis, polychrom-

atophilia, granular basophilia, and an increased colour-index; whilst the marrow of the long bones at the same time becomes red, with a predominance of the megaloblastic type of nucleated cells. This reaction, this blood picture, and the marrow picture are entirely different from those produced in animals by repeated haemorrhage.

This experimental evidence in favour of a haemolytic factor in pernicious anaemia is strongly supported by the anatomical and chemical facts of the disease in man. The excess of iron pigment in the liver-cells, splenic pulp, and renal epithelium, the fact that this iron gives ordinary inorganic tests as though its molecular combination were broken down to something simpler than it is in health, the excess of iron in the urine, and the fact that iron is of little use in treatment as compared with arsenic, all point in this direction. It is known that there is not merely a relative but an absolute diminution in the total quantity of haemoglobin in the body.

It seems clear that the haemolysis occurs mainly, if not entirely, in the portal area; for the excess of iron is chiefly in the liver and in the spleen, the amount in the kidneys being explained as on its way to be excreted in the urine. Moreover, when blood destruction occurs elsewhere in the body, haemoglobinuria usually results, and not urobilinuria as is the case here.

It is less easy to say exactly what part the spleen and the liver respectively play in the haemolysis. It has been suggested, with some probability, that the spleen begins it and that the liver receives the disintegrating haemoglobin from the spleen and completes the process.

(iv.) *What is the Significance of the Bone-marrow Changes?*—Although it is generally allowed that haemolysis is a very important factor in pernicious anaemia, there are greater differences of opinion as to whether the bone-marrow changes precede the haemolysis, or follow it. There are two schools: first, those who believe that the bone-marrow reaction is an attempt to compensate for excessive haemolysis by increased blood-formation; secondly, those who think that the blood-forming powers of the body have deteriorated to such an extent that, even though the marrow of the long bones is called upon to resume its fetal functions in this respect, the blood-corpuscles are so badly made that they soon become disintegrated by the spleen and liver. The second of these views has been gaining ground of late years, but in favour of the first there are three valid arguments: first, the bone-marrow changes are not absolutely distinctive of pernicious anaemia, whereas the iron changes in the liver are; there are no exactly similar deposits of haemosiderin in all the different conditions in which the megaloblastic reaction in the marrow has been observed; secondly, the extraordinary and rapid recuperative power of some of the patients is more easily explained if the bone-marrow activities are regarded as compensatory than if they are looked upon as primary to the haemolysis; and thirdly, cases of pernicious anaemia have been recorded in which these bone-marrow changes have been comparatively slight, whereas in no case of undoubted pernicious anaemia have

the iron deposits in the liver been absent. The conclusion that the haemolysis precedes the marrow changes, and that the latter are compensatory, seems rational.

(v.) *What is the Evidence in Favour of the View that a Toxin is the Cause of the Disease?*—The use of the word toxin almost connotes ignorance. The question here is whether there is any evidence that a chemical substance, of unknown nature, may be the initial cause of pernicious anaemia. Although absolute proof is wanting, there are several arguments in favour of this hypothesis. In the first place, we may recall the attempts to reproduce pernicious anaemia in animals by chemical compounds, such as toluylenediamine, ricin, saponin, pyridine, and pyrogallol. Each of these produces changes very similar to, but not identical with, those of pernicious anaemia. In the next place, there are certain affections of man, acknowledged to be toxic, which, though not in any way to be confused with pernicious anaemia, resemble it in some respects; for example, ankylostomiasis, other helminthic anaemias, chronic poisoning by certain gases, and the septic anaemias which are discussed below. In the third place, the clinical course of the disease suggests a toxic factor, and in this connexion the pyrexia merits particular attention. The degree of fever is nearly always worse when the patient is going downhill, whilst during a period of recovery the patient's temperature may return completely to normal. This is what would be expected if a microbial poison were the cause of the mischief.

It seems more than possible, therefore, that a toxin is concerned in the production of the disease; and further, from the constancy of the clinical picture, it is possible that the toxin is specific, that is to say, the same in all cases.

(vi.) *What is the Evidence in Favour of the View that the Toxin is derived from the Alimentary Tract?*—Dr. Hunter believes that the toxin is not only specific, but that it is infective, and that it is derived from the alimentary canal. He lays particular stress upon the part of oral sepsis, infective gastritis and enteritis in the production of pernicious anaemia. The matter is as yet non-proven, but there is a general consensus of opinion that Dr. Hunter's hypothesis indicates the line along which future research upon the subject should be directed. It is quite clear that oral sepsis and other infective conditions of the alimentary tract do not necessarily cause pernicious anaemia, for oral sepsis is very common and pernicious anaemia is rare.

It is equally clear, as Dr. Hunter points out, that oral and other forms of infection may cause profound anaemia and a severe illness which is not pernicious anaemia. Dr. Hunter draws a very strong line of distinction between the *septic anaemia* of which oral sepsis is the *direct* cause, and Addisonian or pernicious anaemia of which he believes oral or gastro-intestinal sepsis to be an *indirect* cause. The cases of septic anaemia were formerly classed with those of pernicious anaemia, but this is now held to be erroneous because the former, however severe they may be, have a low blood colour-index and no Prussian-blue reaction in the liver.

According to Dr. Hunter, infection plays an important part in the development of pernicious anaemia, although however severe the infection may be it is unable by itself to produce it, some additional factor being required. This additional factor is the special and unknown toxin to which the patient is particularly vulnerable if he or she is already the subject of oral sepsis, septic gastritis, or septic enteritis. It is therefore perfectly possible for pernicious anaemia to develop in the absence of any antecedent oral or gastro-intestinal sepsis; and it is well known that, though pyorrhoea alveolaris and either vomiting or diarrhoea or both are frequent in pernicious anaemia, the disease occurs even in those who have been free from all gastro-intestinal symptoms, and have perfectly clean mouths and teeth.

Dr. Hunter's argument that oral and gastro-intestinal sepsis dispose to pernicious anaemia and pave the way for the specific haemolytic toxin is probably valid, but it is not so easy to accept his further contention that the specific toxin is gastro-intestinal in origin. It is true that the haemolysis occurs mainly if not solely in the portal system, but the spleen and liver are the only organs that are known to have the function, normally, of dealing with effete red corpuscles, and that they do so to an abnormal extent in pernicious anaemia does not prove that the toxin is absorbed from the portal area in the first instance. It might be inhaled, for example, or it might arise endogenously. There is no constant lesion, distinctive of pernicious anaemia, to be found in the alimentary canal. Many observers doubt even the so-called atrophy of the bowel. No special micro-organism can be shewn to be responsible for the toxin, and there is no conclusive proof of the presence of increased intestinal putrefaction in pernicious anaemia; the indican and the other phenol compounds in the urine often lie within the normal limits. Not only are gastro-intestinal symptoms sometimes absent when pernicious anaemia is developing, but even when they do occur they may be nothing more than accidents, due to intolerance of arsenic for example, or to anaemic dilatation of the heart.

In short, although it may generally be allowed that pernicious anaemia is a specific disease, due to the action of some toxin which causes extensive haemolysis in the portal area; that the changes in the bone-marrow are compensatory; and that oral sepsis, septic gastritis, and septic enteritis dispose to the action of this toxin though not themselves the actual cause of the disease,—the nature of the toxin and the site of its formation are unknown, although there are some who hold that it is an infective toxin derived from the alimentary canal.

Symptoms.—The following quotation from Addison's original paper gives a concise summary of the symptoms of pernicious anaemia: "The disease presented in every instance the same general character; and, with scarcely a single exception, was followed after a variable period by the same result. It makes its approach in so slow and insidious a manner that the patient can hardly fix a date to his earliest feeling of that languor which is shortly to become so extreme. The countenance gets pale, the

whites of the eyes become pearly, the general frame flabby rather than wasted, the pulse perhaps large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement. There is an increasing indisposition for exertion with an uncomfortable feeling of faintness or breathlessness on attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth, and waxy appearance; the lips, gums, and tongue seem bloodless; the flabbiness of the solids increases; the appetite fails; extreme languor and faintness supervene, breathlessness being produced by the most trifling exertion or emotion; some slight oedema is probably perceived about the ankles. The debility becomes extreme; the patient can no longer rise from his bed; the mind occasionally wanders; he falls into a prostrate and half-torpid state, and at length expires. Nevertheless to the very last, and after a sickness of perhaps several months' duration, the bulkiness of the general frame and the obesity often present a most striking contrast to the failure and exhaustion observable in every other respect." Addison's description scarcely depicts the peculiar lemon-yellow colour of the skin in advanced cases, nor does it tell of the remarkable, if temporary, remissions of the illness exhibited by most of the patients when suitable treatment is employed; it does not mention the liability to haemorrhages or the pyrexia shewn by the subjects of the disease. Nevertheless it is a remarkable picture of the main symptoms of the complaint. It must be remembered, however, that the earliest indications of the malady are often so slight and insignificant as to be disregarded; it is often not until the disease is well advanced that its true nature is recognised. This early stage lasts months or even years rather than weeks or days, though now and then the onset is more rapid.

The *initial symptoms* in the great majority of cases consist in failing strength and inability for exertion, physical or mental. It is not that the patient would not work if he could; he often tries to do his daily task in spite of his increasing lassitude and languor, and the inability to work often renders him despondent, low-spirited, and capricious in temper. Appetite fails; there may be discomfort after food, more than half the patients suffering from nausea, vomiting, or diarrhoea, even before arsenic has been administered. The gastro-intestinal symptoms may be so prominent as to lead to a suspicion of a gross lesion in the alimentary canal. Notwithstanding this, it is remarkable how the patient's body maintains its bulk; it is rare for emaciation to occur in pernicious anaemia; the weight as a rule decreases more or less, and there is often a complaint of loss of flesh, but the patient's body looks plump and well-covered. Accumulation of subcutaneous fat counterbalances the loss of muscle, so that while the bulk remains fairly constant the weight of the body falls. The absence of severe wasting is in marked contrast to the condition even in malignant disease.

Gradually the signs of anaemia become more evident, and the patient's friends may tell him he is "jaundiced," on account of the lemon- or

primrose-colour of the skin. The sclerotics, however, remain white, and there is no bile-pigment in the urine. Weakness increases; breathlessness, palpitation, and even syncopal attacks occur on the least exertion, and the patient is compelled to abandon his calling and stay in bed. Most commonly the onset is ushered in by languor and anaemia, but in some cases nervous symptoms are the first to attract notice (Gulland). These symptoms may be indefinite, the patient complaining of numbness and tingling in the fingers, pains in the back or limbs, and so forth; or they may comply with all the diagnostic signs of spastic paraplegia, tabes dorsalis, or peripheral neuritis, and may then so focus attention that for months, or even years, the blood condition at the root of them may be overlooked (*vide* article "Combined Sclerosis," Vol. VII.). Ultimately these cases progress precisely as do those in which the onset is by languor and anaemia. In a small number of cases the first symptom is a severe haemorrhage, such as epistaxis or purpura; the course in these is usually acute.

The *later symptoms*, those, that is to say, that may arise after the disease has become declared, may best be described individually; they occur with variable frequency, and some that might almost be regarded as characteristic are occasionally conspicuous by their absence.

Anaemia sooner or later becomes extreme; and with it may appear any of the symptoms that profound anaemia, whatever its origin, may cause. The pallor of the skin is striking, often in marked contrast with the previous good colour of the individual. The skin and mucous membranes are almost devoid of colour, save that the former, especially of the face, generally assumes a yellowish tint, sometimes compared to that of a lemon, or of a primrose, wholly different from the whiteness of the subject of pulmonary tuberculosis, the earthy pallor of the cancerous cachexia, the muddy tint of the malarial subject, or the bronzing of the malady discovered by Addison in his search for an adequate cause of "idiopathic" anaemia. This complexion, however, is sometimes met with in the chlorotic, in cases in which a large pelvic haematocele is undergoing absorption, occasionally in organic disease of the stomach, and in various toxic anaemias such as those due to infective endocarditis, or to parasites such as *Ankylostoma duodenale* (cf. Vol. II. Part II. p. 895). It cannot be deemed pathognomonic, but when it occurs with few symptoms, and without evidence of blood-loss, it may lead to suspicion of the grave nature of the malady. It is all the more suggestive when it occurs in a male subject of mature age whose previous health has been excellent, whose main complaint is languor, and who is not emaciating. There is no constant condition of skin as regards perspiration. Some have noticed undue sweating in the earlier and later periods of illness, but it can hardly be regarded as essential. The skin often shews the soft and smooth character described by Addison as characteristic of the subjects of fatty degeneration.

Breathlessness becomes prominent on any exertion, but as long as the patient remains in bed there is little or no dyspnoea, although the

respiration-rate is more often over than under 20 to the minute. Orthopnoea and cyanosis are quite unusual except when oedema of the lungs occurs towards the end. Bronchitis, pneumonia, or tuberculosis of the lungs are exceptional even as terminal affections.

Pyrexia is noticed in almost every hospital case; it is usually slight, the temperature in the mouth seldom exceeding 101° F., but regularly rising to between 99° F. and 101° F. every evening, and falling to normal every morning. Hypothermia, such as that of chronic valvular disease of the heart, is seldom seen in pernicious anaemia. The temperature chart is not unlike that of many cases of cirrhosis of the liver. The patient himself does not feel feverish, and rigors are very rare, apart from some intercurrent affection. There may be periods without pyrexia, particularly when the patient's general condition is improving; but during the severe stages of the illness moderate pyrexia every evening is rarely absent, a point which seems to favour the toxaemic explanation of the disease.

Circulatory disturbances are generally well marked, and may even lead to an erroneous diagnosis. The patient may complain of palpitation from an early period, and at times may be attacked with faintness or actual syncope. Throbbing in the head, buzzing or drumming noises in the ears, and various subjective intracranial symptoms are frequently complained of. The pulse, generally quicker than normal, is markedly affected by exertion or emotion, the difference between its rates as influenced by posture being considerable. It is usually soft and full. The cardiac impulse is undulating, and percussion may afford evidence of some dilatation of both sides of the heart. It is noteworthy, however, that the cardiac impulse is seldom markedly displaced; in a few cases it may be in the left nipple line, or even external to it, but in the majority it remains very nearly in its normal position. A blowing systolic murmur, loudest in the second left intercostal space close to the sternum, is generally audible over the whole cardiac area. Its haemic origin is confirmed by the presence of a similar murmur in the large arteries, and a loud hum in the jugular veins. The carotids sometimes pulsate violently, and a distinct thrill may be felt over them and the large veins in the neck.

The *blood* is profoundly altered. From the bloodless condition of the tissues it may be somewhat difficult to obtain sufficient for its examination. The drop has a bright pale-ruby colour; it clots less readily than usual, and it is thinner and more translucent than is a drop of normal blood. The following are the main features of the blood-count in a characteristic case: The number of red corpuscles per c.mm. of blood is greatly diminished. The degree of this oligocythaemia depends upon the stage and severity of the disease; but it is not unusual to find the number of red corpuscles reduced to 1,000,000 per c.mm., or 20 per cent of the normal; and as the case progresses they may fall considerably below this figure, the lowest estimation on record being 143,000 (Quincke). The haemoglobin is also greatly diminished, but the reduction in its percentage

is proportionately less than is the reduction in the red corpuscles. Thus, in a case in which the corpuscles have fallen to 15 per cent, the haemoglobin may have only fallen to 20 or 25 per cent. Hence it follows that the individual corpuscles have a larger relative content of haemoglobin than in health; in other words, the colour-index—which is the ratio $\frac{\text{percentage of haemoglobin}}{\text{percentage of red corpuscles}}$—is greater than 1. This *high colour-index* in a case of grave anaemia is almost pathognomonic of pernicious anaemia. The number of leucocytes per c.mm. of blood is seldom above normal; it is quite rare for them to reach 10,000; in the majority of cases they do not exceed 5000, and very often there is leucopenia with a count between 1000 and 5000; in a few cases less than 1000 leucocytes per c.mm. of blood may be found. Microscopical examination of films shews notable changes in the red cells. Their tendency to form rouleaux is almost lost, and they exhibit great variations in size and shape. Many are no longer circular, but pear-shaped, oval, or hour-glass shaped, a condition named by Quincke poikilocytosis. Many are much larger than normal (megalocytes), and some appear as small spherical bodies (microcytes).

Poikilocytosis and megalocytosis, particularly the latter, are more marked in pernicious anaemia than in any other condition; but neither is pathognomonic, for both may be observed in other severe anaemias. It is not possible, therefore, to diagnose pernicious anaemia with certainty from films alone. The discovery of marked megalocytosis is considerable evidence in its favour, but to clinch the diagnosis the colour-index of the blood must be determined too. The red corpuscles stain fairly well in most cases, probably because each is rich in haemoglobin; sometimes, however, when methylene-blue-eosin is used some of the red corpuscles assume a purplish colour, or exhibit a fine speckling with blue granules instead of taking up only the eosin; this tendency to stain with both basic and acid dyes was pointed out by Ehrlich, and it has been variously termed polychromasia, polychromatosis, polychromophilia, polychromatophilia, or punctate basophilia, the last expressing the condition best. Dr. Copeman has found that the haemoglobin separates from the stroma with undue readiness in pernicious anaemia, but this is not so evident in films as it is in solutions. Nucleated red corpuscles, named gigantoblasts, megaloblasts, normoblasts, and microblasts, according to their size, are not infrequently present; roughly speaking, they are more numerous the more severe the patient's illness. If stained films contain numerous megaloblasts, the disease is almost certainly severe pernicious anaemia; but, contrary to the opinion of some authors, pernicious anaemia can be diagnosed even in the absence of this megaloblastic reaction. Dr. Moorhead's observations suggest that there must be quite a large number of cases of the malady in which the nucleated cells suddenly burst out into the blood during the last days of life, particularly when any acute infection has supervened. Should the disease abate for a time, nucleated red corpuscles may disappear, and poikilocytosis and megalocytosis diminish considerably. Megalocytes are amongst the most persistent of the

abnormalities to be noted in films from a patient who is recovering for the time being.

The *differential leucocyte-count* does not shew any constant characters; it may be abnormal, but in the majority of cases there is a relative increase in the small lymphocytes and a corresponding diminution in the polymorphonuclear cells. The numbers of hyaline corpuscles are not usually abnormal. The coarsely granular eosinophil cells are occasionally absent; more often they are present in normal numbers, or in slightly increased relative proportions, up to 3, 4, and even 5 per cent; they seldom exceed this. It is not at all uncommon to find one or two basophil corpuscles and an occasional myelocyte in an examination of 250 consecutive leucocytes.

The following is an example of a characteristic blood-count in a well-marked case:—

Red corpuscles	800,000 per c.mm., or 16 per cent of normal.
Haemoglobin	19 per cent of normal.
Colour-index	$\frac{19}{16}$ or 1·188.
Leucocytes	3,200 per c.mm.

Nucleated red corpuscles, 4 to every 100 leucocytes.

Poikilocytes and megalocytes numerous.

Differential leucocyte count:—

Small lymphocytes	39·0 per cent.
Large hyaline lymphocytes	6·0 „
Polymorphonuclear cells	51·0 „
Coarsely-granular eosinophil cells	2·2 „
Basophil cells	1·2 „
Myelocytes	0·6 „

It must be noted, however, that whereas the marked oligocythaemia, the high colour-index, the poikilocytosis, and the megalocytosis are all well marked when the illness is pronounced, these features of the blood may, and often do, disappear again if the patient rallies under treatment. The high colour-index is the pathognomonic point in the disease, but during a remission of the symptoms the index frequently returns to normal, or even becomes less than 1, as shewn in the following case:—

	Red Corpuscles. Per c.mm.	Red Corpuscles. Per cent of Normal.	Haemoglobin. Per cent of Normal.	Colour-Index.
Nov 18, 1905	981,250	19	25	1·32
„ 30, „	843,750	17	20	1·18
Dec. 12, „	1,100,000	22	25	1·14
„ 30, „	2,231,250	45	40	0·90
Jan. 4, 1906	3,325,000	66	50	0·75

The patient died the following autumn, and the diagnosis was confirmed by necropsy; at that time the colour-index had again become greater than 1:—

Oct. 5, 1906	679,687	14	20	1·42

The same remarks apply to the early stages of the disease before the anaemia has become pronounced. Moreover, it is not at all uncommon to find that a patient whose blood has a high colour-index one week may have an index which is not high the next. The sudden changes to which the blood is thus liable have been called blood crises or storms. Their pathological significance is not clear, but their diagnostic importance is obvious; for, by reason of these blood-storms, or by reason of the return to a normal or subnormal colour-index when the disease exhibits a partial remission, it is not possible to exclude pernicious anaemia when a single blood-count fails to shew a high colour-index. It is practically certain that a case is one of pernicious anaemia if there is well-marked oligocythaemia, no leucocytosis, a high colour-index, and considerable megalocytosis; but the converse is not necessarily true. In doubtful cases the blood examination must be repeated at intervals; if the colour-index of the blood is constantly less than 1, pernicious anaemia is unlikely; but if it is now and then greater than 1, pernicious anaemia is the probable diagnosis, even though the index on many other occasions is 1 or less than 1.

Oedema round the ankles may occur in those who remain up and about in spite of their illness, but it is hardly such a frequent feature of pernicious anaemia as it is of chlorosis. It rarely amounts to more than a slight pitting on pressure over the malleoli; it is the exception for it to become more extensive even late in the disease, though occasionally there is a terminal anasarca. In nearly a third of the patients there is no oedema at all from start to finish. In rare cases, however, there may be sudden outbursts of general oedema, including effusions into the serous cavities; these attacks have been described as "crises," after which the patient either improves considerably or rapidly succumbs.

Gastro-intestinal symptoms are amongst the earliest and most frequent features of the malady. The tongue is pale and flabby; in a few cases it presents multiple acute shallow ulcers, especially along its sides and at the tip. Dr. Hunter has laid some stress upon these as being characteristic in appearance, but there is not sufficient evidence to prove that they differ in any essential particular from those of acute superficial ulcerative stomatitis in general. The teeth are often in bad condition. The gastric juice is not always abnormal, but it is apt to be deficient in hydrochloric acid, which in some cases may be entirely absent (achlorhydria). Digestion is therefore apt to be slow, and the appetite impaired. Bilious attacks, dyspepsia, and flatulence are common. Constipation as a spontaneous symptom is very unusual, though it may occur occasionally as the result of treatment for undue looseness of the bowels. The majority of the patients suffer from vomiting, or diarrhoea, or both, at some period of their illness, and these two symptoms merit special discussion on account of their possible relations to the pathology of the condition. The arsenic which is used in the treatment of the disease may be responsible, in part at least, for attacks of sickness or diarrhoea in the later stages; it is only when these attacks have occurred before any arsenic has been given that they can be regarded as intrinsic.

Dr. Hale White has shewn clearly that vomiting and diarrhoea are common in pernicious anaemia quite apart from the administration of arsenic. His statistics are more than confirmed by the following summary of the gastro-intestinal symptoms spontaneously complained of, before arsenic was given, in 58 consecutive cases :—Both vomiting and diarrhoea, 11 cases; diarrhoea, but no vomiting, 11; vomiting, but no diarrhoea, 9; flatulence, but no marked vomiting or diarrhoea, 7; no marked vomiting, diarrhoea, or flatulence, 15; no note made, 5; total, 58 cases. The attacks were not infrequently very severe, and in several of the above cases, before the anaemia was declared, diagnoses, such as gastric ulcer, cholera, or enteric fever, had been suggested. The vomiting might partly be accounted for by anaemia and cardiac dilatation (Beddard), but these would not account for the diarrhoea. It is probable, therefore, that diarrhoea and vomiting are not adventitious but genuine symptoms of pernicious anaemia.

Jaundice does not occur except as the result of some complication, though the patient's friends often interpret the yellow colour of his skin as due to it. Although the integuments have a lemon tint, the conjunctivae remain white, and bile pigments are absent from the urine, except in rare cases such as those referred to by Chauffard.

The *liver* is seldom very large, but its edge is palpable in about one-third of the cases. It is smooth and soft.

The *spleen* is also palpable in about one-third of the patients, but it seldom comes more than just below the ribs: in a few cases it extends as much as 3 or 4 inches below the costal margin, but this is exceptional. It may be palpable when the liver is not, and vice versa. The peripheral lymphatic glands are not enlarged.

The *urine* is fairly abundant as a rule, of normal or diminished specific gravity, acid, and free from deposit. It is often pale, but in the course of the illness it may become high-coloured without any corresponding increase in its specific gravity. This coloration is frequently due to urobilin, which, in nearly half the cases, is present at one time or another in sufficient quantity to be detected by immediate spectroscopic examination. There may be an excess of indican, and free iron has been observed (Finny). Uric acid is sometimes in excess; the amount of urea varies directly with the amount of protein food digested. Albuminuria is uncommon, though in a few cases a trace of albumin may be noticed; the same applies to blood in the urine. Microscopical examination of the deposit reveals little unless centrifugalisation has been thorough. An occasional hyaline tube-cast may then be found, a few red corpuscles, crystals of uric acid in small numbers, and renal epithelial cells. The latter not infrequently contain fine granules, which have been shewn by special methods to contain iron. Tyrosine and putrescine have already been referred to (p. 734).

The *nervous symptoms* have received especial attention, since the presence of definite structural change in the spinal cord in cases of profound anaemia was determined. As a rule, the symptoms are not so much

those of definite nerve diseases as those which are usually regarded as functional. The patient is frequently irritable, and complains of a growing inability to concentrate his attention, of loss of memory, and often of insomnia. Headache is not prominent until the anaemia becomes extreme, but more than half the patients complain of buzzing or throbbing sensations in the head. Tingling in the hands or feet is not uncommon; numbness with or without tingling is frequent, and sometimes there are severe pains in the arms, shoulders, chest, legs, or back, suggesting peripheral neuritis, acroparaesthesia, or lumbago. Definite peripheral neuritis with extreme emaciation and reaction of degeneration in the muscles is distinctly uncommon, and when it does occur it may be due to arsenic rather than to the pernicious anaemia itself. Towards the end a low form of delirium is frequent, and there may be pre-agonal convulsions passing into coma, or a lethargy deepening into coma without convulsions. The intellect often remains unimpaired almost to the close, but in a few cases symptoms resembling those of mania, extreme neurosis, hypochondriasis, or general paralysis of the insane are noted. Visual hallucinations may be caused by retinal haemorrhages. Cerebral haemorrhage with its concomitant nerve symptoms is uncommon. The autopsy may disclose degenerative lesions in the posterior and lateral columns of the spinal cord without any definite symptoms of these having been noticed during life; on the other hand, it is not uncommon to find the knee-jerks unequal or exaggerated, with some degree of ataxy or spasticity in the legs. A small proportion of cases have pronounced nervous symptoms, and Dr. Gulland has pointed out that the case may be diagnosed as one of spastic paraplegia or of tabes dorsalis some time before the anaemia attracts any particular attention. The following is a summary of the nerve symptoms and signs noted in 58 consecutive cases at Guy's Hospital:—Buzzing or other noises in the head, 22 cases; numbness or tingling, or both (moderate, 18; severe, 3), 21 cases; symptoms of approaching insanity, 6 cases (delusions, 2; hypochondriasis, 2; mania, 1; like general paralysis of the insane, 1); knee-jerks exaggerated, 6 cases; knee-jerks lost, 5 cases; extensor plantar reflex, 3 cases; retention of urine with overflow, 1 case; extreme peripheral neuritis (alcoholic?), 1 case.

Optic neuritis has sometimes been described in pernicious anaemia, but it is far from common. Retinal haemorrhages are frequent, but the disc itself escapes. Out of 58 consecutive cases 1 only had macroscopic changes in the optic nerve; and as this instance shewed choroidal degeneration and optic atrophy, it may have been syphilitic.

Liability to haemorrhage is a noteworthy feature of the disease, but only in quite a small proportion of the cases is it in itself of serious degree. Most commonly there are small capillary haemorrhages only, and their most frequent site is the retina. Sir Stephen Mackenzie has shewn that retinal haemorrhages are prone to occur in any form of prolonged anaemia in which the red corpuscles remain below 50 per cent of the normal; and as this degree of intensity is the rule in pernicious anaemia, their occurrence here is comparatively common. Haemorrhages may be

confined to the retina. They do not usually cause impairment of vision, but they have sometimes led to visual hallucinations, or even to blindness. A few petechiae under the skin, especially on the legs, a little bright red blood with the motions suggesting piles, epistaxis, and a liability to persistent oozing after tooth extraction, are the next most common haemorrhages. It is exceptional for the same patient to exhibit them all, but now and then a case is met with in which the haemorrhagic tendency is almost as severe as it is in purpura haemorrhagica. The following is a summary of the haemorrhages that were noted in 58 consecutive cases:—Retinal haemorrhages, 16 cases; bright red blood with the motions, 12; purpura, 11 (slight, 9; severe, 2); epistaxis, 8 (slight, 7; severe, 1); haemoptysis, slight, and possibly not from the lungs, 4; bleeding gums, 2; haematemesis, slight, 1; cerebral haemorrhage, fatal, 1. The presence of an occasional red corpuscle in the urinary deposit is not here counted as haematuria. Amongst the 58 cases, in 2 only was the haemorrhagic tendency in itself grave, and in 23 cases no haemorrhages were noted at all.

Pigmentation of the skin is common, usually as brown, freckle-like specks and spots on the trunk and limbs. Occasionally there is a more generalised increase in the epidermal pigment, distinct from and in addition to the lemon-yellow tint. The tendency to pigmentation is certainly increased by arsenical treatment, but in some cases the freckling of the body has begun before any arsenic has been given. This pigmentation sometimes increases the difficulty of distinguishing pernicious anaemia from Addison's disease, particularly since, as Dr. Hale White pointed out, cases of pernicious anaemia treated with arsenic sometimes shew extensive pigmentation of the buccal mucosa, even though the suprarenals are not diseased. Out of 58 cases, considerable pigmentation was present inside the mouth in 2, the diagnosis of pernicious anaemia being confirmed by autopsy in both cases.

The *lungs* and the *serous membranes* very seldom give rise to symptoms. Haemoptysis has been mentioned, but it is quite possible that the blood comes from the mouth, nose, pharynx, or trachea rather than from the lungs. Pneumonia, even as a terminal event, is rare, and pleurisy with effusion, pericarditis, and ascites are all exceptional.

Uterine disorders in the past attracted considerable attention, but it is now generally agreed that the severe anaemias ushered in by uterine troubles are not really pernicious anaemia, though they sometimes simulate it superficially. Women with pernicious anaemia may also have disease of their pelvic viscera, but uterine symptoms are not as a rule prominent. Though menorrhagia sometimes occurs, the menstrual flow is more commonly scanty or even absent.

Tenderness of the long bones, particularly of the lower extremities, is not uncommon; it appears to be related to the changes in the bone-marrow.

Diagnosis.—The diagnosis of pernicious anaemia can only be made with certainty by examination of the blood. When the number of red

corpuscles per c.mm. is markedly diminished, the colour-index high, leucocytosis absent, and eosinophilia absent or very slight, the condition is almost certainly pernicious anaemia.

It must be remembered, however, that because a single examination shews that the colour-index is low, or is not high, we are not justified in excluding pernicious anaemia; for as the result of improvement under treatment the colour-index falls below normal, and further in the earlier stages of the illness the colour-index is not necessarily high. Even when the patient is extremely ill the colour-index may not be constantly above normal. In cases of doubt the blood should therefore be examined on several occasions. Provided the counts are trustworthy, the occurrence of a high colour-index on one occasion is more important than the occurrence of a low one on several others.

In the early stages of pernicious anaemia diagnosis is extremely difficult, because the colour-index at that time is not usually high; but when the anaemia is at all pronounced the diagnosis is usually easy—a persistently low colour-index excludes it, whilst a high colour-index on more than one occasion eliminates almost everything else.

Differential Diagnosis.—The various diseases that may be mistaken for pernicious anaemia, or for which pernicious anaemia may be mistaken, unless blood-examinations are made, may be summarised as follows:—

When anaemia, languor, and breathlessness are the main symptoms: carcinoma of the stomach, advanced syphilis, malarial and tropical cachexia, chronic parenchymatous nephritis, infective endocarditis, chlorosis, leukaemia, septic anaemia (Hunter), plumbism, ankylostomiasis, *Bothriocephalus latus*, lardaceous disease.

When the symptoms are mainly gastro-intestinal: gastric or duodenal ulcer, carcinoma of the stomach, non-ulcerative or ulcerative colitis, chronic dysentery.

When anaemia, pyrexia, bruits, and petechiae are the main symptoms: infective endocarditis.

When bleeding is the main symptom: gastric ulcer, duodenal ulcer, cirrhosis of the liver, uterine fibromyoma or polypus, haemorrhoids, rectal or sigmoid polypus, purpura, haemophilia.

When nerve symptoms predominate: neurosis, peripheral neuritis, lumbago, tabes dorsalis, disseminated sclerosis, primary spastic paraplegia, mania, melancholia, general paralysis of the insane.

When pigmentation is a marked feature: Addison's disease.

The only three that need further discussion are Addison's disease, ankylostomiasis, and nerve diseases.

The pigmentation that may occur not only over the body but also in the mouth in some cases of pernicious anaemia, particularly if treated by arsenic, has been described above. Without a blood-examination, or repeated blood-examinations, such cases might be regarded as obvious examples of Addison's disease. The blood-examination will exclude the latter, for in Addison's disease the colour-index is low.

Ankylostomiasis may give rise to a blood-picture extremely like that

of pernicious anaemia, with in a few cases even a high colour-index. The difficulty of diagnosis in a sporadic case may therefore be great unless attention be paid to two further points. These are, first, the differential leucocyte-count, which usually shews a very definite eosinophilia in ankylostomiasis, and at most a slight eosinophilia in pernicious anaemia; and, secondly, the faeces, which in the former disease may be found to contain the parasites or their ova after an anthelminthic remedy has been given.

Finally, symptoms of nerve disease may precede the anaemia by many months in some cases, and it is only as time goes on that the diagnosis can be changed from that of primary nerve trouble to that of pernicious anaemia.

Prognosis.—The outlook in a case of established pernicious anaemia is grave. The danger, however, is not as a rule immediate, and one of the features of the disease is the way in which many of the patients can recuperate for the time being. The remission is sometimes complete; that is to say, the red corpuscles may return to 5,000,000 per c.mm., and the distressing symptoms entirely pass away for a while. More often it is found impossible to raise the red cells to more than perhaps 60 per cent of the normal. During such a remission the patient may be sufficiently well to return to business, but in almost every case the recovery is short-lived, and a relapse follows in a few weeks or months. The recuperative power after one relapse is not so good as it is in the first instance, but there may be a second temporary recovery, partial as a rule, and in a few cases as many as four or even five alternations between recovery and relapse before the end comes. It would, perhaps, be too much to say that the disease must necessarily end fatally, for cases are recorded in which the patients were restored to health and remained well for years. On the other hand, in about half the cases seen in hospital the illness is already so grave that no remission occurs at all. It is important to recognise the malady in the earliest stage possible. The less severe the anaemia at the time the diagnosis is first made, the greater are the chances of temporary recovery under treatment; though even when the red corpuscles have fallen to 20 per cent of the normal remarkable recuperative power may still be left.

Recognition of the disease in the early stages is not easy, but that it may some day be possible to detect it sooner is suggested by the consideration that numbers of the patients have been suffering from symptoms directly continuous with those of the pernicious anaemia for months or years before the blood-examination revealed the diagnosis. Thus, amongst 58 consecutive cases the patients themselves dated their illness back for the following lengths of time prior to its recognition :—

For less than 1 month	in	2 cases.
„ between 1 and 3 months	„	12 „
„ „ 3 „ 6 „	„	6 „
„ „ 6 „ 9 „	„	3 „
„ about a year	„	11 „
„ between 1 and 2 years	„	9 „

For between	2	and	3	years	in 4 cases.
„ „	3	„	4	„	„ 7 „
„ over	5	years			„ 4 „

It does not follow of course that the pernicious anaemia was itself present all the time previously, but the figures leave room for hope that blood-examinations will lead to earlier diagnoses in the future.

It is in the rarest instances only that the disease does not end fatally sooner or later, but there are all degrees in the acuteness of the process. Sometimes it is almost fulminating. More than one-half the patients die within a year from the date when the disease was recognised, but a certain number survive a year or two, and some for longer still. The result of 11 out of the above 58 cases is not known; the histories of the remaining 47 were ascertained up to February 1, 1909. Seven were still alive, but 5 of these would probably not live long; one was still fairly well two years, and another eight years, after the disease was recognised. The interval between the recognition of the pernicious anaemia and the time of death in the remaining 40 cases was as follows:—

Less than	1	month			5 cases.
1 to	3	months			8 „
3 „	6	„			5 „
6 „	12	„			7 „
12 „	18	„			3 „
18 „	24	„			2 „
1 „	2	years			2 „
2 „	3	„			3 „
3 „	4	„			1 case.
6	years				1 „
8	„				2 cases.
10	„				1 case.

The prognosis therefore is poor, but it might be much worse.

Treatment.—It is essential that a patient who is suffering from decided pernicious anaemia should be kept absolutely at rest in bed, or at least in the recumbent position, until recovery is well advanced. Artificial warmth to the feet is needed when the weather is at all cold, and the bed-clothes, without being heavy, should be warm. If the patient does not object, the night-gown should be of fine flannel. Plenty of fresh air and of sunshine are desirable, and a wealthy patient, in whom the disease is not advanced, may with advantage winter in a brighter and a more equable climate than this country affords.

No hard and fast rules as to dietary can be laid down, because every patient has certain idiosyncrasies as to what he can and what he cannot eat and digest; one patient may be able to take almost any ordinary wholesome food, another may suffer so much from anorexia, nausea, and possibly diarrhoea, that it may be very difficult to find any food that can be taken. The cooking should always be of the best, and all food should

be presented to the patient in an attractive form and in comparatively small amounts at a time. The meals need not be restricted when the patient's appetite is good, but the sight of a large quantity at a time is apt to paralyse any desire for food. Whenever possible the diet should be liberal, and many of the patients can eat toast, bread, fish, meat, vegetables, and puddings well. Small quantities of alcohol in the form of claret, Burgundy, hock, or weak but good whisky and water may promote digestion. When, however, appetite is capricious, milk and milk foods should be the basis of the dietary, and the patients may perhaps be persuaded to take meat-juice, egg beaten up in the milk, jellies, and so forth as well. There is no particular kind of ordinary food that is bad for the patient, provided it can be taken without repulsion, and without subsequent dyspepsia. The better the patient can eat, the more likely is improvement to follow.

Red bone-marrow, fresh and uncooked, has been recommended by Sir T. Fraser; in the form of a thin sandwich, seasoned with pepper and salt, it is not unpalatable, though the thought of eating it may at first be distasteful. It is given in the hope that the consumption of fresh marrow may increase the blood-forming activity of the patient's own marrow. It has been tried repeatedly, but, though some have reported good results, there is little evidence that the marrow acts otherwise than as a food.

The bowels are often troublesome, and for diarrhoea, which is not uncommonly present, salicylate of bismuth in full doses acts well. Constipation is rare, but the greatest caution should be observed as to the remedy employed; a purgative is contra-indicated; a mild laxative is the most that should be necessary. More harm is likely to accrue from excessive looseness of the bowels than from any ordinary constipation.

Any source from which bleeding occurs—for example, in the nose or the uterus—should be treated locally.

Bad teeth should be immediately attended to. If the patient is too weak to go to the dentist, the dentist should, in order to prevent delay, attend the patient in bed. Tartar should be removed, useless stumps taken out, and carious cavities stopped. Any pyorrhoea alveolaris may be alleviated by the use of a tooth-brush and one of the numerous antiseptic mouth-washes several times a day; a useful fluid is hydrogen peroxide solution, of a strength varying from 1 part of the liquor in 10 to 1 part in 2 according to circumstances. Cleansing the mouth serves three purposes: first, it diminishes the patient's distaste for food; secondly, it lessens the number of micro-organisms which when swallowed infect the stomach and cause septic gastritis; and thirdly, as a result of this, it is likely to decrease the vomiting. The question of a dental plate is of much less importance than is that of making the mouth clean quickly.

Sleeplessness is not very common; but its occurrence should be met by the use of the milder hypnotics, as it is extremely important that the patient should sleep well.

The heart seldom needs direct treatment when the patient is absolutely

at rest; digitalis, given in full doses in water, is the drug to rely on when cardiac symptoms are pronounced, but this seldom occurs when the patient is in bed.

Finally, certain drugs should be given for the disease itself. Arsenic, first employed by Dr. Byrom Bramwell, is the remedy *par excellence*, though many others have been advocated. Although it will not do good in every case, and although some patients do not bear it well, the experience of those who have treated any large series of cases in different ways is that, whatever else may be given, a series treated with arsenic shews a larger proportion of remissions than is met with in a series treated with other drugs. The arsenic may be given in the form of Fowler's solution or of the liquor arsenici hydrochloricus, beginning with doses of 2 to 3 minims, three times a day after food. The dose should be increased by 1 minim every five or six days until, if no symptoms of intolerance appear, 10 minims or more are given at a time. The pill of arseniate of iron is another convenient form. It is well to continue the drug for some time after the signs of improvement are manifest. When arsenic in any of its commoner forms cannot be taken on account of vomiting or diarrhoea, a trial may be made of the cacodylates or of di-sodium methyl-arsenate, which are sometimes better borne. Sodium anilarsenate (atoxyl), which contains 27·2 per cent of arsenic and affords a means of giving large quantities of the latter without toxic effects, has not been used in pernicious anaemia, but it would seem probable that benefit would result from its administration in the same way as in sleeping sickness.

It might have been expected that in a disease in which haemolysis plays such a prominent part, haematinic remedies would do good. It is remarkable, however, that the chief of these—iron—is in most cases useless. At least, iron alone does not seem to do any good. When given along with the arsenic, however, it often appears to assist the action of the latter.

Another line of treatment that has been much advocated is the use of antiseptic drugs, such as glycerin of carbolic acid, salol, β-naphthol, and salicylate of bismuth. Their efficacy is ascribed to their direct antagonism to the supposed infective processes which yield a haemolytic poison in the intestine. A notable instance of rapid recovery, which, moreover, was sustained for a long time, has been recorded (G. A. Gibson); it followed the prescription of β-naphthol, after the failure of arsenic. Dieballa quotes a case in which, after a number of remedies, namely, ferratin, bone-marrow, oxygen, arsenic, iron, and quinine, had been tried for nearly four months without any benefit, the administration of salol, continued with occasional intermissions for three months, was followed by a restoration in the corpuscular richness which seemed to have been due to the change of remedy. Other isolated instances of good results from this line of practice, including that of lavage of stomach and intestinal irrigation, have been recorded, but not infrequently these methods have led to no good result. The same applies to treatment by antistreptococcal serum. This was advocated at the time when the

distinction between septic anaemia, on the one hand, and pernicious anaemia on the other, was less clear than it is now. At that time it was thought that pyorrhoea alveolaris was itself the direct cause of pernicious anaemia. The chief organism in the alveolar pus was found to be a streptococcus, and it was thought that these streptococci produced the toxin responsible for pernicious anaemia. Antistreptococcal serum was therefore given daily, every other day, or twice a week, subcutaneously or per rectum. The treatment was followed by improvement in some cases, and it is possible that it really does do good when there is severe pyorrhoea alveolaris or evidence of septic gastritis or enteritis. Even though the serum has no direct action on the toxin of pernicious anaemia, it may help to check the associated septic troubles, and thus assist in bringing about recovery. It is also possible that good effects are due to the serum apart from any specific bodies contained in it. The pain necessitated by the hypodermic method of administration is, however, a grave objection to its use; and since it has not been proved that the serum exerts a beneficial influence, it is improbable that it will be employed as a routine measure. The so-called "Crawitz" method of treating pernicious anaemia consists essentially of a strict diet of milk and vegetables, daily enemas, the administration of arsenic and hydrochloric acid by the mouth, and lavage of the stomach on alternate days.

Inhalation of oxygen has been tried in some cases, sometimes with benefit, sometimes with none. Lactobacillin has also been employed with success (Dill). Another line of treatment recently advocated by Vetlesen in Norway is by the administration of a dram of pure glycerin thrice daily by the mouth. Several cases so treated have improved wonderfully, but it is too early yet to say whether this recovery was really due to the glycerin.

There are as yet no statistics to shew whether *x*-ray treatment is of any use in pernicious anaemia as it is in some cases of leukaemia (*vide* p. 826).

There are, indeed, few maladies in which the results of treatment are more capricious. It is impossible to prophesy in any given case whether any given remedy will be useful or not. The reasons for the frequent failure of a remedy in one case, and for its success in another, are not known. Thus, the success attending the use of red marrow, introduced by Sir T. Fraser, has been repeated by some physicians, but never attained by others. A like diversity of experience is to be found in the records of cases treated, often, no doubt, in the last resort, by blood transfusion or saline injections. Excellent and even remarkable results of transfusion have been published—amongst others by Quincke, Brakenridge, and Affleck,—results which often seem quite out of proportion to the amount of blood injected; as if the healthy serum had exerted some specific effect, either in stimulating haemogenesis or, as some think, possibly by exerting an antitoxic influence upon the assumed haemolytic virus. Yet in very many cases this measure has proved futile.

The inconstancy of therapeutical results may be taken as evidence that there is still much to learn of the intimate pathology of the disease. All that can be done in the presence of the progressive blood-destruction is to make trial of each of the several remedial measures that have been found at times to be efficacious; of these, we would place first the administration of arsenic, and next to it that of intestinal antiseptics.

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The above list by no means exhausts the very copious literature of the subject, which of recent years has been greatly added to; nor does it take account of the numerous articles and monographs upon the various forms of parasitic anaemia, notably ankylostomiasis and bothriocephalus anaemia.

Since this article was written Vol. IV. of Osler and M'Crae's *System of Medicine* has appeared, with an article by R. C. Cabot, who analyses 1200 cases, collected from his own practice, from the practice of his friends, and from literature. His conclusions are very similar to those arrived at in this article.

H. F.

SPLENIC ANAEMIAS

By R. HUTCHISON, M.D., F.R.C.P., and J. C. G. LEDINGHAM, M.D.

ENLARGEMENT of the spleen may occur as an incident in secondary anaemia due to various causes, such as malaria, syphilis, and tuberculosis. In the diseases to be dealt with in the present section, however, the splenic enlargement is apparently idiopathic, and constitutes the most

striking feature in the clinical picture. It will be convenient to consider such diseases (1) as they occur in the adult and in later childhood (splenic anaemia), and (2) as met with in infancy (splenic anaemia of infancy or anaemia pseudoleukaemica infantum).

Splenic Anaemia (adult type)

History and Nomenclature.—Shortly after the discovery by Hughes Bennett and Virchow of the association of splenic enlargement with leukaemia the existence of cases of idiopathic splenic enlargement without any increase of leucocytes in the blood was recognised, and to this condition the general term pseudoleukaemia was applied by Cohnheim. Gretsel, in 1866, described such a case in a child from Griesinger's clinic and was the first to introduce the term splenic anaemia to describe such cases. In the following year Müller published several cases under the same title. In spite, however, of the sporadic publication of cases by H. C. Wood, Strümpell, and others, it was not until the appearance of Banti's monograph in 1883 that the disease was brought prominently before the profession; since then Prof. Osler's papers have done much to gain general recognition for the disease. Meanwhile in France a condition identical with splenic anaemia had been described by Debove and Bruhl as "splénomégalie primitive," a term which has since been adopted by other writers. Cases of splenic anaemia are also frequently spoken of as Banti's disease, a description, however, which should more strictly be reserved for cases presenting hepatic cirrhosis and ascites in addition to splenomegaly and secondary anaemia.

It may be granted at once that the term splenic anaemia has often been used rather loosely, and that several conditions have in the past been described under it which would now be classified differently, but, as Prof. Osler has remarked, it is useful provisionally, and until we have further knowledge, to group together cases of idiopathic enlargement of the spleen with anaemia and without lymphatic implication, and to label the condition splenic anaemia. Such cases, however, constitute a clinical rather than a pathological group, and it is probable that they have a varied pathological basis. One type of the disease indeed—that associated with the name of Gaucher—has a morbid histology which is so characteristic as to entitle it to a place by itself. Gaucher published his case in 1882 as one of "idiopathic hypertrophy of the spleen," and described the pathological condition of that organ as an "épithéliome primitif." Similar cases, amounting in all to 13, have since been described (Collier, Picou and Ramond, Bovaird, Brill, Springthorpe and Stirling, Schlagenhaufer, and Marchand, and others). Gaucher regarded his case as identical clinically with "splénomégalie primitive," which, as we have seen, is the term used by some French authors to describe splenic anaemia; but Brill believes that although splenic anaemia and cases of the Gaucher type ("épithéliome primitif") have much in common, they can

yet be distinguished clinically. The features common to both are the splenic enlargement, the occurrence in adult life, the chronicity of the affection, the haemorrhagic tendency and anaemia of the chlorotic type without leucocytosis. He believes, however, that in splenic anaemia the duration of the disease is much shorter,—that anaemia in cases of the Gaucher type is not pronounced and appears late, whereas it is an early and prominent symptom in splenic anaemia. Further, that the cases he describes are characterised by a peculiar tint of skin which is quite different from the pallor of splenic anaemia, that they are less amenable to treatment, and are remarkable for their feeling of comfort and well-being, and by the entire absence of any subjective sign of distress. To these points of distinction it might be added that the liver tends to be larger in cases of the Gaucher type than in ordinary splenic anaemia. It is noteworthy also that cases of "épithéliome primitif" tend to occur in families, affecting different members of one generation; indeed, of the 13 cases on record, 3 only were isolated examples in a family, the other 10 occurring in four families. This peculiarity is not met with, or at all events not to the same extent, in cases of ordinary splenic anaemia. Whilst, for reasons which are more fully given below, we fully recognise that cases of the Gaucher type are distinct pathologically from other cases classed as splenic anaemia, yet we cannot admit that the special features described by Brill are sufficiently distinctive to justify us in placing such cases in a separate clinical class. In the account of the disease which follows, therefore, such cases are included under the general clinical description splenic anaemia, although their morbid anatomy and pathogenesis will be dealt with separately.

Etiology.—Under this head but little is known. The ordinary causes of splenic enlargement such as syphilis, malaria, and alcoholism, do not appear to play any part in the production of the disease.

Age.—It is commonest in early adult life. In a collection of 48 cases the age at which the patient came under observation was as follows:—

Age.	Cases.
Below 10	3
From 10-20	9
„ 20-30	14
„ 30-40	13
„ 40-50	6
Above 50	3
	48

There seems little reason to doubt that the disease may sometimes begin quite early in life, and that a few of the cases are really survivals of the splenic anaemia of infancy. The cases described by Dr. Cowan may perhaps fall into this category.

Sex.—Of the 48 cases above referred to, 30 were in males, 18 in females. Males, therefore, seem to be more commonly affected.

There seems to be a slight tendency for the disease to occur in more than one member of a family. Collections of such "family" cases will be found in Dr. Cowan's and J. P. Simond's papers, most of them being of the Gaucher type. On the other hand, there is no evidence that heredity really plays any part in its production. R. H.

Morbid Anatomy and Pathogenesis.—It will be convenient, in considering this part of the subject, to deal with the ordinary type of splenic anaemia and cases of the Gaucher type ("épithéliome primitif") separately.

(1) **Ordinary Type of Splenic Anaemia.**—There is no doubt that Banti's view regarding the important part played by the spleen in the causation of splenic anaemia, which received support from Senator, Chiari, and others, has induced many subsequent workers to neglect the search for a more satisfactory etiological factor. This consideration will be fully discussed on p. 764, but it must be borne in mind throughout the following description of the morbid anatomy and histology.

Gretsel's case of splenic anaemia, the microscopic features of which were described by Cohnheim in 1866, belonged to the infantile type, and, therefore, although of historic interest as the first case to which the name splenic anaemia was applied, does not concern us here. Banti, in 1882, was the first to give a systematic account of the histology of adult splenic anaemia. Apart from the hepatic condition, the morbid changes met with presented no essential difference from those found by him in the syndrom "Splenomegaly with Cirrhosis of the Liver" recorded in 1894, and again more fully in 1898. This latter description will be closely followed here, after which the additions made by recent authors to our knowledge of the pathology will be dealt with.

The *spleen* is greatly enlarged, preserves its normal form, and may attain a weight of 2-3 pounds, though even greater weights have been recorded. The capsule is thickened and presents patches of perisplenitis, but adhesions to neighbouring organs are not usual. On section the splenic substance is tough, and dark red in colour. Small hard white nodules representing sclerosed Malpighian bodies are scattered throughout.

Microscopically the great thickening of the trabeculae passing from the capsule to the interior is a prominent feature (*vide* Fig. 27). Some of the lymphoid nodes appear quite healthy, but the great majority shew sclerotic changes proceeding from the sheath of the follicular artery, and have on this account lost their normal appearance. These nodes may be completely converted into fibrous tissue, but it is always possible to demonstrate that the fibrosis extends from the periarterial sheaths.

Banti has also noted the presence in many Malpighian bodies of irregularly shaped hyaline clumps staining deeply with eosin, and in such cases there are generally in the neighbourhood of these masses epithelioid cells undergoing a hyaline necrosis. The follicular artery may also contain a hyaline thrombus. The venous sinuses of the pulp though not dilated are richly lined with endothelial cells, and many such

lie in the lumen. Mitosis in these endothelial cells was not observed by Banti. Phagocytic cells containing red blood-corpuscles are rare. The reticulum of the pulp shews a very notable thickening and hyaline transformation of its fibres, and the cellular elements enclosed in the meshwork are very few. To this thickening of the reticulum Banti has given the name of fibro-adénie, and he has suggested that it may be due to a secretión from the degenerated cells of the pulp.

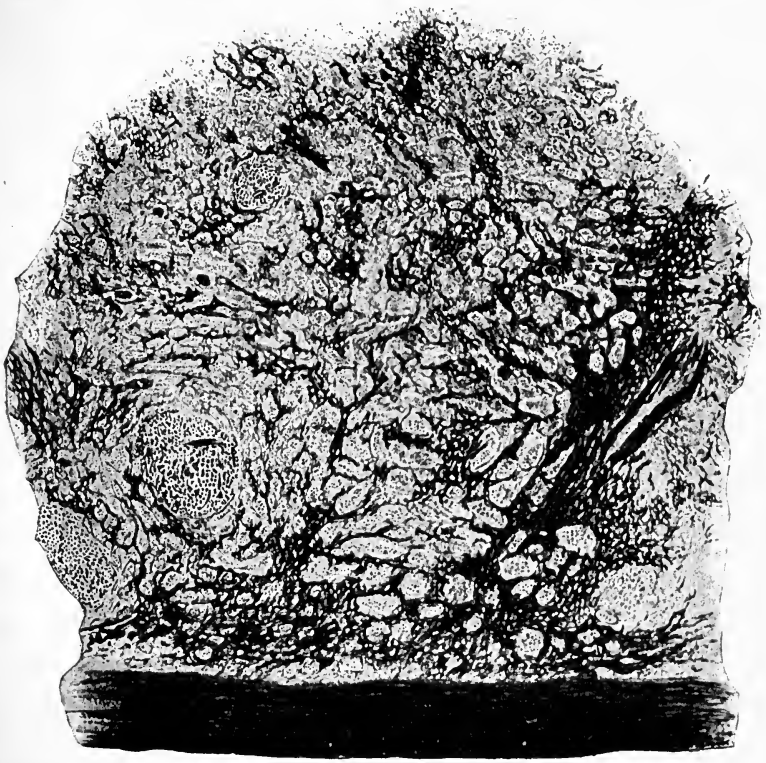

FIG. 27.—Spleen from a case of Banti's disease shewing the thickened capsule, thickened reticulum (Fibro-adénie), and atrophy of the Malpighian bodies. × 60. (Nager and Baumlin.)

To this description of the histological features of the spleen subsequent writers have added but little, although their views as to the etiological factors in particular cases have differed widely.

In one of the early cases reported in this country, Dr. R. T. Williamson observed numerous phagocytic cells containing red blood-corpuscles, but the presence of these cells in the spleen in splenic anaemia has not been subsequently observed. The endothelial proliferation, noted by Banti, was so extensive in their two cases that Harris and Herzog considered it the essential splenic lesion, and suggested that an erythrolytic

enzyme was elaborated by these cells. To this latter point we shall refer below, but it is important to observe here that this endothelial proliferation has frequently been confounded, even by the most recent authors, with the peculiar changes found in the Gaucher type of splenomegaly (*vide* p. 766). This confusion must certainly be considered in any estimation we may form of the views and hypotheses put forward by these writers.

Dock and Warthin carefully examined the spleen in two cases. Nucleated red cells were occasionally found, and also megakaryocytes; no unusual cells were observed in sections stained by triacid and polychrome methylene-blue. The endothelial cells appeared to take part in the formation of the new fibrous tissue of the reticulum. Sclerosis and calcification of the vessels of the pulp were noted in one case. Armstrong observed in his case numerous phagocytic endothelial cells containing blood-pigment. Eosinophil cells in large numbers have been reported by Nager and Baumlin; in their case pulp haemorrhages were numerous. The giant cells noted by them were evidently megakaryocytes, which they apparently confused with the peculiar cells met with in the "Gaucher" type of splenomegaly.

Liver.—In cases presenting the complete syndrom of splenomegaly, anaemia, cirrhosis of the liver and ascites, Banti states that during the transitional stage the size of the liver may be normal, but that in the acute stage a great diminution in its size occurs. Its surface is granular, and, macroscopically at least, it has all the features of portal cirrhosis (Laennec). Microscopically, however, the cirrhotic process is never so extensive as in alcoholic cases.

Changes in the liver are not confined to those cases presenting the complete Banti syndrom. Even in splenic anaemia without any macroscopical evidence of cirrhosis, Banti admits that a slight hyperplasia of the interlobular connective-tissue occurs. Indeed, it seems probable from subsequent work that the condition of the liver will not enable us to differentiate between splenic anaemia and Banti's disease. Dock and Warthin and Chiari shewed that cases presenting the symptoms of splenic anaemia during life, may at the necropsy be characterised by decided cirrhotic changes in the liver, thus forming a transitional stage to the Laennec type of portal cirrhosis postulated by Banti in the final stage of the disease described by him. There is no doubt, however, that the condition of the liver is the most variable factor in the syndrom.

Portal, Splenic, and Mesenteric Veins.—The condition of these vessels is a point of great importance in the pathogenesis of splenic anaemia and Banti's disease. In the latter condition, Banti observed that the portal vein and its branches were dilated during the ascitic stage but not in the transitional stage. Atheromatous and sclerotic plaques were generally present in the splenic and portal veins during the transitional period, and the other branches, such as the mesenteric veins, became similarly affected later. It is unfortunate that many observers have omitted at the autopsies to investigate the condition of the portal vein and its tribu-

taries. As will be indicated below, evidence of long-standing thrombotic changes in these vessels may furnish an important clue to the etiology. Dock and Warthin observed stenosis and calcification of the portal vein in two cases of splenic anaemia, the walls of the splenic and mesenteric veins being also greatly thickened. Edens, Nancrede, and others have reported similar changes in these vessels.

Lymphatic Glands.—Banti found in the syndrom bearing his name that the lymph glands were not enlarged and appeared quite healthy. He alleged that in some reported cases of splenic anaemia the lymphatic glands were hypertrophied, a condition which was never found in the Banti syndrom. Subsequent observers have not confirmed this statement. Neither in splenic anaemia nor in Banti's disease have the lymphatic glands ever shewn hypertrophy. In the cases of Dock and Warthin and of Stengel the lymphatic glands of the mesentery were atrophied, and presented areas of hyaline and calcareous change. These authors found a notable hyperplasia of haemolymph glands lying along the thoracic aorta and in the retroperitoneal region. Enormous numbers of cells containing red blood-corpuscles and blood-pigment were present in these glands, and in view of the fibrosis which involved the loss of the haemolytic function of the spleen, they concluded that this hyperplasia of the haemolymph nodes was compensatory.

Bone-marrow.—Little attention has been paid to the condition of the bone-marrow in cases of splenic anaemia and Banti's disease. Banti noted that the marrow presented fetal characters and that nucleated red cells were not numerous. Dr. R. T. Williamson reported large numbers of cells containing red corpuscles similar to those present in the spleen of his case. In Dock and Warthin's cases the marrow was lymphoid in type, nucleated red cells were increased, and phagocytes containing blood-pigment were present. Stengel, on the other hand, in one of his cases found a lymphoid marrow but an absence of normoblasts.

Gastro-intestinal Tract.—In the light of the frequency of gastro-intestinal disturbances in the course of splenic anaemia and Banti's disease, the absence of severe pathological lesions affecting the stomach and intestines is remarkable. Thickening of the intestinal wall and opacity of the peritoneal coat were noted by Banti, but in the third or ascitic stage only. Hedenius attaches great importance, from the pathogenetic point of view, to the presence in his case of a localised thickening of the intestinal wall at the ileo-caecal junction; the ileo-caecal valve was considerably narrowed, and the mesentery at this point was much thickened, the vessels being embedded in firm fibrous tissue; the subserous and muscular layers contained extensive areas of cellular infiltration in the neighbourhood of the vessels. The intestinal mucosa has generally been reported as atrophic. Considerable importance must be attached to the frequent occurrence of oesophageal and haemorrhoidal varices. Rupture of a cardiac varix has not infrequently been the immediate cause of a fatal issue (Senator, Schlichthorst, von Starck, Dock and Warthin).

Pancreas.—Dock and Warthin observed dilatation of the pancreatic veins and thickening of their walls. A moderate degree of sclerosis of the organ was noted by Stengel and by Dr. Stanley. Phleboliths were found by Simonds.

Kidneys.—Very little information as to the condition of these organs is available; they have generally been found to shew a moderate degree of fibrosis. Hyaline and calcareous changes in the glomeruli were noted in one case (Dock and Warthin).

Suprarenals.—In one case Dr. Stanley found fatty change, and in another case extreme atrophy. Some importance must be attached to their condition on account of the peculiar brownish pigmentation of the skin observed in many cases of splenic anaemia (Osler), although the administration of arsenic may play a part in its causation in some instances.

Pathogenesis.—For many years discussion has centred round the question whether splenic anaemia and Banti's disease should be regarded as definite pathological entities or as mere symptom-groups possessing a varied etiology. The following is a brief summary of the views that have been held on this subject and the criticisms that have been passed upon them. From the accumulation of cases in recent years and their more careful study, it is now possible to take a more comprehensive survey of the whole question than could be done some years ago. Banti based his opinion that the spleen is primarily responsible for the morbid phenomena on the following considerations:—In the first place, the splenomegaly always preceded the anaemia, whilst the hepatic changes appeared last of all; secondly, the changes found in the spleen (fibro-adénie) appeared to him to be peculiar to this disease; lastly, the remarkable success of splenectomy undoubtedly suggested that the diseased and enlarged spleen played the chief part in the causation of the disease. He believed that toxic substances elaborated in the spleen produced anaemia and, at a later stage, endophlebitis of the splenic vein and hyperplasia of the connective tissue of the liver. That some poison of intestinal origin might be a factor in producing the hepatic changes was considered by him highly improbable, on the ground that whereas hepatic cirrhosis due to digestive disturbances was considered to shew enlargement which passed into the atrophic stage only after many years, in Banti's symptom-group the liver is reduced to a state of so-called complete atrophy in the course of a few months. From careful examination of the recorded cases it is quite clear that the stages described by Banti are highly artificial, and that probably no two cases run a similar course. The early appearance of the splenomegaly, however, has been attested by numerous observers, and this has been a stumbling-block to those critics who maintain that a cirrhosis of the liver is the cause both of the splenomegaly and the anaemia, or, at least, that some toxic agent affects the liver and spleen simultaneously. Now, there is no doubt that the splenomegaly which occurs in 50-80 per cent of all cases (Klopstock) of cirrhosis of the liver is not due simply to stasis in the portal circulation, as it appears

before stasis is established (Oestreich). Further, the histology of the spleen in hepatic cirrhosis differs considerably from that found in simple stasis. In cirrhosis there is, as a rule, hyperplasia of the pulp, but in some cases there may be very considerable fibrosis of the connective-tissue framework of the organ. Very large spleens, such as have been reported in Banti's disease, are rare in portal cirrhosis of the liver, but it may quite reasonably be supposed that in certain circumstances the unknown toxic agent responsible for the hepatic changes may at the same time induce a greater reaction on the part of the spleen than usually occurs.

Apart from the question of splenomegaly, the liability to gastro-intestinal haemorrhages common to Banti's disease and to hepatic cirrhosis certainly suggests a close relationship between these diseases.

We have next to consider whether the histological changes in the spleen which were so minutely detailed by Banti are, as he contended, peculiar to this disease. As already mentioned, subsequent writers have described very similar changes without, however, maintaining that these changes were, so to speak, pathognomonic, and might not occur as the result of a number of morbid processes. The lesions may, indeed, be fairly described as those common to the leucopenic splenomegalies of non-parasitic origin. Marchand found these changes in a case which was in all probability of syphilitic nature, and put forward the view that many cases of so-called Banti's disease may be due to permanence of a congenital syphilitic splenomegaly. Dr. Coupland's and Hochhaus' cases are also interesting in this connexion. Chiari, while admitting that syphilis gives rise to this syndrom, believed that cases of luetic origin should be removed from the category of Banti's disease. Gout (v. Jaksch), chronic malaria (Cohen and Rosenberger, Osler, Stengel), kala azar (Marchand and Ledingham), may also be associated clinically with the symptom-group of splenic anaemia. Moreover, the influence of thrombosis of the portal vein and its tributaries has not been sufficiently realised as a causative factor in the etiology. It is certainly suggestive that many cases (Carr, Armstrong, Barr, Harris and Herzog, Fichtner) shewing symptoms of splenic anaemia or Banti's disease have presented a history of severe abdominal injury; for thrombosis of the portal vein with consequent splenomegaly, anaemia, and moderate cirrhosis of the liver has been proved on several occasions to follow injury (Heller, Ponfick, Saxer (51), and Schmorl). A swelling of the spleen has, indeed, been noted within a few weeks of the occurrence of an abdominal injury. In Heller's case of traumatic portal thrombosis the wall of the vessel presented on section more or less extensive ruptures of the elastic layer. This layer was also the one chiefly affected in Edens' case, although there was no definite history of any abdominal injury. The patient had been a policeman, however, and in this capacity may unwittingly have received injury. It is important to observe that in the cases of Saxer (51), Heller, and Schmorl, death took place eight years, two years, and six months respectively after the injury. Baumgarten has also recently

reported a case shewing Banti's syndrom, associated with permanent patency of the umbilical vein.

Several cases also have been found to date their illness from a protracted and difficult pregnancy (59, 65), and enteric fever has also figured in the history of one or two cases. There is no doubt that portal thrombosis of long standing, reported not infrequently in autopsies of cases of Banti's disease and splenic anaemia (22, 31, 62), may be the result of an earlier pylethrombosis. Banti and his present supporters maintain that the success of splenectomy is a strong argument in favour of the view that the spleen is primarily at fault. This does not necessarily follow. It may well be, as some critics have suggested, that the improvement in well-being is due to the removal of an excessively heavy and mechanically troublesome body from the abdomen, and partly to the collateral circulation artificially set up. Cirrhosis of the liver has, it is alleged, been arrested by splenectomy, but post-mortem evidence only can be accepted as proof of this. Moreover, the subsequent history of many of these spleenless patients has not been reported. It is improbable, as Wentworth points out, that a fibrotic spleen would produce toxins. Sippy's experimental results in rabbits, with the extract of spleen from a case of splenic anaemia, are quite inconclusive; the death of two rabbits within twenty-four hours after an intravenous injection of 2 c.c. of the splenic extract cannot be taken as even probable evidence of "an abnormal toxic substance of some nature present in the spleen." The metabolism experiments of Umber before and after splenectomy require further confirmation. In any case, the return to normal conditions of metabolism after splenectomy does not necessarily imply that the spleen had been acting as a toxic focus.

Harris and Herzog's hypothesis that the proliferating endothelial cells of the splenic sinuses secrete an erythrolytic enzyme whereby an excessive destruction of red cells is brought about has not sufficient histological evidence to recommend it. Stengel, indeed, came to the directly opposite conclusion that the normal haemolytic function of the spleen was lost, and that the haemolymph glands were hyperplastic in consequence.

The anomalous cases of Banti's disease reported by Stengel, Borissowa, and Swart will be considered in the section on the Gaucher type of splenomegaly.

In conclusion, it is highly important that the previous histories of cases should be more thoroughly investigated, especially as regards injury and intestinal disorders, and that examination of the portal vein and its branches should never be omitted at autopsy.

(2) **Splenomegaly of the Gaucher Type.**—The splenomegaly of the type first described by Gaucher in 1882 is characterised by an absolutely unique histology, and on this ground alone must be set apart from all other splenomegalies hitherto recorded. Thirteen cases occurring in seven families have been reported up to 1908; but of these 13, 8 only have been confirmed by histological investigation. Dr. W. Collier

of Oxford, and Professor Marchand of Leipzig, have most kindly sent me pathological material from their cases.

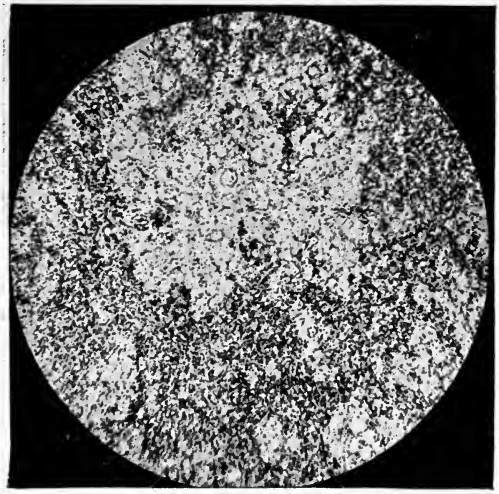

FIG. 28.—Spleen from a case of the Gaucher type of splenomegaly shewing the areas of clear glassy cells. × 50.

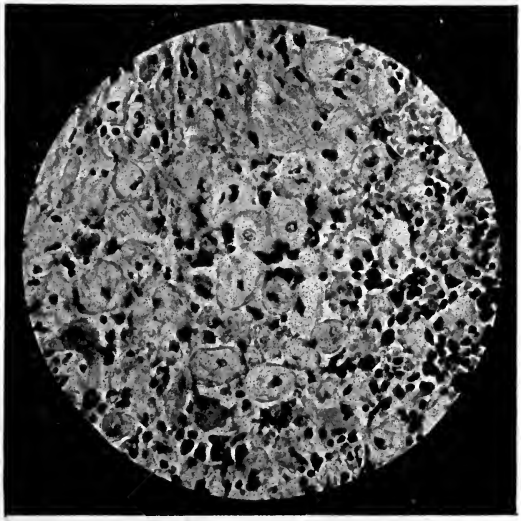

FIG. 29.—Bone-marrow of Gaucher type shewing the characteristic cells with small deeply-stained nuclei. × 250.

The *spleen* retains its usual form but is enormously enlarged, the average weight of 7 adult cases being ten pounds (a little over $4\frac{1}{2}$ kilos).

On section the splenic substance presents a reddish-grey appearance, with numerous whitish points and streaks scattered throughout.

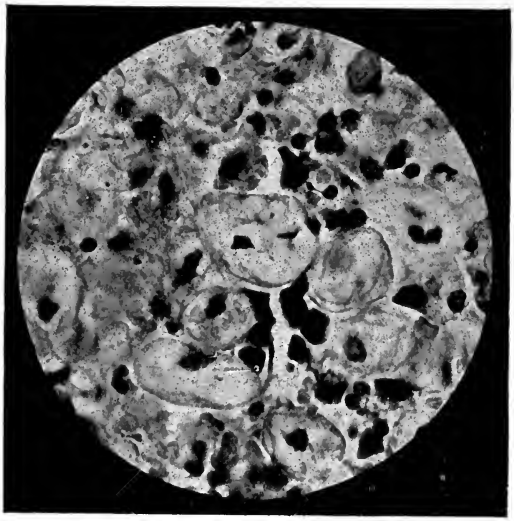

FIG. 30.—Portion of bone-marrow of Gaucher type shewing the Gaucher cells. × 500.

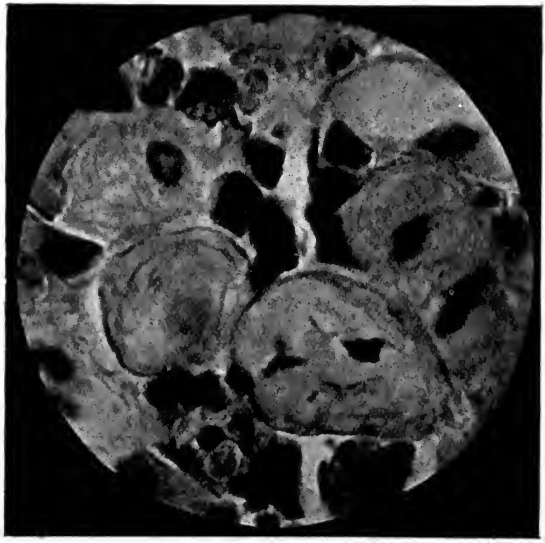

FIG. 31.—Bone-marrow of Gaucher type shewing the Gaucher cells. × 1000.

Microscopically the Malpighian bodies are few in number, or may be entirely absent, the essential feature being the transformation of the

splenic parenchyma into alveolarly arranged spaces filled with large cells possessing certain peculiar morphological characters. A zone of fine fibres of connective tissue separates these spaces from the venous capillaries. The cells which lie loosely within these spaces are very commonly polyhedral, and vary in size from 20 μ to 40 μ. The cytoplasm is rich in amount, and has a peculiar glancing homogeneous appearance almost suggesting a crystalline structure. A fine granular striation can generally be demonstrated in the cytoplasm, which, however, is very frequently vacuolated, and in sections stains very feebly. The nucleus is small in comparison with the cytoplasm; it often occupies an eccentric position in the cell, and stains deeply with nuclear dyes. Many of the cells contain several nuclei distributed irregularly throughout their interior. Mitosis in these cells is very rarely seen.

The *liver* almost invariably presents a considerable enlargement, which is due to the presence in Glisson's capsule of groups of cells similar to those met with in the spleen. They may be so closely packed together in this situation as to resemble a plasmodial mass. The portal vein and intra-alveolar capillaries have also been found to contain these cells in small numbers.

The *lymphatic glands* have not been examined in all the recorded cases, but usually there is a slight enlargement. The pathological changes met with are of the same nature as those in the spleen, but, as a rule, a segment only of the gland is invaded by the peculiar large cells. The supporting tissue of the gland is greatly increased.

Bone-marrow.—The same large cells occur in the marrow, either in isolated masses or scattered about irregularly. No important changes have been found in other organs of the body. It may be noted, however, in view of the peculiar pigmentation of the skin associated with this disease, that large masses of yellow pigment granules have been found in the spleen, lymphatic glands, marrow, and muscular tissue of the uterus (Schlagenhaufer).

The authors who have recorded the cases in question have differed greatly in their conception of the nature of these peculiar cells in the haemopoietic organs. They were regarded by Gaucher as epithelial, and this view was shared by Picou and Ramond, who adopted Birch-Hirschfeld's suggestion that pancreatic "rests" in the spleen might be the starting-point of carcinoma. From examination of Picou and Ramond's specimen, Cornil maintained that the condition was a primary splenic hyperplasia with proliferation of the reticular tissue. He had observed similar cells not infrequently in hyperplastic lymphatic glands. Dr. Collier's case was commented on by Dr. Rolleston; and the Morbid Growths Committee (Targett, Pitt, Shattock) of the Pathological Society of London, to whom the preparations were submitted, referred to the endothelial character of the cells, and also added that similar cell elements were to be found in hyperplastic lymph-glands. Bovaird (1900), Brill (1901), and Brill, Mandlebaum and Libman (1905) apparently shared the endothelial view. The epithelial origin of the cells was rightly considered by Schlagenhaufer

(1907) to be quite untenable. Regarding the endothelial view, he maintained that there was no resemblance between the cells and the endothelia of the vascular sinuses, which could always be distinguished by the presence in them of granules of blood-pigment; and, further, the absence of mitoses in the endothelial cells of the sinuses militated against the view that they gave rise to the large cells in question.

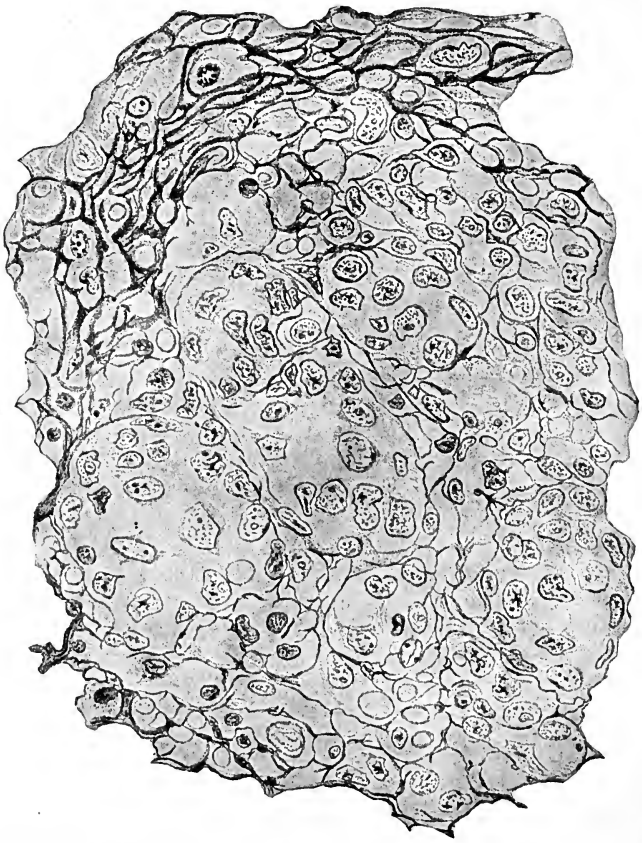

FIG. 32.—Spleen of Borissowa's case shewing proliferation of endothelia. × 750.

Schlagenhaufer agrees with the conclusions of Cornil and the Morbid Growths Committee, and attributes the condition to a proliferation of the reticular tissue in the haemopoietic organs. He regards the disease as a systemic one involving the lymphatic and haemopoietic organs, and due to some unknown, probably toxic, agent. From the existence of tuberculosis in his case (as in Gaucher's) he suggests that possibly the disease is a manifestation of the tubercle bacillus. The frequent association of tuberculosis with lymphadenoma thus forms an interesting parallel,

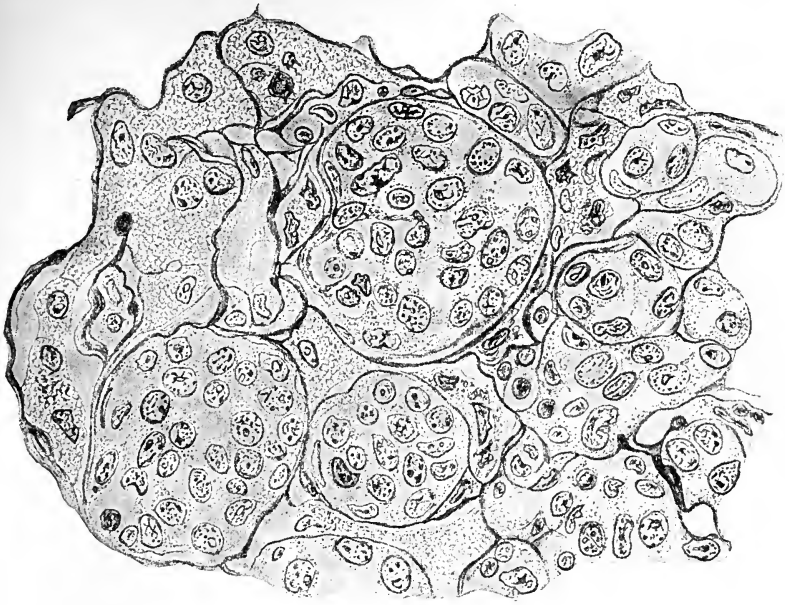

FIG. 33.—Liver of Borissowa's case shewing atrophy of liver cells produced by accumulation of endothelia. × 750.

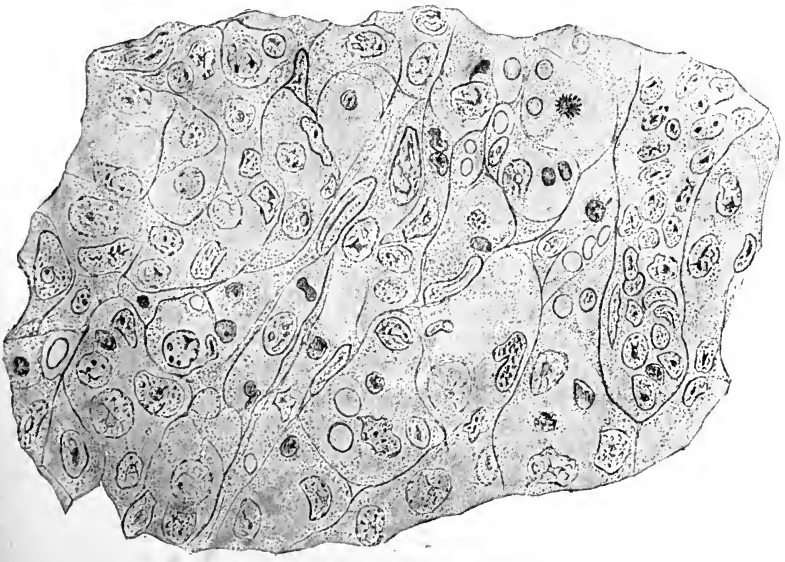

FIG. 34.—Bone-marrow of Borissowa's case shewing proliferation of endothelia. × 750.

especially in connexion with Sternberg's belief that lymphadenoma is a form of tuberculosis (*vide* Vol. IV. Part I. p. 460). Some fresh light has been thrown on the question by Marchand, who examined these peculiar cells in the fresh state at the necropsy. He was particularly impressed by the homogeneous, hyaline, or amyloid-like character of the protoplasm of these cells, and concluded that the enlargement of the cell was due to the deposition in it of some foreign substance. That

FIG. 35.—Spleen from Stengel's case shewing umbilicated projections. × ½.

this latter was not of fatty nature was shewn by the absence of reaction to osmic acid. In a personal communication (March 1908) Professor Marchand tells me that the origin of the large cells from reticular cells or endothelial cells is not improbable. In sections, from bone-marrow especially, he had found so many transitional forms between the large cells and the marrow-cells, that the evolution of the former from leucocytes, pulp-cells, and marrow-cells seemed in the highest degree likely. The nuclei of the large cells resembled exactly those of neighbouring small marrow-cells. He was certainly not of opinion that the condition represented a neoplastic process. The nature of the foreign substance

deposited in these cells must be left for future investigation, and it is to be hoped that the services of the pathological chemist will be called into requisition when these rare cases turn up in future.

The cases of Borissowa, Swart, and Stengel present certain peculiar features which make it impossible to include them in the category either of Banti's disease or the Gaucher type of splenomegaly. The endothelial proliferation which was so noticeable in the cases of Harris and Herzog (*vide* p. 762) was exaggerated in Borissowa's (1903) case, in which there was an enormous accumulation of endothelial-like cells in the venous sinuses of the splenic pulp, the liver capillaries, and the bone-

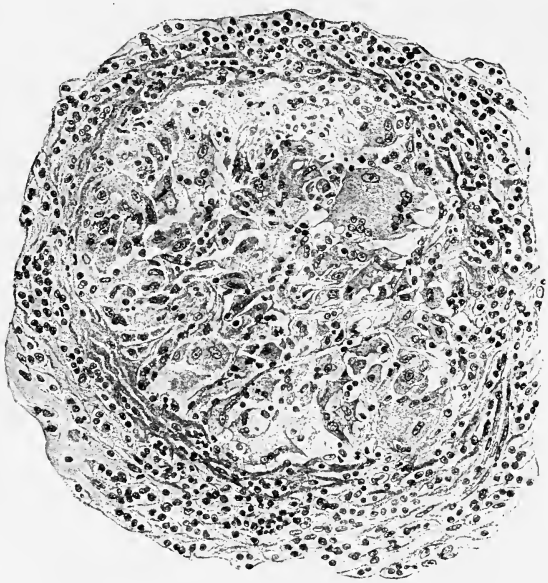

FIG. 36.—Spleen of Stengel's case shewing the clear multinucleated cells. × 142·5.

marrow (*vide* Figs. 32, 33, 34). A considerable atrophy of the liver-cells resulted. The authoress believed that the infiltrating cells resembled those of the Bovaird or Gaucher type, but from her description and drawings there can be no doubt that she was dealing with an entirely different type of cell. The infiltrating cells found in the liver capillaries were considered by her to have been washed into this organ from the spleen. Other features in this case, such as the presence in the blood of a marked leucocytosis and nucleated red cells, justify us placing it at present in a niche by itself.

The four infantile cases of Swart (1905) may, however, be provisionally grouped with Borissowa's case. In Swart's cases there were collections of similar cells in the spleen and liver, but the author was firmly of opinion that they were not of endothelial origin as Borissowa

believed. He considered them to represent primary wandering cells (in Saxer's sense), and thus to be a manifestation of persistent fetal blood-formation in the spleen and liver.

Stengel's case of splenomegaly in a female of twenty-one years is unique in that the surface of the spleen, removed by operation, presented numerous umbilicated projections resembling secondary growths (*vide* Fig. 35). In cross section these masses were seen not to be separate new growths, but projecting parts of a large invading mass occupying the greater part of the organ. Microscopically, alveolar spaces were found containing large clear cells with pale nuclei and also giant cells. Vesicular nuclei were frequent. The clear glistening appearance of the protoplasm is of great interest, but from the drawings and general description it is impossible to class this case in the Gaucher category. The condition of the other organs could not be investigated, as the patient survived the splenectomy. Stengel's own opinion was, that his case and all cases of the Gaucher type represented primary splenic neoplasms.

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CLINICAL PICTURE.—For reasons already stated, it has been considered best to describe the symptomatology of cases of ordinary splenic anaemia and those of the Gaucher type together.

The Symptoms, which come on gradually, fall into three groups: (1) *Those which are the result of anaemia*, such as loss of strength, palpitation, breathlessness on exertion, and, in the more severe cases, oedema of the feet; (2) *those which are the direct result of the splenic tumour*, such as a feeling of weight, distension, or dragging in the left side of the abdomen, with sometimes the addition of pain. These may be the first symptoms of which the patient complains; (3) *haemorrhages from mucous membranes*; of these, epistaxis is perhaps the commonest and earliest met with. Next in frequency is haemorrhage from the alimentary tract, haematemesis or melaena, or both. Gastric haemorrhage may be severe and frequently repeated, and is sometimes fatal. It may lead to a mistaken diagnosis of gastric ulcer (*vide* p. 776). Haemoptysis, oozing from the gums, and haematuria and menorrhagia occur more rarely, and in severe cases petechial haemorrhages into the skin may be seen.

Signs.—The general nutrition of the patient is generally well maintained except in the final stages. The complexion is usually pale, sometimes distinctly chlorotic, and occasionally the conjunctivae are slightly jaundiced. In some cases pigmentation of the skin (melanodermia) is observed; this may perhaps be the result of the prolonged administration of arsenic, although it has been noticed to disappear after splenectomy. Haemic murmurs may be audible over the heart, the cavities of which may be somewhat dilated.

The *spleen* is usually greatly enlarged, reaching down to or beyond the umbilicus. It is smooth, firm, rarely tender, and a bruit, probably

of venous origin, can sometimes be heard over it (Sippy, Rolleston). The superficial lymphatic glands are not enlarged, a point of considerable importance in diagnosis.

The condition of the *liver* is variable; as a rule it is not appreciably enlarged, but in some cases, especially it would seem in those of the Gaucher type, a considerable increase in size is found.

Ascites may occur even in the absence of hepatic cirrhosis, possibly as a result of direct irritation of the peritoneum by the splenic tumour, and in the later stages when cirrhosis is present it may be a prominent feature.

The *urine* is usually normal, but it may be scanty and high-coloured in the later stages.

The temperature may be normal throughout, but irregular pyrexia of some days' duration is not infrequently met with in the course of the disease.

The Blood.—The blood changes may be summed up in the statement that there is a reduction in the number of red cells, a relatively greater reduction in the amount of haemoglobin, and a diminution of the leucocytes.

The reduction of red cells is not often extreme, counts between 3 and 4 million being most commonly met with. It is rare for the number to fall below 2,000,000. In some cases the number of red cells at the time of observation has been normal. Poikilocytosis and polychromatophilia are exceptional, and only occur when the oligocythaemia is extreme. Nucleated red cells are not often met with, and, when they do occur in severe cases, normoblasts always predominate over megaloblasts; this may be of diagnostic importance. The haemoglobin is usually reduced in a greater degree than the red cells, so that the colour-index is below normal, but the reduction is not usually so great as in chlorosis. In the later stages of the disease, when the number of red cells is greatly reduced, the colour-index may rise to normal, or above it.

The leucocyte-count appears to vary a good deal, but leucopenia is the rule, counts between 2000 and 4000 being commonly met with. The differential count is also inconstant, but when the leucopenia is considerable the reduction seems to take place chiefly at the expense of the polynuclear cells, so that a relative lymphocytosis results. In advanced cases a small number of myelocytes may be met with, and in some instances the presence of as many as 5 per cent of mast-cells has been described (Da Costa). In two cases recorded by Dr. Cowan there were present a number of atypical cells of the lymphocyte class, such as are met with in the anaemias of infancy.

There is certainly nothing absolutely characteristic about the blood picture in splenic anaemia; since chronic enlargement of the spleen from any cause (for example, malaria, tropical splenomegaly, lymphadenoma), combined with secondary anaemia, may give similar appearances, including leucopenia with relative lymphocytosis.

Diagnosis.—The chief features which distinguish splenic anaemia

from other conditions which simulate it are: (1) The extremely prolonged course of the disease; (2) notable enlargement of the spleen for which no cause can be found; (3) the absence of a leucocytosis and of glandular enlargement; (4) the tendency to haemorrhages.

Myeloid leukaemia may resemble it very closely in general clinical characters, but can usually be at once distinguished by examination of the blood. Occasionally, however, in cases of myeloid leukaemia the characteristic blood-changes are temporarily in abeyance, and in such an event it might be impossible to distinguish it from splenic anaemia. The point is one of importance, as the operation of splenectomy seems to be invariably fatal in cases of leukaemia, whereas in splenic anaemia it is perhaps the most effective method of treatment. In a doubtful case, therefore, splenectomy should never be recommended until the patient has been under observation for a considerable period, during which the blood has been repeatedly examined. Splenic anaemia can be easily diagnosed from *leukanaemia* (*vide* p. 812) by the characters of the blood; normoblasts and myelocytes, which are prominent features in the film from a case of leukanaemia, being absent or very scanty in splenic anaemia. The course of leukanaemia, too, is much less chronic than that of splenic anaemia.

From *pernicious anaemia* the disease under consideration is distinguished by the relatively much greater enlargement of the spleen in splenic anaemia, by the low colour-index, and by the rule that even when nucleated red cells are present their type is not predominatingly megaloblastic.

Absence of glandular enlargement serves at once to differentiate splenic anaemia from ordinary cases of *lymphadenoma*; but assuming that a purely splenic form of lymphadenoma exists, a question, however, which is still undecided, it would be impossible to distinguish it during life from a case of splenic anaemia.

From chronic *malarial splenomegaly* splenic anaemia can be diagnosed by the history and by the absence of parasites in the blood.

From *syphilitic enlargement* of the spleen, in consequence of the presence of gumma or waxy disease, or both, accompanied by secondary anaemia, it may be impossible to diagnose splenic anaemia except by observing the effect of a course of antisyphilitic treatment. In a case recorded by Dr. Coupland, the spleen of a woman who presented the symptoms of splenic anaemia was removed with great improvement in the general condition. Two years later, however, she succumbed with haematemesis and ascites, and the autopsy shewed syphilitic disease of the liver.

Cases of splenic anaemia, in which haematemesis is frequent and severe, and in which the enlargement of the spleen is not so pronounced as usual, may simulate *chronic gastric ulcer* rather closely. In the case of a woman twenty-eight years of age who had been admitted to the London Hospital thirteen times in fifteen years for severe haematemesis this mistake was made for a time, although some degree of splenic enlargement had been noted at the period of her second admission. When, however,

the possibility of such an error is borne in mind, consideration of the whole course of the case, the presence of an enlarged spleen, and the occurrence of haemorrhage from other mucous membranes, especially epistaxis, will usually lead to a correct conclusion.

Thrombosis of the portal vein, when it does not lead to a rapid termination, may, from the presence of splenomegaly and periodic haemorrhages from the gastro-intestinal tract, closely simulate splenic anaemia.

In its later stages, when ascites has supervened, splenic anaemia may present a close resemblance to *hepatic cirrhosis*, especially as haematemesis may occur in both conditions. In alcoholic cirrhosis, however, the spleen is relatively not so much enlarged as in splenic anaemia, in which, as a rule, the splenic enlargement has for long preceded that of the liver. Some cases of metasplenomegalic hypertrophic biliary cirrhosis, in which the spleen is enlarged before the liver, may imitate closely the final stages of splenic anaemia (Gilbert and Lereboullet). As already pointed out, also, the manifestations in delayed inherited syphilis may be almost indistinguishable from the ascitic stage of splenic anaemia as described by Banti. Several such cases have been put on record by Marchand (38).

The combination of an enlarged cirrhotic liver, splenic enlargement, and pigmentation of the skin which constitute *haemochromatosis*, may simulate splenic anaemia rather closely, especially as ascites and haemorrhages may occur in its later stages. In haemochromatosis, however, anaemia is not a marked feature, and diabetes (diabète bronzé) is a terminal and distinguishing feature.

Splenic anaemia resembles kala azar in exhibiting marked leucopenia, but differs from it in the absence of Leishman-Donovan bodies in the splenic blood.

Course and Prognosis.—As a rule, the disease runs a prolonged course, cases in which splenic enlargement had been present for twelve or more years being not uncommon. The duration seems to be specially protracted in cases of the Gaucher type; in Gaucher's own case, for instance, the spleen had been enlarged for twenty-five years before death. Death may occur as the result of intercurrent disease or from a profuse haemorrhage. Banti (3) in 1894 described cases with a terminal cirrhosis of the liver with ascites, and the name Banti's disease is now frequently applied to cases which exhibit these symptoms with splenomegaly. Whether this is the natural mode of termination of all cases of splenic anaemia which run their full course is still an open question, but there can be no doubt that in its earlier stages Banti's disease is indistinguishable clinically from ordinary splenic anaemia. On the other hand, there can be little doubt that the Banti "syndrom" may result from several kinds of pathological processes of which splenic anaemia is only one; such, for example, as thrombosis of the splenic or portal vein, or the late form of congenital syphilitic cirrhosis. This point, however, has been more fully referred to under the head of Pathology.

Treatment.—(1) *Hygienic.*—Rest, fresh air, sunshine, and the administration of abundant and nutritious food are all of the greatest value, and

sometimes effect a striking improvement in the patient's general condition. If the patient is able to go about it may be advisable to support the spleen with a suitable belt

(2) *Medicinal.*—No drug has any specific effect on the disease, but the administration of iron and arsenic is sometimes helpful, although these drugs are probably of less value than in most other forms of anaemia. Haemorrhage must be treated on general principles.

(3) *Treatment by X-Rays.*—The application of *x*-rays to the spleen as in myeloid leukaemia has been tried, and some successful results recorded (Einhorn). In two cases in which I have tried this treatment the spleen became somewhat smaller and harder with coincident improvement in the general condition, but although the application of the rays was continued for several months, in neither case could the disease be described as really arrested.

(4) *Surgical Treatment.* — There is now abundant evidence that splenectomy can completely cure the disease, and as other measures are powerless to do more than retard its progress, operation should be seriously considered in every case in which the patient's condition offers a fair chance of success. In 1906 Armstrong published a collection of the results of the operation up to that time in 32 cases. In 22 there was complete recovery (69 per cent); in 9 the operation proved fatal (usually from haemorrhage or shock); in 1 the patient was unrelieved. If the patient survives operation complete restoration to health can usually be promised; the anaemia disappears, the haemorrhages cease, and the liver diminishes if it be enlarged. A severe degree of anaemia seems to add greatly to the risk of splenectomy, and the consideration of operation should therefore not be postponed too long.

In the later stages of the disease, when the liver exhibits marked cirrhosis and ascites is present, it may be advisable to combine the Talma or Drummond-Morison operation with splenectomy. In a case reported by Tansini this was done with complete success.

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SPLENIC ANAEMIA OF INFANCY

History and Nomenclature.—Attention was first directed to anaemia associated with enlargement of the spleen in infancy by Italian writers. Somma in 1884 described a series of such cases under the name "anemia splenica infantile." He was followed by Di Lorenzo, who first introduced the designation infective in connexion with them, a term which was subsequently adopted by Fede, Cardarelli, and others. Most of these writers regarded the disease as due to bacterial infection, and described different micro-organisms found in the spleen which they believed to be the specific cause. Meanwhile von Jaksch recorded cases of anaemia with splenic enlargement in children, which he considered to be characterised by reduction of red cells and haemoglobin, high and persistent leucocytosis, enlargement of the spleen and sometimes of the lymphatic glands, and to a less extent of the liver. His descriptive title "anaemia pseudoleukaemica infantum," though widely adopted, is

unfortunate, for there can be no doubt that the "anemia splenica infettiva dei bambini" of the Italian writers and the disease described by von Jaksch are really identical, and that the word "pseudoleukaemia" has caused much confusion. For the present, therefore, it would seem best to adhere to the terminology employed by those who first described the disease, and to speak of it simply as the "splenic anaemia of infancy."

Recent writers on the disease are divided into two camps: (1) Those

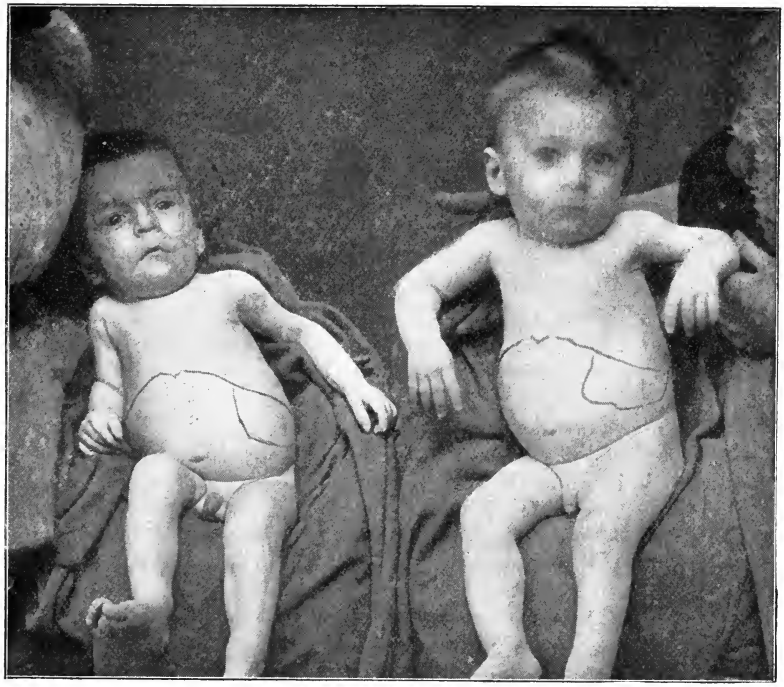

FIG. 37.—Splenic anaemia of infancy affecting twins.

who hold that the splenic anaemia of infancy is merely a severe secondary anaemia, which owes its peculiarities to the fact of its occurrence in early life; (2) those who regard it as a disease *sui generis*. The arguments for and against these two views cannot be considered in detail here, but the balance of evidence is in favour of regarding the disease, for clinical purposes at least, as having a separate existence, and although the ordinary causes of secondary anaemia which are in operation in infancy may be predisposing factors in its causation, yet there is probably concerned in its production some specific, possibly toxic, agency which imparts to the disease its special characters.

Etiology.—Males appear to be slightly more often affected than

females; out of 35 well-marked cases, 21 were in boys and 14 in girls.

Rickets is a very frequent concomitant but may be entirely absent; it is probably the result of the same factors which produce the anaemia rather than itself a cause of the latter. Congenital syphilis certainly seems to play a part in some cases; thus, out of 42 well-marked examples of the disease it was certainly present in 6, in 15 it was doubtful, whilst in 21 (or 50 per cent) it could be excluded with a great degree of certainty.

The disease is not specially apt to affect several children in one family, but twins seem to be peculiarly liable to it. I have seen this happen in five instances (one of which is shewn in Fig. 37), and others have drawn attention to it also. A liability to tuberculosis is common in the clinical history of these cases, but it is doubtful if it is found with a frequency which can be described as greater than is met with in the ordinary run of hospital patients.

Of other possible etiological factors mention must be made of too prolonged breast-feeding. The association of this factor with tumefaction of the spleen in infants was pointed out as long ago as 1849 by Battersby, and is probably the cause of the unusual frequency of splenic anaemia amongst the children of Polish Jews in the East End of London—a frequency which has been pointed out both by myself and by Dr. Clive Riviere—for prolonged suckling is well known to be a habit of that race.

Much importance has been attached by some writers to gastro-enteritis as an etiological factor in the production of the splenic anaemia of infancy. It is true that a history of chronic diarrhoea can often be obtained in such cases, but it must be remembered that chronic diarrhoea is of very frequent occurrence in all delicate and rickety infants, whilst it is only in a small number of such cases that splenic anaemia appears.

R. H.

Morbid Anatomy and Pathogenesis.—*The spleen* may be enlarged to eight or ten times the normal size in children between the first and second years. The average weight of 6 cases recorded by Cohen was 93 grams with extremes of 1 ounce, 3 drams (40 grams), and nearly 6 ounces (170 grams). Most observers are agreed that the capsule and trabecular septa are thickened as in adult splenic anaemia. This thickening may also extend to the reticulum, with the result that the Malpighian bodies are encroached upon and in some cases reduced to mere fibrous nodes (Glockner, Hutchison). In other cases there is no evidence of increase in the interstitial tissue or of thickening of the reticulum (Scott and Telling, Gianturco and Pianese, Hutchison). As a rule the Malpighian bodies are few and of small size (Cohen), but large, well-defined, and even hyperplastic follicles have been reported (Glockner, Fowler, Fede, Audeoud). Regarding the pulp, many authors have been content to note simply a cellular hyperplasia. In some cases the

endothelial cells of the blood-sinuses have been increased (Glockner, Gianturco and Pianese), as in Banti's disease, whilst in others no such increase has been apparent (Hutchison, Scott and Telling). Small lymphomas or areas of round-cell infiltration have been found in the neighbourhood of the capillaries (Cohen, Audeoud). The available data regarding the question of red-cell destruction in the spleen are extremely meagre; in some instances there was no evidence of haemolysis (Glockner, Scott and Telling).

It would be desirable to have more evidence on the question of the resumption by the spleen of its haemopoietic function. No indication of this appeared in the cases of Luzet and of Hutchison, although the former laid great stress on the presence in the liver of erythroblastic foci. In Drs. Scott and Telling's case, however, which was thoroughly examined by modern staining methods, very distinct evidence was obtained of a myeloid transformation of the spleen pulp (*vide* Vol. IV. Part I. p. 437). Numerous indifferent cells (Wolff), or basophil myelocytes (Dominici), neutrophil and eosinophil myelocytes, and nucleated red cells pervaded the pulp, and it was abundantly evident that the spleen was functionally active as a haemopoietic organ. Marked changes like those described by Drs. Scott and Telling, in the spleen, liver, and lymphatic glands (see below), have not been reported by other observers in cases designated as infantile splenic anaemia, and the question whether Drs. Scott and Telling's case may not more properly fall into the category of the so-called leukanaemias will be discussed on p. 784.

Liver.—No constant histological picture is met with in the liver. In two cases reported by Hutchison no changes of any kind were noted. Fatty infiltration may be present in some cases and absent in others. The interstitial connective-tissue of the organ was found increased by Cohnheim (in Gretsel's case), Gianturco and Pianese, Mya and Trambusti, v. Jaksch, and Cohen. Small lymphomas were also noted by v. Jaksch and by Cohen. Luzet, Mya and Trambusti, and Ewing found evidence of a resumption by the liver of its fetal haemopoietic function, but Hutchison and Fowler were unable to demonstrate such erythroblastic foci. The liver in Drs. Scott and Telling's case was distinctly fetal, as evidenced by the large number of indifferent cells and neutrophil and eosinophil myelocytes in the liver capillaries.

The *lymphatic glands* have not been examined in many cases. Occasionally a moderate enlargement has been reported. The supporting tissue of the glands is generally increased in amount, and there may be slight proliferation of the endothelia of the lymph-sinuses (Hutchison). In Drs. Scott and Telling's case the glands presented on section the appearance of red bone-marrow. Numerous giant-cells of megakaryocyte type were present, many of which were acting as phagocytes. The endothelial cells of the sinuses also frequently contained red cells in process of dissolution.

The *thymus* in Drs. Scott and Telling's case did not shew any evidence of myeloid transformation.

Bone-marrow.—Most observers (Hutchison, Ewing, Scott and Telling, etc.) have found evidence of marked cellular activity on the part of the bone-marrow. The formation of red cells appears to be proceeding rapidly.

Little attention has been paid to the condition of the other organs. Some observers have reported catarrh of the intestinal mucosa with enlargement of the Peyer's patches and the solitary follicles. The frequent association of gastro-intestinal disturbance is sufficient to account for such changes.

From the above survey of the morbid anatomy and histology it will be obvious that the splenic anaemia of infancy possesses no *pathological* picture peculiar to itself. The only case in which definite and peculiar lesions were found was that of Drs. Scott and Telling, and it is doubtful whether this case should be placed in the category of infantile splenic anaemia. The number of erythroblasts in the circulating blood was abnormally high (7900 per c.mm., *i.e.* 44 per 100 leucocytes, the usual number being 5 or 6 per 100 leucocytes). Further, the percentage of myelocytes and mast-cells (of each 2·1) though small, undoubtedly suggests a resemblance to the blood-condition in so-called leukanaemia. I have had an opportunity of observing exactly parallel histological changes in the organs of a leukanaemic case, and in those of a leukaemic case which had been under radiotherapeutic treatment. Setting aside Drs. Scott and Telling's case, therefore, it may be said at once that the histological changes differ in no essential particulars from those found in uncomplicated rickets and in congenital syphilis, the two diseases whose influence is so difficult to estimate either as causative or disposing factors in infantile splenic anaemia.

Luzet's erythroblastic foci are well-known features in the liver of congenital syphilis (Erdmann). The perivascular infiltrations in the spleen and the thickening of the adventitia of the small arteries are also found in syphilitic splenomegaly. In many cases, however, syphilis can certainly be excluded, and perhaps in a few rickets also; and to such cases it is impossible, in the present state of our knowledge, to assign any definite cause. A toxaemia of intestinal origin has been suggested by more than one observer as an exciting cause, and it is not unlikely that some light may be thrown on the subject as the result of the increased attention now being paid to the bacteriology of the intestinal tract in children.

Many Italian writers (Somma, Fede, Cardarelli, etc.) have insisted on the infectious nature of the disease, but they have not supplied any bacteriological evidence to substantiate their position.

One feature of the disease, already mentioned (p. 782), deserves special mention from the pathological point of view, viz. the peculiar liability of twins to suffer from it. In this connexion it should be noted that Marchand has recently reported the presence of extreme splenomegaly in male twins, both of whom died a few days after birth. Hydramnios was present in both cases. The mother had three living

female children, but two males had died during the first two days of life. The grandmother had borne five females who survived, and male twins on three occasions, all of whom succumbed shortly after birth. Syphilis could almost certainly be excluded. The blood of both children shewed moderate leucocytosis and enormous numbers of nucleated red cells. In the liver there was very marked evidence of new formation of red cells. The etiology of such cases is at present quite obscure. It is just possible, however, that had these twins survived they might have presented at a somewhat later stage in their life-history the clinical symptoms of infantile splenic anaemia.

Finally, the recent discovery by Nicolle in Tunis of kala azar parasites (Leishmania) in the organs of 3 cases of infantile splenic anaemia, must be mentioned. In 1905, Pianese of Naples had previously reported the presence of similar parasites in 5 cases of infantile anaemia. In tropical countries, therefore, and along the Mediterranean seaboard, the possibility that the parasite of kala azar may be responsible for adult and infantile splenic anaemia must always be remembered.

J. C. G. L.

Symptoms.—The child is usually between ten months and two years old, and the onset of the disease has been gradual, the patient being brought to the doctor because he is pale or "not getting on," or on account of rickets or one of its complications.

The complexion is generally of a waxy yellow tint and the mucous membranes blanched. There is usually a greater or less degree of rickets, and very often the head shews prominent bosses over the frontal and parietal eminences (so-called hot-cross-bun head). There are often loud haemic murmurs over the heart and large veins. On abdominal examination the spleen can easily be felt. It is smooth, hard, and not tender, and may reach down to the iliac crest and as far as, or even beyond, the umbilicus. The liver is also enlarged in most cases, sometimes notably so, and like the spleen feels smooth and firm. The superficial lymphatic glands are sometimes but not always palpable. There is no ascites. Haemorrhages from the mucous membranes, with the exception, perhaps, of epistaxis, never occur, but in severe cases a slight petechial eruption may be noticed, and is always of grave omen. The temperature is frequently irregular. Various complications may be present, bronchitis, bronchopneumonia, diarrhoea, and vomiting being the most frequent.

The Blood.—The red cells are always reduced in number, but rarely to an extreme degree, from two to three millions per c.mm. being the common figure. Poikilocytosis is present in all but the mildest cases, but, as a rule, the size of the cells is affected more than their shape. Nucleated forms are common, as in all severe anaemias in childhood, and may amount to as many as 2500 per c.mm. The majority are normoblastic, their nuclei often exhibiting mitosis, but megaloblasts are also common. Dr. J. S. Fowler found them in 13 out of 20 cases.

The haemoglobin is always reduced, and the colour-index is usually

low, being on the average about 0·45, but in estimating the reduction the low ratio of haemoglobin which is normal in infancy must be taken into account.

Leucocytosis is usually, but not invariably, present, and in a certain number of cases the white cells are actually diminished. An increase, however, is commoner, and may be as high as 50,000 per c.mm., but the tendency is to overestimate it, forgetting that between the ages of one year and eighteen months, at which the majority of these cases occur, the number of leucocytes is normally from 12,000 to 14,000 per c.mm. In some cases the leucocytosis is due to an actual increase in the granular cells, which may depend on an ordinary leucocytosis called out by the existence of some complication, such as bronchopneumonia, although in others no such cause can be discovered. More usually the increase is chiefly to be ascribed to an augmented number of non-granular cells, which tends specially to affect the larger lymphocytes and "transitionals," but every intermediate grade between these and small lymphocytes is met with, so that accurate differential counting is almost impossible. Among the larger lymphocytes a good many may have granules staining with basic dyes, whilst some take on both basic and acid dyes. Myelocytes are usually present, to the extent of almost 2 per cent, but the number may rise as high as 14 per cent. They are often small in size, and exhibit but sparse granulation. Eosinophilia is rare, but these cells vary greatly in number in different cases and at different times; eosinophil myelocytes are very rare. In a few cases the mast-cells are markedly increased. The "heteromorphism" of the leucocytosis is perhaps the most striking feature of this form of anaemia, transitional forms between small and large lymphocytes, between large lymphocytes and myelocytes, between neutrophils and eosinophils being specially common.

To sum up: in a well-marked case of the splenic anaemia of infancy the blood exhibits the features of a chlorotic anaemia along with the presence of a high proportion of nucleated red cells, both normoblasts and megaloblasts, and, usually, a leucocytosis, the latter chiefly affecting the non-granular leucocytes, but shewing a high degree of "heteromorphism," intermediate types of cells of all sorts being met with, the presence of myelocytes also being a constant, although not a striking, feature.

Diagnosis.—In well-marked cases the diagnosis usually presents no difficulty, as splenic anaemia is the only disease associated with such marked tumefaction of the spleen at this time of life; myeloid leukaemia, which most closely resembles it, probably never occurs so early. In a doubtful case the comparatively low degree of leucocytosis and the small percentage of myelocytes in splenic anaemia would be determining features.

Cases of rickets or congenital syphilis accompanied by secondary anaemia and a moderate degree of splenic enlargement may give rise to difficulty, and it may, indeed, be impossible to distinguish such a case from a mild form of splenic anaemia; but the points in favour of the

latter would be the presence of a "heteromorphous" leucocytosis and of normoblasts in the blood film. Fortunately an exact diagnosis in these borderland cases is of no practical importance. (For relation to Ponos see Vol. II. Part II. p. 609.)

Prognosis.—The disease is by no means necessarily fatal, recovery taking place in a fair number of cases. Valuable prognostic indications are furnished by the blood, a marked degree of anaemia and a high and especially a very "heteromorphous" leucocytosis being unfavourable, whilst the number and character of the erythroblasts and the presence of a few myelocytes are of little significance. The presence of a purpuric rash is also of bad omen. On the other hand, the size of the spleen has apparently little influence on the outlook.

Death when it occurs is usually the result of a complication, such as bronchopneumonia or diarrhoea, or of some intercurrent disease such as measles. It is probable that in some cases splenomegaly persists long after the anaemia has been recovered from, whilst other cases may perhaps pass into the splenic anaemia of adult life. Dr. Cowan has recorded 2 cases in which this seemed to take place.

Treatment.—Good hygienic surroundings, including abundance of sunshine and fresh air, are of the first importance. The diet will usually require revision, and should contain plenty of animal ingredients, such as pure milk, yolk of egg, and raw-meat juice or scraped meat. On the other hand, the amount of starchy food must often be cut down. Oat flour is a useful article of diet in these cases, as it is rich in fat, protein, iron, and organic phosphorus; it may be used to thicken some of the milk. Amongst drugs, iron and cod-liver oil are of most service; arsenic is probably of little value. In some cases extract of red marrow has seemed to do good.

The application of the *x*-rays to the spleen deserves a trial in severe cases, but it is certainly not nearly so effective as it is in true leukaemia.

Splenectomy is never justifiable.

Complications must be treated on the usual lines.

R. HUTCHISON.

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LEUKAEMIA

By Prof. Robert Muir, M.D.

Leukaemia or leucocythaemia may be briefly described as a disease in which there is great, and usually permanent, increase in the number of leucocytes in the blood, associated with, and apparently due to, overgrowth of the leucocyte-forming tissues, these being affected in a varying manner in different cases. Further, the leucocytes in the blood are not only increased in number, but, taken as a whole, are altered in character also.

Introductory.—Though conditions which can now be identified as cases of leukaemia had been described before, the definition of the group of symptoms of which it consists dates from the independent and almost simultaneous publications of Hughes Bennett and Virchow on the subject. In October 1845 the former recorded a case which, from the microscopical characters of the blood, he described as one of "suppuration of the blood, with enlargement of the spleen and liver"; and a month later Virchow gave an account, under the title "white blood," of a similar condition in which he noted the association of splenic enlargement, epistaxis, and a peculiar richness of the blood in leucocytes. In both of these cases the important changes were observed after death. Afterwards Bennett gave the name *leucocythaemia* to the disease, whilst Virchow called it

leukaemia. A short time after his first case Virchow observed another in which the leukaemic condition of the blood was associated with enlargement of the lymphatic glands, whilst the spleen was only slightly enlarged; and in subsequent papers he drew a distinction between a *lymphatic* form of the disease in which there is an admixture in the blood of leucocytes from the enlarged lymphatic glands—"lymphaemia," and a *splenic* form in which he believed the excess of leucocytes to be produced in the enlarged spleen—"splenaemia"; the cells in the blood being of smaller size in the former than in the latter variety. Neumann, in 1870, not long after his discovery of nucleated red corpuscles in the bone-marrow, found that this tissue is often profoundly altered in cases of leukaemia, and this change he regarded as primary. After much discussion of Neumann's views a *medullary* form was added. A considerable amount of confusion, however, arose from this classification of cases based on the organs affected, as, according to this nomenclature, most cases were found to be of a mixed kind.

Renewed interest in the subject was aroused by the researches of Ehrlich and others on the characters of the cells in the blood and their reactions to various aniline stains; and much of the work in recent years has been along the same lines. The result has been that the characters of the leucocytes in the blood in leukaemia have been universally accepted as the basis of distinction in different cases. Ehrlich distinguished two types of leukaemia, namely the *medullary*, in which the granular cells are increased, and the *lymphatic*, in which those of the lymphocyte class are increased. Although the two types are not so distinct from each other as he supposed, his classification, nevertheless, is of fundamental importance in relation to the pathology of the disease.

Within recent years special attention has also been directed to the more acute forms of the disease; and, in consequence, cases which formerly would have been overlooked have been identified as leucocythaemia. The extensive haematological work which has been carried on has also demonstrated the occurrence of a considerable proportion of cases in which the blood picture may be called *atypical*; and, although there are still many points in dispute, the different appearances are coming to be explained in accordance with our knowledge of the genetic relationships of the different forms of leucocytes.

The essential feature in leukaemia is the proliferation of cells of the leucocyte class, leading to an excess in the blood. From a more comprehensive standpoint, all conditions in which an excessive proliferation of such cells occurred might be included in one class whether the blood was involved or not. Nevertheless, the blood picture is so important from the clinical point of view that it may be regarded as the differentiating feature; reference will afterwards be made to allied conditions in which leukaemia is not present (*vide* p. 811 *et seq.*).

It is unnecessary to describe the different forms of leucocytes and their characters, as this has been done elsewhere (Vol. I. p. 675); but real knowledge of the varieties of leukaemia depends so much on the genetic

relationships of the different forms of leucocytes to one another that a short preliminary consideration of this subject will facilitate discussion at a later period. Different writers have expressed widely divergent opinions on this subject, but the points of disagreement are now in the main of minor importance. In attempting to formulate a general statement, we must take into consideration the development of the leucocytes in embryonic life, the varieties and seats of proliferation in adult life, the mode in which cells of the leucocyte class react in infections and other conditions, and, lastly, the cells which appear in excess in different cases of leukaemia. From a study of the question from all these points of view, the following general statement may be made. It is generally agreed that all the forms of leucocytes are derived from a primitive non-granular cell with basophil protoplasm, closely similar in appearance to the large lymphocyte. Up to about the third month of intra-uterine life practically all the leucocytes of the human fetus are of this character. From this primitive cell are derived the two great series of leucocytes, namely, the granular and the non-granular. In the case of the former, granules of three kinds, namely eosinophil, neutrophil, and basophil appear in the protoplasm, which becomes rather more abundant and less basophil, whilst certain minor changes may be noted in the nucleus. In the adult the bone-marrow is the chief seat of the proliferation of these granular cells which are accordingly called myelocytes (neutrophil, eosinophil, and basophil respectively). The cells intermediate between the primitive leucocyte and the myelocytes are known as myeloblasts or pro-myelocytes. The myelocytes are the mother cells of the corresponding granular leucocytes, and the process of formation of the latter is practically the same in each case. The granular myelocytes divide by mitosis, giving rise to smaller cells with nuclei which, at first rounded, subsequently become indented, horseshoe-shaped, and then by constriction at places become changed into the typical polymorphous state, the polymorphism being rather more pronounced in the neutrophil leucocytes than in the others. During the process the protoplasm becomes less basophil, till in the polymorphonuclear cell it is practically uncoloured by basic aniline stains. In the case of the neutrophil class, and also sometimes in the eosinophil, the granules undergo a change which may be called a ripening, as shewn by increase in the oxyphil reaction. This is well seen in myelocytes stained by Jenner's stain, the granules in the younger forms being somewhat violet, whilst in the polymorphonuclear leucocyte they are red. The granular leucocytes as seen in the blood may thus be regarded as the terminal and most highly differentiated cells of this series, and it is to be noted that the mother cells, the myelocytes, do not appear in the circulation in normal conditions.

From the primitive lymphocyte or lymphoid cell is also derived the second series of cells which remain granule-free—the lymphocytes of different sizes; these multiply by mitosis in the germ-centres of the lymphatic glands, spleen, etc., and also in the bone-marrow, giving rise

to smaller cells with nuclei rich in chromatin and strongly basophil protoplasm. The small lymphocyte of the blood is in its characters furthest removed from the dividing lymphocyte of the germ-centres, and is thus in a sense more differentiated. It is also seen in long-standing collections of lymphocytes in the tissues, which appear to be in a passive condition. On the other hand there is evidence that it can increase in size again and become a large lymphocyte. The distribution of the lymphocyte is very widespread, in fact it may be said to occur in practically all the tissues. The mononuclear leucocyte of the blood or hyaline cell (splenocyte of Pappenheim) with feebly basophil protoplasm is also regarded as a derivative from the lymphocyte, and from this again the so-called transitional cell is generally believed to take origin. Some observers (Naegeli, Schridde) believe that the primitive cells of the granular series (myeloblasts) can be distinguished from those of the lymphocyte series (lymphoblasts) by the character of the nuclei, and by the lymphoblast containing the so-called azur granules which can be demonstrated by Giemsa's stain; others, however, deny this. The point is of relatively minor importance, as it is merely a question as to the stage at which characteristic differentiation appears.

As already stated, practically all observers recognise the important distinction into the two great groups, but opinion is divided as to how far transitions may take place from the one to the other. Against Ehrlich's original view that the cells of the myeloid and lymphoid series were quite distinct, certain objections have been brought. Thus, it is argued that cells intermediate between lymphocytes and myelocytes may be found, for example, in normal marrow, and that in cases of leukaemia transitions are met with. Again, it has been found that as a result of infections in animals a myeloid transformation may occur in certain lymphoid tissues, such as the spleen (Dominici). Many haematologists appear to lay too much emphasis on merely histological points, and fail to take a broad view of the question. Consideration of the cells found normally in active division shews that these are the lymphocytes in the germ-centres, and the myelocytes (especially the neutrophil) in the bone-marrow. The proliferation of neutrophil myelocytes with well-formed granules in cases of leucocytosis is a very striking feature, and I have failed to find that the supply of these cells is kept up by transition from non-granular cells. Evidence is wanting that the reactions of the different granular cells to chemiotactic agencies depend upon a continuing differentiation of indifferent cells such as occurs in embryonic life. The erythroblasts also, it should be borne in mind, are derived in ontogenetic development from primitive lymphoidal cells, but evidence is wanting, as Dr. Gulland puts it, that this occurs in adult life, the mitotic division of the erythroblast being sufficient for the production of red corpuscles. We shall probably be fairly correct in concluding that in normal conditions of extra-uterine life the different varieties of leucocytes behave as if they belonged to separate and self-sufficient classes, and that at the same time the leucocyte-forming tissues probably

contain non-differentiated lymphoid cells which are capable of undergoing differentiation along separate lines. It is not surprising that in leukaemia, which in many ways is analogous to tumour growth, there should be a reversion to more primitive and less differentiated types giving rise sometimes to a complicated blood-picture. The conditions of the blood in this disease also shew that there is a wider distinction between the granular and non-granular series than between the different members of the granular series.

Varieties of Leukaemia.—On the basis of the classification explained above there are two chief forms of leukaemia. In the first, the granular cells of the myeloid tissue are specially affected, and there is not only an increase of granular leucocytes in the blood, but the corresponding myelocytes also appear in the circulation—myeloid, myelogenic, or myelocytic leukaemia, myelaemia or myelocythaemia (most of the cases formerly described as splenic or spleno-medullary leukaemia belong to this class). In the second form there is an increase of the non-granular cells or lymphocytes—lymphatic or lymphocytic leukaemia, lymphaemia or lymphocythaemia. In a few cases the cells do not correspond to lymphocytes but are of the large mononuclear or hyaline class. The great majority of cases of the disease readily fall into one of these two groups, but in a certain proportion of cases the cells all seem to be derived from the two great groups, and to these the term mixed or atypical leukaemia has been applied. It is to be noted, however, that the title mixed-celled leukaemia is sometimes used to indicate myeloid leukaemia; the significance of this group will be considered on p. 796. Cases of leukaemia have also been distinguished according to their clinical characters as *acute* and *chronic*. The recognition of acute leukaemia, first made in the case of the lymphatic form, is comparatively recent, dating from Ebstein's work in 1887; observations since that time shew that the acute form is much commoner than was formerly supposed. More recently still a number of acute cases of the myeloid type have been published; acute myelogenic leukaemia is accordingly recognised. Whilst there is not a strict correspondence between the characters of the leucocytes in the blood and the course of the disease, the general statement may be made that the more differentiated the cells in the blood the more chronic is the case likely to be. Thus, myeloid leukaemia in its ordinary form is a distinctly chronic affection, and lymphatic leukaemia with small cells is chronic in a considerable number of cases. In acute lymphatic leukaemia an excess of large lymphocytes is present in many cases, and sometimes this is very striking; in other cases, however, the small lymphocytes are in excess. In many cases of acute myeloid leukaemia a considerable number of the more primitive non-granular cells have been observed. In the present state of our knowledge the different classes of leukaemia should be regarded as varieties of the same affection.

PATHOLOGICAL ANATOMY AND HISTOLOGY.—**The blood.**—The appearance of the blood may shew little change on naked-eye examination, or,

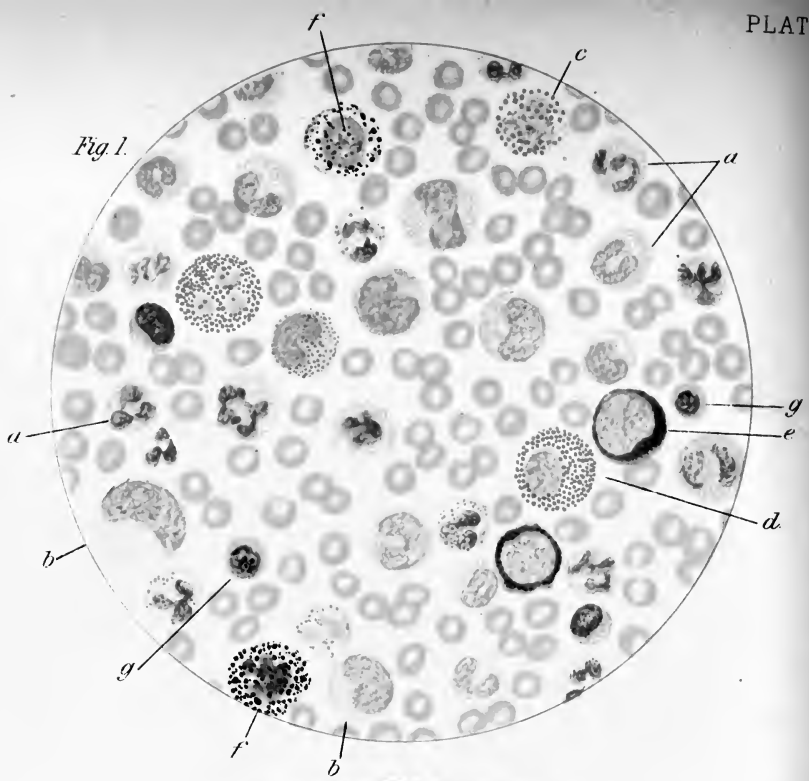

Fig. 1.

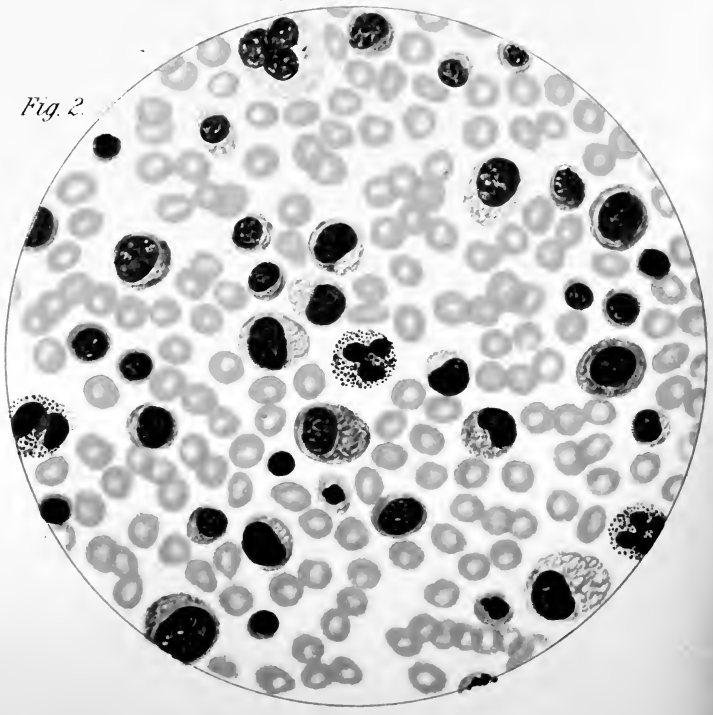

Fig. 2.

PLATE II.

FIG. 1.—Film of blood from a case of myeloid leukaemia, shewing the varieties of cells usually present. Note that the majority of the cells have fine neutrophil granules stained red.

a, Neutrophil polymorphonuclear leucocytes.
b, Neutrophil myelocytes.
c, Eosinophil leucocyte.
d, Eosinophil myelocyte.
e, Large lymphocyte (pro-myelocyte ?) with basophil protoplasm.
f, Basophil cells.
g, Nucleated red corpuscles.

Jenner's stain. ×700.

FIG. 2.—Film of blood from a case of lymphatic leukaemia, shewing the high proportion of lymphocytes of different sizes. Leishman's stain. ×700.

on the other hand, it may be strikingly altered. In cases in which the number of leucocytes is very much increased, it is pale and slightly turbid in appearance, as if mixed with pus; and if, in addition, marked anaemia be present, it is thin and watery and may have a yellowish tint. It usually coagulates less readily than normal blood, especially when there is much anaemia.

On microscopic examination of the fresh blood, the change is generally obvious at once, the number of leucocytes being notably in excess. But, as will be shewn hereafter, it must not be inferred that when the increase is apparently trifling the case is not one of leukaemia. Examination should be carried out by means of dried films, the most suitable stains being Jenner's stain or Ehrlich's triacid mixture after fixation by heat. The following are the characters of the blood:—

A. *Myeloid Form.*—As already stated the chief increase is on the part of the granular cells with the appearance of myelocytes in the blood. As a rule the great majority belong to the neutrophil series, these often numbering 70 to 80 per cent of the whole. The proportion of myelocytes to polymorphonuclears varies very much in different cases, the myelocytes not infrequently equalling the latter in number, though it is rather exceptional for them to be in decided excess. The average number of neutrophil polymorphonuclears may be placed at about 50 per cent and of myelocytes about 35 per cent. All transitional stages between these two types of cells can be met with, and there may also be variations in the staining of the granules. Sometimes a number of the leucocytes may be without granules, and sometimes unusually small or dwarf cells may be present. Occasionally mitotic figures can be observed in the myelocytes. The number of the eosinophils is practically always increased, and the percentage is also often above normal—5 to 10 per cent being by no means uncommon. Here again myelocytes are present and transitional forms between these and typical leucocytes can be seen. According to my observations the fully-formed neutrophil and eosinophil leucocytes, when examined on a warm stage, have active amoeboid movements as in normal blood; the large myelocytes are practically non-amoeboid, whilst intermediate forms naturally possess varying degrees of motility. The basophils (mast-cells) vary greatly, but they are increased in many cases, and often their percentage is above normal; occasionally cases occur in which these cells are extremely numerous, percentages of 40 and over having been recorded. Some are of the myelocyte type, but not infrequently a large proportion are comparatively small polymorphonuclear cells, the nucleus staining rather faintly. The granules usually give the metachromatic reaction. The proportion of lymphocytes is usually decreased, and sometimes these cells are very scanty, but, as a rule, the absolute number is above normal. The chief features of the blood are illustrated in Fig. 1, Plate II.

It will thus be seen that the blood-picture is of a very varied kind. The average number of leucocytes per c.mm. may be said to be about 300,000, and it is rather exceptional for the number to rise to about

600,000. Cabot, however, records a case in which the number reached over one million. The total number of leucocytes and the proportion of different forms may alike shew considerable variations from time to time. I do not consider that any conclusion as to the probable course of the disease can be drawn either from the total number of leucocytes or from the varieties present. In some cases under treatment, the number may fall to normal; in such instances the blood usually remains altered as regards the varieties of cells, myelocytes still being present. In one or two instances the blood has been described as returning to a normal appearance. The condition of the red corpuscles usually resembles that in a secondary anaemia of slight degree, the colour-index being rather below normal. Marked anaemia, however, is not common, and sometimes the number of red corpuscles is practically normal. In this form of the disease, the presence of nucleated red corpuscles is almost constant, and they are often present in larger numbers than are met with in any other affection; not infrequently they number 10,000 per c.mm., and even higher figures are not uncommon. Most are of the normoblast type, but sometimes a considerable number of megaloblasts may be present. The blood-plates are usually increased in number and sometimes the excess is very notable.

B. *Lymphatic Form.*—In this form the outstanding feature is the great absolute and relative increase of lymphocytes (Fig. 2, Plate II.), these cells usually numbering more than 90 per cent of the total leucocytes present. In some cases they are almost exclusively of the small form, rather smaller than red corpuscles; in other cases, they may be chiefly of the large lymphocyte type, and again all intermediate forms may be found. Most observers find that there is a tendency for the large lymphocytes to preponderate in the more acute cases of the disease; with this I agree, but we are not justified in going further than this general statement, as numerous exceptions are found in both directions. It is also to be noted that the proportion of small to large lymphocytes varies very widely in the same case from time to time, and it is not uncommon to find an increase in the proportion of larger lymphocytes when the case is running an unfavourable course. The neutrophil leucocytes are not infrequently absolutely as well as proportionately diminished, and occasionally very few cells of this kind can be found. Neutrophil myelocytes may be present in small numbers, but chiefly in acute cases towards the end of the disease. Eosinophils and basophils are also usually very scanty. In dried films the lymphocytes often shew irregularity in form; the protoplasm is apt to be frayed out, and sometimes gives off irregular projections. Degenerative forms are also often to be met with; both the protoplasm and the nucleus may become vacuolated or broken up, and the characteristic staining reaction is lost. Cells also sometimes shew a marked friability so that in film preparations a considerable number may appear as irregular blebs without distinct structure, although in fresh blood they may be of normal appearance; this is specially noticeable in the more acute cases. Prof. McWeeney also found that when the blood was

mixed with salt solution containing a basic aniline dye, the nuclei of the cells took up the stain, whereas those of normal leucocytes did not. This is probably due to diminished vitality on the part of the cells. The total number of leucocytes in the blood is on the whole lower in the lymphatic than in the myeloid form; the average may be said to be 100,000-200,000 per c.mm., but sometimes very high counts are met with.

Even in chronic lymphatic leukaemia the anaemia tends to be rather more pronounced than in corresponding cases of the myeloid form, but the red corpuscles otherwise present much the same condition. In acute cases, however, a rapidly advancing anaemia is more prominent, the number of red corpuscles falling markedly within a short time; not infrequently the number falls to 1,000,000 per c.mm. or lower before death. In cases of this kind polychromatophilic degeneration and poikilocytosis are common features. Nucleated red corpuscles are not infrequently absent in lymphatic leukaemia and are almost always scanty, there being in this respect a contrast to what obtains in the myeloid form. They are perhaps most abundant in some of the acute cases, in which a fair proportion may be of the megaloblast type. Another point of interest is that in the acute form the anaemia may depart from the secondary type and come to resemble the condition found in pernicious anaemia, the colour-index being above 1; out of 13 cases collected by T. McCrae, this condition was found in 4. The blood-plates are usually diminished in number and are sometimes very scanty.

C. *Atypical and Rarer Forms.*—The above account applies to the blood conditions in the great majority of cases of leukaemia. In some recorded cases, however, the cells have been of the non-granular type with a simple round nucleus, but have resembled the large mononuclear or hyaline cells of the blood, though many are of larger size. The protoplasm stains more faintly than the nucleus, and the cells in question are generally accepted as being distinct from large lymphocytes. Such cases have been recorded by Wolff, Veszprémi, Schultze, and others. The number is not very great, but probably the occurrence of such cases is more frequent than appears, inasmuch as the cells are sometimes simply described as "lymphocytes." From the clinical point of view they correspond with cases of lymphatic leukaemia, the tissues being the seat of infiltration, or tumour-like masses consisting of these cells, in which many mitotic figures are sometimes present. In some cases of chloroma the blood-picture is of this type (Sternberg). The relationship of the cells in question has been variously interpreted; some, such as Wolff, regard them as the primitive or least differentiated leucocytes, the original cell from which the others are derived. Others, again, regard them as derivatives from the large lymphocyte, the latter being looked upon as ontogenetically the older cell (Pappenheim and others). Sternberg, on the other hand, regards the cell as an atypical form which is specially associated with the formation of deposits of sarcoma-like nature, and gives the term leuko-sarcomatosis to the condition. Against this view it may be urged that in some cases this cell is present in great

excess in the blood without there being any tumour-like masses, and on the other hand, that the tumour-like growths are met with in association with typical lymphocythaemia. The true significance of the condition from the haematological point of view is not settled, but in its general features this form corresponds to lymphocythaemia with a tendency to run a rapid course.

In a number of recorded cases, usually described as mixed leukaemia (*vide* p. 792), the most frequent condition is the association of a considerable proportion of non-granular lymphocyte-like cells with cells of the myeloid series. A considerable number of such cases have now been described; some of these have been acute, some chronic. So far as the changes in the organs are concerned, they conform to myeloid leukaemia. The most probable explanation, at least in the majority of the cases, is that the large lymphocytes in question represent the non-granular precursors of the myelocytes, and as a matter of fact all stages can be traced between them in the blood. In other words, the blood-picture includes a stage further back in ontogenetic development than is usually seen in myeloid leukaemia. Again, the presence of myelocytes in small numbers is not infrequently to be noted in lymphatic leukaemia, but in some cases these cells may be comparatively abundant, and thus again a mixed affection may be simulated. A similar condition is sometimes seen when the marrow is the seat of secondary malignant growths, and the explanation generally given is that in the cases referred to, the appearance of the myelocytes is the result of disturbance of structure by the lymphocytic infiltration; that is, the presence of the myelocytes in the blood does not represent an active proliferation of these cells as part of the leukaemic condition. As a rare variety may be mentioned a condition in which there are numerous small mononuclear cells with neutrophil granules, or "neutrophil pseudo-lymphocytes," and all transitions between these and typical myelocytes. A few cases have been recorded (Wilkinson, Melland) in which a blood-picture of the myeloid type was succeeded by one of the lymphatic; these are probably also to be explained on the lines indicated above. So far as we know, there is no instance in which the essential changes of myeloid and lymphatic leukaemia were present concomitantly both in the blood and in the tissues.

Changes in the Viscera.—The morbid changes in the viscera are often very extensive, though they vary much in different cases; they chiefly depend upon the following processes:—(*a*) Accumulation and infiltration of leucocytes within organs, leading to general enlargement or to tumour-like swellings; (*b*) the occurrence of leucocytic thrombosis; (*c*) haemorrhages, which may be of small or large size; and (*d*) the progressive anaemia which produces fatty degeneration and aids in the production of the general oedema which may be present. We shall afterwards consider whether any of the changes in the organs are to be regarded as primary in nature.

Bone-marrow.—As indicated above, the changes in the bone-marrow are of special importance in relation to the pathology of the disease;

even in the rare cases in which it appears normal to the naked eye important alterations are to be found on microscopical examination. In most cases, especially of myeloid and chronic lymphatic leukaemia, the marrow is a soft cellular tissue of pale-reddish colour. In acute lymphatic leukaemia it may have the same appearance or it may be of deep red colour, often described as like currant jelly. In some cases again the marrow may be very soft and of pale-yellowish tint like pus—the "pyoid" marrow of Neumann. This appearance occurs in the myeloid and also in the acute lymphatic type and is due to degenerative change in the cells. The colour may even be greenish, approaching that of the lesions in chloroma, with which it may be associated, though it may occur apart from that condition. The altered marrow fills not only the spaces in the small bones, but also takes the place of the fat in the shafts of the long bones, and occasionally causes considerable absorption of the bone, extending along the vessels to the periosteum. The marrow usually shews the same character throughout, but sometimes patches of the pyoid condition may be present. In some rare cases of acute leukaemia the transformation of the yellow marrow is incomplete. The presence of tumour-like nodules is also very rare. The marrow should be examined by means of film preparations and also by sections. For the latter the marrow in the shafts of the long bones will be found most convenient, as it can readily be removed in pieces. The marrow may also be expressed from the short bones into fixing fluid and thereafter embedded in paraffin, though in this case the structural arrangements are disturbed. The process of decalcification, in our experience, interferes with the examination of the minute structure of the cells.

Microscopically, the marrow in the myeloid form is found to contain very much the same cellular elements as are found in normal marrow. The neutrophil and eosinophil myelocytes, however, preponderate, and the proportion of the corresponding leucocytes is much smaller than in the blood. A considerable number of mitotic figures in the myelocytes may be found, though the ordinary conditions under which examination is made are not suitable for their preservation. Nucleated red corpuscles are also fairly numerous, and some of them may be of the megaloblastic type. Cells containing red corpuscles in various stages of disintegration may also be present, but these are often met with in the marrow in a great variety of other conditions. In sections it is usually found that the fat has been completely replaced by a richly cellular tissue which has the structural arrangements of an active marrow, with an excess of the colourless cells. The vascular channels are badly defined, the blood-stream percolating between masses of cells loosely held in position. Giant-cells, generally of smaller size than usual, may be scattered through the section in considerable number. The change may be described in general terms as a hyperplasia of the marrow, the colourless cells, especially those of the granular series, however, preponderating.

In the lymphatic form, in which the marrow may present very much the same naked-eye appearances as in the other variety, there is found a large proportion of lymphocytes, which displace to a considerable extent the cells proper to the marrow. This often takes place to a remarkable degree, so that very few granular cells of any kind are to be found. The relative proportion of large and small lymphocytes varies much, but as a rule it corresponds to the condition present in the blood during life. Nucleated red corpuscles are few in number, and giant-cells are also scanty. The condition is really a lymphocytic infiltration of the bone-marrow of the same nature as in other organs. Its significance as a primary or secondary change is discussed on p. 807.

Spleen.—The splenic enlargement is one of the most striking features of the disease; in most cases it is marked, in some cases extreme. The largest spleens are met with in chronic cases, which are usually of the myelogenic, though sometimes of the lymphatic type; the weight of the organ is often from 5 to 6 lbs., and weights up to $18\frac{1}{2}$ lbs. have been recorded. In the more rapid cases the enlargement is not so marked, and the organ may be less than 1 lb. in weight; in a considerable number of the acute cases it has been found to be of normal size. Cases described as acute leukaemia in which the spleen is large and firm are probably chronic cases with an acute terminal course. The enlargement is generally uniform, so that the form of the organ is maintained; the notches in the anterior border are usually so strongly marked as to be palpable during life. Spleniculi, if present, may share in the enlargement. On the surface of the spleen there may be cartilage-like plates of fibrous thickening, or there may be fibrous adhesions. On section the enlarged organ usually has a fairly uniform red colour varying in depth in different cases, and a somewhat dry appearance; and it may contain infarctions of various numbers and ages: sometimes it is studded with them. The substance of the organ is usually pretty firm (the more chronic the case the firmer it becomes), owing to a general thickening of the supporting stroma; nevertheless it is often somewhat friable. The Malpighian bodies are, as a rule, indistinct, and it may be impossible to define their outline; sometimes, though rarely, they are very distinct. In the more acute cases the organ is generally rather soft, and shews on section a uniform reddish-pink colour.

Microscopically, the change is found to consist in a packing of the general pulp with leucocytes similar in character to those found in the blood. Thus in myelogenic leukaemia neutrophil myelocytes as well as polymorphonuclears, eosinophils, and basophils are present in large number; giant-cells of the bone-marrow type are sometimes present. In the lymphatic form the cells are almost exclusively lymphocytes, corresponding in character to those in the blood. A general thickening of the reticulum of the pulp may be present in the chronic cases, and thickening of the trabeculae and vessel walls is also common, the fibrous tissue often shewing a hyaline appearance. These latter changes are, however, no doubt secondary to the chronic distension of the spleen,

aided probably by abnormal metabolic processes; they occur in all conditions of long-standing enlargement of the organ. In the cases which run an acute course, on the other hand, the stroma of the organ may be quite unchanged. The Malpighian corpuscles usually shew no alteration; they appear few in number owing to their being separated by the enlargement of the pulp; and in the myelogenic form they are sometimes atrophied. In a small number of lymphatic cases they are enlarged. The infarctions, when present, shew the usual minute structure; they are apparently due to leucocytic thrombosis. The significance of the splenic changes is discussed on p. 808.

Lymphatic Glands.—In the myelogenic form distinct enlargement of the lymphatic glands is not common. In the majority of cases the disease runs its course without any of the glands being affected; sometimes, however, enlargement occurs, but it usually involves only small groups of glands here and there, and to a small extent. In chronic lymphatic leukaemia, on the other hand, enlargement of the glands is the rule, though not quite invariable. A single group of glands may shew enlargement; usually several groups are affected; more rarely is there a general enlargement. The cervical, axillary, inguinal, and mesenteric glands are most frequently enlarged. The enlarged glands may reach the size of small plums, and usually remain separate and freely movable. Large masses may be formed by their aggregation, though pressure symptoms produced by them are less common than in lymphadenoma. They are somewhat soft in consistence, and on section appear succulent and of whitish or slightly pink colour, though there may sometimes be small haemorrhages into their substance. In acute lymphatic leukaemia glandular enlargement never reaches the same degree. In most cases it occurs but is often confined to one group of glands, most frequently the cervical, and is of moderate extent. A considerable number of cases, however, have now been recorded in which there was no appreciable affection of glands up to the time of death.

In the enlarged glands in the myelogenic form there are large collections of neutrophil myelocytes, polymorphonuclears, eosinophils, etc., similar to those in the blood and readily distinguishable from the lymphocytes of the adenoid tissue. These cells may be derived from the blood or may be carried to the glands from the tissues by the lymph stream. In favour of the latter occurrence is the fact that in glands of normal size they may be found in the cortical sinuses. There is distinct evidence that they undergo proliferation, forming areas of myeloid tissue.

In the lymphatic form of the disease the enlargement of the glands is due to an accumulation of lymphocytes, which closely crowd the various parts of the gland and give a uniform appearance throughout. Here again the accumulation may be specially dense in the cortical lymph-sinuses; the capsule of the gland may also be infiltrated with lymphocytes. The lymphocytes may be chiefly of the small or of the large variety, corresponding as a rule with the characters of the lympho-

cytes in the blood. In some acute cases nearly all the lymphocytes are of the large variety, and by some writers this has been interpreted as due to an extension of the germ-centres to the whole substance of the gland. The appearance, however, seems rather due to an overrunning of the tissue with the particular cell in excess, similar to what is seen in other organs. In acute cases a considerable number of mitotic figures may be found in the lymphocytes. Other varieties of leucocytes are comparatively rare, though sometimes there is a fair number of eosinophils and occasionally giant-cells of the type found in the bone-marrow. There is usually no thickening of the stroma of the gland, and caseation does not occur unless some other condition be superadded.

Thymus.—Occasionally in lymphatic leukaemia the thymus undergoes considerable enlargement and forms a pretty firm mass, somewhat irregular on the surface, in the anterior mediastinum. This condition may sometimes be recognised by percussion during life. It may occur in the adult as well as in the young subject. In a woman aged twenty-five I found great enlargement of the thymus along with enormous enlargement of the spleen, but scarcely any enlargement of the lymphatic glands. Microscopically, the enlarged thymus shews a well-formed fibrous stroma enclosing pretty large spaces, which are filled with lymphocytes, there being a small amount of delicate reticulum between them.

Liver.—This organ generally shews some degree of enlargement, and is often 5 or 6 lbs. in weight. In one case at least, a weight of over 13 lbs. has been recorded. The enlargement is generally uniform, the surface usually smooth, and there may be small haemorrhages under the capsule, though these are not very common. The consistence may be unaltered or may be diminished, and usually the colour is distinctly paler than normal. This pallor may be pretty uniform, but is often more marked round the portal tracts, thus giving a lobular marking. Occasionally tumour-like masses may be present. Microscopically, there is found an infiltration of the connective tissue of the portal tracts with leucocytes, and the infiltration may extend for some distance into the lobule between the liver-cells and the capillary walls. The cells are chiefly of the myeloid or of the lymphoid series according to the nature of the case. These leucocytic infiltrations occur in varying degrees in all types of the disease, but, as elsewhere, they are usually most marked in the lymphatic form. The capillaries contain large numbers of leucocytes, and some may be plugged by them. Further, in advanced cases there may be a considerable amount of atrophy of the liver-cells; as the result of the anaemia, in many cases these shew fatty degeneration, which is usually most distinct in the centre of the lobules. The presence of iron-containing pigment in the liver-cells may be shewn in a fair proportion of the cases by the naked-eye tests; it is rarer to find distinct granules on microscopic examination. It is difficult to explain its irregular occurrence, as in some cases it is very well marked whereas in others of an apparently similar nature it is absent. There is no evidence that any cirrhotic change ever occurs as the result of leukaemia.

Kidneys.—In the myelogenic form the kidneys are usually of normal size and may shew nothing abnormal beyond a slight degree of pallor. On microscopic examination, however, some degree of leucocytic infiltration of the myeloid type is usually to be found. Occasionally the infiltrations give rise to visible whitish areas, often surrounded by red zones. More rarely there is a diffuse leucocytic infiltration of the connective tissue. The tubules may be normal, but there is very often fatty degeneration of their cells, and occasionally there may be haemorrhage into their lumen. Sometimes also there are evidences of catarrh. In the lymphatic form marked changes are much more common. These may be in the form of masses of lymphocytic aggregations like new growths, or of a diffuse infiltration which may lead to great enlargement. Haemorrhages are not uncommon. In the case of a boy aged eight, reported by Dr. John Thomson and myself, each kidney weighed 16¼ ounces, and the left kidney was easily palpable below the spleen during life. The enlargement usually affects both cortex and medulla, in a uniform manner and in equal proportion. The tissue is pale and the markings are regular, though there may be small haemorrhages here and there. The consistence may be nearly normal, or it may be distinctly soft, so that the kidney substance bulges somewhat when the section is made. Microscopically there is found in these cases simply an enormous infiltration of lymphocytes in the connective tissue of the organs, so that the tubules and other elements become widely separated from one another. The tubules themselves may remain normal, or any of the conditions mentioned above may be present.

Occasionally infarctions are found in the kidneys as the result of leucocytic thrombosis, but these are rare.

Other organs, such as the *suprarenals*, *thyroid*, *ovaries*, may shew changes similar in character to those in the kidneys, though they are less frequently affected. When such affection is marked their tissue becomes softer, and has usually a diffuse pinkish colour, the normal markings being somewhat blurred.

Bizzozero has observed numerous mitotic figures in the leucocytes infiltrating the tissues, and Hindenburg found them in the leucocytes in the spleen pulp, in the capillaries of the liver, and in the sinuses of lymphatic glands, but not specially in the germ-centres of lymphoid tissue.

Alimentary Canal.—The lymphoid follicles in connexion with the various parts of the alimentary canal may undergo enlargement in the lymphatic form of the disease, and there may be in addition more diffuse infiltration of certain parts. This latter may occur in the tissues of the gums, leading to marked swelling which may be followed by ulceration, or even by deep necrosis; haemorrhage from the affected parts is common. The tonsils in some cases may undergo considerable enlargement, and the lymphoid tissue of the pharynx and neighbouring parts may be similarly affected. The solitary glands in the stomach have also been found enlarged in a few cases. In the intestines the changes are

occasionally of a striking character. Swellings of considerable size may be produced by enlargement of the Peyer's patches or solitary glands, or by irregular leucocytic infiltration of the mucous membrane. Such changes may be found both in the large and small intestine, but usually one part of the intestine is affected in a special degree. The swelling may be followed by ulceration, which is usually irregular, though the ulcers in some cases have been described as "typhoid-like." Along with these intestinal changes there is usually enlargement of the mesenteric glands, though this latter may occur independently of any affection of the intestines. These lesions are essentially similar in nature to those described above.

Heart.—Fatty change in the muscular fibres of the heart is often present, and, in cases in which there has been marked anaemia, the inner surface of the organ may shew extensive pale-yellowish mottling. The organ often contains yellowish-white coagula which, owing to the large number of leucocytes contained in them, may appear as if pus were mixed with the fibrin—a condition which attracted the attention of earlier observers. As a rare condition may be mentioned the occasional occurrence of patches of *myomalacia cordis* in the heart wall, the results of thrombosis of the branches of the coronary arteries. Leucocytic infiltration may be present, but as a rule it can only be detected on microscopic examination. We can find no evidence that any hypertrophy of the heart takes place as the result of leukaemia, though some writers mention its occurrence. If present, it is due to some coexisting complication.

Lungs.—In the lungs also the connective tissue may be the seat of leucocytic infiltration. The lymphoid tissue in the walls of the bronchi and the peribronchial tissue are chiefly affected, and the condition may be diffuse or localised; the change is usually to be found only on microscopical examination. Many of the small vessels may be found to be plugged with leucocytic thrombi, and haemorrhages may be seen around them. The lungs are generally oedematous, and various other conditions may be present as complications; pneumonic consolidation is not uncommon.

Haemorrhages.—Small haemorrhages have already been mentioned as occurring on the surface or in the substance of various organs, and they are also common on serous membranes generally, in the periosteum, and in the skin. Haemorrhages of larger size may be found in various parts; sometimes they are apparently spontaneous, sometimes produced by slight traumatism; and often they take place from mucous surfaces. Special mention must be made of the occurrence of cerebral haemorrhages on account of their importance, as they are not infrequently the direct cause of death. The haemorrhage is sometimes single and of large size, tearing up the brain substance to a great extent, and may occur in any part. It is usually progressive and leads to a fatal result, though occasionally arrest and recovery may take place. Sometimes multiple haemorrhages are found, as in one case observed by the writer, in which there were

fully a dozen haemorrhages of various sizes in the cerebrum and cerebellum, both in the superficial and in the deep parts. These haemorrhages are almost certainly the result of leucocytic thrombosis occurring in badly nourished vessels, the thrombosis probably beginning in the small veins. Many of the small vessels in the neighbourhood of the haemorrhage may be found plugged in this way, and small haemorrhages with large numbers of leucocytes may be seen in their perivascular sheaths.

Nervous System.—Apart from a certain amount of leucocytic infiltration along the perivascular lymphatics to be found on microscopical examination, and the occurrence of cerebral haemorrhage just mentioned, the central nervous system is practically exempt from leukaemic lesions. The eye and ear may be affected in like manner; namely, by the occurrence of haemorrhages, and of leucocytic infiltrations of their tissues. In the retina minute haemorrhages are common, and are often associated with leucocytic infiltrations along the lines of the vessels and in patches—the condition described by Liebreich as *retinitis leucaemica*, though it is not really of inflammatory nature. Occasionally a more diffuse leucocytic infiltration of the layers of the retina has been found. Thrombosis of the central vessels has occasionally been recorded. Haemorrhage into the vitreous is rare. Similar infiltrations have been found in the structures of the inner ear, and have been associated with subjective symptoms, such as vertigo; in a few cases haemorrhage has been found as the cause of sudden deafness. Haemorrhages into the sheaths of the cranial nerves, especially the facial and the auditory, are amongst the rare occurrences. In some cases degenerative changes in the columns of the spinal cord have been observed, of similar nature to those in pernicious anaemia.

Pathological Chemistry.—At a comparatively early date chemical analyses were made of the blood and organs in leukaemia, but many of the results are vitiated to a considerable extent by the fact that the material used was obtained after death, and therefore at a time when important changes had been brought about by bacterial action. In some cases, however, analyses have been made of the blood obtained by venesection, and of the spleen excised during life; even in these circumstances there is considerable discrepancy in the results. The statement formerly made, that the blood has an acid reaction, depended upon examination of blood in which acidity had been produced by post-mortem change, and is incorrect; though the alkalinity is usually diminished. The fibrin has been found by some to be increased in amount, by others to be normal; coagulation takes place slowly, according to most observers, though others have found the coagulation-time to be normal. Slow coagulation has been ascribed to the presence of peptone, but this has not been proved. Matthes, and also more recently Schumm, found deutero-albumose in the blood taken fresh, but no peptone. On the other hand, A. E. Taylor, as the result of careful analysis, found no albumoses. As the neutrophil leucocytes are rich in autolytic enzymes the production of proteoses will be apt to occur when the blood is allowed

to stand. Erben found that this occurred to a marked degree in myeloid but not in lymphatic leukaemia.

As the result of many independent analyses, xanthine bases have been found in increased amount. This was discovered many years before any definite opinions were formed regarding their origin. According to the view which has now obtained pretty general acceptance, these bodies are formed chiefly from nucleoproteins especially of leucocytes, and rather from their breaking down than as a product of their metabolism. Kossel and also Horbaczewski traced the formation both of the xanthine bodies and of uric acid to this source. The latter found that from portions of spleen outside the body, by varying the conditions, he could at one time obtain uric acid, and at another xanthine bases. Salomon found that hypoxanthine forms in ordinary blood after it has been allowed to stand; but in fresh leukaemic blood, obtained by venesection, a considerable quantity is present. According to most authors, uric acid is not found in the blood, though some have asserted its presence. The presence of certain organic acids—lactic, formic, and succinic—has also been affirmed, the first-mentioned being found by Salomon in the proportion of ·05 per cent in fresh blood. By some observers, other substances—leucine, nucleo-phosphoric acid, guanine—have been found as abnormal bodies or increased in amount, but chiefly in specimens obtained after death.

One more point of considerable interest is the occurrence in the blood and organs after death of the minute crystals known as Charcot's crystals. They are not present in the fresh blood, but may be found after it has been kept for some time. They are specially abundant in the spleen and in the bone-marrow; and, according to Neumann, they are present specially in the myeloid form, being usually absent in the lymphatic form. They are usually regarded as a post-mortem product, though not necessarily produced by bacterial action. Westphal, however, found them in blood taken from the spleen during life and examined at once on a warm stage; hence he concludes that, in the spleen at least, they may be present during life. They are not peculiar to leukaemia, but may be found in the marrow in other conditions; and, as Leyden first discovered in the case of bronchial asthma, they may be found in the sputum. They are minute, elongated, symmetrical octahedra, and usually measure 10 μ in length; though smaller and larger forms are also found. They are soluble in warm water and in solutions of alkaline carbonates, very sparingly soluble in cold water, and insoluble in alcohol, ether, and chloroform. There is some doubt regarding their exact constitution, but at any rate they contain phosphorus; according to Schreiner, they are a compound of phosphoric acid and a base spermine which has the formula C_2H_5N. They are probably nucleo-protein derivatives (*vide* also p. 50).

Chemical examination of the organs has given results somewhat analogous to those described above. Both in the liver and in the spleen, obtained after death, various observers have found a considerable quantity of peptone, also of xanthine bodies (especially of xanthine itself, hypoxanthine being less abundant or absent), also of organic acids, especially

lactic, formic, and succinic, and leucine and tyrosine in small and varying amounts. In most analyses uric acid has not been found. Bockendahl and Landwehr obtained from a leukaemic spleen excised during life—peptone, 1 per cent; lactic acid, ·012 per cent; succinic acid, ·002 per cent; xanthine, ·038 per cent: leucine was present, but no tyrosine, uric acid, or glycogen.

The amount of iron in the liver and spleen has been estimated in a few cases, and has been found somewhat increased; v. Bemmelen found a proportion of 0·22 to 0·27 per cent of dried substance in the liver, and Prof. Stockman 0·337 per cent in the liver and 0·29 per cent in the spleen. Stockman attributes the increase in his case to the numerous haemorrhages in the body. Granboom also found more iron in the liver in leukaemia than in a number of other diseases investigated; namely, 0·09 per cent of liver substance (not dried).

The general result of chemical investigation in the disease has thus not been to reveal any very striking change in metabolism; the various chemical substances found in the blood, organs, and also in the urine (*vide* p. 820) being, so far as evidence goes at present, chiefly the result of excessive disintegration of leucocytes, with the increased formation of nucleo-protein derivatives—uric acid, xanthine bases, and phosphoric acid.

Conditions of Occurrence and Remoter Causes.—A distinct difference is to be noted in the age-incidence of acute and of chronic leukaemia respectively. Although, as has been stated, a hard and fast line cannot be drawn between the two forms, some general statements may be made as to their occurrence. Chronic leukaemia (myeloid and lymphatic) is most common in middle adult life—from thirty to fifty years of age. The results of statistics independently compiled agree in shewing that it is twice as common in men as in women. Cases are most numerous about the age of thirty in men and forty in women, but it appears to affect men at a greater age than women, being exceedingly rare in the latter after sixty, whilst a good many cases have been recorded in men above seventy. Acute leukaemia on the other hand is commonest in the second and third decades of life, the average age being about twenty; a considerable proportion, about 15 per cent, of cases occurs before the age of ten. A greater proportion of cases of the lymphatic than of the myeloid type occurs in the early years of life; but both varieties may affect children a few months or even weeks old. Pollmann records a case in which the disease was present at birth. Leukaemia is found in people of all classes of society, its occurrence being apparently little affected by the conditions of life and surroundings; though it is sometimes stated to be more common in the poorer classes. It appears to occur in various countries with much the same degree of frequency: statistics of the proportion of cases of leukaemia to the total number of cases in various Continental hospitals for ten years, given by v. Limbeck, shew the average proportion of cases of leukaemia to other cases to be about 3 to 10,000.

Hereditary influences appear to play little or no part in the proclivity to the disease. Only a few cases are on record in which more than one member of the same family have been affected by the disease. Such cases have been recorded by Chambers, Senator, and Eichhorst. Senator, quoted by Eichhorst, observed the disease in twins. Instances in which one member of a family has suffered from leukaemia and another from splenic or glandular enlargement are also few in number, and the occurrence of leukaemia in one of the parents and in one of the children of the same family is almost unknown. Leukaemic women bear children free from the disease; on the other hand, the child of a healthy mother may shew the disease when but a few weeks old.

As *remoter causes* syphilis, rickets, rheumatism, acute febrile diseases, depressing mental conditions have been mentioned by writers on the subject, but these would probably be found to be the most common antecedents of a large number of cases of any chronic disease. With regard to malaria, however, there may be some connexion which is more than accidental. Sir W. R. Gowers found a history of previous intermittent fever in a fifth of a number of cases, and exposure to malarial influence in a quarter. Though his results have not been entirely confirmed by the statistics of others, still they suggest that malarial fever may probably act as a disposing condition. In many cases of acute leukaemia there has been a history of pre-existing inflammatory or ulcerative conditions about the mouth, fauces, or intestine; but it is possible that these were early results of the disease itself (*vide* p. 818). A history of a blow over the spleen, or of injury to the bone, has been noted in one or two cases, but the coincidence must be regarded as accidental.

In woman sexual processes have been regarded by many as having an etiological relation to the disease, which has frequently been observed to start during pregnancy, after parturition, and, especially, during a prolonged lactation. Without denying that these processes may have some relation to the disease, still, in view of the considerable proportion of the adult life of a woman which on an average is thus occupied, and of the fact that at such times any abnormal condition is more likely to be noticed, we consider that the connexion is only accidental.

Our knowledge regarding the conditions of occurrence may be summarised by saying that leukaemia may occur at any age; that no connexion with the surroundings and conditions of life of the patient can be traced, and that, with the possible exception of malaria as a remote cause, no relation to any previous disease has been established. In the great majority of cases the individuals affected had previously been in good health.

Further—and this is a point of importance—the disease affects the lower animals, cases having been observed in the dog, cat, ox, sheep, pig, common fowl, and others.

Etiology and Relationships.—Excessive and apparently purposeless proliferation of leucocytes has been shewn to be the essential change in leukaemia, and the involvement of one or other of the chief classes of

leucocytes has given the basis of classification. The seat of formation of cells of the granular series in the adult is practically confined to the marrow, and nearly all observers agree that myeloid leukaemia (in the sense explained above) has its site of origin in the marrow. Hence the disease might be described as hyperplasia of the marrow with extension of its cells to the blood stream and to various tissues in the body. In the case of lymphatic leukaemia the lymphatic glands were formerly believed to be the chief site of origin of the disease; but recent observations shew that here also the marrow plays a very important part. Neumann was the first to believe that leukaemia in all its forms had its origin in the bone-marrow, and this conception has recently received a considerable amount of support. That lymphocytes are produced in the bone-marrow as well as in the lymphatic glands is admitted, and this supplies a basis for the origin of the disease in the marrow. Furthermore, in quite a considerable number of cases of lymphatic leukaemia, chiefly of the acute form, the bone-marrow has been the only tissue to shew morbid changes, the spleen, lymphatic glands, and other lymphoid structures not being enlarged; so that in these cases the disease in all probability originated in the marrow. Probably also there is no case of either form of leukaemia in which the marrow has not shewn at least histological changes of importance. But this does not prove that in every case the primary change is there; for with few exceptions the marrow throughout the body shews characteristic changes, and accordingly we must assume either that there is a general primary affection of the marrow or that the disease has started locally, and that the other parts have been affected secondarily. If the latter alternative be adopted, the importance of the marrow changes as indicating primary affection is lost, as manifestly a similar secondary affection might occur through the blood, say from the lymphatic glands. As a matter of fact, examination of the vascular arrangements of the marrow and of the close relation of its cells to the blood stream shews how readily a lymphocythaemia may lead to a corresponding affection of the marrow. The initial change in the marrow is often spoken of as if it were a general change, but if this view is adopted it would be unjustifiable to deny that the lymphoid tissues in other parts of the body might not sometimes be first affected in a similar manner. Moreover, in some cases enlargement of glands has preceded the leukaemic condition of the blood, though in some of these there has been a high percentage of lymphocytes. We are therefore brought to the conclusion that the lymphoid tissue in any part of the body may be the starting place of lymphocythaemia; but there is no evidence to decide whether and to what extent there is a simultaneous affection of different parts, or whether the origin is, as in most cases of tumour growth, quite local.

It is also doubtful how far the leucocytic deposits and infiltrations should be regarded as metastases, and to what extent they may be formed in situ. A study of the changes in myeloid leukaemia would seem to indicate that most of the cells in the tissues come from the blood, though they subsequently undergo proliferation, as shewn by the presence of

mitotic figures. Active mitosis in the tissues is also seen in acute lymphatic leukaemia, especially in the large-celled variety. A myeloid transformation in the spleen and other organs, that is a formation of cells of the granular series from primitive non-granular cells in these positions, has been described as occurring in infections in animals (Dominici and others). It is possible that such a process plays a part in the tissue changes in leukaemia, but no definite decision can be formed. In an interesting case of the lymphatic type Dominici found myeloid change in some of the lymphatic glands, apparently a myeloid metaplasia of compensatory nature. Schridde considers that the collections of myeloid cells in the tissues are derived from the vascular endothelium, but there does not appear to be sufficient evidence in support of this. When groups of glands undergo great enlargement, as in lymphatic leukaemia, it cannot at present be stated whether this is due to transference of proliferating lymphocytes after the manner of tumour cells, or whether gland after gland successively undergoes the morbid change underlying leukaemia. In the absence of any knowledge as to etiology of leukaemia, it would be futile to discuss a purely speculative question such as this, since arguments with equal force can be urged in favour of either interpretation. Ehrlich, in addition to distinguishing myelogenic and lymphatic leukaemia on histological grounds, also considered that they were different in nature; he regarded myeloid leukaemia as a mixed leucocytosis due to some chemiotactic stimulus of unknown nature, and the lymphatic form as allied to tumour growth, the distribution of the cells being a passive or mainly mechanical process. There are no good reasons for maintaining this distinction, and until the etiology is known we must consider that the same pathological disturbance underlies the different forms of leukaemia.

The important question arises whether the leukaemic proliferation is analogous to tumour growth, however this may be caused, or whether is it of the nature of a reaction to some infection or some chemical stimulus in the widest sense? Some German writers speak of it as a hyperplasia of leucocyte-forming tissues as distinguished from tumour growth, but nothing is known of such a condition unless it be of the nature of a reaction. The analogy with tumour growth is in many respects close. If we imagine a condition affecting leucocytes in the same way as sarcoma affects connective-tissue cells, we might expect to get changes similar to those found in leukaemia. The increase of the cells in the blood and the diffuseness of the lesions in the tissues in most cases as contrasted with tumour masses might be readily explained as due to the wandering character of the cells concerned. Of course in certain cases tumour-like formations do actually occur. Then again, as regards the duration of the disease, analogies might be drawn with tumours of different degrees of malignancy with corresponding variations in the types of cell. The chronicity of myeloid leukaemia, in which the most highly differentiated cells are in excess, and the comparatively undifferentiated or more primitive type of the cells in most acute cases of the disease, also bear on this question. Both in leukaemia and

in new growths there is a resemblance in the variable manner in which the different organs are implicated, but this is also shared by the infective granulomas. The association in chloroma (p. 812) of tumour masses of lymphoid cells with a lymphocythaemia is also highly suggestive in this connexion.

Anaemia in the myeloid type, as has been already stated, is usually slight and may be practically absent, whereas in lymphatic leukaemia, even of the chronic type, it is apt to be more marked. The natural explanation of this is that in the latter condition the place of myeloid tissue of the marrow is largely taken by lymphocytes, so that erythroblasts are diminished in number, and blood formation is interfered with. Siderosis in the organs occurs in an irregular manner, and may in part be secondary to haemorrhages, but in some acute cases the anaemia advances so rapidly that we are practically forced to assume the presence of some haemolytic agent. In the clinical characters, especially as regards the marked pyrexia, these acute cases resemble an infective process, and some writers consider that the disease, at least in its acute form, is really of that nature. It is a question, however, as to what extent toxaemia may be due, in some cases at least, to superadded infections in connexion with the mouth or other parts. Some writers have suggested that the destruction of lymphocytes gives rise to the formation of toxic bodies, producing haemolytic and other phenomena; but there is no direct evidence of this.

At present there is no proof that the leukaemic condition is the result of a proliferation in response to an infection. Löwit described protozoa in the blood in both the myeloid and lymphatic forms of the disease, to which he gave the names *Haemamoeba leukaemiae magna* and *Haemamoeba leukaemiae parva* respectively; and more recently White and Proescher considered that lymphatic leukaemia is due to *Spirochaeta lymphatica*; but these statements have not been confirmed, and it may be definitely accepted that as yet the existence of a parasite peculiar to leukaemia has not been demonstrated, and that the disease has never been experimentally produced *de novo*. The bone-marrow is now known to react in a striking way to intoxications and infections. Thus a neutrophil, an eosinophil, and recently also a basophil reaction have been described, but in each case it is the one variety only of the granular cells which responds, and no one has been able to produce the characteristic blood-picture of myeloid leukaemia. It is therefore clear that in the present state of our knowledge there is no satisfactory reason to regard myeloid leukaemia as a mixed leucocytosis. Experiments have been made on animals by injections of chemiotactic substances over a long period of time, for example, of peptone by Vehsemeyer and also by A. E. Taylor, but the only result has been a marked neutrophil leucocytosis.

Recently K. Ziegler states that he has produced leukaemic changes in rodents by exposing them to Röntgen rays. He found that the effect of exposing the spleen for several hours to the action of the rays was in the first place chiefly on its lymphoid tissue; the cells in the Malpighian bodies

were destroyed and disappeared, and at the same time there was a fall in the number of lymphocytes in the blood. There then occurred a compensatory reaction on the part of the myeloid tissue, myelocytes appearing in the blood and settling in large numbers in the spleen pulp, where they produced a myeloid transformation with some enlargement, though the size of the organ usually never reached more than twice the normal. Sometimes collections of myelocytes were observed in other organs. He considers that the essential factor in myeloid leukaemia is a damage to the lymph follicular tissue, and thus a disturbance of the normal relation which subsists between it and myeloid tissue; whereupon there follows a hyperplasia of the latter with myeloid transformation of the spleen, etc. According to this view myeloid leukaemia has no specific cause, but may be brought about by a great many pathological processes, which damage the lymphoid tissue of the spleen. Space does not permit a detailed criticism of this work, but it may be said that whilst the results are of high interest in connexion with the reactions of the leucocyte-forming tissues, they neither prove that leukaemia can be produced experimentally, nor explain the ontogeny of the disease. As already stated, leukaemia has been observed in a number of the lower animals, and it appears that it is in this direction that the greatest hope for the elucidation of the nature of the disease lies. Experiments made by injecting leukaemic blood or emulsions of organs from the human subject into animals have all been fruitless, and Weil and Clerc injected the blood of a leukaemic dog into another dog without result. Recently, however, Ellermann and Bang report success in transmitting the disease to fowls. By injecting the cells from a leukaemic fowl they were able to continue the disease over three generations with a comparatively large proportion of positive results. One interesting point is that in some of these experiments a leukaemic condition of the blood was not present, although the characteristic changes in the organs were found, a point of importance in connexion with pseudo-leukaemia. They also produced the disease by injecting cell-free fluid from an emulsion of leukaemic tissue, and accordingly concluded that in the transmission of the disease the proliferating cells were not essential as in the case of malignant growths, but that the disease was the result of an organised virus of unknown nature. Further observations will be necessary, but it is quite evident that these results, if confirmed, will prove to be of the highest importance. At present, therefore, we must speak with due reserve as to the possible etiology of the disease. Most of the data bring it into close relation to tumour growths, but a toxic phenomenon is also present in many cases, the pathology of which, even with this supposition, would still be obscure. It is therefore impossible to say more than that the essence of leukaemia is an excessive and apparently purposeless proliferation of leucocytes. Recent knowledge as to the so-called infective lymphosarcoma of the dog—a growth structurally similar to a malignant neoplasm, and yet manifestly the result of infection by some undiscovered organism—shews how closely tumours and infective granulomas may approach each other.

We have now to consider the relation of leukaemia to certain allied conditions. There is, in the first place, the disease known as *pseudo-leukaemia* (Cohnheim), regarding which there has been considerable confusion. The word is now generally used by German writers, as indicating an affection with the tissue changes of lymphatic leukaemia, but without the characteristic alteration in the blood, that is, an aleukaemic stage of lymphatic leukaemia; this is the sense in which the name, if used at all, should be employed. There are present in such cases the same enlargements of glands, infiltrations of various tissues, and lymphomas in various organs, which are essentially composed of aggregations of lymphocytes as in lymphatic leukaemia. Pinkus states that a characteristic feature is the high proportion of lymphocytes in the blood with a normal total count, but the observations of others shew that this is by no means constant, and it cannot be regarded as essential. Such cases, often of a chronic nature, usually run their course without the leukaemic state ever occurring; in a small proportion there is a transition into ordinary lymphatic leukaemia. Pseudo-leukaemia in this sense and lymphatic leukaemia are to be regarded as essentially the same affection, the only difference being the state of the blood; but how the leukaemic condition is prevented from occurring in the former we are in complete ignorance. In cases of myeloid leukaemia again, as the result of treatment or other factors, the number of leucocytes may fall to normal, though the abnormal elements are usually present, and in some acute cases extensive marrow changes are present with little alteration in the leucocyte-count. Some of the cases recorded as leukanaemia (*vide* p. 812) would also come into this group. The condition in these would correspond to a myeloid pseudo-leukaemia, comparable to the ordinary lymphatic pseudo-leukaemia.

Another group of cases, however, has been included by many writers, such as Paltauf, under the heading of "pseudo-leukaemia," as a hard variety, and many at least of these are examples of a different disease. Various American writers—Dorothy Reed, Longcope, and W. G. MacCallum —following Greenfield's description, recognise the true character of this affection. The disease in question is characterised by chronic enlargement of lymphatic glands as in pseudo-leukaemia, and often by a similar affection of the Malpighian bodies in the spleen; but the histological changes are quite different, being essentially of the nature of a reaction on the part of the supporting elements of the lymphoid tissue, with great proliferation of the endothelial cells and formation of small giant-cells. In the older lesions the tissue becomes fibrous and sclerosed. The changes in the internal organs are of the same nature. The blood in adults generally shews a moderate leucocytosis with increase of the neutrophils, or the leucocytes are little altered. My own observations shew that the histological changes are quite different from those of lymphatic leukaemia, that the disease is of the nature of a chronic infection with tissue reaction, and that it is not tuberculous in nature, though this infection sometimes becomes superadded. The name lymphadenoma might be reserved for this affection (*vide* art. Vol. IV. Part I. p. 459).

Closely allied to pseudo-leukaemia, as above defined, is the condition known as *myeloma* or myelomatosis ossium, characterised by the occurrence of multiple tumour-like nodules throughout the osseous system, attended with considerable softening of bone (*vide* art. Vol. III. p. 77). In one form the growths appear to start from myeloid tissue, and the cells composing them may contain fine granules of neutrophil or of allied character. The growths are confined to the bone-marrow, there is no leukaemia, and the condition is attended with the well-known Bence-Jones albumosuria. In another variety of myeloma the growths are composed of non-granular lymphoidal cells (Parkes Weber), and may also occur in the lymphatic glands. Cases of this kind would appear to form a link between the ordinary myeloma and lymphatic pseudo-leukaemia.

The condition known as *chloroma* is of considerable interest, as it seems to form a connecting link between leukaemia and malignant growths, especially lymphosarcoma. The chief feature is the occurrence of tumours of greenish colour, most frequently in connexion with the bones of the head, especially in the orbits and temporal fossae, and in connexion with the vertebrae. Most of the cases have been in young subjects, the majority being males; the blood has shewn lymphocythaemia, the larger lymphocytes usually predominating. In some cases the cells have been chiefly mononuclear leucocytes (Sternberg). The condition may therefore be regarded as a modification of the leukaemic process, the masses in the tissues, which are composed essentially of the same cells as those in the blood, presenting the infiltrating properties of new growth, and being also characterised by their colour and their distribution. Cases of chloroma of myeloid type have recently been recorded by Klein and Steinhaus, Türk, and by Sternberg; in these the tumours have also been of a green colour, but their cells have contained neutrophil granules. The changes in the marrow are those of myeloid leukaemia, and the blood shews a large number of myelocytes along with non-granular pro-myelocytes—atypical myeloid leukaemia. It is interesting to find that in chloroma again we have a corresponding lesion affecting both the lymphoid and myeloid tissues. Why the green pigment should be formed in these cases is not known, but it is noteworthy that a similar colour may be met with to a varying degree in the bone-marrow in cases of leukaemia without the presence of tumours.

Under the heading of *leukanaemia* Leube described a condition with marked change both in the leucocytes and in the red corpuscles, such as are usually seen in leukaemia and pernicious anaemia respectively. A considerable number of these cases have been published, and in this country Drs. Parkes Weber, Bushnell, and Drysdale have paid special attention to the subject. The cases recorded have certain features in common, but they also present important differences. There is in all a rapidly progressing anaemia with poikilocytosis, high colour-index, presence of nucleated red corpuscles in the blood, many of which may be megaloblasts. As regards the leucocytes, there may be leukaemia in the ordinary sense, or if the number is not increased the qualitative change brings the

condition into line with leukaemia. In some the large lymphocytes have been chiefly in excess sometimes along with myelocytes, or some other variety of atypical leukaemia has been present. Eosinophils and mast-cells have usually been scanty. The changes found after death in the various organs also vary. In some cases the bone-marrow has shewn myeloid hyperplasia, and in others lymphatic: in Hirschfeld's cases lymphomas were present. The condition of the spleen and lymphatic glands has also varied considerably. In all the cases except one there has been an absence of siderosis in the liver, and so no evidence in this respect of a haemolytic anaemia; but in Hirschfeld's case this condition was well marked. The word "leukanaemia" connotes nothing more than a condition of extreme anaemia, often of the megaloblastic type, with disturbances of leucocyte formation which may or may not result in the blood-picture of leukaemia. As stated above, in some cases of acute lymphatic leukaemia the anaemia advances very rapidly, and may be associated with a high colour-index; but all degrees of such affection may be present, and there is no reason to assume that in the most rapid cases some other distinct morbid condition has been superadded to the existing leukaemia. In most of the cases of leukanaemia the blood-picture has been atypical, and leukaemia with this condition as a rule runs a rapid course. The use of the term is at present unjustifiable from a pathological point of view, and its clinical use is more likely to lead to confusion than to be of convenience.

Our views as to the relationships of the different affections under discussion may be shewn by the following scheme. The arrangement in the absence of knowledge as to etiology must of course be regarded as merely provisional:—

A. Overgrowth of myeloid tissue.
   (*a*) With leukaemia: (1) Myeloid leukaemia, acute and chronic, including atypical forms with non-granular pro-myelocytes. (2) Myeloid chloroma.
   (*b*) Without leukaemia: (1) Diffuse overgrowth—aleukaemic stages of myeloid leukaemia, some cases of "leukanaemia." (2) Tumour-like growths—myeloid myeloma.

B. Overgrowth of lymphoid tissue.
   (*a*) With leukaemia: (1) Lymphatic leukaemia. (2) Chloroma (ordinary lymphatic form).
   (*b*) Without leukaemia: (1) Diffuse overgrowth — lymphatic pseudo-leukaemia. (2) More localised tumour-like growths, including lymphoid myeloma.

Notes.—The chloromas have been put by themselves, as some of their characters resemble those of new growths, especially lymphosarcoma; this is, however, somewhat arbitrary, as the same features are found in some cases of leukaemia without chloroma. It is also recognised that some leukaemias with large non-granular cells may belong to the myeloid series, the cells representing pro-myelocytes, or perhaps cells even further back in the ontogenetic scheme. A similar remark applies also to the lymphoid form of myeloma; it can hardly be regarded as determined whether this

is a derivative of lymphoid or pro-myelocytic tissue. If the former is the case, it is closely similar to ordinary pseudo-leukaemia.

Symptoms.—In describing the symptoms of leukaemia, we may distinguish an acute and a chronic form; these are fairly well defined, though cases of intermediate character occur. We shall first give an outline of the course of the disease in the two forms, taking first the chronic form, which is the commoner. The great majority of chronic cases are of the myeloid variety, but a certain proportion belong to the lymphatic type.

The onset of the disease is generally gradual and insidious. In many cases the earliest symptoms are produced by the splenic tumour; a dragging sensation or pain in the left hypochondriac region or a general swelling of the abdomen may first be complained of. In others, weakness, breathlessness on exertion, giddiness, or gastric symptoms are the first indications. In chronic lymphatic leukaemia the enlarged glands often lead the patient to seek medical advice. Sometimes haemorrhage from the nose, more rarely from the bowels, is the earliest symptom. At this stage the patient usually looks in pretty good health, and has not lost flesh, though a certain degree of pallor may be present. Examination of the blood may shew a moderate or great increase of the leucocytes, and the red corpuscles may be only slightly diminished. The spleen, even at this early period, may shew enormous enlargement, and its lower margin may be at the iliac crest. The changes in the blood and the condition of the spleen usually render the diagnosis easy. If the temperature be taken regularly, slight irregular pyrexia may sometimes be detected. This generally occurs at night, the temperature rising a degree or more on some days, with intervals of a normal condition; it may be accompanied by sweatings; though, independent of rise of temperature, such a tendency to sweating is not an uncommon symptom. Disturbances of the alimentary system often appear, vomiting or diarrhoea from time to time being not infrequent.

Such are the common symptoms in the early stages of the disease; and in distinctly chronic cases patients may remain in pretty much the same condition for months, or even for one or two years. In some cases, in fact, they may enjoy tolerably good health with the condition of the blood well marked and the spleen of great size. More frequently the general health is considerably impaired, more prominent symptoms occurring at intervals and tending to become aggravated. In this stage, under suitable treatment, considerable improvement in the general health may take place, and the number of leucocytes may even diminish considerably. Periods of relapse, however, follow, and in the course of time a greater or less degree of cachexia usually supervenes. Pallor and breathlessness become more marked, the pulse is often feeble and rapid, the temperature is more frequently elevated and still shews the same irregular character. The abdomen may shew considerable tumidity, owing partly to the splenic enlargement, partly to chronic flatulent distension, and partly to the ascites, which is an occasional complication. The

patient loses flesh, becomes more and more asthenic, and is confined to bed. Even at this stage a certain amount of improvement may occur, but too often the course is steadily downhill. A tendency to haemorrhage, if not present before, often appears now, and in this way the prostration is increased.

A fatal termination may be brought about in various ways. In some cases advancing cachexia and anaemia are followed by the occurrence of general dropsy, which gradually increases, and the patient dies from heart failure with pulmonary oedema. This, indeed, is the usual sequence of events unless some fatal complication occur. In the lymphatic form the symptoms characteristic of acute leukaemia may precede the final issue. In other cases severe haemorrhage from the nose, bowels, or elsewhere may be the immediate cause of death; and in a certain proportion of cases death is produced suddenly by the occurrence of single or multiple haemorrhages in the brain. Occasionally severe diarrhoea contributes largely to the fatal termination; in other cases intercurrent affections, such as pneumonia or peritonitis.

Such, in outline, is the course of the disease in its chronic form, and most cases of myeloid leukaemia in adults conform to this description. The disease in this form usually lasts for from one to two years after the first symptoms, though a longer duration is not uncommon. After distinct cachexia sets in, the fatal result generally follows in a few months, though it may occur at any time.

In another group of cases the disease runs a much more rapid course, and to these the name **acute leukaemia** has been given, though it has only a relative significance. As stated above, leukaemia is more apt to have this character in the earlier years of life, especially when the disease is of the lymphatic variety. In some such cases a fatal result may follow as early as four or five weeks after the first noticeable symptoms, or even earlier; how long after the beginning of the disease we cannot, of course, say. The characters of the disease are of the same nature as in the chronic form, but are exaggerated in degree and in rapidity of course. Rapidly advancing pallor and weakness, or severe haemorrhage, may be the first indications of the disease. Irregular pyrexia, often with great perspiration, thirst and anorexia, vomiting, diarrhoea, repeated bleedings from the nose, gums, or bowels, and subcutaneous extravasations, are amongst the most usual symptoms during its course. Enlargement of the lymphatic glands is sometimes well marked, and may be one of the earliest changes to be noted by the patient. Death may be preceded by a typhoid condition; sometimes it results from general oedema and heart failure, sometimes directly from haemorrhage. In such acute cases the splenic enlargement is usually only moderate in degree, or may even be slight; though the increase of leucocytes is generally great and the anaemia sometimes extreme.

After this outline of the main features of the disease the more important clinical conditions may be described in greater detail.

The condition of the *blood* is always of importance, and when examined

from time to time may give valuable indications as to the course of the disease; these indications are discussed below under *Diagnosis* and *Prognosis*. As stated above, it is impossible to draw any definite conclusions as to the course of myeloid leukaemia either from the total number of leucocytes or from the proportions of the different varieties. It is not the rule to find a gradual increase in the number according to the duration of the disease, although when the condition of the patient grows worse the number of the leucocytes often increases. Occasionally, under treatment, the leucocytes may become considerably diminished, and may even fall to normal. It is not possible, however, to say that the patient is cured, though the diminution is usually accompanied by an improvement in the general health; the abnormal elements remain in the blood, and the splenic enlargement is sometimes little altered, though sometimes it is considerably diminished. It is also a fact of great importance that the incidence of acute intercurrent infections, such as erysipelas, pneumonia, influenza, and acute tuberculosis, usually leads to a notable fall in the number of leucocytes. Dock has collected recorded cases of this kind and in about half of these the leucocyte number fell to normal; sometimes there is even leucopenia. The diminution in number is associated with an increase in the proportion of neutrophil polymorphonuclears, and sometimes there is a diminution in the size of organs, such as the spleen. When recovery from the infection takes place there is usually a return to the former condition of the blood. Throughout the greater period of the disease in the chronic type the red corpuscles are usually little reduced in number, their number remaining almost stationary for a considerable time, though falling considerably towards the close of the disease. It is always a grave sign when the number of the red corpuscles steadily diminishes in spite of treatment. Moreover, it should be borne in mind that when the condition of the blood is stationary, or even improving, a rapid aggravation leading to a fatal result may set in at any time. In the more acute cases a considerable augmentation in the number of leucocytes may be observed in the course of the disease, and, as there is usually much diminution of the red corpuscles at the same time, the proportionate increase is more marked still. (For further details see p. 793.)

The *splenic enlargement* corresponds in general characters with that met with in other conditions. It is greatest in long-standing cases, and may exceed that met with in any other disease. The enlargement, for anatomical reasons, extends mostly forwards and downwards; but sometimes, when the downward extension is interfered with by adhesions or by a powerful costo-colic ligament, the extension upwards is very marked. The lower margin may be as low as the anterior superior iliac spine, or even lower; whilst the anterior border may reach beyond the middle line, occasionally even as far as the anterior superior iliac spine on the right side. The form of the organ is maintained, and, as its consistence is usually firm, its rounded margin can be readily palpated, the notches in the anterior margin being often well marked. The enlarged spleen

often gives rise to a sense of dragging or heaviness, the uneasiness being increased after food; and sometimes, owing to the occurrence of perisplenitis, actual pain of a dull or sharp character may be present, especially on movement. It may also interfere to a varying extent with the movements of the diaphragm, and complicate respiratory troubles. When such great enlargement has been reached, the size remains as a rule fairly constant, shewing only slight variations from time to time. Sometimes, however, considerable diminution takes place, which may or may not be accompanied by an improved condition of the blood. In the more rapid cases the enlargement of the spleen is usually at most only moderate and in a fair proportion of cases is absent; even when the organ is enlarged, palpation of its border is not readily effected, as its consistence is less firm. In acute cases the organ may not infrequently be found to undergo enlargement during the progress of the disease. Between the size of the spleen and the number of leucocytes in the blood there is no fixed relation.

The *lymphatic glands*, when enlarged, may give rise to considerable swellings which are readily visible; in other cases the condition is discovered by palpation. The anatomical changes have already been described (*vide* p. 799), and the clinical characters correspond. The enlarged glands are usually free from matting or induration around, are neither painful nor tender, and may shew considerable fluctuations in size from time to time. In some cases the enlarged mesenteric glands give rise to a considerable abdominal tumour. Pressure symptoms are rarely produced, though their occurrence from enlarged mediastinal and bronchial glands has been recorded. In acute lymphatic leukaemia the glandular enlargement is usually moderate in degree and limited in extent; in a considerable number of cases now recorded it has been absent. The cervical glands are those most frequently implicated in acute cases and the affection may be limited to them; a general enlargement, however, may be present, although in certain of these cases we may be dealing with an acute stage supervening on a chronic. In chronic lymphatic leukaemia great enlargement of many groups of glands may be present for a considerable time. In the great majority of myeloid cases glandular enlargement is slight or absent.

The changes in the *bone-marrow* are usually unaccompanied by any symptoms. Mosler was the first to describe tenderness over the sternum as a symptom in the disease: this he found to be due to an overgrowth of the marrow, with absorption of the bone; and a like condition has been noted in other cases. Occasionally there is a dull pain in addition to tenderness, and these symptoms may be present in other bones besides the sternum. Such symptoms are, however, the exception rather than the rule, and it may be definitely stated that an extensive hyperplasia of the marrow may be present without any subjective indication whatever; though relatively more frequent in myelogenic leukaemia they also occur in the lymphatic form.

The *thyroid*, when it is the seat of leucocytic infiltration, may be obviously enlarged during life. I have only once observed this, a

symmetrical enlargement of moderate degree and painless, occurring in a case of acute lymphatic leukaemia. So far as I can ascertain, no symptoms referable to the suprarenals occur when these are the seat of leucocytic infiltration.

Disturbances of the *alimentary system* are common, especially in the more acute cases, and may give rise to most troublesome symptoms. The tonsils and lymphoid tissue of the pharynx may be enlarged and interfere somewhat with deglutition, especially when an inflammatory condition is superadded, as is sometimes the case. The enlargement, as in the case of the lymphatic glands, may shew fluctuations from time to time. In a considerable number of acute cases the chief early symptoms are related to lesions of the mouth. These are due partly to swelling of the tissues as the result of lymphocytic deposits and partly to infective processes which supervene. The gums may become much enlarged, spongy, inflamed, and bleed readily; the teeth may become loosened and the proper closing of the mouth may be interfered with. There is often decomposition of the secretions and blood with marked fetor. The tissues are easily injured and thus necrosis and ulceration occur, sometimes even gangrene may be superadded. Similar changes affect also other parts of the mouth, the soft palate, inside of cheek, pharyngeal wall, etc. The relation of such lesions to leukaemia was first recognised by Mosler, who applied the term leukaemic stomatitis.

The appetite varies considerably. In the earlier stages in chronic cases it is usually little if at all impaired; in a few cases it has been described as unusually great. Discomfort after a full meal is a common symptom, and is to be ascribed in part to the pressure of the enlarged spleen on the stomach. In the later stages of the disease, when there is cachexia, and especially in the acute cases, gastric symptoms may be very prominent. There is complete loss of appetite, very feeble digestive power, vomiting, and occasionally haematemesis; though bleeding from the stomach is not so common as from the nose or bowels, and usually occurs only late in the disease.

Intestinal symptoms are comparatively common. There may be flatulent distension and constipation alternating with diarrhoea; a tendency to the latter is often well marked throughout chronic cases. But diarrhoea is sometimes severe in degree, especially in the stage of cachexia; and it may largely contribute to a fatal result. It is sometimes accompanied by tenesmus and by bleeding from the bowels, the bleeding varying greatly in amount, but being sometimes profuse and occasionally the cause of death. In such cases often no lesion of the intestinal mucous membrane can be found after death, there being apparently a general oozing of blood from its surface; occasionally with the lymphatic variety of the disease the lesions above described are found associated.

Acute peritonitis may supervene and determine a fatal issue. In leukaemia the general resistance to bacterial infection is lowered and in the cachectic stage invasion of the blood by bacteria is not uncommon. Thus, plugs of micro-organisms, especially cocci, may be found in the

organs after death. The peritoneum may be infected by the blood-stream, though sometimes infection would appear to come indirectly by means of the spleen. In other cases peritonitis may be set up by the process of tapping.

Enlargement of the liver can often be ascertained by percussion, and its lower margin is sometimes palpable; but usually no symptoms are produced by the affection of this organ. Jaundice is not met with, unless as the result of some superadded condition. Great leucocytic infiltration of the portal tracts may, however, possibly aid in the production of ascites, which is often present towards the close of the disease. The ascites may occur as part of a general dropsy, but sometimes the effusion into the peritoneum is well marked when there is little or no dropsy elsewhere, and may require repeated paracentesis. Spontaneous haemorrhage into the peritoneum has been described, but is a very rare occurrence.

The symptoms in connexion with the *circulatory* and *respiratory* systems are mostly referable to the general condition, and especially to the anaemia. Palpitation, breathlessness on exertion, giddiness, and the like tend to become worse as the disease advances. The pulse becomes softer and more rapid, but is usually regular, even in the later stages of the disease, when, owing to the fatty change which is often present, the heart's action may be very feeble. Systolic haemic murmurs may be heard over the heart, and a bruit over the veins at the root of the neck. The heart is sometimes displaced upward and slightly to the right side by the splenic enlargement and the abdominal distension. Dyspnoea is often a distressing feature in the late stages of the disease, even to the full extent of orthopnoea. Several factors are concerned in the production of this symptom. In addition to the anaemia present and the feeble action of the heart, effusion into the pleural cavities may largely contribute to it, and the condition is aggravated by the abdominal distension which displaces the diaphragm upwards and restricts its movements. Oedema of the lungs usually precedes death, which may come about very gradually. In one case, observed by the writer, in which death took place somewhat suddenly, there was extensive leucocytic thrombosis in the small pulmonary vessels, along with large pale coagula in the large trunks. Bronchial catarrh is not uncommon throughout the disease, and the cough, in some cases very troublesome, is attributed to reflex causation. Pleurisy and pneumonia may be mentioned as complications.

Dropsy is common in chronic cases in which there is advancing cachexia; it results from the anaemic condition, general malnutrition, and gradual heart failure. Anasarca may be of extreme degree, the epidermis may be raised in blebs, and an erysipelatous condition sometimes supervenes. Effusions into the various serous cavities are common, and, as I have said, ascites is often considerable.

Haemorrhage into the tissues, or from mucous surfaces, occurs, at some period of the disease, in the majority of cases, but is a specially prominent feature in acute leukaemia. Epistaxis is of frequent occurrence in the

chronic as well as in the acute variety, being probably the most frequent form of haemorrhage in chronic leukaemia. It may occur at any period, and is not uncommonly an early symptom. It may recur frequently throughout the disease and be moderate in degree; sometimes it is very severe and may be the cause of death. Bleeding from the lesions in the mouth (*vide* 818) is common in acute leukaemia. Haemorrhages from the stomach or from the bowels, though less frequent than epistaxis, are by no means uncommon, those from the bowels being the commoner. The amount and frequency of the haemorrhages vary greatly in different cases. In the case of intestinal bleeding, for example, there may be only a small amount of altered blood in the stools; the faeces may be pulpy and contain a considerable admixture of blood, or almost pure blood may be passed from the bowel. Haemorrhages from the lungs and kidneys and from the female genital tract are rarer events. Purpuric spots are often present in acute leukaemia; they also occur in the chronic form, but usually only in the advanced stages of the disease. They are generally in association with marked anaemia. Sometimes in the more rapid cases the skin haemorrhages may be much larger and of more diffuse character, as in purpura haemorrhagica. Haemorrhage into the joints has also been recorded. Haemorrhage into the deeper tissues, or muscles, is another complication, sometimes resulting from slight trauma, sometimes apparently spontaneous. I have seen more than a pint of blood effused into the abdominal muscles, as the result of paracentesis when the puncture was made a little to one side of the middle line. Haemorrhage into the brain has been mentioned above as a not infrequent cause of death. Fatal cerebral haemorrhage may occur suddenly, or may be preceded by symptoms in the case of smaller initial haemorrhages. As the haemorrhage is in some cases multiple and in other cases very extensive, localisation during life is usually very difficult. In giving a prognosis in cases of leukaemia, the possibility of the occurrence of cerebral haemorrhage should be kept in view.

Elevation of the *temperature* at some period of the disease is almost invariable. In the early stages in chronic cases slight irregular elevations, more marked at night, may occur from time to time, with periods of normal temperature between. In the later stage, and especially in cases running an unfavourable course, the pyrexia is more marked, though still shewing an irregular character. In the typically acute cases marked elevation of temperature is common; it shews sometimes an almost typhoid-like course, though more frequently it has the irregular character of a septic condition. A temperature of 103° F. is not uncommon and even 105° has been recorded. Occasionally slight rigors occur with the rise of temperature, the causation of which is obscure.

The *urine* is generally normal in quantity, though towards the end of the disease it may be diminished. On the other hand, in some acute cases the amount of the urine has been found to be much increased, this being associated with evidence of increased breaking down of nucleoproteins, as described below. Its specific gravity varies, but is usually pretty high; an acid reaction is usually well marked. The amount of

urea has been found to vary in different cases, though it is often little altered ; but increase in the quantity of uric acid, observed by Virchow at an early date, is an almost invariable occurrence. The amount of the latter has been recorded as reaching over 3 grms. a day, but more recent analyses shew that such a figure is rare. A deposit of urates often appears in the urine after standing, and uric acid crystals may also be found. The xanthine bases, of which traces are found in normal urine, are also increased in amount, and some of the rarer members of the series—heteroxanthine, guanine, etc.—have been found by different observers. Bondzynski and Gottlieb, in a case of myeloid leukaemia, found that the xanthine bases exceeded three to four times the normal amount. These changes in the urine are to be associated with those in the blood and organs described above, and probably all are due to the excessive breaking down of the nucleo-protein of the leucocytes. Most observers have found these changes most marked in myelogenic leukaemia, but Magnus-Levy has found that the most important factor is the rapidity of the case. In acute leukaemia, for example, he found on comparing the intake and output that there was a great nitrogen loss, sometimes amounting to 20 grms. in the day ; that there was a great increase in uric acid and in varying proportion of purine bodies in the urine, and also that there was an increased excretion of phosphoric acid, combined in unusually high proportion with fixed bases. The amount of uric acid and xanthine bases manifestly varies much, and there is no fixed relationship between it and the number of leucocytes in the blood. Formic, lactic, and other organic acids in small quantities have been found in the urine in some cases (for example, by Kolisch and Burian, who also found histone in one case) ; and peptone and albumoses have been observed occasionally. Various observers have found that *x*-ray treatment results in increased disintegration of nucleo-protein, evidenced by increased nitrogen loss, increase of uric acid and xanthine bases in the urine, and sometimes the excretion of amino-acids. On the other hand Dr. Ledingham found, as the result of extensive observations, that there was no evidence in the urine of increased breaking down of leucocytes, and came to the conclusion that *x*-rays produced their effect by interfering with leucocyte formation. Albumin may be present towards the close of the disease, but, as a rule, the urine is free from it ; haematuria, though occurring occasionally, is rare. There may be great enlargement of the kidneys due to leucocytic infiltration, without a trace of blood or albumin. The occurrence of renal calculi from the increased excretion of uric acid and urates is not common, though a few cases have been recorded.

In the *skin* the occurrence of multiple tumour-like nodules, often reaching a hazelnut in size, was first described by Biesiadecki, and a considerable number of cases have since been recorded. The condition, however, is to be placed amongst the rarer leukaemic lesions. The nodules occur most frequently in the skin of the face and may give rise to much disfigurement ; less frequent sites are the arms, especially the back of the hands, and the legs. Sometimes they are pale, but usually they have a

reddish or even purplish colour. Microscopically they are found to consist of masses of lymphocytes, which appear first around the deeper vessels of the skin and extend upwards to the papillae. They have usually been associated with chronic lymphatic leukaemia with much glandular enlargement. In the condition described by Kaposi as lymphodermia perniciosa there occurs a diffuse redness and swelling of the skin attended by itchiness, and later, tumour-like nodules appear. The position of this as a true leukaemic affection has, however, been called in question by recent writers, *e.g.* Nékám. As other skin lesions may be mentioned, papular urticaria and sometimes harder and firmer nodules which disappear after a time; the nature of these latter is unknown. A tendency to boils has been noted in some cases of leukaemia. Other changes, haemorrhages, etc., in the skin have already been mentioned.

Symptoms in connexion with the *nervous system*, apart from those produced by haemorrhages, are on the whole rare. Mental affection, especially of a melancholic type, has been observed in some cases, chiefly towards the close of the disease; but it is not sufficiently frequent to indicate any special proclivity. In some of the acute cases delirium and coma have occurred before death, sometimes apart from marked pyrexia. In addition to the symptoms produced by cerebral haemorrhage, which has been referred to above, paralyses of certain of the cranial nerves, due to haemorrhage or leucocytic infiltration in their sheaths, have been recorded, and several observers have noted the occurrence of sudden deafness: in one or two cases this has been found to be due to haemorrhage into the inner ear. In some other cases impairment of hearing, subjective aural sensations, giddiness, and the like, have been observed. Dr. Parkes Weber has collected nine cases of leukaemia with Menière's symptoms; most of the cases shewed haemorrhage into the internal ear, but leukaemic infiltration without haemorrhage may be the condition found after death (Politzer).

The *retina* on ophthalmoscopical examination very often shews distinct changes, which depend chiefly on the altered condition of the blood with the occurrence of haemorrhages. When the anaemia is well marked the fundus is pale and sometimes of yellowish tint; the veins are usually dilated, tortuous, and paler than normal, whilst the arteries are narrow. There is sometimes swelling of the optic disc. Haemorrhages in the retina are common, and are most frequently situated at the periphery, though they may also occur in the region of the macula; their occurrence in the acute form is said to be practically invariable. They vary in size, though they are usually small; in shape they are irregular and have sometimes a striated appearance. Pale spots, usually close to the vessels and often surrounded by traces of haemorrhage, are also seen sometimes; occasionally they may reach a considerable size. They are composed chiefly of collections of leucocytes and degenerated nervous elements. In some other cases a uniform opacity of the retina has been observed, which has been found to be due to leucocytic infiltration of the layers of the retina. Interference with sight may be present or absent, according

to the position of the lesions. As these are most common at the periphery, usually nothing abnormal is noticed by the patient, but in some cases, in which the more central region is involved, defect of the field of vision may result. In a few cases such symptoms have first led the patient to seek advice, and in this way have led to the discovery of the disease. Haemorrhage into the vitreous has already been mentioned as a rare occurrence.

Reproductive System.—In women there is often irregularity of the menstrual function. There is sometimes menorrhagia, occasionally metrorrhagia, but as the disease advances amenorrhoea is not infrequent. Women suffering from the disease have been known to pass through more than one pregnancy and to bear healthy children. In man the occurrence of persistent priapism, lasting sometimes as long as eight weeks, is a curious symptom which has been noted in a considerable number of cases (Leube, Ward). It has been attributed to thrombosis in the veins or in the sinuses of the corpora cavernosa, and in a case recorded by Kast evidence of such thrombosis was found after death, the priapism having occurred a year and a half before.

DIAGNOSIS.—In most cases of myeloid leukaemia the diagnosis is very easy. Frequently attention is first drawn to the great enlargement of the spleen, and thereafter an examination of the blood reveals the nature of the disorder. The number of leucocytes may be so great as to leave no doubt possible; but it must be borne in mind that occasionally their number may not be much above normal, and also that in a number of other diseases the leucocytes may be increased in number. Here the examination of the characters of the leucocytes in stained films is essential. The attempt to distinguish leukaemia from leucocytosis by the number of leucocytes is quite unscientific—the difference being one not merely of degree but of nature. In leucocytosis the increase is almost exclusively on the part of the polymorphonuclear leucocytes, so that the proportion of these to the other leucocytes may be increased three or fourfold, and no abnormal elements are present. In leukaemia, on the other hand, the leucocytes have the characters already described, the most important change being the presence of numerous neutrophil myelocytes; increased number of eosinophils, especially when some are myelocytes, and of basophils, and the presence of many erythroblasts are also important points, though considerable variations are met with. In the rare cases in adults when a normal or only slightly increased leucocyte-count is associated with the presence of the abnormal elements mentioned, we are probably dealing with an aleukaemic phase of myeloid leukaemia, usually of temporary character. Accordingly, when such a condition is found the case should be closely watched and the blood examined from time to time. Examination of the blood will also distinguish myeloid leukaemia from other diseases with great splenic enlargement, such as ague or splenic anaemia. In the latter disease the number of leucocytes may be slightly increased, normal, or even diminished; but they never shew the alterations in character met with in leukaemia.

In the case of children diagnosis is often difficult as the anaemias generally, including the so-called *anaemia pseudo-leukaemica* of v. Jaksch (p. 780), are often attended with the presence of myelocytes in the blood, and the leucocyte picture may shew the variegated characters of leukaemia. Here again repeated examinations are necessary; if the leucocyte-count mounts to a marked degree the condition will evidently be leukaemia, but if it does not or does so only to a slight extent it must be admitted that in the present state of our knowledge a definite diagnosis may be impossible (*vide* p. 776).

In lymphatic leukaemia the high leucocyte-count with great excess of lymphocytes is conclusive. In some cases of pseudo-leukaemia as above defined in our experience, especially in children, the number of leucocytes may be only slightly increased or normal, while the proportion of lymphocytes is high. Lymphocythaemia may sometimes be found to develop on subsequent examinations. But pseudo-leukaemia may be present with a normal condition of the leucocytes. In the condition in which the glandular enlargement is chiefly due to reaction of the supporting elements of the tissue, and which we have separated under the name lymphadenoma, the blood sometimes shews an ordinary leucocytosis, sometimes no abnormality in the leucocytes; the glands are usually of firmer consistence than in lymphatic leukaemia. But with regard to all this group of affections we may say that a definite diagnosis can only be made with certainty from the blood examination when the typical picture of lymphocythaemia is present. In the absence of this, diagnosis can only be made by the microscopic examination of an excised gland.

Some cases of acute leukaemia with extensive haemorrhages may be mistaken for severe purpura and like conditions; and this is the more liable to occur as the enlargement of the spleen may not be sufficiently great to attract special attention. In other acute cases, with high temperature and without special enlargement of lymphatic glands, the condition, as Ebstein pointed out, may even be mistaken for enteric or other fevers. When the lesions of the mouth described above (p. 818) are present, often associated with pyrexia, the case may readily pass for one of ulcerative or gangrenous stomatitis. In such conditions the examination of the blood should always be undertaken, and will usually reveal the condition at once, if it be one of acute leukaemia. Here again the importance of distinguishing it from a mere leucocytosis may be noted.

Prognosis.—Though we cannot affirm that leukaemia always ends fatally, yet, so far as prognosis is concerned, it must be regarded as a condition of the gravest nature. A few cases are recorded in which a cure is said to have taken place; but in most of these one cannot but regard the evidence as inconclusive, as the diagnosis in some of the cases was uncertain, and in others the subsequent history was insufficient. Cases, however, certainly occur in which great improvement in the general health takes place, the number of leucocytes also diminishing greatly; and this improvement may last for a year or two. Accordingly, whilst the disease

practically always leads to a fatal issue, the duration of life after the recognition of it is very variable. In some chronic cases the disease has lasted as long as seven years; in other cases it has run an acute course in a few weeks or less. In relation to the probable duration in different cases a few general facts may be given.

In the first place, as regards age, the disease is usually of shorter duration in young subjects, the lymphatic variety being often of an acute type; myeloid leukaemia also, though it is comparatively rare, tends to run a comparatively rapid course. Myeloid leukaemia in adults, when there are no bad symptoms, is usually chronic, and often lasts one or two years. Some writers consider that it is rather more rapid in women, but there is probably little or no difference between the sexes in this respect. The number of leucocytes in itself does not give much indication, nor does the character of the cells present, with the possible exception that an atypical blood-picture, *e.g.* the association of numerous non-granular cells with many myelocytes, is often attended with a somewhat rapid course. The degree of anaemia present is of more importance, and a steady decrease in the number of red corpuscles is especially grave. The size of the spleen affords little assistance, except, perhaps, that a very great enlargement points to a comparatively slow course so far, a circumstance which may sometimes affect the prognosis.

In cases of lymphatic leukaemia the important point is to determine whether it is of an acute or chronic character. The presence of a large proportion of large lymphocytes is more frequently present in acute cases, but many exceptions to this occur. The condition of the mouth, presence of stomatitis, etc., the course of the temperature, the degree of anaemia, etc., are of much more importance in estimating the probable duration of a case. If acute leukaemia is present the general symptomatology will soon indicate this. It is, however, to be kept in view that even in very chronic cases an acute exacerbation may occur at any time and lead to a fatal result.

Haemorrhages have a varying significance according to their position and extent. Haemorrhage from the nose is not infrequent in the early stages of the disease, and, though it may lead to a fatal result, may occur from time to time in cases which run a very chronic course. Haemorrhages from the stomach and bowels are much more serious symptoms, and usually indicate a condition of special gravity. So also haemorrhages in the skin are generally the omen of rapidly advancing cachexia. The possible occurrence of cerebral haemorrhage at any time, even in chronic cases, should always be kept in view. The presence of dropsy, well-marked or continuous pyrexia, or persistent diarrhoea naturally makes the prognosis specially grave.

TREATMENT.—Leukaemia is a disease for which there is no specific remedy, and it is one which too often runs a steady course towards a fatal termination. But while this is so, under careful and judicious treatment life may be considerably prolonged in many cases, and great improvement may be effected in some. It ought to be regarded as a con-

dition in which death may be much hastened by indiscretion on the part of the patient; but an intelligent knowledge of the features of the disease and the complications which are likely to arise will sufficiently guide the physician in this matter.

It is rather the rule than otherwise for patients in the earlier stages of chronic leukaemia to improve when under treatment in hospital. The regulation of the condition of the alimentary canal is of great importance. The diet ought to be arranged so as to exclude anything likely to lead to a gastric disturbance, but otherwise should be as full and nourishing as the condition of the patient will allow. If a tendency to constipation be present, the bowels ought to be kept regular by mild laxatives or intestinal stimulants; constipation is apt sometimes to be followed by diarrhoea. Powerful purgatives, however, are contra-indicated in all conditions which may arise in the course of the disease. Excess in eating and drinking, exposure to cold, over-exertion, and such like must be carefully avoided. Such general measures as these, along with good hygienic conditions, have a distinct effect on the general condition of health apart from treatment with drugs. The tendency to haemorrhage should be kept in mind in connexion with any surgical interference which may be incidentally called for in a patient suffering from leukaemia.

A large number of drugs have been employed in the treatment of the disease, and with regard to each it may be stated that whilst in some cases improvement or even cure is recorded, in the majority it has been found ultimately to fail. Of all the drugs employed, arsenic is of the greatest value, and in many cases great improvement results from its use. It ought to be given at first in ordinary doses, to be gradually increased, and pushed as far as possible. Under its use the number of leucocytes may diminish greatly and may even fall to normal; the size of the spleen also may become considerably less, though sometimes it is little affected. Arsenic and atoxyl have also been administered subcutaneously and by direct injection into the spleen, but there are manifest objections to these methods, especially when the haemorrhagic tendency is well marked. Some observers consider quinine in large doses to be of considerable service, but it is distinctly inferior to arsenic. Good results have been reported from the use of phosphorus in one or two cases, but the general experience is that it is of no value. In other cases improvement has followed the use of tonic medicines—cod-liver oil, iron, with or without quinine in small doses. In our experience, however, arsenic is the only drug which seems to have a distinct effect on the leukaemic condition.

X-ray treatment has recently been employed in leukaemia with a considerable degree of success, so far as amelioration of symptoms is concerned. The spleen, the sternum, and the epiphyses and the shafts of the long bones have been exposed to the *x*-rays; sometimes only one of these situations, sometimes several of them have been selected for treatment. The exposure has usually lasted for ten to twenty minutes on successive or on alternate days. Treatment has in certain instances been continued

for two or three months. The general result has been that in a considerable proportion of cases of chronic myeloid leukaemia marked improvement has resulted. The number of leucocytes has diminished, the fall in the first instance being generally on the part of the myelocytes, and in several cases the number has fallen to normal in the course of a few weeks. There has also sometimes occurred an increase in the number of red corpuscles, and the general well-being has been improved. The effect on the size of the spleen has been variable. Not infrequently a distinct, though slight diminution, has occurred; in a few cases this has been marked. The results in the case of chronic lymphatic leukaemia have been less successful. Usually only a moderate decrease in the leucocytes has occurred, and the general improvement has been slight. Harris concludes that the action of *x*-rays is associated with the production of a leucolytic body or bodies in the patient. As occasional untoward results may be mentioned erythema, dermatitis, and burns of the skin, and sometimes obscure toxic symptoms, headache, nausea, and so forth. These must be guarded against on ordinary principles. As a general conclusion it may be stated that although there is no case which can be said to have been cured by the treatment, still a considerable improvement has resulted in many cases of myeloid leukaemia. Some writers consider that the treatment is not more successful than that by arsenic, but the general results appear to us on the whole to have been more favourable.

On the view that the spleen is the primary seat of disease, a number of measures have been adopted to produce diminution of this organ. Such are the use of certain drugs—eucalyptus, quinine, and piperine (Mosler), the faradic or galvanic current applied over the organ, electropuncture, the cold douche to the splenic region, and so forth. All these measures, we believe, are without effect. Excision of the spleen has been performed in a considerable number of cases, but almost invariably with a fatal result; it must be regarded as absolutely unjustifiable, and it is also, we believe, useless. Transfusion of blood has also been tried without any satisfactory result. Inhalations of oxygen have been administered in a considerable number of cases, sometimes alone, sometimes along with other remedies, especially arsenic. In the hands of some observers benefit has followed, chiefly in the early stages of the disease; but in many cases this treatment has entirely failed. The amount of oxygen employed has usually been about 30 litres daily, though sometimes as much as 100 litres have been used. Bone-marrow has been administered in this disease, but there seems to be no scientific basis for this treatment, yet in a disease in which all known remedies may be without avail the method is worth a fair trial. The marrow may be administered either in the fresh condition or in the form of prepared tablets. Dr. J. H. Drysdale had under his care a case of comparatively acute myeloid leukaemia with intestinal symptoms, in which remarkable success was obtained by means of naphthalene tetrachloride. The condition of the blood (the leucocytes numbered 40,000, of which

over 60 per cent were myelocytes) returned to normal; the number of red corpuscles increased from about a million per c.mm. up to the normal; and the slight enlargement of the spleen and lymphatic glands which was present disappeared. The drug was given in doses of 8 grains at first every three hours and later every two hours. The result is of so striking a nature that the drug should be tried in such cases.

The complications occurring in the course of the disease and most frequently calling for treatment are the haemorrhages from various sources, the gastric and alimentary disturbances, and, in the later stages, the heart-weakness, dyspnoea, and dropsy. All these are to be met by the usual methods. In the more acute forms all remedies fail, and the aid of the physician is limited to the relief of the more distressing symptoms.

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The literature on leukaemia is so extensive that only a number of representative papers can be quoted. In making a selection I have endeavoured to cover the subject in all its aspects; full references to other works will be found in the papers cited, and the subject-matter of those bearing on more special points has been indicated. The earlier literature on the subject may be found in the article "Splenic Leucocythaemia" by Sir W. Gowers in the *System of Medicine* edited by Russell Reynolds, whilst a full account of the modern work with references to cases with peculiar features will be obtained in the *Folia Haematologica* edited by Pappenheim, the first volume of which was published in 1904. For details as to the cytology of the blood, etc., the works on haematology by Cabot, Coles, Da Costa, Ewing, Grawitz, v. Limbeck, and O. Naegeli may be consulted.

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R. M.

POLYCYTHAEMIA AND ERYTHRAEMIA

By F. Parkes Weber, M.D., F.R.C.P.

The various forms of **polycythaemia**, or "polycythaemia rubra," that is to say, increase in the number of red corpuscles in the circulating blood, though considered in the article on the "Clinical Examination of the Blood and its Significance" (Vol. I. p. 666), must be referred to here, in order that the special class of cases to which the term polycythaemia is now sometimes restricted may be examined and distinguished. Polycythaemia may be (i.) relative or (ii.) true. (i.) *Relative polycythaemia* is due to concentration of the blood, such as may be caused by choleraic diarrhoea or other excessive fluid discharges from the body, and is doubtless almost always temporary only.

(ii.) In *absolute* or *true polycythaemia* (polycythaemia rubra vera) the total number of red corpuscles in the body is increased, and there is evidence that in most if not in all cases the total volume of blood is also increased. Cases of absolute polycythaemia may be divided into the following classes:—(*a*) Those due to imperfect oxygenation of the blood and tissues brought about by the circulatory disturbance in chronic cardiac and pulmonary diseases. In this class may also be included the polycythaemia occasionally following carbon monoxide poisoning (33), phosphorus poisoning (39), and other toxic conditions interfering with the proper oxygenation of the blood. (*b*) Those connected with residence at high altitudes and diminished oxygen-tension in the inspired air. (*c*) Those in which no recognised exciting cause of polycythaemia can be ascertained, and which have been described under the headings splenomegalic polycythaemia, myelopathic polycythaemia, and erythraemia. These cases should not be designated polycythaemia with chronic cyanosis, for cyanosis is entirely absent in some instances, and in other examples is only occasionally present. Moreover, cyanosis is often a striking feature of cases in class *a*. These cases cannot be distinguished from other forms of absolute polycythaemia (*a* and *b*) either by evidence of increase in the total blood-volume or by evidence of excessive erythroblastic activity in the bone-marrow, since probably all forms of absolute polycythaemia are due to increased formation of erythrocytes in the bone-marrow, and are always associated with more or less polyhaemia (plethora vera (46)). Neither does splenic enlargement appear to be an invariable characteristic of these cases. Since an increase of the haemic leucocytes, when known to be a reactive response to infection or toxaemia, is spoken of as leucocytosis, and so distinguished from leukaemia, it is reasonable to differentiate between an apparently primary increase and a secondary (reactive) increase in the number of the red blood-corpuscles. We may therefore, as suggested by W. Türk,

H. Hirschfeld, and W. Osler, designate as erythraemia the cases (class *c*) in which no definite cause for the increase of red corpuscles can be ascertained, and with Hirschfeld employ the word erythrocytosis for any reactive increase in the number of erythrocytes resulting from imperfect oxygenation of the blood and tissues of the body.

Erythraemia

Synonyms.—*Splenomegalic polycythaemia; Myelopathic polycythaemia; Polycythaemia with chronic cyanosis; Erythrocytosis megalosplenica* (Senator), *Vaquez's disease, Osler's disease.*

Definition.—A disease, or at least symptom-group, characterised by well-marked persistent relative and absolute polycythaemia (increase in the number of red blood-corpuscles), due to excessive erythroblastic activity of the bone-marrow, without the presence of any recognised, or at all events sufficient, exciting cause; it is also characterised by persistent increase in the viscosity and total volume of the blood, and usually by a cyanotic appearance of the patient and by enlargement of the spleen.

History.—In 1892 H. Vaquez described a peculiar form of cyanosis accompanied by excessive and persistent polycythaemia ("hyperglobulie"), and in a supplementary note (1895) drew attention to the existence of splenomegaly and the absence of cardiac lesions in his case. This was followed by other cases of polycythaemia associated with splenomegaly (Rendu and Widal (1899), Moutard-Martin and Lefas (1899), R. C. Cabot (1899 and 1900), Cominotti (1900), M'Keen (1901), Saundby and Russell (1902), and W. Türk (1902 and later)). In a prefatory note to Dr. Russell's description of Prof. Saundby's case the condition was characterised as a "clinical entity," but it was probably the appearance of two papers by Prof. W. Osler (1903 and 1904) that widely drew attention to the subject in England and America. Dr. L. G. J. Mackey in 1907 was able to collect over forty cases. Reports of many more exist, and I know of several as yet unpublished cases. Erythraemia cannot be quite so rare as it has been supposed to be. There have been several autopsies; the first complete one was published by Dr. Watson and myself in March 1904. In former times cases of erythraemia were probably described as plethora, general venous congestion with cyanosis; and possibly Cuffer and Sollier's two cases of "congestive venous diathesis" were, as Dr. Herringham points out, examples of erythraemia.

Etiology.—Nothing certain is known in regard to etiology. Nervous excitement or mental worry has been suggested as the exciting cause in some cases. According to various hypotheses the abnormal activity of the bone-marrow (giving rise to the polycythaemia) is due to toxaemia originating in the spleen, lungs, or alimentary canal (20, 45); or, it is suggested, the polycythaemia may be regarded as the result of a compen-

satory reaction towards some hypothetical disturbance in the gas-exchanging functions of the blood (v. Korányi, Bence), which disturbance may in its turn be of toxaemic (for instance, alimentary or digestive) origin (16). Further investigation into the functional capacity of the red blood-corpuscles and into the respiratory exchange (this subject has been specially discussed by Lommel) in cases of erythraemia is certainly required. The blood has been examined in one or two cases for methaemoglobin and sulph-haemoglobin with negative results (16). The condition chiefly affects middle-aged persons of either sex, but has been observed in persons after sixty and before thirty years of age, and, according to Ambard and Fiessinger and Blumenthal, may possibly even be congenital. Nothing is known as to the relation of the condition to climate (atmospheric temperature) and race.

Morbid Anatomy.—There have been necropsies made in several cases (2, 7, 8, 14, 16, 17, 19, 23, 27, 34, 36, 42, 48, 50), including the five fairly complete ones recently discussed by Hirschfeld. Evidence of increased erythroblastic activity in the bone-marrow has been found in almost every case in which the shafts of the long bones have been examined with regard to this point. Much of the marrow of the shafts of the long bones, which is normally of the pale fatty kind, has been found converted into red (erythroblastic) marrow, so that the total amount of erythrocyte-producing marrow in the body must have been enormously increased, though the red marrow normally present may not have been much altered. A striking feature of uncertain significance in Dr. Watson's and my case was the great proportion of non-granular mononuclear cells of the large lymphocyte type (probably to be regarded as non-granular myelocytes or "myeloblasts") seen in sections of the altered marrow. The spleen has been almost always found enlarged and engorged with blood, but in the cases carefully examined this organ shewed little if any erythroblastic or myeloid transformation; in many cases it contained anaemic infarcts, apparently of thrombotic origin. In one or two cases no enlargement of the spleen was found either during life or after death (16). The extreme vascular engorgement of the liver noted in some cases is quite distinct from that found in chronic venous engorgement. In every case the distension of the visceral blood-vessels has been very striking, the mesenteric venules sometimes looking as if they had been forcibly injected for anatomical purposes. The following morbid changes have been found occasionally: a certain amount of pulmonary emphysema, arteriosclerosis, fibrosis of the cardiac muscle (Hutchison and Miller), slight changes in the cardiac valves, hepatic cirrhosis, and the results of disease of cerebral blood-vessels. Primary tuberculous nodules in the spleen were reported in two cases (27, 34), in which it was scarcely possible that anaemic infarcts could have been mistaken for tuberculous caseous masses. In view of the greatly increased viscosity of the blood the absence of much cardiac hypertrophy in most cases is remarkable.

Pathology.—Most of the signs and symptoms of erythraemia may be

accounted for by the increased formation of red blood-cells in the bone-marrow. The results of this excessive erythroblastic activity of the bone-marrow may be compared with what would be the consequences of persistent slow transfusion of blood into the veins of an animal. Experimental sudden transfusion of blood in animals (von Lesser, Worm-Müller) leads to temporary plethora, followed quickly by polycythaemia, and it is reasonable to suppose that a slow transfusion of blood, lasting not for a few minutes only, but for months and years, were it possible from the experimental point of view, would give rise to a condition of persistent absolute polycythaemia associated with true plethora, such as is met with in cases of erythraemia (46). Dilatation of capillaries and venules would necessarily follow, and probably for a time at least there would be increased arterial blood-pressure. Ultimately degenerative changes in the vascular system would be likely to occur, leading to true passive congestion, cyanosis, bleeding from the gums, thrombosis in various organs, and local circulatory disorders. The excessive erythroblastic activity of the bone-marrow in cases of erythraemia may be supposed to be a primary change, a return to a fetal condition or analogous to the increased leucoblastic activity in leukaemia, but there is no proof that it may not be secondary as already pointed out (p. 832). In connexion with the possibility that the polycythaemia is secondary, the question of individual reactive power must not be overlooked. Chronic cardiac and pulmonary insufficiency may in some adults give rise to great polycythaemia (13, 32), but in others to none. The enlargement of the spleen found in most cases seems to be due partly to engorgement with blood, the organ acting as a kind of elastic blood-reservoir, and partly to hyperplasia of the splenic pulp, possibly connected with the increased haemolysis (Abeles found increase of iron in the urine in polycythaemia), which must necessarily accompany all conditions of absolute polycythaemia unless the erythrocytes are specially long-lived (for which there is no evidence in erythraemia). Thrombotic infarcts, past malaria, or tuberculosis may sometimes partly account for the splenomegaly. At future necropsies great care should be taken to examine for changes in the splenic vein. Both splenic infarcts and obstruction in the splenic vein may give rise to more or less splenomegaly, and in this connexion it may be remembered that in certain cases supposed during life to have been examples of splenic anaemia or Banti's disease, the splenic enlargement has been shewn to be connected with obstruction in the splenic vein, and in two cases of polycythaemia with cyanosis and splenomegaly (van der Weyde and van Ljzeren, Lommel's first case) the necropsies shewed thrombotic obstruction in the portal vein. At present it is impossible to be sure that all the cases classed as erythraemia are pathologically identical. Provisionally the cases may be divided into those with splenic enlargement and those without. The cases without obvious splenic enlargement may be further subdivided into those with exaggerated blood-pressure ("Hypertonia polycythaemica" of Geisböck and Hess), and those with normal or low blood-pressure (W. Pfeiffer, Herringham).

Signs and Symptoms.—The patient may complain of lassitude, headache, migraine, vertigo, Menière's symptoms, sensation of fulness in the head, abdominal pains, dyspepsia, constipation, distressing thirst, menorrhagia, epistaxis, bleeding gums, or symptoms resembling erythromelalgia of a lower extremity. On the other hand, there may be almost no symptoms. The vascular engorgement or cyanosis of the skin, most obvious in the face and ears, varies much in different cases and in the same patient at different times. Exposure to cold and some emotional influences may intensify the cyanosis of erythraemia as well as other forms of cyanosis. Prof. Osler (30) points out that a warm room and mental excitement may occasionally cause blueness of the face in these patients to give place to redness. In erythraemia the vascular engorgement is, of course, not confined to the skin, but may be observed in the mucous membrane of the mouth, fauces, and larynx, in the conjunctivae, and by ophthalmoscopic examination in the interior of the eyes. Especially characteristic is the bluish-red appearance of the tongue. Sometimes there is slight cutaneous pigmentation. The spleen can generally be felt moderately or considerably enlarged and hardened, and not uncommonly the liver projects below the costal margin. The splenic region is occasionally painful or tender. The urine may be pale and abundant, or highly-coloured and containing excess of urobilin (48), as shewn by spectroscopic examination without concentration. It often contains a little albumin and sometimes hyaline and granular casts. The blood-pressure is frequently, but not invariably, above the normal. The most important signs are, of course, those yielded by examination of the blood. The red cells are increased in number (7 to 12 millions per c.mm.), and on the average rather increased than decreased in size (43), but usually normal in appearance. In regard to the white cells the only constant feature is the excessive proportion of the polymorphonuclears (not rarely up to 80 per cent or higher). A few normoblasts and one or two myelocytes have occasionally been noted. The haemoglobin value may reach 170 or 180 per cent, or even higher, but the colour-index is often below 1·0. Nothing abnormal has been found by cryoscopic examination of the blood. The specific gravity is generally raised, but further observations are required. The viscosity is increased, more or less in proportion to the degree of polycythaemia. The coagulability is probably sometimes increased and sometimes diminished. The resistance to haemolysis was found in one case (44) decreased, and in another case (45) normal. The total blood-volume, as estimated during life by Dr. Haldane and Prof. Lorrain Smith's carbon-monoxide method is greatly above the normal (6, 46), and this clinical observation is confirmed by the appearance of the viscera at necropsies.

Complications.—The presence in two cases of primary splenic tuberculosis has already been alluded to. In two other cases pulmonary tuberculosis was the ultimate cause of death. The following complications have been occasionally noted: jaundice (41), hepatic cirrhosis (5), renal disease (8), ovarian tumour (45); a certain amount of pulmonary emphy-

sema, bronchitis (31); bronchiectasis (20); slight valvular lesions of the heart, myocardial fibrosis (19); arteriosclerotic changes, thrombotic infarction of the spleen, the results of vascular disease in the brain, erythromelalgia (45, 49); Menière's attacks, tabes dorsalis (14); and insanity (48).

Diagnosis.—The plethoric or cyanotic appearance of the patient, the presence of splenomegaly of uncertain origin, symptoms resembling erythromelalgia (45), or other circumstances lead to examination of the blood. The diagnosis of erythraemia then depends, as has already been pointed out, on the recognition of a condition of persistent absolute polycythaemia and the absence of obvious cause for any considerable erythrocytosis.

Prognosis and Course.—Some cases appear to be stationary, or to improve with or without special treatment. Some have died in a sudden exacerbation of cyanosis (16, 48), and others of complications due to vascular disease in the brain (7, 19).

Treatment.—Subjective improvement seems to have followed spontaneous haemorrhages (49), and treatment by an occasional copious blood-letting has been carried out with at least temporary relief of symptoms in an as yet unpublished case of Dr. T. D. Acland. In a case of moderate polycythaemia with a history of malaria, reported by Schneider, splenectomy was performed and the number of red cells decreased, but shortly after the operation the patient developed progressive pulmonary tuberculosis. In other cases the operation of splenectomy was fatal (5), or was followed by a fatal septic complication (9). The application of *x*-rays did not benefit my second case (45), but I have heard of apparent improvement in another case. Arsenic, quinine, and a number of drugs have been tried, but generally without any satisfactory effect. Begg and Bullmore recorded improvement from quinine and inunction of iodide of mercury ointment. Bence thought that the polycythaemia could be reduced by oxygen inhalations, but Stern failed to obtain any such result.

On general principles patients should, as far as possible, avoid mental fatigue, excitement, impure air, constipation, excess in tea, coffee, tobacco, and stimulating meats and spices, and abstain from alcohol on account of its action on the blood-vessels, from chalybeate drugs in view of their effect on the erythroblastic tissues, and from coal-tar products, such as antipyrin, phenacetin, and acetanilide, which occasionally produce cyanosis. The plentiful use of German "sour milk" or some similar preparation, on account of the effect on the flora of the large intestine, might be worth a trial, and a lacto-vegetarian diet (Stern) or one rendered as poor in iron as possible (P. Ehrlich, quoted by Stern) has likewise been suggested.

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ENTEROGENOUS CYANOSIS

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Introduction.—That certain toxic substances, including some which are employed as drugs, are capable of changing the haemoglobin of living blood has long been known. Some of these, such as carbon monoxide and sulphuretted hydrogen, form special compounds with the blood-pigment, whereas others convert oxyhaemoglobin into methaemoglobin. In cases of poisoning by potassium chlorate an active haemolysis also occurs, and methaemoglobinuria, and sometimes jaundice result. Other poisons such as nitrobenzol and aniline derivatives do not induce haemoglobinuria, but the altered colour of the pigment in the corpuscles produces a kind of cyanosis. (For poisoning by aniline and nitro- and dinitro-benzol, *vide* article, Vol. II. Part I. p. 1023.)

Dittrich, who has made a careful study of toxic methaemoglobinaemia, arrived at the conclusion that, although when the change is extreme the red corpuscles laden with methaemoglobin are broken down, when the amount of methaemoglobin contained in them is smaller the injured corpuscles are capable of recovering, and that restoration of the altered haemoglobin may take place within them, apart from any haemolysis. When the methaemoglobin of the destroyed corpuscles is free in the plasma, it is quickly disposed of, partly by the liver which converts it into bile pigment, and in part by the kidneys which excrete it in the urine if the quantity present be greater than the liver can deal with. The phenomenon of methaemoglobinaemia is therefore better seen in cases in

which the methaemoglobin circulates in the corpuscles, and in which no active haemolysis takes place. The cyanosis in such cases has a different tint from that which results from mere deficiency of oxygen, and has been styled "false cyanosis."

It was the last of the many services of the late Prof. Stokvis to clinical medicine to shew that a similar cyanosis is produced, in exceptional cases, by poisons which are presumably formed in the intestine and thence absorbed, and are not introduced into the alimentary canal from without. He thus laid the foundations of our knowledge of the rare conditions here to be described under the name of enterogenous cyanosis. The publication of Stokvis' posthumous article in 1902 was soon followed by records of further cases of the kind by other observers in the Netherlands, Talma and Hijmans van der Bergh. Talma, in 1902, described three more cases of enterogenous methaemoglobinaemia resembling that recorded by Stokvis; but whereas the latter observer had based his diagnosis upon the spectroscopic examination of the living tissues of his patient, Talma, by investigating the blood, proved that the abnormal pigment was wholly intracorpuscular, and that the serum which did not shew any abnormality of tint, when examined with the spectroscope did not give the absorption-bands of methaemoglobin. Hijmans van der Bergh (1905) found that the absorption-band in the red which the blood of his first patient shewed, and which he at first ascribed to methaemoglobin, agreed in position with that of the compound first described by Hoppe-Seyler under the name of sulph-haemoglobin, and differed from the very similar band of methaemoglobin. In a second case the blood shewed the band of methaemoglobin, and the differentiation of the pigments present in the two cases was confirmed by a further test. Thus it became evident that the rare examples of enterogenous cyanosis fall into two distinct classes. In Stokvis' and Talma's cases the differentiation from sulph-haemoglobinaemia was not established, but the associated clinical symptoms strongly suggest that they really belonged to the methaemoglobinaemic rather than to the sulph-haemoglobinaemic class. In a later article van der Bergh and A. Grutterink described some further cases of both varieties.

Since then the subject has attracted attention in this country. In 1906 Drs. G. A. Gibson and Carstairs Douglas recorded a further case of methaemoglobinaemia; in 1907 Drs. S. West and T. Wood Clarke described the first case of sulph-haemoglobinaemia diagnosed in England, and additional cases of the same kind have been put upon record by Dr. A. E. Russell and by Dr. W. Essex Wynter. Of the 15 cases of enterogenous cyanosis now recorded, the abnormal blood-pigment was methaemoglobin in 8, if we include Stokvis' and Talma's cases, and sulph-haemoglobin in 7.

Diagnosis of Enterogenous Cyanosis and its Varieties.—The presence of cyanosis which may persist for years, although varying in intensity from time to time; the peculiarity of tint of the skin and mucous membranes, and the absence of any lesions of the heart or lungs capable of

explaining the phenomenon, will suggest the diagnosis of enterogenous cyanosis. If the spectroscopic examination of the skin and mucous membranes of the patient, or better still of his blood, shews the presence of an absorption-band in the red of the spectrum in addition to the bands of oxyhaemoglobin, the suspicion will be greatly strengthened, but even then it is necessary to exclude the continuous taking of an aniline derivative or other drug to which such a blood-change might be due. If the band in the red is found to correspond in position to that of sulph-haemoglobin this latter causation is practically excluded, for no compound which is used as a drug is known to induce sulph-haemoglobinaemia, and I do not know of any record of such persistent cyanosis resulting from continued inhalation of minute quantities of hydrogen sulphide in sewer-gas or otherwise. It is possible to observe the spectroscopic change in the blood by examining the reflex from the cyanosed skin or mucous membranes with a pocket spectroscope; more readily by examining the light which penetrates between the apposed fingers, and better still by utilising the light which has traversed the pinna of the ear, from a small electric lamp fitted with a conical reflector which concentrates its rays upon the back of the pinna.

It is far more satisfactory to examine the blood itself. If a few drops, obtained from the lobe of the ear, are mixed with distilled water in a small pipette the spectrum of the diluted and haemolysed blood may be well studied, and if some further drops are mixed with normal saline solution and centrifuged, the absence of any tint from the serum may be readily established. Differentiation of the spectra of methaemoglobin and sulph-haemoglobin by mere inspection is hardly possible even for experts in spectroscopy, and certainty can only be attained by accurate measurement of the position of the band in the red, or by direct comparison of the spectrum with that of control specimens of the two compounds. The band in the red of sulph-haemoglobin, which is really complex and consists of two narrow black bands united by a dark shading, is somewhat narrower than that of methaemoglobin, and is situated nearer to the oxyhaemoglobin bands. The respective positions of the two bands as measured in wave-lengths are as follows:—

Methaemoglobin band λ 620 – λ 645;
Sulph-haemoglobin band λ 610 – λ 625, or in concentrated solutions λ 630.

The action of ammonium sulphide affords a valuable distinctive test; when a very small quantity of a solution of that substance is added to a blood containing methaemoglobin the band in the red promptly disappears, whereas that of sulph-haemoglobin is not affected by the reagent. Excess of ammonium sulphide removes the band of sulph-haemoglobin also, and this point must be borne in mind, seeing that a too free addition of this reagent may easily lead to an erroneous conclusion.

We owe an additional test to Drs. Wood Clarke and Hurtley, who found that when a stream of carbon monoxide, carefully freed from any

admixture of acid, is passed through a solution of sulph-haemoglobin all the bands of the spectrum are shifted towards the violet, the place of the two bands of oxyhaemoglobin is taken by those of CO-haemoglobin, and the band in the red is shifted from λ 610 – λ 625 to λ 605 – λ 620. When carbon monoxide is passed through a solution of methaemoglobin no such change is observed. In the blood of patients with enterogenous cyanosis the band in the red is often rather faint, and may not be clearly seen with the dilutions necessary to render the oxyhaemoglobin bands clearly visible. Somewhat concentrated solutions which, before the spectroscope, obliterate the whole of the green and blue of the spectrum should therefore be employed. By means of these three tests, namely, measurement of the band in the red, the effect of a trace of ammonium sulphide, and that of a stream of acid-free carbon monoxide, it is possible to establish beyond question the differential diagnosis between methaemoglobinaemia and sulph-haemoglobinaemia. In both conditions the cyanosis which is the conspicuous outward sign depends upon the colour of the abnormal pigment, and not upon the presence of reduced haemoglobin as in ordinary cyanosis from deficient oxidation. The hue of the skin and lips has been variously described as violet, leaden and otherwise, but perhaps it is most accurately spoken of as blue with a mauve tinge. In neither condition has more than a small portion of the blood pigment undergone change, and the oxygen-carrying power of the blood is not seriously impaired. Hence, unless other complicating conditions are present, such as cardiac dilatation or anaemia, dyspnoea is not a conspicuous sign nor an essential feature of enterogenous cyanosis.

The tint of the skin in enterogenous cyanosis is so distinct that when once seen it should not be confused with the pigmentation of Addison's disease, ochronosis, argyria, or haemochromatosis. From polycythaemia (*vide* p. 831), a blood examination will at once distinguish it.

Methaemoglobinaemia. — *Etiology.* — Intestinal disorders attended with looseness of the bowels are, apparently, the underlying cause of enterogenous methaemoglobinaemia, but the conditions responsible for the diarrhoea seem to have been of different kinds. Three of the patients had resided in the Dutch East Indies, on military service, and had there acquired the intestinal maladies which had resulted in chronic diarrhoea. Of these, Stokvis' patient passed fluid and offensive stools, of acid reaction, which contained many flagellated protozoa; after death, the mucous membrane of the intestines was swollen and hyperaemic, with superficial ulceration of some Peyer's patches. In one of van der Bergh's cases, *Anguillula stercoralis* was found in the stools on several occasions. Some patients had not resided in the Tropics, and in one of van der Bergh's cases the intestinal disturbance was comparatively slight, being only manifested by the passage of two or three loose motions in the day.

Symptoms. — Headache and feebleness of the limbs have been conspicuous symptoms in most cases of methaemoglobinaemia, and would seem to be those most directly associated with the blood change. Inter-

current maladies of various kinds have been observed, and in more than one of the patients cardiac dilatation and signs of backward pressure have been present. In Stokvis' case there was conspicuous clubbing of the fingers, although no morbid condition of the thoracic organs, such as usually underlies such clubbing, could be detected during life or at the necropsy. In two of Talma's patients lymphatic glands were enlarged. Anaemia is not an essential feature of the condition, and blood-counts may not present any abnormal features.

The cyanosis of methaemoglobinaemia is known to have lasted for seven and eight years in two instances. It is wont to vary much in intensity, and the variations have sometimes been due to changes of diet. Talma observed great improvement on a diet of milk alone; and Hijmans van der Bergh found that on such a diet the cyanosis might completely disappear, but only to reappear with undiminished intensity after a single meal of meat. The urine of the patients has not shewn any abnormal pigmentation, and no methaemoglobin has been found in it. In Stokvis' case the proportion of ethereal sulphates was notably high, and excess of indican was observed by Talma and by van der Bergh. The substance present in the urine of Stokvis' patient, which converted oxyhaemoglobin into methaemoglobin, was probably a nitrite, such as is found in decomposing normal urines. Hijmans van der Bergh and Grutterink were able to demonstrate by more than one method the presence of nitrites in the blood of a patient, and that it was contained in the corpuscles and not in the plasma. An unusual amount of nitrite was also present in the saliva. To the presence of such compounds in the urine and faeces they attach little importance. Drs. Gibson and Carstairs Douglas confirmed these observations in their case, and as they found traces only of nitrites in the patients' faeces, which did not convert oxyhaemoglobin into methaemoglobin, they were inclined to regard the nitrite in the blood as formed in the circulation. From blood from their patient's ear they obtained a pure culture of an organism of the coli group, probably *Bacillus coli communis*, but the organism in question failed to produce nitrites in a watery peptone medium. They are, however, inclined to ascribe the presence of nitrite in the blood to the bacillus, and proposed for the condition the alternative name of "microbic cyanosis." Blood cultures carried out in other such cases are greatly to be desired; but whether or no bacterial agencies are actually at work in the formation of nitrites in the blood itself, rather than in the intestine, the observations quoted leave little doubt that such compounds, which are well known to effect such conversion of blood pigment, are the active agents in the production of the methaemoglobinaemia. At a later stage of Dr. Gibson's case, when the cyanosis had practically disappeared, when the blood no longer shewed the methaemoglobin band, and when nitrites were only detected in it in traces, a culture from the ear proved sterile. The improvement in this case was brought about by a course of intestinal antiseptics, and the employment of such drugs seems clearly indicated in the treatment of enterogenous methaemoglobinaemia, whereas the

repeatedly observed effects of a diet of milk suggest that such a diet is suitable while antiseptic treatment is being carried out.

Sulph-haemoglobinaemia.—*Clinical Aspects.*—The cyanosis due to sulph-haemoglobinaemia may also persist for years; in Dr. Essex Wynter's case there was a clear history that the symptoms had existed for twelve years, and Dr. Russell's patient had been under observation for eight years. The clinical details of several of the recorded cases are wanting, but symptoms similar to those complained of by methaemoglobinaemic patients may be present, such as headache and extreme muscular weakness. Blood-counts do not reveal any special peculiarity of the blood, and do not shew any evidence of active haemolysis. There may be associated anaemia, but this is no constant feature of the malady. In Drs. West and Clarke's case cultures of blood obtained from a vein proved sterile. Nor are there any noteworthy changes in the urine; Dr. Wood Clarke found no excess of indican nor any undue ratio of ethereal to mineral sulphates.

Various intercurrent maladies have been observed. In Dr. Essex Wynter's case alone there was considerable enlargement of the spleen. As in Stokvis' case of methaemoglobinaemia, there was pronounced clubbing of the fingers and toes in one of van der Bergh's sulph-haemoglobinaemic cases; examination of the heart and lungs revealed no intrathoracic cause for this, and that the clubbing was intimately connected with blood-change was strongly suggested by the fact that when complete recovery ensued the fingers and toes resumed their normal shapes. The intestinal derangement upon which the sulph-haemoglobinaemia apparently depends takes the form of obstinate constipation, and the cyanosis may disappear when the bowels are kept freely open. Van der Bergh's case, just referred to, is peculiarly instructive in this connexion. The patient, a boy aged nine years, born with imperforate anus, had been operated upon in the first days of life and had acquired a urethro-rectal fistula. The faeces were mixed with decomposed urine; marked improvement followed dilatation of the contracted anal orifice, and the retention of a catheter in the urethra; and subsequently a plastic operation, which closed the fistulous opening and allowed complete evacuation of the retained faeces, brought about a complete cure of the enterogenous cyanosis. The treatment, therefore, consists in the prevention of constipation.

Pathogeny.—Any attempt to explain the development of the sulph-haemoglobinaemia is confronted with serious difficulties. It would not appear that there is excessive formation of hydrogen sulphide in the alimentary canal in these cases, and it is not apparent why, of the thousands of patients who suffer from obstinate constipation, such cyanosis should appear in a few exceptional ones. Organisms which form this gas are present in normal stools, and were isolated by Hijmans van der Bergh and by Wood Clarke from the faeces of their patients. The latter, who employed a method of decimal dilution, obtained blackening of lead acetate in bouillon cultures of the patient's stools after incubation for

forty-eight hours, either anaerobically or aerobically, up to a dilution of 1 : 10,000,000, whereas four controls from other patients on similar diets produced the same effect in dilutions from 1 : 10,000 to 1 : 1,000,000,000. Even at times when the blood shewed the sulph-haemoglobin band clearly, neither of the observers quoted was able to detect hydrogen sulphide, by chemical methods of extreme delicacy, in air or carbon dioxide which has been allowed to bubble through the blood in a wash-bottle. In the course of his experimental investigations of hydrogen sulphide poisoning in animals, Erich Meyer found that chemical methods were far more delicate than the spectroscopic one. He found, however, that whilst it was possible to remove by the passage of air, or better, of carbon dioxide, the sulphide contained in the blood as such, or in the form of sodium sulphides, the sulph-haemoglobin already formed remained intact after prolonged passage of gases. Thus it is possible for a specimen of blood to shew the spectrum of sulph-haemoglobin, whereas no hydrogen sulphide can be found in it by the chemical method. This is the explanation which Hijmans van der Bergh advances of the negative result of the chemical examination of the blood in cases of sulph-haemoglobinaemia, for it may readily be supposed that small quantities of the sulphide are quickly removed from the plasma by oxidation, whereas the haemoglobin compound remains unaffected. The blood of warm-blooded animals which have been poisoned by inhalation of an atmosphere containing hydrogen sulphide usually does not shew the absorption-band of sulph-haemoglobin, whereas in frogs so poisoned the band is always seen in the blood. It would seem that the inspired gas kills in virtue of its effects upon the nervous system, before there is time for the development of the characteristic blood-change. When administered per rectum, the gas proves less toxic, and Erich Meyer observed the band of sulph-haemoglobin on examining the blood of a rabbit after such injections. The smaller the quantity of a solution of hydrogen sulphide that is added to the blood, the longer the appearance of the absorption-band is delayed; Dr. Wood Clarke found that the change to sulph-haemoglobin occurred with much higher dilutions in specimens placed in an incubator at 37° C., but Erich Meyer observed that mixtures kept at temperatures of 40° C. shewed a feebler sulph-haemoglobin band than those left at the temperature of a cold room. As the higher temperature would tend to expel the hydrogen sulphide from the serum, it may be that the use of open and closed vessels explains the discrepant results.

Drs. Wood Clarke and Hurtley, who recently studied the properties and formation of sulph-haemoglobin anew, found that the presence of a reducing agent such as hydrazine greatly hastened the appearance of the characteristic absorption-band. They are of the opinion that sulph-haemoglobin is a true sulphur compound, but found that it was only formed by the addition to solutions of haemoglobin of sulphur compounds which exert a reducing action.

It is as yet too early to formulate any hypothesis of the origin of sulph-haemoglobinaemic cyanosis. That it is due to a chronic poisoning

by hydrogen sulphide seems evident, and there is much to suggest that the poison is absorbed from the intestine. If further observations should bear out the conclusion that hydrogen sulphide is not produced in abnormal quantities in the intestine of these patients, it will be necessary to fall back upon the supposition that there exist, in such cases, conditions unusually favourable to its absorption, or that, as Drs. Wood Clarke and Hurtley suggest, the actual morbid agent is some compound of reducing properties which favours the formation of sulph-haemoglobin in the presence of traces of hydrogen sulphide which need hardly be classed as abnormal.

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PURPURA

By the late Sir STEPHEN MACKENZIE, M.D., F.R.C.P.

Definition.—Spontaneous extravasations of blood into the skin, mucous membranes, and internal organs of the body, sometimes accompanied by free haemorrhages from mucous surfaces.

Etiology and Pathology.—Morbid anatomy simply reveals the existence and extent of distribution of haemorrhagic effusions, often accompanied by evidences of anaemia. In a minority of cases in the mucous membranes, and more rarely in the skin, erosions or ulcerations are met with in connexion with the haemorrhages, but these are clearly the effects and not the cause of them; in mucous membranes the moisture of the part, and in some organs the digestive property of the secretions, tend to produce this result. In the hollow viscera blood may be found in con-

siderable quantities, and the serous cavities may contain blood or blood-stained serum. Besides the skin and mucous membrane, haemorrhage occurs in the solid organs and in the serous membranes. They are found in the lungs, kidney, spleen, liver, suprarenals, brain, and retina; indeed, there is no part in which haemorrhages may not occur. In the brain, from the delicacy of its structure and feeble resistance, the haemorrhage may reach considerable magnitude, and may be fatal. The pleurae, pericardium, peritoneum, and pia-arachnoid are often dotted over with small extravasations. The haemorrhages vary in size from a pin's head to a patch as large as the palm of the hand. On post-mortem examination the most important changes found, other than haemorrhages, are in the liver (cirrhosis and acute yellow atrophy), kidneys, suprarenals, and lungs. Slight degrees of diffuse or parenchymatous nephritis are relatively common. Congestion and oedema of the lungs are frequently present, and are often the determining cause of death. Ulceration of the intestine, especially of the large intestine, and enlargement of the solitary and agminated glands are sometimes present.

The changes in the suprarenals require more detailed notice. There is a considerable amount of evidence as to the association of changes in the suprarenals and purpura. Loeper points out that the vascularity and feebly supporting structure of these organs renders them prone to haemorrhage. They secrete a vaso-constrictor substance—adrenalin—and it is more than possible that all secretory disturbances may greatly modify the tonicity and vascular resistance of the secretory organ. Thus it happens that anatomically and physiologically the suprarenals are disposed to haemorrhage, and the damage done to their structure will necessarily diminish the pressor secretion and still further add to the existing tendency to haemorrhage in other parts of the system. The symptoms referred to haemorrhage into the adrenals have been dealt with elsewhere (Vol. IV. Part I. p. 424). Dr. Graham Little has collected 11 cases in which severe purpura was associated with haemorrhage into the suprarenals. Rapidly fatal cases of haemorrhage into the adrenals, however, without purpura are on record. In two of his cases streptococci were found in the blood-vessels. Dudgeon and Loeper are of opinion that the adrenal haemorrhages may be primary and idiopathic. In purpura neonatorum, visceral haemorrhages, especially into the suprarenals, are said to be very frequent. Cases have been published in which adrenalin administered subcutaneously or by the mouth has arrested purpura that has resisted other coagulative and vaso-constrictor remedies, as calcium salts, gelatin, and ergot.

With regard to the mode of escape of the blood in this as in other conditions in which spontaneous haemorrhages take place, it may be by *rhexis*—by rupture of blood-vessels, or by *diapedesis*—by the escape of blood-corpuscles through unbroken vessel-walls. The former is most probably the process in the great majority of cases. Though many observers have failed to discover rupture of blood-vessels at the seat of the extravasations, Unna and his pupil Sach have shewn they are to

be detected by certain methods of examination. According to Unna, it is the veins that give way; and he has pointed out that the laceration occurs especially at the junction of the superficial part of the subcutaneous tissue with the lower part of the cutis. At this point, which he regards as one of less resistance, the vessels lose their well-marked adventitia, and lack the support of the highly elastic cutis. The extravasated blood from its seat of origin percolates the epidermis, and occasionally the sebaceous and sweat glands; in some cases sero-haemorrhagic extravasations take place also in the subcutaneous and intermuscular tissues. The causes that lead up to and actually determine the escape of blood are probably many and complex. Search has naturally been made in the walls of the blood-vessels for changes apt to cause them to give way. In some cases inflammatory changes have been found, and may in such instances have been the cause of the ruptures. In the majority of cases, however, the inflammation is the result of the violence to which the coats of the vessels have been subjected, an inflammation which may extend to vessels at some distance from the rupture. Hyaline degeneration, either of the intima or of the adventitia, or both, has been found by some observers. In the case recorded by Wilson Fox a lardaceous change was found in the vessels of a syphilitic subject. Unna properly remarks, and experience of these changes in other circumstances confirms his opinion, that these hyaline and lardaceous changes would rather have a tendency to restrain than to encourage haemorrhage. In connexion with disease of the blood-vessels, reference must be made to the eruptive angiomas, of which several forms have been recorded. Cases of interest bearing on the present subject have been recorded by Osler, Rendu, Brown Kelly, Hawthorne, Parkes Weber, and others. Prof. Osler's first paper was entitled "On a family form of recurring epistaxis associated with multiple telangiectases of the skin and mucous membranes" typifies these cases. The reader is referred to valuable articles, founded on cases of their own by Dr. Colcott Fox, and by Dr. Parkes Weber who arrives at the following conclusions: (1) That the disease affects and is transmitted by both sexes; (2) That the haemorrhage is in most cases only from the nasal mucous membranes; (3) That in most cases the morbid syndrom is not connected with any haemophilic tendency, or any diminution of blood-coagulability; (4) That the cutaneous angiomas usually first attract attention towards middle life; (5) That in most cases a tendency to nose-bleeding has been present from early life, or, at all events, many years before any cutaneous angiomas have been observed; (6) That with advancing years both the attacks of haemorrhage and the anaemia become more severe. The bearing of these observations on the pathology of purpura is uncertain, but every condition of the blood-vessels and blood giving rise to haemorrhage must be studied in order that light may be thrown on this difficult subject. Moreover, minute telangiectases have been mistaken for purpuric petechiae. Venous thrombosis, as in so-called "purpura thrombotica," has been met with occasionally; but probably it stands in the relation of effect rather

than of cause. Capillary emboli have been found in sarcoma (Hilton Fagge), in leucocythaemia, and in pyaemia, and may have a direct causal influence; but numerically such cases are very infrequent, and afford no explanation of the majority of cases of purpura in which they are absent. Hayem, Silbermann, and Bona believe that embolism and thrombosis of the capillaries, due to granular precipitation of blood-platelets, block these vessels. Attention has been devoted to the search for micro-organisms in the blood, in the blood-vessels, and in the tissues. Various bacteria have been found by different observers in some cases, but in other cases the same observers have failed to discover them. The presence of micro-organisms in the blood-vessels, even in large numbers as in diphtheria or anthrax, does not necessarily give rise to haemorrhage; moreover, apart from the negative results of the search for bacteria, the circumstances in some cases in which purpura occurs make it unlikely that its causes are of this kind. Though thus not necessarily leading to rupture of vessels or diapedesis, they may nevertheless affect the vessel walls indirectly, by inducing some chemical change in them, as suggested by Sir Watson Cheyne and Unna. Further, as Sir Watson Cheyne has pointed out, the presence of bacteria does not necessarily imply that their entrance into the blood is the starting-point of the disease; the alternative view, however, may be entertained that, although the primary cause may be of quite a different nature, the result may be such an alteration of the fluids of the body that, of the innumerable organisms present in the mouth and intestinal tract, certain species may be enabled to penetrate into the blood and to live in it. The introduction of an alien serum into the body may be followed by purpura. This has been shewn to occur experimentally when as a result of a previous hypodermic injection of serum a condition of hyper-sensitiveness or anaphylaxis has been induced. It is quite possible, also, that some toxin or albumose formed in other parts of the body may be absorbed, and act chemically upon the blood-vessels, or on the vasomotor nerves, producing variations of blood-pressure which at the weakest points they are unable to resist. The organisms most frequently found have been streptococcus, staphylococcus, pneumococcus, *Bacillus coli*, especially the first-named. Kolb described a *Bacterium haemorrhagicum* found in the blood-vessels of the skin, as well as in the lungs and kidneys; Dr. Klein a *Staphylococcus haemorrhagicus*. Dr. Poynton has found the diplococcus which he connects with rheumatism, in the blood in a case of rheumatic fever with purpura. In another case of a girl of eighteen, with rheumatic fever, active endocarditis, erythema, and purpura, there were nodules, and one nodule was the centre of a patch of purpura. These nodules were the result of subcutaneous deposits of the diplococci. In the whole class of specific diseases, whether in those in which micro-organisms have been demonstrated, or in those in which so far they are only assumed, the bacteria or their products must play an important part in the production of the cutaneous haemorrhages which are an occasional

feature of nearly all members of this group of diseases. The fact that purpuric phenomena are not uncommon in certain of them, such as typhus, small-pox, and measles, in which no specific micro-organisms have as yet been demonstrated, should make us chary of denying the possible existence of bacterial influence in the purpura of other diseases in which up to the present no micro-organisms have been found.

Purpura also occurs in connexion with pneumonia, cerebrospinal meningitis ("spotted fever"), pyaemia (including infective endocarditis), and in septicaemia, in which organisms are found.

It is noteworthy that the occurrence of haemorrhages in the infective diseases is almost confined to the specially severe cases—so-called malignant—in which the whole aspect of the case suggests an active poison, the toxin of microbes. The frequency of the presence of albuminuria clinically, the proved toxicity of the urine in some cases, point strongly to a poison circulating in the blood and eliminated by the urine. Purpura is occasionally seen in acute cases of tuberculosis and phthisis.

It is certain that cutaneous haemorrhages are sometimes determined, and in all probability primarily caused by nervous influences; as in the case of purpura occurring in the situation of the lightning pains of tabes (Straus), and in connexion with certain neuralgias (Weir Mitchell). The mechanism of the haemorrhage in such cases is hitherto purely conjectural; but it seems most probable that, by acting on vasomotor centres, it produces variations of vascular pressure under which the blood-vessels give way in the situation already indicated as the point of least resistance. Though purpura is one of the manifestations of haemophilia, the histopathology of the latter need not be fully discussed here (see "Haemophilia," p. 918), nor would it materially elucidate the pathology of the majority of cases of purpura. Haemophilia is believed, however, by some authors to be due to a congenital defect in the vascular walls. It is quite possible that in some cases of purpura a haemophilic taint may be an element in the haemorrhagic tendency.

Venous stagnation plays a part in the production of purpura. Though not of itself a sufficient explanation of haemorrhage, it is evidently a factor of importance, as in many cases of purpura the haemorrhages begin and are most marked in the lower extremities, the veins of which have to support a longer and heavier column of blood than those of other parts, or on the back if recumbent. As a rule, however, something more than stagnation is necessary to bring about rupture or diapedesis. When hyperaemia co-operates with stagnation the conditions are favourable to haemorrhage (Unna).

The Blood.—Coagulability.—According to Hayem the blood coagulates either at the normal rate or more slowly, but what is characteristic is the absence of retraction of the clot and transudation of the serum. This he attributes to a chemical alteration in the blood. Persistence of this phenomenon is said to be of bad omen, whilst its disappearance would be a favourable sign, and Bensaude confirms this. It is said by Lenoble

that this peculiarity of clotting is confined to the myeloid variety of purpura.

Red Corpuscles.—The number may be, in the early stage of the disease, normal or nearly so, but in the majority of cases they diminish as the disease progresses, and in the worst and fatal cases they may fall to a degree only equalled in traumatic and massive internal haemorrhages and pernicious anaemia. When the disease has lasted some time and, as would be anticipated, when copious internal haemorrhages have taken place, still greater reduction in numbers takes place. Hayem has recorded a case in which the red corpuscles fell below 1,000,000, Quinquaud a case with only 740,000, and Hérard a case in which there were 1,885,000 when first counted, and later 620,000 per c.mm. John S. Billings, jun., had a case with a count of 483,000, and haemoglobin 17 per cent. The blood that exudes in such cases of extreme anaemia is only tinged with red, appearing as a thin serous fluid. Nucleated red blood-corpuscles, great and small, may be present or absent. Microcytes are sometimes found, and occasionally poikilocytes.

Haemoglobin varies in different cases. It may fall and rise pari passu with the red cells, especially where massive haemorrhages occur, but it may be more deficient than the red cells, so that the corpuscular value may be below normal, as in chlorosis, to which type of anaemia such cases approach; this is said to be the case in myelogenous purpura. In other cases, on the contrary, the red cell loss is greater than the haemoglobin, so that though the anaemia is greater the corpuscular value is increased as in pernicious anaemia.

White Blood-corpuscles.—A certain degree of leucocytosis is common in purpura, but it is not invariable. There are great discrepancies in regard to differential counts. It is usually due to increase of the polymorphonuclears, but in some cases there is a relative excess of lymphocytes; in some instances eosinophilia has been reported.

It is doubtful if our present knowledge is sufficient to allow of a haematological classification of cases of purpura. Lenoble, however, thinks that it is, and lays down the following basis:—True or genuine purpura (Myeloid purpura)—(1) Absence of retraction of clot and of transudation of the serum; (2) constant myeloid reaction, sometimes intense; (3) remarkable changes in nucleated red corpuscles, diminution in number, increase in size (Hayem), and, in addition, material changes in their structure. This myeloid purpura is, according to him, a true morbid entity with toxaemia as its cause, its well-defined symptoms and localised anatomy. It is a disease, if not *the* disease par excellence, of the bone-marrow. It is very similar to myelogenic leukaemia, and microscopically is so similar as to be misleading. The clinical characteristics are absence of fever, and hypertrophy of all blood-making organs—liver, spleen, and glands.

But whilst anaemia, or a deficiency in the quantity and quality of the blood-corpuscles, is very common or almost constant in purpura, and may be either a consequence or cause of it, haemorrhages from mucous

surfaces and even fatal cerebral haemorrhage may occur in polycythaemia (*vide* p. 836).

In addition to the changes described, other alterations may be present; thus, deficiency or excess of some of the saline constituents of the blood as in scurvy, alterations in the reaction, alterations in the specific gravity, deficiency in the fibrin-forming elements may all play their parts in the initiation of changes in the vessel walls and in their permeability. Sir A. Wright is of opinion that the defective coagulation of the blood (in haemophilic children at least) is undoubtedly a defect of one of the elements of the blood, *i.e.* in the fibrin, due to a diminution of the alkalinity of the blood caused by bacteria. Lastly, the presence in excess of some organic matters such as bile, urea, and other products of metabolic changes as in jaundice or uraemia, or the addition to the blood of extraneous matters, have all a tendency to promote some chemical or vital changes which render the vessels liable to rupture or increase the permeability of their coats. In the latter category we have important evidence of the effects of certain chemical substances. The observations of Prussak, confirmed by Dr. Wickham Legg, have demonstrated that chloride of sodium injected into the vessels or subcutaneous tissues of the frog gives rise to diapedesis of coloured corpuscles which, under the microscope, may be seen to pass through the intact walls of the blood-vessels (18). Similarly, in certain persons, iodides, as well as other drugs, such as boric acid, give rise to purpura. Though the exact mode of operation of such agents has not been worked out, we must ascribe some influence, direct or indirect, to chemical action on the blood or walls of the blood-vessels.

Finally, it must be pointed out that a diminution of support to the blood-vessels by the tissue immediately surrounding them, may lead to their rupture. Thus purpura occurs in those who have wasted much from severe or protracted diseases (purpura of convalescence); in the wasting, loss of elasticity, and vascular degeneration of the aged (senile purpura), and in the newly-born (purpura neonatorum). Summarising what has been said as to the conditions that appear to cause or at least attend purpura, nearly all may be classified as *vascular*, involving alterations in the blood-vessels, congenital or acquired, or in the blood, or in both. With regard to the blood, this embraces infective diseases (including provisionally at least rheumatism) with bacteria and toxic products, organic and chemical poisons which may either gain admission from within or be introduced from without the body; alterations in numbers or character of the formed constituents of the blood or of its plasma; absence of some normal constituent (scurvy?); conditions interfering with the free circulation of the blood, local and general, by pressure or want of support; irregular and varying arterial, venous, and capillary tension. The influence of the nervous system is rarely, if ever, alone primarily effective, but there is evidence that it may determine the occurrence and site of the haemorrhages.

In the absence of a common cause, of a definite clinical course, of

constant pathological changes, it is obvious that purpura is not a consistent or uniform symptom-group, but is itself a symptom entering not into one only but into many groups. As a symptom it may be primary or secondary.

The best notion of the circumstances in which purpura occurs will be conveyed by an analysis of 200 cases from the records of the London Hospital. They were not selected, but taken consecutively, so far as the records permitted. They are given in the following table :—

TABLE of 200 Cases of Purpura in the London Hospital, arranged as regards probable Causes or associated Conditions.

	Males.	Females.	Total.
Rheumatism	33	28	61
Doubtful rheumatism	7	3	10
Bright's disease	7	2	9
Heart disease	3	5	8
Anaemia	3	3	6
Leucocythaemia	1	0	1
Scurvy	6	0	6
Privation and dietetic	3	2	5
Pyaemia	0	2	2
Infective endocarditis	2	0	2
Malaria	0	1	1
Rickets	1	0	1
Whooping-cough	0	1	1
Congenital syphilis	1	1	2
Tuberculosis	3	1	4
Alcoholism	2	0	2
Toxic (drugs)	3	0	3
Cirrhosis of liver	1	0	1
Convalescence	2	0	2
Injuries	2	0	2
Haemophilia	0	1	1
Varicose veins	0	1	1
Peripheral neuritis	1	0	1
Unexplained	31	37	68
Totals	112	88	200

This table does not present any instances of purpura in connexion with the specific fevers, for these, with the exception of enteric fever, are not admitted. Nor are there any cases of P. neonatorum or P. senilis.

Age incidence will be best shewn by the subjoined table :—

TABLE of 200 Cases of Purpura arranged in Decades.

	Up to 10 years.	11 to 20.	21 to 30.	31 to 40.	41 to 50.	51 to 60.	61 to 70.	Totals.
Males	24	29	31	13	9	2	4	112
Females	25	28	17	10	7	1	0	88
Totals	49	57	48	23	16	3	4	200

From these figures, which fairly represent the conditions in which purpura occurs, apart from the eruptive fevers and in the newly-born, it will be observed that, at any rate in a general hospital, purpura is more common in the male than in the female sex, in the proportion of 14 males to 10 females—not quite 1½ males to 1 female. This holds good for all ages with the exception of the first decennium, in which the females exceed the males by one. In the second decennium the numbers are nearly equal, with the preponderance of one in the males. It will also be observed that the greatest number of cases occur in the first three decades, 77 per cent in persons under thirty years of age. In the fourth decade the numbers rapidly fall to less than half of those in the third decade; still fewer cases occur in the fifth decade, and only 7 cases occur in persons of either sex over fifty years of age.

The number of cases here dealt with is probably larger than in any published series: but it will be seen how comparatively rare purpura is when I say that these 200 cases represent the number occurring amongst 63,834 medical cases in 16½ years. They only amount to 0·3 per cent of the medical cases, and this is probably a fair calculation of its occurrence in purely medical practice.[1]

The great variety of supposed causes or associated conditions is sufficiently striking. Still more so is the fact that in one-third of the cases tabulated no explanation was afforded for the purpura, though in several of the cases a necropsy was made. It will thus be seen how extremely complex is the pathology of purpura. All we can do in the present state of our knowledge is to accumulate further information, and to exhaust every means—histological, bacteriological, and chemical—in the investigation of cases. It will be observed that in by far the majority of cases in which anything definite can be ascertained as to the causation of purpura this is of a vascular character—some known or probable alteration of the blood, or some condition which brings about a change in the blood-vessels; and, arguing from the known to the unknown, it seems probable that, in those in which no definite causation can be ascertained, purpura is due to one of these two kinds of change.

Symptoms.—The one symptom common to all cases of purpura is the occurrence of red, purple, green, or brown spots in the skin, which do not disappear on pressure at any stage of the disease. Certain phenomena are common to most cases of purpura.

Changes in the Extravasated Blood.—Recent extravasations appear of a more or less bright red or crimson colour. They are usually oval or round, but may occur in lines or streaks—vibices. In a short time they become of a dull purple, and later of a brownish-red tint; lastly, a brownish stain persists for a considerable time. In some cases a bluish-green colour is present. In quite superficial haemorrhages, spots, as they fade, present a yellowish hue, passing into a faint brown, so well observed in the universally known "black-eye." As regards the changes in the

[1] A very few cases, too few to affect the calculation, were omitted as the notes were incomplete.

blood effused, when the haemorrhage takes place into the cutis, there begins, according to Unna, very soon after the occurrence of the bleeding solution of the haemoglobin, which is partly reabsorbed with the blood-plasma, and partly crystallised in the tissue (precipitated). Where large masses of blood-corpuscles are closely packed, they break up, without previously giving up their haemoglobin, into yellow or brownish flakes, which are gradually converted into pigment granules, and as such are partly taken up by the connective-tissue cells.

Pyrexia.—A certain degree of fever is present in more than half the cases. In the majority it is slight and transient; in others the disease runs a moderately febrile or highly febrile course (P. febrilis), and hyperpyrexia has been known to occur. The decidedly febrile cases are nearly always characterised by a greater severity, and are therefore attended with greater danger than those which are non-febrile; otherwise no important differences are noticeable.

Albuminuria, apart, of course, from cases in which it is plainly due to Bright's disease, is of rather frequent occurrence in purpura; it occurs in both febrile and non-febrile cases, and corresponds with the statement (p. 846) that in fatal cases the kidneys are frequently found diseased. Urobilin, creatine, and indican have been found, and the urine has been found to have toxic properties due to an organic intoxication (Carrière et Gibert).

Digestive System.—Derangement of the stomach and intestine is common. Apart from anorexia, which is frequent, colic in severe paroxysms, vomiting and diarrhoea are so pronounced in some cases as to have been constituted into a special form of the disease (Henoch's purpura).

Haemorrhages. — Haemorrhage may occur from any of the mucous surfaces. Epistaxis is the most common; next, haemorrhage from the gums and throat, and, following these in frequency, from the intestines, urinary passages, stomach, lung, and sexual organs. Intra-visceral and interstitial haemorrhages also occur; and haemorrhages in the retina may be detected during life by the ophthalmoscope. Retinal haemorrhages are, however, rare in purpura.

The following kinds will be described here:—(i.) Purpura simplex, (ii.) purpura haemorrhagica, (iii.) purpura rheumatica, (iv.) iodic purpura, (v.) Henoch's purpura.[1] There is no fundamental distinction between P. simplex and P. haemorrhagica; the former is a mild form of purpura, the latter a severe purpura with haemorrhages from mucous surfaces. Both are symptomatic of a great number of causes.

PURPURA SIMPLEX.—With or without preceding constitutional dis-

[1] Neurotic purpura, or purpura of nervous origin, cannot be made into a well-defined variety; but the name neurotic purpura may be applied to cases in which the haemorrhages can be confidently attributed to nervous influence. Weir Mitchell has described cases of neuralgia in which haemorrhages occurred in the skin about the penis; Straus and others, purpura in connexion with tabes. Purpura is also met with in angina pectoris, meningitis, whooping-cough, and epilepsy. In the latter categories the immediate mechanism is probably vascular, and consists in a local increase of blood-pressure.

turbance, haemorrhagic extravasations make their appearance in the skin. They frequently begin in the lower extremities, but become generally disseminated over the whole surface. They may present a rough symmetry, or have a random distribution. The spots are generally circular or rounded, but may occur in streaks; they vary in size from mere petechiae to extravasations as large as half-a-crown or larger. The attack may be ushered in by a slight rise of temperature, or febrile disturbance may arise in the course of the attack. Many cases are afebrile throughout their course. The disease is most common in young persons. The patient may be anaemic, or may present a healthy appearance, and be well nourished. There may be some malaise, digestive troubles, diarrhoea (Graves), and other constitutional disturbance; or these may be wanting. The first spots fade, passing through the changes of colour described, and new ones appear; so that all varieties of colour are present. After lasting a variable and indefinite period, usually a week or two, no fresh spots make their appearance, the old ones fade, and the attack comes to an end, leaving pigmentation of the skin where the haemorrhages have been present, for some weeks or longer.

PURPURA HAEMORRHAGICA (*Morbus maculosus Werlhofii*).—The etymologically meaningless name P. haemorrhagica—for all purpura is haemorrhagic—is applied to cases in which not only cutaneous extravasations are present, but in which haemorrhages take place from mucous surfaces also. It represents the more severe and dangerous kind of purpura. No more than P. simplex is it to be regarded as a uniform symptom-group, for it occurs under a variety of conditions.

It may begin with more or less constitutional disturbance—headache, debility, gastric pain, and vomiting, and be followed by extravasations into the skin and mucous membrane, and free haemorrhages from the latter. Or it may begin as P. simplex and later become P. haemorrhagica, as bleedings take place into and from the mucous surfaces. The haemorrhages vary in size as in P. simplex, but tend to be larger, and are often accompanied by haemorrhagic oedema in large patches—as large as the hand or larger—appearing in certain parts, raised, reddish, or purple-blue in colour, and pitting on pressure. The orbits, the penis, and scrotum, parts with loose subcutaneous tissue, occasionally become extremely swollen, and the skin tense and of a livid colour. The appearance may suggest a fear of sloughing, and indeed the fear may be justified. Blebs may form over the haemorrhages in the skin (P. bullosa). The cutaneous haemorrhages pass through the same stages as in P. simplex, but appear in rapid succession, and are often of large extent. Haemorrhages in severe cases are usually met with in the mucous membrane of the mouth and throat; and in this situation they may give rise to alarming symptoms, and even occasion a fatal issue. In several recorded cases haemorrhages have taken place into the palate and tongue. When occurring in the latter organ acute swelling of the tongue, resembling acute glossitis, has been produced, necessitating incisions for the relief of

the consequent dyspnoea. In one or two cases sloughing of the tongue, with shedding of its apex, has occurred.

Of the haemorrhages that take place from the mucous membranes epistaxis is the most common; haemorrhages from the mouth and throat are also very common: in some cases haemorrhages occur from the stomach, intestines, lungs, and genito-urinary organs. The bleedings from the mucous membranes may be very severe and frequently repeated, and in some cases are uncontrollable. Though in some cases anaemia may not be present at the outset, it rapidly makes its appearance, which is not surprising when we consider the large amount of blood lost from the mucous surfaces and into the skin.

Fever is present in the majority of cases of P. haemorrhagica. It may reach a high grade—104° F. or higher, and may be hyperpyrexial—105·5° or higher. Cases with high fever, extensive extravasations, and copious and repeated haemorrhages from the mucous membranes, may run a very rapid course, and end fatally in the course of a few days. Such cases have been described as P. fulminans. In severe cases haemorrhages may take place into the brain, and may occasionally be seen during life in the retina. In P. haemorrhagica pains are often present in the joints and limbs, even in cases in which there is no reason to believe the condition to be of rheumatic nature. Schebey Buch has drawn attention to effusion into the joints in non-rheumatic cases. Albuminuria, with or without blood, is often present in cases of P. haemorrhagica. In fatal cases pulmonary oedema, often associated with haemorrhage into the lung due to exhaustion and heart failure, is commonly the determining cause of death.

In cases which pursue a favourable course, or which do not end fatally, the haemorrhages into the skin and from the mucous membranes recur from time to time over a period of days, or, more usually, of weeks, in a fitful manner, and eventually cease; the patient being left extremely weak, anaemic, and often much wasted.

Purpura Rheumatica (Schönlein's *Peliosis rheumatica*).—This kind has gradually gained increased recognition, though thirty years ago it was scarcely ever diagnosed. Schönlein's description is worth reproducing, as differences of opinion have arisen as to the meaning of the name he used.

"The patients have either already suffered from rheumatism, or rheumatic symptoms accompany the attack: slight periodic throbbing pains in the joints (in the ankles and knees, rarely in the hand and shoulder-joints), which are oedematously swollen and tender on pressure. The characteristic spots of the disease in the majority of cases first appear on the extremities, especially on the lower extremities, and here only as high as the knee (rarely on the upper). The spots are small, of the size of a lentil to that of a millet seed, bright red, not raised above the skin, *disappearing under the pressure of the finger* [italics not in original]; they gradually become dirty brown or yellowish, the skin over them slightly

desquamates with a branny scale. The eruption comes out in crops, often during several weeks. Ever so slight a change of temperature, as for example passing into a colder room, may occasion a fresh outbreak. The eruption usually appears with some fever, of a remittent type. Towards evening the symptoms are at their height, with a recession in the morning. There is frequently a deposit in the urine." It is clear from Schönlein's own words that he described an erythema papulatum, for he expressly notes the colour "disappearing under pressure." Further, in discussing the diagnosis, he gives the diagnostic criteria from Werlhof's disease (P. haemorrhagica). The majority of writers, following Schönlein, regard purpura rheumatica as a purpuric erythema, though this is scarcely justified from his description that the colour disappeared on pressure. Some go farther and appear to regard all purpura as erythematous in nature. Though an allied process, I believe it better to keep the two conditions distinct, and in the following description of purpura rheumatica I shall restrict the name to a condition which is purpuric from the beginning, and in which the spots do not disappear on pressure at any stage. In other respects Schönlein's description of the eruption coming out in crops, and of the aggravation of disease in the evening, is singularly apt.

The disease occurs with about equal frequency in the two sexes, and is most common in the second, third, and fourth decennia (from eleven to forty); it is rare before ten years of age and after forty. In some cases the purpuric eruption makes its appearance while the patient is suffering from acute or subacute rheumatism. More commonly the arthritic symptoms arise coincidently with the purpuric eruption; in a few cases, in which arthritic symptoms are doubtfully present in the attack, or are entirely absent, an attack of arthritic rheumatism may appear at some subsequent period, thus revealing the rheumatic nature of the purpura; or, perhaps, to be more exact, thus demonstrating that the patient is a rheumatic subject. Apart from cases in which acute or subacute rheumatism ushers in the purpura, the very characteristic onset and course of the disease is as follows:—The patient has pain in the lower extremities, which may be of a dull aching character, but frequently and characteristically is a sense of tension—a "sensation of bursting" in the parts affected, as patients frequently describe it; often there is itching. When these symptoms are present (and patients who have had a previous attack know well their meaning), bright red spots, which do not disappear on pressure, are seen on the legs. In the majority of cases when they first make their appearance they are raised (P. papulosa). The eruption and its accompanying discomforts usually make their appearance in the later part of the day, afternoon or evening. The knee and ankle joints are usually painful and often swollen and tender, sometimes the skin over them is slightly reddened. A slight degree of oedema of the lower part of the leg, of the ankle, and of the dorsum of the foot is present in nearly all cases. By the following morning the pain remits, and inspection shews that the spots are now of a purple or dull red colour,

and no longer raised. On the second evening, or after an interval of two or three days, the same phenomena are repeated—the aching of the legs, the pains in the joints and oedema, and the appearance of another crop of bright red spots similar to those first observed. The spots pass through the usual stages of discoloration characteristic of haemorrhages into the skin, and if the patient is seen after the occurrence of two or three outbursts, and at a time when a fresh crop has recently appeared, we observe:—1. Bright red raised spots, varying in size from a millet seed to a threepenny piece or larger, not disappearing on pressure. 2. Spots of a similar size of dull red or purple colour, but not raised above the surface, and unaffected by pressure. 3. Yellowish-brown stains. The affected limbs are tender to pressure and slightly oedematous. In most cases, as already stated, there are pain and swelling of the joints of the lower extremities, and in some of the elbows and wrists; even in cases in which the skin of these parts is not affected by haemorrhages. The joint affection often persists between the outbursts of haemorrhages, though exacerbations of pain and swelling occur in the attacks. The first outburst of haemorrhages is usually confined to the lower part of the legs and feet. In subsequent outbursts there is a tendency to an extension of range, so as to involve the upper part of the legs, and, later still, the thighs and buttocks. In slight cases the eruption is limited to the lower extremities, but in more severe cases the forearms and arms are affected also. Usually when the thighs are affected the skin above and below the elbow is the seat of haemorrhages. The eruption is so far symmetrical that if one leg is affected the other leg is affected also; and if it attacks the upper extremity both will be attacked. The eruption shews no marked predilection either for the flexor or extensor surfaces of the limbs. In the great majority of cases it is confined to the extremities; but in the more severe cases, especially those in which the arthritis and pyrexia are great, the trunk and face also are affected. Haemorrhages into and from the mucous membranes are rare, but in a few cases small haemorrhages may be seen in the buccal mucous membrane; and in rare and very severe cases extensive haemorrhages may take place into the tongue (intra-muscular) and throat. In about one-third of the cases some degree of pyrexia is present, and probably, if careful thermometric observations were made in the evening at the time of the eruption, some elevation of temperature would be found in nearly all of them. Sweating is not a marked symptom unless the arthritis be pronounced. The amount of constitutional disturbance is variable, this being slight in the majority of cases; but in some malaise and debility are present. The majority of patients are able to walk about stiffly in the early part of the day, but locomotion is very difficult and painful in the later day, especially at the time of the outbreaks of haemorrhages. Any exertion tends to bring on an attack. The department for diseases of the skin, of which I had charge, was open in the morning, and patients have told me they had a bad attack in the afternoon or evening of the days when they had been to see me. Exertion seems to me to determine

attacks much more than changes of temperature, to which Schönlein referred them. The eruption usually lasts an indefinite time, unless treatment of a certain kind is adopted for several weeks, or months; I have known it to persist for two years. The disease is occasionally, though extremely rarely, fatal. Usually it is a benign affection. It is very apt to recur.

The assemblage of symptoms is very definite and characteristic. The occurrence of haemorrhages—usually confined to the extremities, appearing in crops, usually in the latter part of the day—the arthritic pain and swellings, and its protracted course, distinguish it from other forms of purpura, and from erythema exudativum multiforme. It has undoubtedly close clinical alliances with the latter, which also, in a large proportion of cases, is of a rheumatic nature, and the two may occur in the same subject; but in the cases to which I would restrict the name purpura rheumatica the eruption from first to last is purpuric, and not erythematous. The evidence of its connexion with rheumatism is, in the majority of cases, extremely distinct. The arthritis, which is present in many cases, is characteristic, and may precede the purpura; so that the diagnosis of acute or subacute rheumatism is already made. In other cases the patient has previously suffered from rheumatic fever. In a considerable proportion of cases valvular disease, usually mitral incompetence, is present; and in a few it may arise during an attack. Many patients have had other affections belonging to the rheumatic series, such as tonsillitis, endo- and peri-carditis, pleurisy, chorea; and a family history of rheumatism is very common. I have seen two brothers with purpura rheumatica at some years' interval. The second one died of heart disease a few years later. In a certain number of cases the arthritic symptoms in the attack are equivocal or absent; but the complex of symptoms described have been definite and identical with those in which the rheumatic nature was beyond dispute; so that when the symptoms above described are present, I am of opinion that we are justified, even in the absence of arthritis, in diagnosing purpura rheumatica. I have seen a case in which no arthritis accompanied the purpura, yet (at an interval of a year or more) an attack of rheumatic fever subsequently appeared. In the list I have given of the ascertained causes of purpura, rheumatism, it will be observed, stands very high, giving in the 200 cases 30·5 per cent, exclusive of doubtful but still probably rheumatic cases.

Iodic Purpura.—Fournier was the first to give a good description of this form of purpura. The eruption is generally confined to the lower extremities, and in the majority of cases to the parts below the knee. The eruption consists of discrete miliary haemorrhagic spots, bright red when recent, not elevated, not obliterated by pressure, unattended with heat, pain, or swelling. The eruption comes out at an early period of the iodide treatment, and continues to appear for two or three days. It remains for a certain time as a staining of the skin, the

blood undergoing the changes of colour usual in cutaneous haemorrhages, and finally disappears by the end of two or three weeks. During its progress a renewed attack may sometimes be induced by augmenting the doses, and then the bright red recent haemorrhages contrast very markedly with those that are fading. Though usually confined to the legs, it may affect the trunk and the face, as in a case I have recorded. The purpuric spots are usually more pronounced in the anterior than in the posterior parts of the legs. Successive outbreaks are usually less profuse than the original one. It may be accompanied by some oedema of the legs, but this is not usually the case. The various salts of iodine seem to produce purpura, but exceptions to this rule are met with; some persons can take sodium or ammonium iodide without inducing it, whilst potassium iodide is operative; or potassium iodide may fail to produce it, whilst ammonium iodide may be operative. As potassium iodide is the salt most frequently prescribed, purpura is most frequently met with in patients taking this preparation. It is held by Besnier that pure iodine will not cause the haemorrhages, and he has illustrated this fact in the person of a man who had purpura in the lower limbs every time he took iodide of potassium; yet, although tincture of iodine caused symptoms of iodism in him, no purpura appeared. Iodic acid has been known to produce it. Purpura is a very rare consequence of the administration of potassium iodide. Usually it is quite a benign and unimportant affection, but one to be borne in mind, lest it be misinterpreted. Occasionally, moreover, the salt may give rise to very grave symptoms and even prove fatal; as in a case I have recorded. In this case fatal purpura followed a single dose of $2\frac{1}{2}$ grains of potassium iodide in an infant five months of age. In prescribing iodides to young children a small dose should be first given, and if tolerated, the dose may be augmented.

The reaction is clearly due to idiosyncrasy, as it occurs in a very small minority of persons. It does not depend on the debilitated state of the patient, whose nutrition may be quite good. It is possible that syphilis favours its occurrence; but the frequency with which iodides are administered for syphilis and the rarity of iodic purpura shew that personal peculiarity or idiosyncrasy is the determining factor. It is probable that the cause of the iodide purpura is some chemical action of the drug on vasomotor centres producing variations in pressure in the area in which purpura appears; but it is possible that the drug may have a selective action on particular vascular areas, rendered more vulnerable than usual by incidental influences.

Henoch's Purpura.—Though Willan many years previously had described a case of this kind very graphically, it was not until Henoch published a series of cases that attention was prominently directed to this form, often called "Henoch's purpura." Couty recorded a number of cases which he recognised as similar in nature to those described by Henoch; and Prof. Osler, who takes a more general view of purpura

than I have done in the present article (including it under erythema exudativum), has particularly directed attention to the visceral complications.

The marked feature of this disease is the association of abdominal symptoms (vomiting, colic, intestinal haemorrhage) with purpura and arthritic swellings. The attack may begin with rheumatic pains and swellings of the joints, and be followed by purpura and colic with vomiting and blood in the stools. Or it may begin with gastro-intestinal derangement, and the purpura and articular swellings and pains follow. What is especially characteristic of it is the occurrence of repeated outbreaks of colic, vomiting, and haemorrhage from the bowels, with purpura and pains and swellings in the joints. The illness generally consists of a series of such events over a period of some weeks or months; but intervals of months may occur, and fresh outbreaks then take place. Recurrence is one of its most characteristic features, and it may extend over several years.

The colic is generally of a very intense character. The abdomen is usually tender, especially over the colon. The possibility of suprarenal haemorrhage should be borne in mind. The vomiting is often severe and protracted, frequently bilious, occasionally but not frequently bloody. The stools contain more or less coagulated blood, but in some of the attacks no blood may be passed. The acute abdominal symptoms have led to laparotomy, for example for intussusception (Greig); intussusception indeed has occurred in association with Henoch's purpura (Sutherland, Lett). In some cases albuminuria is present, and well-marked symptoms of nephritis set in which may prove fatal; or this complication may slowly subside. Epistaxis, haematuria, haemoptysis may occur, but are not frequent. In the majority of cases the eruption is purely haemorrhagic, but in others, in addition to the purpura, purpuric oedema, angioneurotic oedema (Don), exudative erythema, and urticaria may be present. Most commonly the eruption is confined to the extremities, but it may involve the face and trunk; and haemorrhages may occur in the mouth and throat. In the attacks the joints are usually affected. There may be only pain and stiffness, or there may be effusion and redness of skin over the articulations. The dorsa of the feet are often swollen, as in purpura rheumatica. There is as a rule little pyrexia, and it may be entirely absent. In one of Prof. Osler's cases great coldness of the feet was a prodromal symptom of the attacks, and in one case the spleen was enlarged. Silbermann has published a fatal case: a child, aged ten years, was attacked on December 15, 1887, with fever and pains in the knees. On the 16th there was an outbreak of purpura, with colic, haematemesis, and melaena, and after persisting for three days the symptoms disappeared. The attack recurred in January with great severity, and on the 20th, 21st, and 22nd there were signs of peritonitis. The autopsy shewed acute peritonitis, which had resulted from a perforation at the fundus of the stomach. There was no ulceration in the bowels, but the mucosa was swollen and congested.

There were necrotic foci in the stomach and intestines, and thrombi were found in some of the blood-vessels.

Henoch's purpura is relatively most common in childhood, but it occurs in adults also. As to the nature of such cases the evidence is inconclusive, and whether the colic and vomiting stand in relation to the haemorrhage from the bowels and stomach as cause or effect is uncertain. Silbermann's case, however, suggests that haemorrhage is the primary event and may lead to ulceration and perforation, as haemorrhage is an exceedingly rare or almost unknown event in colic of the most severe degree, as in lead poisoning. It has also been thought that the condition is due to toxaemia of intestinal origin. Some of the cases appear to be of a rheumatic nature—the patients, as in some recorded by Henoch, having previously had a rheumatic attack without purpura or colic. Couty regards the disease, by the exclusion of other causes, as of nervous origin, affecting the vasomotor nerves.

Diagnosis of Purpura.—It must be reiterated that purpura is rather a symptom than a disease. It is not sufficient, therefore, to recognise purpura, but the nature of the process in the individual case must be ascertained. To recognise the symptom purpura is an extremely easy matter. The occurrence of haemorrhages in the skin and mucous membrane is demonstrated by an eruption of blood-colouring matter not of traumatic origin, the colour not disappearing under pressure. In many forms of exudative erythema there is blood extravasation, but this is accompanied by overfilling of the blood-vessels, which may be emptied by pressure, the colour returning when the pressure is removed. To this condition the name purpuric erythema may be applied; but the name purpura should strictly be applied to cases in which the haemorrhages are primary, unattended with erythema, and not due to injuries. Purpura may be simulated by coal-tar pigments, and an appearance like bruises or ecchymoses may be produced. These, it is needless to say, "do not disappear on pressure," but do by washing.

Having decided that purpura is present the observer has next to search for its cause. It is for this reason that some clinical classification is not merely desirable, but absolutely essential. The first step is to ascertain whether the purpura is an expression of one of the specific diseases prone to be attended with haemorrhage. Small-pox, scarlet fever, measles, pyaemia, syphilis, pneumonia, and rheumatism have especially to be borne in mind. The diagnosis of purpura rheumatica has been sufficiently given. Next, the various primary blood diseases have to be considered—pernicious anaemia and leucocythaemia and haemophilia in particular. The appearance of the patient may afford a clue, but the most important matter is a complete microscopical examination of the blood. The coagulability of the blood may be ascertained by means of Sir A. E. Wright's coagulometer. In the next place the possibility of scurvy must be remembered. In this disease, in addition to the cutaneous haemorrhages, subcutaneous and intra-muscular extravasations occur, producing brawny, blood-stained

patches in the hamstring muscles and calves of the legs, and in the skin over the patches; and the gums are swollen and bleeding. Evidence of insufficiency of fresh vegetable or animal food is generally obtainable. In doubtful cases the effect of treatment will assist in the diagnosis, as scorbutic cases rapidly improve when treated with fresh vegetables and meat juice. It must be remarked, however, in this connexion that in certain cases of pernicious anaemia the gums may be swollen and bleeding as in scurvy. To these cases the name "scorbutic anaemia" has been applied. Scurvy being excluded, the possibility of some poison having been accidentally or intentionally taken must be considered—phosphorus, mercury, mineral acids, etc., being borne in mind; or some medicinal substance, especially iodide of potassium. A certain proprietary "blood mixture" containing iodide of potassium has caused several cases. Nor must the possibility of a nervous origin be forgotten; the history of the case, and an examination of the nervous system, will determine whether this cause be in operation. Powerful emotion apparently may produce purpura. Carrière and Gibert have recorded a case in a male aged twenty-one. Unjustly suspected of theft, one hour afterwards epistaxis occurred, which was repeated during eight days. Purpura one month afterwards.

Finally, in a considerable number of cases no definite cause can be ascertained for the purpura, and such cases are indicated by the name P. idiopathica. They must temporarily be relegated to the class purpura simplex or purpura haemorrhagica, according to the symptoms presented. It must be remembered, however, that this indefinite name serves but to remind us of our ignorance; and the observer must ever be on the alert to discover the cause which will immediately remove the case to its own category.

Prognosis.—Most cases of purpura end in recovery. The mortality is probably about 14 or 15 per cent. Thus of the 200 cases above analysed the mortality was 28, or 14 per cent. Sex does not appear to exercise any decided influence—the mortality in males, in the 200 cases, being 14·2, whilst in females it was 13·6. Age exercises some influence, the gravity appearing to increase, on the whole, with the age of the patient. But in the 200 cases analysed the mortality in the first decade was 16 per cent; in the second decade, 10 per cent; in the third decade, 14 per cent; in the fourth decade, 13 per cent; in the fifth decade, 25 per cent; in the seventh decade, 25 per cent. It is thus seen that the greatest mortality occurs in patients under 10 and over 40 years of age. Cases of P. simplex almost invariably end in recovery; but, on the other hand, purpura simplex may be the beginning of a severe and fatal case of purpura haemorrhagica. The gravity of the case is generally stamped early upon it. The severity and frequency of the cutaneous haemorrhages, the occurrence of haemorrhages from mucous surfaces, the degree of pyrexia, the constitutional depression, the degradation of the blood, as proved by the haemoglobinometer and haemocytometer, and the occurrence of marked albuminuria, will draw

attention to the danger attaching to the case. At the same time it must be borne in mind that the most severe and apparently dangerous cases sometimes end in recovery.

Treatment.—The patient in all kinds of purpura should be confined to bed. Whenever a definite cause for the purpura is discoverable, a clue to the treatment will be supplied. In the infective diseases it invariably indicates a very grave condition, and calls for support by nourishing fluid food and perhaps stimulants; whilst at the same time some of the haemostatics to be subsequently mentioned, especially turpentine, should be administered. In syphilitic purpura iodide of potassium should not be given, for it appears in some cases to increase or to initiate the haemorrhages. In many cases of P. rheumatica oil of turpentine appears to act as a specific; it should be given in ten or twenty minim doses in capsules, or suspended by means of tr. quillaiae saponariae or mucilage. The following mixture I have used in numbers of cases with the happiest results:—Ol. terebinth ℥ x., tinct. quillaiae sapon. ℥ x., aquam cassiae ad ℥j. To be given three times a day. Dr. Eustace Smith advocates much larger doses, and gives to a child of five or six years of age 2 drams of turpentine with an equal quantity of castor oil, and if the first dose is insufficient increases it. He has prescribed as much as ½ oz. with the same quantity of castor oil to children of ten or twelve years. As given with castor oil it acts as a purgative, and probably not much of the turpentine is absorbed. He only recommends these large doses in the case of well-nourished, full-blooded children. Boeck of Christiania recommends antifebrin in five or ten grain doses in these cases. Salicylates, in my experience, as well as in that of Boeck, have little or no influence for good. Dr. Longley has recorded a case of severe Henoch's purpura with haematuria in which adrenalin 2 minims, liq. arsen. 3 minims, every four hours, acted like a charm. Adrenalin certainly deserves trial, especially in cases in which other remedies have failed. A solution of adrenalin chloride (1-1000) may be given by the mouth in doses from 5 to 30 minims; or adrenalin extract (dry) from ½ to 3 grains, tablets 5 grains, liq. ext. 10 to 15 minims, hypodermically 1 to 5 minims.

In cases in which no discoverable cause can be ascertained, as well as in many in which there is a recognised cause, turpentine is, on the whole, the best remedy. Ergot and hamamelis may be tried, but they have not proved very efficacious in my hands. Calcium chloride or lactate, suggested by Sir A. Wright, is indicated when deficient coagulability of the blood is proved or suspected, and certainly should be tried when other remedies fail. It should be given to adults at first in twenty-grain doses, every three or four hours, the dose being reduced later to fifteen or ten grains: as when given in excess it diminishes the coagulability of the blood. Sansom had a successful case treated with sulphocarbolate of sodium in gr. xxx. doses. Iron, as preparations of the perchloride or persulphate, appears useful in some cases in the attack, and should be given in convalescence to remove the anaemia which so

commonly results in severe cases. In Henoch's purpura Henoch himself has seen benefit from an ice-bag applied to the abdomen; in chronic cases he recommends perchloride of iron. Prof. Osler in two cases saw benefit from arsenic, which appeared to control the tendency to recurrences. In other cases, however, it failed.

The hypodermic injection of fresh animal serum has been employed (Leary, Larrabee).

PETECHIAE.—Minute haemorrhages in the skin, the size of a flea-bite. Such haemorrhages vary in colour from bright red, dark red, to purple; and have this characteristic, that the colour does not disappear on pressure. Petechiae may be one of the expressions of purpura, in which case they will be almost invariably associated with larger haemorrhages in the skin, and in these circumstances own the most varied causes (see Purpura). Or they may be caused by the bite of the common flea. In the latter case, when recent there is a small circular spot of erythema with a pin-point haemorrhage in its centre. The erythema disappears on pressure, to return when the pressure is removed, whilst the central punctum remains, as it does also when the erythema spontaneously subsides. When due to flea-bites, recent lesions, with the above characters, will almost invariably be found, affording a clue to their nature. Their position, on covered parts of the skin, as well as the evidence of want of personal cleanliness of the patient and clothes, will be of assistance in determining their nature. There is some evidence that cachectic conditions and want of food favour the persistence of the minute haemorrhages due to flea-bites, and their abundance undoubtedly implies neglect. When associated with pyrexia they may cause mistakes in diagnosis, especially as regards typhus and measles; so that the subject is not unimportant. Care with regard to the above points will enable the observer to avoid errors in diagnosis. The term petechial is applied to diseases, especially fevers, accompanied by haemorrhage.

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S. M.

HAEMORRHAGES IN NEW-BORN CHILDREN

By John Thomson, M.D., F.R.C.P., Ed.

The haemorrhages which occur in new-born children may be divided into two groups: (1) **Traumatic or Accidental Haemorrhages,** which are the direct result of injury at the time of birth; and (2) **Spontaneous Haemorrhages,** which occur without any apparent external cause.

The cases of spontaneous haemorrhage are best again subdivided into (*a*) *Idiopathic* cases in which the bleeding is the chief or only symptom—the so-called "haemorrhagic disease of new-born children"; and (*b*) *Symptomatic* cases, in which the haemorrhages are secondary to some serious organic disease, such as congenital malformation of the heart, congenital obliteration of the bile-ducts, or some other grave affection of the liver. With this group also may be taken the rare cases in which true haemophilia leads to haemorrhages in early infancy.

A. Traumatic or Accidental Haemorrhages

The traumatic haemorrhages are mainly due to injuries received during birth, either by the pressure of the maternal parts on the child, or by the artificial means used by the accoucheur to expedite delivery. They are consequently more frequent in the case of first-born and male children, in difficult and prolonged labours, and when the presentation is abnormal. There can be little doubt, also, that increase of the blood-pressure, owing either to asphyxia from pressure on the cord, or to pressure on veins or compression of some other part of the body, may be an important cause of their occurrence.

Traumatic cases are of less importance, from the physician's point of view, than those of spontaneous bleeding. Nevertheless they also are of interest to him and therefore worthy of brief mention here because, in not a few instances, they form the starting-point of serious nervous disease in later life.

The most important situations in which the effused blood is found may be stated as follows:—(i.) On the surface of the skull, between the pericranium and the bone—cephalhaematoma; (ii.) Inside the cranium—apoplexia neonatorum; (iii.) Into the substance of the sterno-mastoid muscle; (iv.) Into one or more of the abdominal or thoracic organs.

(i.) **Cephalhaematoma** is the name given to a swelling on the surface of the cranium formed by a collection of fluid blood between the pericranium and the bone. The condition is due to rupture of blood-vessels under the pericranium, owing to mechanical pressure during birth; and it is met with about once in every 200 births. It is much more commonly seen after first labours than after subsequent ones, and is

especially frequent after difficult births in which the head has presented. It occurs, however, sometimes after breech cases, and occasionally also with comparatively easy and normal labours.

In the majority of cases the tumour is situated over the right parietal bone—this being usually the presenting part. Less frequently it is found in the left parietal region; and sometimes it occurs on both sides. It is rarely met with over the other cranial bones. The swelling is generally noticed within the first two or three days after birth. It is rounded in contour, fluctuating and not apparently tender; and it shews no heat or redness. Being under the pericranium it is always distinctly limited to the surface of one bone and never crosses a suture. For four or five days it usually goes on increasing in size, and then, after being stationary for a while, it slowly disappears. When the blood begins to be absorbed, the bone can readily be felt through the tumour, and round its margin a raised ring can be made out. This is due to the formation of bone having gone on under the raised periosteum. Sometimes also from the same cause there is a crackling sensation experienced on handling the surface of the swelling.

Generally the blood tumour is quite absorbed within four weeks of birth, but it often takes two or three months before all trace of the bony ridge round it has disappeared. The prognosis in uncomplicated cases is invariably good, the cephalhaematoma always recovering without any treatment. It should, however, be remembered that in a certain proportion of cases the external swelling is accompanied by an intracranial haemorrhage.

(ii.) **Intracranial haemorrhages** (Apoplexia neonatorum) are unfortunately not very uncommon. They are important, not only because they are a very frequent cause of stillbirth and early death, but also because they are responsible for a large amount of bodily and mental defect in after-life.

Etiology.—Although the state of asphyxia into which many children are brought during birth must be regarded as a strongly predisposing element in the causation of these haemorrhages (Ashby), Dr. Spencer's statistics render it almost certain that they are mainly due to external injuries. These may be produced either by the pressure of the maternal parts on the child or by that of the blades of the forceps. Thus he has found that the frequency of cerebral haemorrhage is greatest with forceps delivery, less when the breech or foot presents, and least of all with natural head delivery.

As to the mechanism by which the lesion is brought about, Spencer suggests that in many cases it is due to displacement inwards of the lower anterior corner of the parietal bone. This corner directly overlies the great anastomotic vein, and being driven inwards during birth, clamps this vessel so as to cause engorgement in its area of distribution. This explains, he thinks, the fact that the haemorrhages are often limited to the parietal region and Sylvian fissure. Compression of the internal jugular vein by the forceps may also favour cerebral haemorrhage in a

similar way. S. McNutt has shewn that haemorrhages limited to the convexity are more frequent in breech than in head deliveries.

Morbid Anatomy.—In a very large majority of the cases the haemorrhage is primarily meningeal, and the injury to the brain itself is secondary and results from pressure from the surface. In some cases, however, the bleeding takes place into the brain substance. Effusion of blood on the inner aspect of the cranial bones, outside the dura mater (internal cephalhaematoma), is sometimes found along with an external cephalhaematoma. It is said that this does not occur unless a fracture of the bone is present (Holt). Generally the blood is poured out into and beneath the arachnoid and pia.

The lesion is more frequently bilateral than confined to one side; and it is much commoner at the base than on the convexity of the brain. It is also commoner towards the posterior part of the skull than anteriorly. As has been already mentioned, haemorrhages are frequently found over the parietal region and in the Sylvian fissure. The ventricles are sometimes distended with blood.

When meningeal apoplexy occurs, it sometimes lacerates the underlying cerebral cortex; in any case, it is apt to interfere with its nourishment by tearing through the blood-vessels which pass into it from the membranes. It also injures it by its pressure, so that softening and atrophy soon follow. Thus permanent atrophy and arrest of development of the cortex are set up along with degeneration of the fibres in the motor tract of the brain and spinal cord.

Clinical Features.—If the damage to the brain be very great, the child will probably be stillborn. The haemorrhage may, however, be tolerably extensive, and yet the infant may survive for several days; or he may even recover and grow to adult age, although generally with a permanently damaged nervous system.

In many cases there are no symptoms at all; and often, even when the haemorrhage is severe, the infant only shews torpor and feeble or irregular breathing; but other indications may be present. There may be obvious paralysis of one or more limbs, or of the cranial nerves if the haemorrhage implicate the base; and the fontanelle may be prominent and tense. If the child live for some days, convulsions often occur; and they are more frequent in cases in which the haemorrhage is over the cortex than in those in which it is at the base of the brain (McNutt).

As the child gets older, although the parents are often slow to see that anything is the matter with him, it will usually soon be found that the limbs are unnaturally stiff and the knee-jerks exaggerated. Later, he is backward in learning to hold his head up, in sitting up, and in walking; or it may be that he displays a lack of interest in his surroundings, which is soon noticed as abnormal. Gradually, as the brain grows, the extent of the damage to its functions becomes more manifest, and the case passes off into spastic paraplegia, hemiplegia, diplegia, imbecility or idiocy with or without paralysis.

Prognosis.—Whilst extensive haemorrhages at the base are usually

fatal, comparatively large ones over the convexity are compatible with life. Small cortical apoplexies may, it is said, be entirely recovered from, but in the great majority of cases more or less permanent injury to the brain results.

(iii.) **Haematoma of the sterno-mastoid** is a collection of blood which forms within the sheath of that muscle when some of its fibres have been ruptured during birth. It is met with most frequently in breech cases or cross-births in which there has been difficulty in delivering the head; often also in difficult forceps cases, and sometimes after labours which are said to have been quite easy. It is probably caused more often by a sudden twisting of the neck than by simple traction on it. In nearly 300 autopsies on children, who were either stillborn or had died soon after birth, Dr. Spencer found this lesion in fifteen.

The swelling may occur at any part of the muscle, but most frequently it is situated about its centre. The muscle of the right side is much oftener affected than that of the left. The tumour is not usually noticed until the second or third week, and often it does not attract attention till much later. This is due to the fact that the swelling caused by the effusion of blood is generally small at first. It is not until the injury to the muscle has occasioned a considerable growth of fibrous tissue ("muscle callus") round it, that it becomes too obvious to be overlooked. It may reach the size of a pigeon's egg, but it is generally smaller. The swelling remains stationary for weeks, and then slowly diminishes. It usually takes six or seven months to disappear; but it may have quite gone by the third month, or it may last more than a year (Pollard).

The connexion between haematoma of the sterno-mastoid and so-called congenital wryneck is certainly a very close one, but it is difficult at present accurately to define it. Out of 106 cases of haematoma which Mr. D'Arcy Power collected from medical records, marked wryneck had resulted in twenty-one at least, whereas only in fourteen had it been specially looked for and not found. Dieffenbach and other older writers on the subject assumed that the wryneck was the simple result of the injury to the sterno-mastoid muscle at birth; but this explanation has been disputed by later authorities (Golding-Bird, Petersen, Koettnitz). The chief difficulty in accepting it is that in most if not all of the marked cases of congenital wryneck there is a very decided arrest of growth of all the structures of the face on the affected side, and it is difficult to imagine how any lesion of the neck only could bring this about. What cerebral lesion could cause it, however, is as yet undetermined. The fact remains that this characteristic facial asymmetry along with wryneck not uncommonly appears as a sequel of haematoma of the sterno-mastoid. Usually little can be effected in the way of treatment owing to the age of the child; but it is probable that judiciously applied massage and manipulations may sometimes be of use.

(iv.) **Haemorrhages into Abdominal and Thoracic Viscera.**—As Dr. Spencer points out, haemorrhages into the abdominal and thoracic

viscera are much more frequent after breech cases than after those in which the head has presented. They may occur into any of the organs, being seen frequently in the lungs, liver, kidneys, suprarenals, and intestine, and comparatively rarely in the spleen.

In most cases of internal haemorrhage the diagnosis is impossible during life for lack of symptoms. Pulmonary infarctions, however, sometimes betray their presence by causing physical signs of consolidation of the lung. They are the cause of death in many cases of children who live for a few days only, and in these the fatal issue is apt to be attributed to congenital heart disease on account of the degree of cyanosis which is present. If the infant live long enough, pneumonia may result.

Haemorrhage into the pyramids of the kidneys may cause death within a few days, with symptoms of suppression of urine; and Dr. Spencer records one case in which a large haemorrhage into the caecum caused complete intestinal obstruction.

B. Spontaneous Haemorrhages

(i.) Idiopathic Cases (the Haemorrhagic Disease of New-born Children)

Description.—The haemorrhagic disease of new-born children may be described as a passing morbid condition of the system which shews itself mainly by a tendency to spontaneous bleeding. The haemorrhages may occur either from the umbilicus, from the stomach or bowel, from the blood-vessels in the subcutaneous tissue, or from other parts; and their occurrence is probably due to poisoning by the toxin produced by any one of various micro-organisms.

The condition is a very rare one. Cases of gastro-intestinal haemorrhage, which is its commonest form, are said to occur once for every 500-1000 births (Runge, Hermary, Kling); whilst umbilical haemorrhage is only met with once for every 5000 confinements (Ribemont).

Clinical Features.—In the great majority of cases no family history of bleeding is to be obtained. The sexes seem to be affected in about equal proportions. This point is of interest when we remember the very much greater frequency with which the male sex is affected in haemophilia—the proportion being stated by Grandidier as eleven boys to one girl (*vide* art. "Haemophilia," p. 918).

Sometimes the patient is in weak health before the bleeding sets in; being premature or feeble, or perhaps the subject of congenital syphilis. Generally, however, he appears quite healthy until the haemorrhage begins. This takes place usually within the first week of life, and rarely after the end of the second; the exact date varies, partly according to the situation whence it comes.

The site of the haemorrhage may vary considerably. In the majority

of cases it comes either from the alimentary tract (mouth, stomach, or bowel) or from the umbilicus. It may also take place into the subcutaneous tissue, or from the nose, conjunctiva, or ears, or into almost any of the internal organs. The bleeding may come from one situation only, as often happens in the slighter cases, or many parts may be affected, either at one time or successively. Thus, of 50 cases reported by Townsend, the umbilicus was affected in 18 (alone in 3); the intestine in 20; the mouth in 14; the stomach in 14; the nose in 12; subcutaneous ecchymoses occurred in 21; bleeding from an abrasion of the skin in 1; from the meninges in 4; cephalhaematoma appeared in 3; haemorrhages into the abdomen in 2; and into the pleura, lungs, and thymus in 1 each.

The amount of blood lost at a time is usually small; but the loss is generally so frequently repeated that pallor, chilliness, and prostration with failure of the pulse are very soon produced. In some cases the temperature is high, in others it is normal or subnormal throughout. In the cases of recovery the bleeding usually lasts one or two days; in the fatal cases death often occurs within twenty-four hours, and rarely later than three days from the beginning. Sometimes diarrhoea appears, and towards the end convulsions not infrequently set in.

In children who recover the convalescence is apt to be prolonged and tedious, although the health is not permanently damaged.

Gastro-intestinal Haemorrhages (*Melaena neonatorum*).—The blood in these cases is more frequently passed by the bowel than vomited. When vomited it is sometimes bright red, often dark brown in colour. Its amount varies greatly in different cases. Sometimes the haematemesis occurs only on one occasion; more frequently small quantities are brought up repeatedly. When passed by the bowel the blood is generally very black and thoroughly mixed with the motions. Sometimes, when it comes from the lower part of the bowel, it is red, and it may be in clots.

The blood is most frequently seen for the first time on the second day of life, or at least before the fifth; but occasionally the haemorrhage may begin as late as the second week.

Spontaneous umbilical haemorrhage usually takes the form of a steady oozing from the point where the cord has separated or is about to separate. The bleeding does not generally come from any visible blood-vessel; it is often intermittent; sometimes it is alarmingly free. Sometimes it takes place into the substance of the cord, or from fissures on its surface.

It generally begins about the fifth day of life, but it may occur earlier, and it may be deferred till the seventh or even the ninth day. It does not generally last more than three days, but in rare cases it may go on much longer. It is often fatal within twenty-four hours.

Subcutaneous ecchymoses may occur at any part of the body, and are as common on protected areas as on those which are exposed to pressure and friction. They are often of small size, but occasionally they become

very large. If they occur without any haemorrhages from other situations the prognosis is generally good.

Bleeding from the female genitals occurs occasionally in cases of multiple haemorrhages. It is, however, much more frequently met with as an isolated symptom; and, when this is so, it is generally the result of some trifling local disturbance and has no serious significance. The haemorrhage begins usually within the first six days of life, rarely after the twenty-first (Busey). The external genitals appear quite normal, but there is a more or less constant oozing of blood from the vaginal orifice, which lasts from two to five days, or sometimes a little longer. Owing to the trivial nature of the ailment very few opportunities have occurred for investigating its morbid anatomy. Eröss in one case found acute haemorrhagic catarrh of the fundus uteri. Only in rare cases does the haemorrhage recur, so that it cannot be regarded as of the nature of menstruation.

Morbid Anatomy.—In most cases of children who have died from haemorrhage there is nothing to be discovered at the autopsy but the traces of the effused blood and a general pallor of all the organs.

In a considerable proportion, however, of the cases of melaena (40 per cent according to Romme), more or less ulceration of the mucous membrane of the stomach or duodenum has been found. The ulcers are usually multiple, and may either consist of superficial abrasions or be of a perforating character. In one case (Landau) a clot was found obliterating the blood-vessels which supplied the area in which the ulcers were situated, but this is not usually the case. In some cases of melaena cerebral haemorrhages have been found (Pomorski, v. Preuschen), but these also are by no means constant. In syphilitic cases endarteritis of the small and middle-sized vessels in the submucous tissue of the alimentary tract has been described (Mraček).

A considerable variety of micro-organisms has been found in the blood and in the tissues in cases of haemorrhage, and especially in those of melaena. The first to record an observation of this kind was Klebs, who, in 1875, described a micrococcus which he had found in large quantities in the organs of nine new-born children who had died of haemorrhage. This he injected into young rabbits, and succeeded in producing haemorrhages in them. His results were confirmed in the following years by Weigert, Eppinger, and others. Since then various micro-organisms have been discovered in these cases by competent observers. Thus, streptococci have been found by Baginsky, Babes, and Bar; *Bacillus pyocyaneus* and staphylococci of various kinds by Neumann, Bar, and Finkelstein, and *Bacterium lactis aerogenes* also by Neumann. Further, Babes found in one case an organism with all the characters of the *Diplococcus pneumoniae*, and v. Dungern one which resembled in every way Friedländer's pneumo-bacillus. In v. Dungern's case it is also recorded that, while the child was in the ward, three other infants died of severe pneumonia. In 1894 Gärtner published an account of two fatal cases of melaena in which he found a short bacillus. Cultures of this organism

were made and injected into the peritoneal cavity of young puppies, and they set up fatal gastro-intestinal haemorrhage. Finkelstein and various other writers have found a similar organism.

Etiology.—A number of very different hypotheses of the causation of this condition have been framed. The following deserve mention:—

1. Von Preuschen and Pomorski have published cases in which melaena and pulmonary infarction of an apparently spontaneous origin were found after death to be associated with traumatic haemorrhages into the cerebral peduncles and the fourth ventricle, damaging the vasomotor centre. They therefore maintain that many if not all of the cases of spontaneous haemorrhage are secondary to cerebral injury. They were able to strengthen their position by means of experiments on animals; for they succeeded in producing melaena in a considerable number of rabbits by puncturing the cerebral peduncles and the walls of the fourth ventricle.

Whilst these observations are certainly interesting and important, they cannot be held as explaining the occurrence of most cases of this disease. Cerebral haemorrhages have only been found in a few instances.

2. Other writers have laid great stress on the local morbid condition. Thus, for example, in dealing with melaena they have given mechanical explanations to account for the presence of ulceration in the stomach and bowel in these cases. The most remarkable of these hypotheses is that put forward by Landau. He noticed that the condition often occurred in premature and weakly infants in whom the function of respiration was established with some delay and difficulty. He accounts for this by supposing that the delayed inspiration favours stagnation and clotting of the blood in the umbilical vein. Then, he further supposes that, from the thrombus so formed or from that in the ductus arteriosus, an embolus is separated and carried through the circulation until it becomes impacted in one of the arterial branches which supply the stomach and duodenum, and ulceration results. In one case of gastric haemorrhage he was able to satisfy himself that the artery supplying the area from which the blood came contained a clot.

Emboli of this sort have not been found by other observers who have looked for them, and Landau's hypothesis has not, therefore, been generally accepted. It must be remembered in this connexion that the formation of ulcers in the stomach and bowel is a frequent result of general infection with organisms of various kinds, and even of poisoning by toxins (Demelin).

3. Considerable stress has been laid by some authors on the fact that many of the patients in these cases are syphilitic or otherwise weakly; and it has been supposed that the bleeding might be attributed to some disease causing special fragility of the blood-vessels.

Evidence of vascular disease, however, has not usually been found; and it seems more probable that debilitated states of the system act as remote causes only in so far as they prepare a suitable soil for the growth of micro-organisms.

4. Of recent years there has been an increasing tendency to regard the spontaneous hæmorrhages in these cases as a manifestation of a micro-organismal disease; and, although there are difficulties in the way of accepting this explanation in all cases, there are many points in favour of it. It is well known, for example, that many pathogenetic organisms have the property of producing a tendency to hæmorrhage. As already mentioned, a large number of different organisms, known and unknown, have been cultivated from the blood and tissues in these cases; and some of them have even been found to cause hæmorrhages when injected into animals. The relation of the micro-organismal invasion to the haemorrhages has been discussed by Lequeux and others. Holt suggests that the organisms may act by producing a substance which, like the so-called "haemorrhagin" found by Flexner and Noguchi in rattlesnake venom, destroys the epithelium of the small blood-vessels.

Diagnosis.—Spurious melaena, that is, the vomiting or passing by the bowel of blood which the child has swallowed during birth, or has sucked from fissures in the mother's nipples, often causes needless anxiety if mistaken for this disease. It is more frequently met with than true haemorrhage. Or the child may have epistaxis or haemorrhage from an ulcer in the mouth or throat, and the blood may be passed with the motions and cause a diagnosis of melaena. Such mistakes are not usually difficult to avoid. If, however, the haemorrhages be confined to the internal organs, they are very apt to be overlooked in the absence of characteristic symptoms.

The occurrence of spontaneous haemorrhages—especially ecchymoses—has, it should be remembered, some interest from a medico-legal point of view, as they may be regarded erroneously as evidence of violence.

Prognosis.—The condition is always a very dangerous one. In Townsend's cases the mortality was 62 per cent. In cases of umbilical haemorrhage it is even larger than this, being variously stated by authorities at from 65 to 84 per cent; whereas in melaena it is usually estimated at from 50 to 60 per cent. Should the infant be syphilitic or otherwise constitutionally feeble, this fact naturally renders the prognosis still more unfavourable.

Treatment.—Great encouragement to prompt and persevering treatment of these cases is to be gathered from the fact that the disease is so brief in its duration. The treatment is to be conducted on general principles, and not confined merely to the administration of drugs. It is especially important, to begin with, that everything possible should be done to conserve the child's vitality. He should be kept lying quietly with his head low, and with his body and limbs wrapped in cotton wool and surrounded with hot-water bottles. French writers recommend the use of an incubator (Dusser, Oui). The local application of ice is to be avoided because of its depressing effect on the general strength. When there is much exhaustion from the loss of blood, very great benefit is sometimes derived from sterilised salt solution (0·75 per cent) either given subcutaneously or very slowly injected into the rectum.

The most valuable drug in these cases is suprarenal extract, and adrenalin chloride (1-1000 solution) is probably the most efficient preparation of it. This may be given by the mouth, in doses of ♏ss.-i., every hour or two. As Holt pointed out, this is often strikingly successful in stopping the haemorrhage in cases of melaena. In some instances, at least, it has also appeared to do good in umbilical haemorrhage. This may be explained by supposing that adrenal insufficiency plays some part in setting up the tendency to haemorrhage in this disease as it seems to do in others (Rolleston).

Another remedy which has been used with success is gelatin. It may be given subcutaneously, as Holtschmidt recommends, in doses of ʒii. or more of a 2 per cent solution; or a 2-5 per cent solution may be given by the mouth (ʒi. every hour) or by the rectum (ʒi.-ii.). Only gelatin which has been very carefully sterilised may be injected, as commercial gelatin often contains tetanus bacilli. Should neither of these remedies be obtainable, ergotin may be administered subcutaneously or by the mouth. During recent years Dr. E. C. Hort and others have drawn attention to the striking effect of fresh sterile animal serums, given by the mouth, in arresting various forms of internal haemorrhage. This method of treatment may, in the future, prove of great value in the spontaneous haemorrhages of new-born children. The subject is scarcely as yet, however, within the sphere of practical therapeutics, especially in the case of an emergency such as melaena.

When the haemorrhage is from the umbilicus, patient and intelligent digital pressure on the bleeding point should be tried along with the local application of adrenalin, gelatin, calcium chloride, nitrate of silver, or plaster of Paris. The actual cautery has often also been successful. Should other means fail, the base of the bleeding point should be transfixed by a hare-lip pin and a ligature applied round it.

In melaena the infant should not be allowed to suck, but small quantities of breast-milk or peptonised milk should be given him by a spoon or medicine dropper, at short intervals. Injections into the bowel are to be avoided as they tend to set up peristalsis.

Haemorrhage from the vagina in new-born children is generally so trivial a matter that no special treatment is required.

(ii.) Symptomatic Cases

Description.—Spontaneous haemorrhages, similar in most respects to those we have been considering, are frequently met with as a symptom of various diseases. Thus we find them occasionally occurring in children with congenital malformation of the heart, rarely in infants who inherit true haemophilia, and frequently in cases of congenital obliteration of the bile-ducts and other serious diseases of the liver accompanied by jaundice.

The tendency to haemorrhage met with in these morbid conditions differs from that seen in the haemorrhagic disease of new-born children

in that it is permanent. With few exceptions it lasts as long as the child lives.

In congenital obliteration of the bile-ducts, and in all other forms of disease which cause lasting jaundice in young infants, haemorrhages are a common and characteristic symptom. Thus, more than two-fifths of the cases of umbilical haemorrhage collected by Jenkins and Grandidier occurred in icteric infants; while in 65 cases of congenital narrowing or obliteration of the bile-ducts tabulated by myself, haemorrhages were noted in more than half of the infants who had lived more than a few days. A similar haemorrhagic tendency is of course well known to occur sooner or later in all cases of severe and continued jaundice.

Clinical Features.—The places from which the bleeding occurs in these cases are just the same as those observed in the case of idiopathic haemorrhages. Their onset, however, is generally later. Thus in Grandidier's cases of umbilical haemorrhage the average date of onset was about the sixth day in the non-icteric and about the tenth in the icteric cases. In the case of gastro-intestinal haemorrhages this difference is very much more marked; for, although jaundiced infants sometimes shew a tendency to haemorrhage from the very first, they often do not begin to bleed until several months after birth. When once established the tendency seems rather to increase as they grow older.

Etiology.—The causation of the haemorrhages in cases of jaundice has never been satisfactorily explained, although many hypotheses have been proposed to account for them. By some they have been attributed to impoverishment of the blood (Budd, Murchison); by others it has been supposed that they are due to bile acids circulating in it, and either acting on the corpuscles (Leyden) or setting up a diseased state of the blood-vessels (Wickham Legg).

It seems, however, more probable that the haemorrhagic tendency is caused in some way by the presence in the blood, not of bile acids, but of some organic poisons. These are formed in the process of ordinary digestion, and the diseased liver is not able to render them innocuous, as it would do if it were in a state of health. The following facts seem to support this hypothesis. It has been found by Roger that the function of the liver, in virtue of which it neutralises the organic poisons formed in the alimentary canal, as well as others, is closely connected with the amount of glycogen it contains. Thus, when the liver contained little or no glycogen, he found that a very much smaller dose of these organic poisons was required to produce a given result than was necessary if the organ were healthy in this respect. It has also been demonstrated by Dr. Wickham Legg and others that the obliteration of the bile-ducts by ligature is followed in animals by disappearance of glycogen from the liver. It would appear that the retention of bile from any cause interferes with the proper discharge of the function of glycogenesis in the hepatic cells.

In the light of these observations, it seems not improbable that in congenital obliteration of the bile-ducts and other serious forms of

jaundice a process of auto-intoxication is set up. If this be so, the poisons which come thus to circulate in the blood will probably induce haemorrhages in the same way as do those toxins which are produced by the action of micro-organisms in the idiopathic cases.

Owing to the serious nature of the diseases present in these cases the **prognosis** is much worse than in the idiopathic group, and the **treatment**, which is to be conducted on the same lines as in the others, is much less likely to be successful.

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SCURVY

By W. Johnson Smith

Synonyms.—*Scorbutus, Scorbut;* It. *Scorbuto;* Russ. *Zinga.*

Scurvy is a general apyretic disorder characterised by mental depression, extreme debility, a tendency to syncope, and special lesions of the mouth, skin, and muscular system, indicative of a morbid change in the composition and properties of the blood. Of these lesions the most frequent and most marked are swollen, deeply congested, and softened gums, petechiae and diffused livid patches on the surface of the skin, and swelling and rigidity of the hams. In severe and advanced cases there may be bleeding from the mouth and nose and from internal organs, and rapid breaking down of ulcerated, injured, or scarred skin.

This disease has occurred from time to time on land in epidemics, differing in extent and severity in different instances, but invariably produced under analogous conditions. The disease seems to have preserved the same type, and the records of recent outbreaks shew that it is capable now of presenting characters equal in virulence and intensity to those recorded in past ages. The history of land epidemics proves clearly that it is very seldom met with save in times of war and famine, or in circumstances of neglect; and that it should always be dreaded in besieged towns, in armies in the field, after a widespread failure of crops, and in badly-provisioned and overcrowded public institutions. These conditions being present, scurvy will not spare the members of the most advanced and civilised communities. Paris suffered severely during the last siege, and both the French and English armies were much stricken in the Crimean War. Of about 110 records of epidemics of scurvy in the course of the last century, collected by Hirsch, 11 occurred in Great Britain.

It is chiefly from its former prevalence at sea that scurvy has excited the most interest. To the recorded experience of naval medical officers the profession is indebted for most of its knowledge of the nature of the disease, and, from their successful efforts to banish this grievous scourge from the service, it has learnt not only how to treat, but also how to prevent it. The oft-quoted passages from the history of Lord Anson's expedition in 1740 give but a partial idea of the ravages caused by scurvy in the Royal Navy in the course of that century. According to Lind, it killed more men than did the hostile French and Spanish armies; and in 1795 the safety of Lord Howe's fleet was seriously endangered by an outbreak of this disease. From this date, when, at the recommendation of Sir Gilbert Blane, lime-juice was introduced into the Navy, scurvy has gradually decreased; and during the past sixty years, except in some few outbreaks arising in exceptional circumstances, it has become so rare as to be practically abolished as an important disease (Bryson). A like

improvement, though long retarded, has also been effected in merchant ships. In 1864 Robert Barnes in an official report pointed out that during the twelve years following 1851 there had been admitted into the *Dreadnought* hospital ship, off Greenwich, 1058 cases of scurvy. In the course of the next twelve years (1864-75) the number of cases admitted into this institution was reduced to 580. Since the end of 1899, 10 cases only have been recorded in the annual reports of Dr. Herbert Williams to the Port of London Sanitary Committee.

Scurvy may occur in any climate; and neither extreme heat, nor extreme cold, nor excess or absence of humidity, can be regarded as an essential factor in the causation of the disease. Though more frequently observed in northern and cold regions it has at times prevailed severely in India and China, and amongst exploring parties in Australia. It attacks in the same way both white and coloured subjects, and no race is exempt. Its greater prevalence amongst adult males is doubtless due to incidental circumstances, as in extensive epidemics on land neither sex nor age affords immunity or even resistance against attack.

Etiology.—This disease, though almost invariably associated with circumstances of privation, is the result of a defective quality of food, and not merely of a reduced supply. The large majority of those who have had actual experience of scurvy, and have carefully studied the records of its epidemics, are convinced that the defect consists mainly in the want of vegetable matter, which forms part of every ordinary and adequate dietary. Whether, as it is held by some, scorbutic symptoms may in certain circumstances be due to the absence of fresh animal food is still an unsettled question, and so must necessarily remain until more is known of the essential nature of the disease. Notwithstanding the expression of opinion by the medical members of the Arctic Survey Committee, in 1877, that scorbutic disease may be due to an absence of fresh meat, and the able though opposed contentions of more recent writers, it seems difficult, on a review of the evidence that has accumulated since the middle of the eighteenth century, to resist the conclusion, first formulated by Bachstrom, that the primary and, in most instances, only cause of this disease is an absence of vegetable food. The question is one of purely scientific interest, and need not at present be brought to bear on measures of prevention and treatment. Whatever may be the differences of opinion as to the causes of this or that epidemic, there is an almost unanimous agreement, amongst both medical men and ship's officers, that the only sure and effectual means of preventing this disease, and of curing it when it has shewn itself, is the supply of fresh succulent vegetables or fruits, or of a pure vegetable juice. As the introduction of lime-juice into the Royal Navy in 1795 was speedily followed by a practical extinction of scurvy, so in recent years a like result has been attained in the merchant service by securing for seamen a good supply of this antiscorbutic, and by a general adoption of a dietary including an increased proportion of vegetable food.

Further evidence, beyond that collected and considered by Dr.

Buzzard in 1870, in support of the conclusion that scurvy is caused by the absence of vegetable nutriment, may be found in the accurate and carefully prepared records of subsequent outbreaks. The appearance of scurvy in Paris in the winter of 1870-71 was due, as Delpech and Bucquoy shewed, to a failure of vegetable and not of animal food; and in the thorough inquiry into the causes of scurvy in the Arctic Expedition of 1875-76, the outbreak was unanimously attributed by the members of the Admiralty Committee to the absence of lime-juice from the sledge dietaries. The latest official returns of scurvy on board British merchant ships also support the same conclusion.

It is necessary to bear in mind that the manifestations of scurvy, as of other constitutional disorders, especially those of a cachectic character, may be much favoured, though not directly caused, by such conditions as are likely to impair physical vigour, and to disturb the maintenance of good health. Amongst the host of such indirect and remote causes mention may be made of exhaustion by hard work, poor diet, previous disease, faulty hygienic conditions such as bad air and water and overcrowding, deprivation of sunlight, monotonous diet, and an almost exclusive use of salt meat. In instances of scurvy on board ship, debility from previous disease, especially dysentery and malarial fever, the most frequent penalties of tropical service, often plays an important part; and very frequently the first manifestations of a scorbutic taint are excited by extreme cold, or by a sudden transition from warm to cold and rough weather. The latter conditions probably exert in most cases a mixed or indirect influence, as cold and bad weather at sea usually necessitate increased work and exhausting or prolonged muscular exertion.

On the other hand, such conditions as a more or less varied diet, freedom from severe physical labour, a good standard of health and vigour, and fair hygienic surroundings will enable those who have been long deprived of vegetable food to resist and even to escape an attack of scurvy. Although it is not strictly true that this disease is exclusively one of the forecastle, there can be no doubt that even in the most severe outbreaks of scurvy at sea the number of officers affected is relatively very much less than the number of men. The existence of absolute immunity from scurvy under a very long-continued or habitual deprivation of vegetables has yet to be proved. It is not impossible, however, that in individual instances immunity may exist from scurvy as from acute infectious disease and many forms of organic poisoning. This quality of immunity, on which so much stress has been laid by some, does not affect the validity of the generally recognised rule as to the causation of scurvy; for, as was pointed out by the Arctic Commission, "although a deficiency or entire absence of fresh vegetable food is an invariable antecedent of a scorbutic attack, it does not follow that the disease invariably occurs during this deficiency or absence."

Pathogeny.—Inquiries into the general pathology of scurvy have hitherto consisted in attempts to determine on the one hand the changes in the blood and urine of scorbutic patients, and, on the other hand, the

special chemical element of food, the absence of which results in the appearance of scorbutic symptoms. No satisfactory information has yet been attained by the examination of the blood and urine. The statements, as a rule, are very contradictory, the results of one observer being diametrically opposed by those of another.

The next questions to be asked are what elements of nutrition are withheld in the absence of vegetable food, and to which of these, whether singly or in combination, the normal immunity from scurvy is to be attributed. We have been taught by wide experience that the most efficient of so-called antiscorbutics are fresh green vegetables, succulent and acescent fruits, and the juices of the latter, especially of the lemon and lime. Of vegetables in common use the most trustworthy are those represented by the lettuce, cabbage, potato, yam, onion, cress and other cruciferous plants. The most prized and useful fruits are such as are juicy, particularly those belonging to the order of Aurantiaceae. Apples also are good antiscorbutics, and their use has done much to protect American seamen against scurvy. Vegetables retain their antiscorbutic properties when preserved, though to a diminished extent. Probably of all forms of preserved vegetable, sauerkraut is the best. As substitutes for succulent fruits, lime- and lemon-juice appear to be by far the most efficient. Malt liquors, spruce beer, and claret possess antiscorbutic properties, and probably also cider, which has certainly had a good reputation in this respect.

It seems to be quite clear that vegetables do not owe their antiscorbutic properties to their free organic acids. Citric and tartaric acids have been found practically worthless as antiscorbutics; indeed the use of the former as a substitute for lime-juice on board British ships has been legally proscribed. Though these acids are present in large proportions in the most succulent fruits, they exist but in small quantities in many antiscorbutic vegetables; and the potato, so it is said, contains no vegetable acids at all.

In 1848 a scientific hypothesis of the etiology of scurvy was based by the late Sir Alfred Garrod on the following conclusions:—(1) That in all scorbutic diets (salt meat, leguminous vegetables, rice, bread, etc.) potassium exists in much smaller quantities than in those which are capable of maintaining health. (2) That all substances proved to act as antiscorbutics contain a large amount of potassium. This hypothesis has now been generally abandoned, as it was soon found difficult to bring the conclusions on which it is based in accord with certain results of common and repeated experience. Although some of the most reliable antiscorbutics, such as lime-juice and potatoes, certainly contain much potassium, the efficacy of antiscorbutic agents bears no relation, as a rule, to the amount of potassium which each contains. Moreover, some articles of diet, although rich in potassium, possess very slight, if any, antiscorbutic properties. The administration of nitrate of potassium, regarded by Dr. Buzzard as a crucial test, has failed both to prevent and to cure scurvy.

Immermann endeavoured to overcome these difficulties by suggesting that the scorbutic disorder may be due, not to an insufficient supply of potassium to the organism, but to an absence or deficiency of this base in the tissues. An insufficient supply in the food, according to this author, is certainly one way, but not the only possible way, in which this absence of potassium in the tissues can be brought about; such absence or deficiency being attributed to faulty assimilation of food, and the disturbing action of disease and debility on the trophic energy of the cells and their capacity for appropriating potassium from the blood. These explanations, whilst removing some of the objections to Garrod's hypothesis, are opposed by the prompt efficacy of fresh vegetables in the treatment of scurvy, notwithstanding the presence of associated disease and exhaustion.

It has been suggested by Dr. Buzzard that the antiscorbutic element in vegetable food is not potassium alone nor the organic acids alone, but a combination of the two. Thus, scurvy is to be attributed to the absence of organic salts of citric, tartaric, and malic acids; especially of the potassium salts, which are present in the growing leaves of plants and in fruits and their juices, and which in the organism are converted into carbonates.

In 1877 Ralfe endeavoured to extend the suggestions of Dr. Buzzard yet further, and from observations on the results attending abstinence from fresh succulent vegetables and fruits, and from the analyses of urine from scorbutic patients, came to the following conclusions:—"The primary alterations in scurvy seem to depend on a general alteration between the various acids, inorganic as well as organic, and the bases found in the blood, by which (*a*) the neutral salts, such as the chlorides, are either increased relatively at the expense of the alkaline salts, or (*b*) that these alkaline salts are absolutely decreased. This condition produces diminution of the normal alkalinity of the blood; and it is suggested that this diminution produces the same results in scurvy patients as happens in animals when attempts are made to reduce the alkalinity of the body (either by injecting acids into the blood or feeding with acid salts); namely, dissolution of the blood-corpuscles, ecchymoses, and blood-stains on mucous surfaces, and fatty degeneration of the muscles of the heart, the muscles generally, and the secreting cells of the liver and kidney." These statements, though surmises rather than positive conclusions, have, as was anticipated, proved of much value as indications of the lines of subsequent research.

In 1895 Sir Almroth Wright proposed his hypothesis of acid intoxication, which, if fully confirmed, would afford the supporter of the old view in regard to the dietetic origin of scurvy, the simplest, most convincing, and most scientific explanation of the pathology of this disease. A long series of observations based on the results of Walter's experiments on the effect of the ingestion of mineral acids upon rabbits, shewed, in the first place, that man, though able to neutralise acids by means of ammonia, will, if plied with such chemical agents beyond a very definite limit, shew

diminution of the alkalinity and coagulability of his blood and finally succumb to acid intoxication. He broadly classifies the components of the human diet as (1) alkaline food-stuffs which leave upon incineration a distinctly alkaline ash; (2) neutral food-stuffs which leave a neutral or almost neutral ash; and (3) acid food-stuffs which leave a distinctly acid ash. The first of these categories includes green vegetables, tubers and roots, fruit and fruit juices, the blood of all animals, and milk, especially that of the herbivora. The second category is made up of the various sugars and of the vegetable fats and oils; and in the third, that of the acid food-stuffs, may be ranged all cereals and all meats. In ordinary human diet there is a comparatively small preponderance of acids over alkalis, because man is continually neutralising some of the excess of acid ingested in the form of acid food-stuffs by the excess of alkali ingested in the form of alkaline food-stuffs. If this adjustment were forcibly interrupted by the omission of all fresh vegetables and fruits from his dietary, man would lapse into a condition of acid intoxication. As experience shews that scurvy supervenes in man when alkaline food-stuffs are withdrawn, it may be provisionally concluded that this disease is a condition of acid intoxication. This hypothesis not only accounts for most of the points in the clinical history and the therapeutics of scurvy, and for the failure of such supposed remedial agents as citric acid and mineral potash salts, but it also explains some of the perplexing difficulties suggested by recent records of Arctic exploration, by including fresh blood as well as milk among the most efficient anti-scorbutics. There are, however, as has recently been shewn by Holst and by Dr. R. Hutchison (22*a*), some difficulties in the way of a ready and full acceptance of this etiological hypothesis. The former, indeed, has been led by the results of laboratory research to the opinion that scurvy is in no way due to acid intoxication; and the latter points out, together with other cogent objections, that scurvy does not always arise in conditions of hyper-acidity of the blood. From a strictly practical point of view an objection to the "acid intoxication" view is the necessity, if this be favourably accepted, of ignoring the well-attested efficacy of lime-juice as both a curative and a prophylactic agent.

The very old belief that scurvy is caused by qualitative and not by quantitative defects has recently been revived by Torup of Christiania, to whom is attributed the opinion that the disease is a form of poisoning due to damaged and imperfectly preserved meat. Drs. Jackson and Harley in 1900, in support of the statement that salted or tainted meat may produce scurvy even when lime-juice or vegetables are being taken at the same time, give the results of experiments on monkeys fed on boiled rice and maize together with tainted tinned meat. The morbid condition produced by this abnormal diet, though distinctly haemorrhagic in character, failed to conform to the distinctive features of scurvy, as the most marked lesion was an inflammatory or intensely congested state of the alimentary canal, and there was an absence of definite tenderness of the limbs, of swelling of the legs, and of purpura.

It has been recently thought that scurvy is really an infective disease, and not due directly to any defect or anomaly of diet. This opinion, based for the most part on a study of the abundant clinical material afforded by some parts of Russia, has been fully and clearly laid down by Berthenson, who, by personal observation of a wide outbreak in St. Petersburg in 1889, was led to the conclusion that the hypothesis of the infective origin of scurvy accounts for many difficulties that cannot be otherwise explained, and that it conforms more readily than other hypotheses to modern pathological teaching. This conception, which has not hitherto received any accepted bacteriological support, seems to have been suggested by outbreaks in which the scorbutic symptoms were either of very uncertain character, or simply complications of other diseases of decidedly infective origin. Moreover, as Holst points out, there is usually much difficulty in these records of land-scurvy in obtaining information concerning the special nutriments of the previous "sufficient" or "satisfactory" dietary. The infective origin of scurvy has gained able and quite independent support from Dr. Myers Coplans, who from observation of an isolated outbreak amongst African natives at Standerton soon after the end of the Boer War, was led to the conclusions that the condition known as scurvy in adults is not brought about by the absence of any particular kind of food, but is more probably a specific bacterial infection. He clearly proves that a disease presenting scorbutic symptoms may prevail to a considerable extent in one community, whilst another neighbouring community living at the same time under precisely similar conditions of food-supply may be practically free. The scorbutic outbreak described by Dr. Coplans, however, clearly presented some exceptional features, and one of these to which special attention is directed, and on which the author's conclusions in regard to both the etiology and treatment of scurvy seem to be mainly founded, was "the occurrence of inflammation of the gums in all cases without exception." Moreover, it was found that this condition of the gums always preceded the other signs of the disease. Swelling of the gums, the inflammatory nature of which in ordinary and uncomplicated forms of scurvy may be questioned, though more striking than most scorbutic signs, is certainly not a constant scorbutic lesion, and, when present, is not always the initial one. It has been pointed out by Holst that more than half of the 225 cases of land-scurvy recorded by Berthenson did not shew any affection of the gums.

In a recent paper on the etiology of scurvy, based on the results of experiments on animals and on careful pathological examinations, Holst and Frölich of Christiania give important support to the old views of a dietetic origin of the disease and of the efficacy, in regard both to prophylaxis and therapeutics, of fresh vegetables. These observers, though aiming mainly at a bare record of scientific research and dealing cautiously with hypotheses, express the opinion that the data on which Lind and so many other writers have concluded that scurvy is caused by a one-sided diet and especially one in which fresh aliments are scanty

or quite absent, are in every respect convincing. Their investigations shew that a one-sided diet consisting of grains, groats, and bread constantly produces in guinea-pigs a condition which resembles scurvy both in its naked-eye and its microscopical appearances. It was found that this disease did not appear when the animals had been fed on fresh cabbage or boiled fresh potatoes only, and that it was influenced favourably by the nutriments which are known in human pathology as antiscorbutics. Finally, examples are quoted shewing that the same or similar nutriments that produce the disease in guinea-pigs rather frequently, have also produced scurvy in man.

Pathological Anatomy.—Our knowledge of the pathological changes produced by scurvy still remains very imperfect, notwithstanding the researches of Duchek and the careful observations made by French pathologists in 1871. One important point that has been well established by the latter, is the exemption of the blood-vessels from morbid change. The condition of the body after death from scurvy is such as might be expected in a case of cachectic disease marked by a tendency to haemorrhagic effusion. An interesting point, to which attention has often been directed, is that, except in protracted and very severe cases, there is very little wasting of the subcutaneous fat and the muscles. Decomposition sets in rapidly, and the petechiae and ecchymotic patches observed in the skin during life are soon obscured by post-mortem lividity. The subcutaneous tissue, especially in the lower limbs, is suffused by blood-stained fluid, and here and there are collections, varying in extent, of effused blood, some quite black and others of a paler colour, from cherry-red to yellow. In the indurated swellings, such as those so often met with at the back of the thigh and knee, the muscles and tendons will be found embedded in a thick and firm clot, and the muscles within their sheaths studded with haemorrhagic foci, which, like the extra-muscular effusions, are soft and ruddy when recent, and pale, tough, and scar-like when of long standing. Similar deposits, though of much less extent, may be found in connexion with bones, in most instances the tibia, just beneath the periosteum; and also, as Immermann asserts, within the bone, especially in the midst of spongy tissue. Effusions are sometimes found between an epiphysis and the shaft of a long bone in a young subject; and also between the ribs and their cartilages. Many of these effusions do not consist merely of altered blood or sanguineous fluid, but of a fibrinous and plastic material which, after a time, is traversed by minute vessels which may be readily injected. Holst has lately referred to some scanty post-mortem records which shew that in ordinary adult scurvy the long bones present pathological lesions resembling those met with in the same structures in infantile scurvy, both the compact and the spongy tissue being rarefied, and the meshes of the medulla filled with lymphatic cells, red corpuscles, and pigment cells. In most cases of mild and uncomplicated scurvy the viscera present but few morbid appearances. The lungs, except at their lower lobes, are usually collapsed, pale, and anaemic. The cavities of

the heart are sometimes empty; at other times they are distended by dark-coloured blood containing soft and gelatinous clots. The organ itself, as a rule, is small and flabby. In many cases the only marked indications of a scorbutic taint are haemorrhagic spots scattered over the pleura and over the roots of the large vessels of the heart. The changes observed in cases of grave inflammatory lesions which may involve the pulmonary organs in scurvy have been fully described by Buzzard. Of these the most considerable are complete engorgement of the lungs; a diffusion of ecchymotic deposits which compress and obliterate little by little the pulmonary tissue, and often form large fluctuating tumours composed of fluid blood and dead tissue. Many medical men versed in severe scorbutic attacks have made mention of effusions of more or less blood-stained serum into the pleural and pericardial sacs. Such effusions, it seems, take place rapidly, are generally abundant, and always associated with fever and other indications of inflammation. Mention has been made also of similar effusions, which, however, are not so frequent, into the abdominal cavity, together with ecchymotic spots and patches on both the parietal and the visceral peritoneum. The abdominal lesions observed in seamen are usually such as are due to tropical diseases; to dysenteric ulceration or pigmentation of the large intestine; a swollen spleen; and a swollen and an engorged liver. Although transient albuminuria is not of infrequent occurrence in scurvy, no constant morbid change nor any special scorbutic lesions have been observed in the kidney. All pathologists agree as to the rarity of any intracranial lesions in scurvy. It has been pointed out by Dr. Buzzard that, considering the delicate structure of the brain, it is remarkable that scorbutic lesions occur by no means so commonly in this organ as in other and less vital parts of the economy. Here clinical and pathological data are in correspondence, as in even the most severe cases of scurvy the intellect remains clear to the last. In considering the few records in which paresis and analgesia are recorded as scorbutic lesions, it would be well to take into account the possibility of confounding scurvy with beriberi, especially in coloured men.

Symptoms.—Scurvy, as a rule, comes on slowly and insidiously; and the appearance of its external lesions is usually preceded by a preliminary stage of extreme physical weakness and mental apathy. In this stage the nature of the illness is indicated by shortness of breath, fleeting pains in the back and lower limbs, and a peculiar sallowness of the skin. As the morbid condition is displayed and the characteristic signs of scurvy manifest themselves, the following symptoms appear:—The patient is listless and weary; the skin is dry and rough, and marked by small purple spots (petechiae), which are most abundant on the thighs and legs and, in many instances, are met with on the lower limbs exclusively. In addition to these spots there are livid patches of varying size and shape, which resemble bruises. Here and there, most frequently in the soft parts of the ham and calf, and behind the ankle, firm subcutaneous swellings may be felt which are widely diffused,

not well defined at their margins, and very tender. The eyelids are slightly swollen, and the conjunctivae often marked by bright red patches of ecchymosis. In some cases the eye is covered by the swollen and purple lids, and the conjunctiva presents the appearance described by Dr. Buzzard as "tumid and of a brilliant red colour throughout." The lips are pale and anaemic, and the gums of a deep red colour, very soft and vascular, and much swollen. The tongue is moist and clean. There is a peculiar and characteristic fetor in the breath. The patient suffers from breathlessness, which is increased by the slightest muscular exertion; he sleeps well and retains a fair appetite. The urine is scanty, and the bowels are usually constipated.

Of these characteristic symptoms of a mild and ordinary scorbutic attack, the earliest and most frequent are those presented on the surface of the skin. In the primary stage, and when all other signs of scurvy are absent, there will be found almost constantly a dirty and pale yellow-stained skin, and a decided dryness of the epidermis with a tendency to desquamation. Duchek has directed attention to the frequent presence of a roughness over the extensor surfaces of the limbs caused by elevation of the follicles. The petechial spots, each of which is formed by a small and circumscribed effusion of blood around a hair follicle, are smooth, level with the surface of the skin, and persistent under digital pressure. The centre of each is usually traversed by a hair. These spots are in most cases confined to the lower limbs; but in a severe and prolonged attack they may arise on other parts of the body, with the exception of the face. The patches of ecchymosis which usually appear later than the petechial spots, and are not constant, are likewise met with most frequently in the lower limbs: although within these limits they have no special seats of election, they often occur just over or near a large subcutaneous swelling. Like the patches of ecchymosis observed in the subjects of haemophilia, they are probably due to slight injuries. The tender subcutaneous swellings which occur so frequently in the popliteal space and the muscles of the calf, and which are sometimes met with in the sheath of the rectus abdominis muscle and the armpit, usually succeed the more superficial lesions.

The affection of the gums and the subcutaneous indurated swelling are the two especial lesions of scurvy. The former, though generally regarded as a test symptom, is by no means constant. In most cases it is an early and well-marked symptom; but sometimes, even though all the other lesions may be present in a severe and advanced form, this may be altogether absent, and the gums may remain smooth and regular, though very anaemic, and of a pale blue colour. The swelling and discoloration may come on suddenly and increase rapidly at an early stage of a scorbutic attack, or may advance very slowly whilst all other symptoms are well marked. The intensity of the gum affection, though, as a rule, most marked in very severe and advanced cases of scurvy, often fails to bear any proportion either to that of the general condition or of the other local symptoms. The first indications of the gum affection are usually

redness and swelling of the tongue-shaped extensions of gingival tissue between the teeth. Afterwards the gums along the dental arches, both in front and behind, form soft and pulpy swellings of a deep red colour, which are tender and bleed readily when rubbed. Where any teeth are absent, there is little or no swelling; and in very old or young subjects who are edentulous the morbid alteration of the gums is reduced to a minimum, or may be quite absent. The swelling is most marked about the necks of carious and broken-down teeth; but certainly it is by no means always absent from the gums of those scorbutic patients who retain a perfect set of teeth.

If the disease be allowed to progress and to acquire an intensity which fortunately is now very rarely seen, the patient rapidly becomes weaker and more lethargic. He suffers much from shortness of breath and palpitation, and the heart's action is so weak that any muscular exertion, such as an attempt to sit up in bed, may cause fatal syncope. The muscular pains in the back and legs still persist and render him more or less helpless. There is decided emaciation and wasting of the muscles, whilst the feet and ankles become oedematous, and the face and eyelids bloated. The petechial spots and patches of ecchymosis become more livid, and make their appearance on the trunk and upper extremities. The indurated swellings increase in size and become more painful, the affected limb, usually the leg, being kept in the flexed position. The swollen gums form large, vascular growths which surround and often hide the teeth, and occasionally project from the mouth and distend the cheeks. These growths break down into large and deep ulcers, which may cause wide destruction of the gingival structure, free exposure of bone, and loosening of the teeth. No other portion of the oral mucous membrane participates in these morbid changes.

At this stage there is a general tendency to effusion of blood or sanguineous fluid. Thus a tender subperiosteal swelling—the so-called scorbutic node—may be formed in front of a long bone, most frequently the tibia; the breathing and heart's action may be suddenly disturbed by the pouring out of fluid into the pleural or the pericardial cavity; or, again, all the symptoms of pulmonary gangrene may be caused by the occurrence of haemorrhagic foci in the lung. Scorbutic effusion into a large serous sac or into a large joint is usually of an inflammatory nature, as indicated by pain and rise of temperature. A marked peculiarity of severe scurvy is the readiness of the skin to ulcerate; not only will any existing sore suddenly thus alter its character, but an old scar, a recent wound or scratch, or even a portion of apparently sound and intact integument may become the focus of a rapidly-spreading scorbutic ulcer, the characteristic feature of which is a dry black slough which, when detached, reveals sharply cut edges and a base of large livid granulations from which there is a profuse and continuous discharge of ichorous fluid. The formation of large vesicles distended by blood-stained fluid, which, according to Immermann, may result in ulceration of the skin, probably occurs only in malignant and very advanced forms of scurvy; it is very

rarely, if ever, met with in the milder and ordinary forms of the disease. The tongue still remains moist, except in cases of visceral complication or extensive ulceration of the skin, but it is usually more or less swollen. There is now a tendency to diarrhoea. The stools in simple cases consist mainly of partly digested food and blood-stained fluid, but in a dysenteric patient, or in one who has been treated by strong purgatives, it may be mixed with large and abundant clots.

Notwithstanding the evident gravity of the lesions presented by scorbutic patients, and the profound morbid changes produced in almost every part of the body, this disease, in the form known to modern observers, is not only attended by a remarkably small mortality, but yields at once to medical treatment and even to a suitable change in diet. Of the 816 cases admitted into the Seamen's Hospital since 1864, 15 only were fatal—a death-rate of 1·83 per cent; and of 208 received during the past twenty-two years (1886-1907), only one was fatal. The usual cause of death in uncomplicated forms of sea-scurvy is syncope. In many cases of death, whether during the attack or after the disappearance of most of the special scorbutic symptoms, the fatal result is due either to extreme weakness from pre-existent disease, or to a complication with dysentery, malarial fever, or some other such exhausting malady. In an uncomplicated case of scurvy, even though very severe, a supply of suitable vegetable food, together with rest, good nourishment, and healthy conditions, is speedily followed by the disappearance of most of the symptoms and by rapid restoration to perfect health. The external lesions usually, though not always, disappear in the following order:—first the firm subcutaneous swellings, next the swellings of the gums, and finally the petechiae and the cutaneous ecchymoses.

A knowledge of the clinical phenomena presented in the final stage of an attack of scurvy in its worst form can only be obtained by reference to the writings of the older authors of this subject. According to Lind, it was not easy to conceive a scene of more diversified wretchedness than that beheld in the third and last period of this disease. Then the swollen legs were covered with livid and fungous ulcers; there was a profuse discharge of altered blood in the stools and urine, and also from the lungs, nose, and stomach; there was a tendency to effusions into the chest and abdomen, and towards the close of the attack there was much oppression of breathing and extreme dyspnoea; there was a troublesome cough with expectoration of fetid and blood-stained sputa; the gums were black and gangrenous; the teeth became loose and fell out; the skin was covered by cold and clammy perspiration; there was a constant involuntary discharge of stools; the urine was retained, and the patient, unless carried off by a sudden attack of dyspnoea, gradually sank from asthenia.

Although in many of the scorbutic outbreaks recorded in the eighteenth century scurvy was often confounded with typhus and other infectious diseases, there can be no doubt that the disease itself was then attended by a very high rate of mortality. The ships of the East India Company

in their voyages round the Cape often lost nearly one-half of their crew; and in Lord Anson's voyage round the globe, 380 out of 510 seamen perished from the disease.

In scurvy it is difficult to draw the line between the special symptoms on the one hand and the complications on the other. Formerly many lesions were regarded as specially scorbutic which were certainly due to casual and extrinsic causes; of late the tendency has been to reject even the least variable and most characteristic signs, and to reduce scurvy to a simple cachexia associated with much mental depression and muscular weakness. Thus, the petechiae are attributed to the rubbing of clothes, the swollen gums to the irritation of carious or dirty teeth, the livid patches and subcutaneous swellings to pressure and injury, and the pleural and pericardial effusions to inflammation. There can be no doubt that, from the peculiar circumstances in which it is produced, scurvy must almost always be associated with other morbid conditions due to insufficient as well as to unsuitable food, to overcrowding, to mental depression, and to exposure to cold; as occurred in the siege of Paris, in 1871, from the failure of fuel during an exceptionally severe winter. As Ralfe truly asserted, simple dietetic scurvy is seldom seen, even afloat. In many instances on board ship it is really a secondary and complicated affection in men laid up from injury or some other disease, subjected to the most unfavourable hygienic conditions, and probably unable to obtain lime-juice. In such cases one would expect to find the patient suffering from diarrhoea the result of dysentery; from stomatitis the result of syphilis, or rather of its treatment; from tertiary affections of the bones and joints; and from one or more fungous ulcers of the legs the result of the chronic ulceration of the lower limbs frequent in seamen. It is very doubtful whether scurvy can exert any particular influence on fractured bones. In the form now observed it never causes the absorption of old callus; and in recent fractures, though like other weakening diseases it may retard union, it is rarely, if ever, followed by a permanent pseud-arthrosis. Indeed, notwithstanding the frequent occurrence of fracture on board ship non-union is very rarely met with amongst seamen.

Much attention has been directed to the frequent association of night-blindness with scurvy. This association may occur in epidemics on land, but has been most frequently met with amongst the large crews of war-ships cruising in tropical waters. Many instances have been recorded by English and French naval surgeons in which a large proportion of men suffering from an outbreak of scurvy also suffered from night-blindness. Some of these writers go so far as to regard this disturbance of sight as a symptom of scurvy, whilst others reject the notion of any connexion between the two affections. Mr. Donald Gunn expressed the latest and most rational view, in stating that night-blindness has no more to do with scurvy than with any other exhausting disease, except that instances of the eye affection were first observed in scurvy patients. Night-blindness is a functional disorder depending primarily on exhaustion of

the retina from prolonged exposure to bright light. Any cause that lowers the general vitality will tend to accelerate the incapacity of the retina to respond to less than the strongest stimuli. Scurvy would be the more likely to act in this indirect way as the special conditions which give rise to it are often associated with exposure of the patient to bright light. That the retinal and not the general state is the cause is shewn by the following considerations :—(i.) Perfectly vigorous well-fed men, if exposed to sufficient glare, become night-blind—as in the snow-blindness of Alpine travellers, which is quite independent of the associated conjunctivitis; (ii.) A man, however depressed by scurvy, or any other disease of malnutrition, will not shew night-blindness unless he be also exposed to very bright light. It has been asserted, as the proof of the retinal, or, at any rate, functional origin of the trouble, that if one eye of a nyctalopic patient be bandaged, this eye will recover sufficiently to enable the patient to get about at night, while the other eye remains quite blind.

Blood and Urine in Scurvy.—In scurvy, according to Duchek, the blood in the heart and large vessels is fluid, of a dark-red colour, and contains soft ruddy clots; thus resembling the blood in enteric fever. In anaemic bodies, after long protraction of the disease and extensive haemorrhages, it is lighter in colour, but still coagulable. When taken from a living scorbutic patient it differs but slightly from healthy blood. There is a secondary anaemia. Hayem found in blood taken during life that there was no leucocytosis, and that there was no alteration in the appearance of the red blood-corpuscles. On the other hand, Laboulbène found the number of leucocytes considerably increased,—a condition, however, which he considered of no special importance with regard to scurvy, as it is observed in many other pathological conditions. The colour-index has been found to be low. The statement of Busk, in 1841, that the amount of fibrin in scorbutic blood is increased, though opposed by Andral on the strength of a very doubtful observation of scurvy, and afterwards by Becquerel and Rodier, has been fully confirmed by more recent observers. Chalvet agrees with Busk that the red blood-corpuscles are diminished and the amount of albumin increased. As a result, no doubt, of the impossibility of obtaining sufficient quantities of blood for such purpose, no endeavour has been made to determine the relative quantities of the different inorganic constituents. The assertion of Becquerel and Rodier, that there is an increase of chloride of sodium and other salts in the serum of the blood, has been disproved by the later investigations of German chemists. By haemalkalimetrical research in severe cases of scurvy Sir A. E. Wright found the alkalinity of the blood strikingly reduced. These results, however, have not been confirmed by later examinations, by the same method, of scorbutic blood.

Haematuria seldom occurs in scurvy, even in the severe cases. The urine during the course of the scorbutic attack is scanty, dark-coloured, clouded, and in severe cases from time to time slightly albuminous. As the symptoms pass off, and the patient becomes convalescent, it increases

in quantity and becomes paler. The specific gravity increases during the attack, and decreases after it. In correspondence with these changes Duchek found a decrease of the solid constituents, except phosphoric acid and potash, in the first stage; and subsequently a restored relation between all the solid elements. In a more recent investigation, to which allusion has already been made, Ralfe found in the urine of scurvy patients (i.) an increase of uric acid; (ii.) a diminution of the acidity of the urine; and (iii.) a reduction of the alkaline phosphates.

Sir Almroth Wright has pointed out that in determining the degree of acidity of the urine in cases of scorbutic acid-intoxication, a mere litmus paper test is quite inadequate, as, in such cases, one may expect to find that the quantity of acid passed as neutralised acid is much greater and of much more serious import than the quantity of acid passed in the free form.

The following are the **complications** most frequently observed in scurvy:—(*a*) Inflammatory effusion in the pleural cavities; (*b*) Pneumonia and gangrene of the lungs. These affections were very prevalent amongst scorbutic patients in the Crimea. It would have been interesting to trace their association with ulceration of the gums, as the excellent descriptions of the pulmonary symptoms given by Haspel and Buzzard seem to indicate an infective rather than a catarrhal origin of these lesions. (*c*) Pericarditis with abundance of sanguinolent effusion. (*d*) Diarrhoea usually of the simple irritative form, but in severe land epidemics and amongst seamen, often of haemorrhagic character, in consequence of the presence of dysentery. (*e*) Dropsy: dropsical oedema of the foot and ankle is a very frequent complication; rapid effusion into the whole of the lower limb on one side was occasionally observed during the epidemic at the siege of Paris. Ascites rarely occurs, and when present is probably the result of renal or hepatic disease. Hydrothorax and hydrarthrosis are not infrequently met with.

In scurvy there is not, as is generally supposed, any marked tendency to bleeding from internal organs. Epistaxis occurs more frequently than any other form of haemorrhage; melaena is met with occasionally as a result of dysenteric ulceration or of the action of strong medicine; haematuria and haemoptysis occur very rarely.

Diagnosis.—In ordinary circumstances no difficulty will be met with in the diagnosis of scurvy. Most of the symptoms are very characteristic. In a large majority of instances the scorbutic symptoms are observed in several persons living together who have been subjected alike to the influence of a diet of insufficient quantity and deficient in vegetable food. In some few cases, however, the nature of the disease may be readily overlooked, or cannot be determined. Sporadic scurvy may occur on land in consequence of abstinence from vegetables through extreme poverty, of aversion to such food, or of too much zeal in enjoining or in carrying out medical instructions. In such instances an absence of one or more of the special lesions of scurvy might give rise to uncertainty. The gums may remain quite healthy, the lower limbs be free from swelling,

and only those symptoms be present which scurvy possesses in common with other diseases. The chief points to be taken into consideration in a doubtful case are the nature of the patient's diet, the presence, both before and during the illness, of cachexia and extreme debility, the absence of continued fever, and the effect on the symptoms of the addition of fresh vegetables, lime-juice, and other antiscorbutics to the patient's diet. Important clinical features of scurvy are the multiplicity and wide diffusion of its lesions, not only of the skin and gums, but also of the muscles, bones, and some of the viscera.

There is very probably but one disease attacking several persons at a time, which is likely to be confounded with scurvy. On board ship, particularly with coloured men in the crew, it might be found difficult in case of an outbreak of cachectic disease to distinguish between scurvy and beriberi. The latter interesting malady presents many symptoms resembling those of scurvy, and indeed Morehead was thus led to attribute to beriberi a scorbutic origin, a view which has recently been supported by Tnocht and Holst. It certainly presents in general neither petechial spots nor livid patches; but these are signs of scurvy which, even if sought for, would be difficult to make out in a black subject. In beriberi, however, it should be borne in mind that the oedema usually begins in front of the tibiae, and not in the foot and ankle; and that the gums are not swollen. Very little importance can now be attached to the presence or absence of nervous symptoms, as it has recently been shewn by the above-mentioned authors that neuritis of the limbs, though an essential symptom of tropical beriberi, is comparatively rare in beriberi occurring on ships.

Although there is at first sight a strong resemblance between scurvy and purpura, particularly that variety known abroad as Werlhof's disease, there are well-marked distinctions between the two affections. Purpura is not due to any special defect in diet, nor is it relieved by an increased supply of antiscorbutics. It shews a marked tendency to epistaxis and bleeding from internal organs; it affects chiefly the mucous membrane and the skin, whilst the muscles, bones, and subcutaneous soft parts remain free. There is no swelling of the gums. The ecchymotic spots and patches are more vivid in colour and more generally diffused than those of scurvy.

It would hardly be possible to mistake sporadic scurvy for haemophilia; the latter being a chronic affection of a congenital and hereditary character, met with usually in young subjects, and presenting signs of haemorrhage from time to time, usually after injury. Some cases of acute lymphatic leukaemia present a considerable resemblance to scurvy from the sponginess, ulceration, and necrosis of the gums, and the occurrence of haemorrhages. The diagnosis depends on examination of the blood. With regard to pernicious anaemia, which resembles scurvy in many respects, the distinction should rest upon the chronic course of the former disease, the absence of any special dietetic fault, a marked difference between the waxy pallor of those affected and the sallow hue

of the scorbutic subject, and the examination of the blood (*vide* p. 742). Dr. Hutchison (22) has described a group of cases of malignant hypernephroma with proptosis and secondary growths with ecchymoses about the orbits in children (*vide* art. "Infantile Scurvy," p. 913).

Prognosis.—The prognosis of a case of scurvy is favourable if the attack have not lasted long, if there be no visceral complications, and if the patient can be supplied at once with efficient antiscorbutics and placed under other good hygienic conditions. In cases of prolonged scurvy, death may occur from prostration and general loss of power. Abundant inflammatory effusion into the pericardial or pleural sacs must be regarded as serious; although, as a rule, such effusions disappear with remarkable rapidity under the influence of an improved and antiscorbutic diet. Dysentery is a serious complication; if it do not lead to a fatal result it will certainly retard convalescence. Notwithstanding the low mortality that has attended scurvy in recent years, care should be taken in every case not to give too favourable an opinion; as, even under the most promising conditions, and at any moment in consequence of a moderate muscular effort,—such, for instance, as that of sitting up in bed,—fatal syncope may occur. Persistence of a normal temperature, a tendency in the haemorrhagic spots and patches to fade, an increased flow of urine, and a clean tongue are all to be regarded as favourable signs. On the other hand, scanty and high-coloured urine, an increased tendency to local haemorrhages, an occasional elevation of temperature, diarrhoea, difficulty in breathing, signs of cardiac failure, are all to be regarded as indications of the steady persistence of the scorbutic attack.

Prevention.—If, as has been assumed, scurvy is usually caused by a much diminished supply or a total absence of vegetable food, then the means for the prevention of the disease must consist mainly in correcting this fault, and in ensuring a full and mixed diet. On land this question, which, except in children, very rarely presents itself in times of peace and plenty, becomes one of pressing urgency in war; and then forms one of the greatest difficulties in military hygiene. In long sea-voyages it is always necessary to take the matter into consideration, and to endeavour to make good the enforced deficiency of fresh vegetable food by the supply of preserved vegetables and fruits, and of some antiscorbutic preparation. Of these substitutes for natural nutriment the former, though not the more efficient, are certainly the more convenient and trustworthy. Lime-juice, when taken day after day, becomes distasteful, and often disagrees with those who take it; as it is not an article of food there is no certainty of its being regularly consumed except under such conditions of discipline as exist in the Royal Navy and in large mail steamers: moreover, in spite of all precautions it may deteriorate after long storage on board ship. Notwithstanding the improved means of preserving vegetables, and the undoubted value, as antiscorbutics, of preserved potatoes, cabbages, carrots, and so forth, they are still much inferior in this respect to vegetables and fruits that are quite fresh. For this reason short voyages are an important factor in the prevention of

scurvy. Curnow, alluding to the decrease of scurvy in merchant ships in correspondence with the increase of steam shipping and the decline in the number of sailing vessels, pointed out that more rapid voyages mean more frequent supplies of fresh food, and thus eventually lead to the practical extinction of this disease. The substitution, proposed by Sir Almroth Wright, of essential antiscorbutic elements (Rochelle salt, calcium chloride, lactate of sodium) for raw materials (lime-juice and fresh vegetables), as a *prophylactic measure* seems open to the objection that except in bodies of highly disciplined men the regular and routine administration of anything in the shape of a medicinal agent is likely to be found a very difficult matter.

Whenever the ship touches at a port no opportunity should be neglected of supplying the crew with fruits and fresh vegetables, and in taking an abundance of these on board. A good supply of preserved vegetables and of lime-juice on board ship would not justify any neglect of this precaution.

To the above-mentioned antiscorbutics, which are strictly of vegetable origin, may be added milk, which contains all the elements required for the nourishment of the body, and also certain beverages such as malt liquors and light wines, especially claret, tea, and very probably cider, which was regarded by Lind as the best of all. Alcohol not only fails to act as an antiscorbutic, but, when taken freely, is undoubtedly an active contingent cause of the disease.

It is necessary, also, to take into consideration the means by which, in the absence of efficient antiscorbutics, an outbreak of scurvy may be averted. These should consist in removing, as far as possible, all other conditions that interfere with the maintenance of good health; in an endeavour to supply good and nutritious food, particularly fresh or well-preserved meat; to avoid exposures to extreme heat and cold; to promote moderate but not excessive exercise; to afford suitable clothing, and to maintain good ventilation and other favourable hygienic conditions.

Treatment.—The treatment of scurvy, provided the attack be free from complication, is very simple. The chief indications to observe are the supply of those elements of food which have hitherto been wanting, to restore strength and vigour, and to relieve the more severe local lesions. In most cases all these indications may be fulfilled by strictly dietetic means; the scorbutic taint being removed by the free use of fresh vegetables, and the general weakness overcome by nourishing and readily assimilable food. Under such treatment the more serious symptoms, such as those of pleural and pericardial effusions, will, in most cases, disappear together with those that are less grave and more superficial. In dealing with a scorbutic patient care must be taken to avoid such articles of diet as might intensify any complicating affection, particularly dysentery; and, in the second place, by keeping the patient in the recumbent position, to prevent syncope or sudden death. The local lesions, even the most severe, usually disappear with singular rapidity, and by the end of the second week the patient may be restored to his former state of health.

The diet should consist of a free supply of fresh vegetable (potatoes, green vegetables) with oranges and other succulent fruits, and eggs, fresh milk, strong soups, and beef tea; to these, as the health improves and the digestive organs become stronger, may be added chicken and lean meat. There is no need, as a rule, to give medicine; nor, if a good supply of vegetables be at hand, even lime- or lemon-juice. In complicated cases only will it be found necessary to resort to medicinal treatment. Dysenteric diarrhoea must be met by appropriate remedies; and in a case of extensive pleural or pericardial effusion it may be advisable to remove the fluid by aspiration. The gums, if much swollen and ulcerated, should be touched with solid nitrate of silver or sulphate of copper; or be brushed over with a solution of one part of chromic acid in five parts of water. If there be any scorbutic ulceration, the swollen and sloughing sore should be douched three or four times a day with cold sterilised water, or salt and water, and be dressed in the intervals with some iron lotion, or boracic ointment. The petechiae will disappear rapidly and need no local treatment. The indurations, if they remain tender and shew but little tendency to diminish, should be treated by gentle massage and the compression of a flannel bandage.

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INFANTILE SCURVY

Syn.—*Scurvy Rickets.*

By W. B. Cheadle, M.D., F.R.C.P., and F. J. Poynton, M.D., F.R.C.P.

Definition.—The scurvy of childhood, like that met with in adults, is a morbid condition of blood and tissues due to defect of diet. It is characterised by great and progressive anaemia, tendency to syncope, cachectic earthy complexion, marked muscular debility, mental apathy and depression, sponginess of gums, and haemorrhages into various structures, notably under the skin and periosteum and into the muscles, especially of the lower limbs.

The disease has a definite dependence upon the privation of fresh food: in the case of adults usually of fresh meat and fresh vegetables; in the case of infants of fresh milk or other fresh food which supplies the same antiscorbutic property; in both it is immediately relieved and rapidly cured by the administration of the fresh elements which have been wanting.

History.—The existence of scurvy in young children, in sporadic form, apart from its occurrence in common with adults under the special conditions of epidemics, has only been recognised within a comparatively recent period, although Glisson in 1651 gave a description of the condition as a complication of rickets in his treatise on that disease. It appears from the researches of Sir Thomas Barlow that isolated cases of similar character had been observed and recorded in Germany from the year 1859 to 1873, by Möller, Bohn, Hirschsprung, and Senator, as examples of acute rickets. The first suggestion of their real nature seems to have been made by Ingelev, a Swedish physician, in recording a case which came under his care in 1873. The first case observed in this country was recorded in the *Pathological Transactions* by Sir T. Smith, in 1876, under the provisional title of Haemorrhagic Periostitis, but the condition was not recognised as scorbutic. In 1878, in a clinical lecture on three cases in young children, published in the *Lancet*, one of us (W. B. C.) identified the affection as true scurvy, and traced it to the want of antiscorbutic element in the food, and reported similar cases again in 1879 and 1882. In 1880 Dr. Dickinson noted cases of

haematuria in children which he recognised as scorbutic, and described in his work on *Renal and Urinary Disease.* Other cases, distinguished by swelling of the lower limbs, attracted the attention of Dr. Gee, in 1881, who described them under the designation of Osteal and Periosteal Cachexia. In 1883 Mr. Herbert Page recorded a case of subperiosteal haemorrhage which he judged to be scorbutic. The credit of completing the investigation of the disease and adding the final proof of its nature belongs to Sir Thomas Barlow, who in the same year published an account of 31 cases, with an exhaustive description of the morbid changes found on post-mortem examination, and shewed that the lesions found were identical with those met with in the so-called sea or true scurvy of adults. Since that time these conclusions have been fully confirmed by later observers, and a great number of cases have been recorded. In 1901 the collective investigations of the American Pediatric Society reported upon 356 cases, which were summarised by Griffith, who added 18 more from his personal observations; and one of us (W. B. C.) had up till October 1908 met with 90 cases.

Morbid Anatomy.—For an accurate knowledge of the morbid changes which are associated with the signs and symptoms described, we are chiefly indebted to the careful investigations of Sir T. Barlow, who, in a paper published in the *Medico-Chirurgical Transactions* for 1883, has given an exhaustive account of the appearances met with after death, and has shewn conclusively that in this respect also the conditions observed are identical with those found in the true epidemic or sea scurvy of adults. These conditions have been further examined and confirmed by other observers in this country and abroad, and again by Sir T. Barlow himself, who has set forth the results in the Bradshaw Lecture for 1894. The details of morbid changes given below are largely drawn from this source.

The principal lesions found after death are due to increased vascularity and extravasations of blood into various tissues. The most extensive and important of these are found in connexion with the periosteum, the bones, and the muscles. These changes are most common and extreme in the lower limbs; but they are met with also, although less frequently and in minor degree, in connexion with the bones of the upper extremities, and of the skull. The periosteum of the long bones of the leg and thigh is highly vascular, and blood is effused more or less extensively round the shaft beneath it, detaching it from the bone and forming a thick sheath of blood-clot between periosteum and shaft; the tibia and femur are usually most affected in this way (Fig. 2, Plate IV.). The extravasations correspond with and account for the exquisitely tender and sensitive swellings observed during life. In some cases similar haemorrhages occur under the periosteum of the humerus, of the scapula, of the ribs, and of the cranial bones, corresponding to the swellings described there. One of the most characteristic of these, when it occurs, is the extravasation into the loose tissue which connects the roof of the orbit with its periosteum, and accounts for the curious proptosis which

has been described in some cases, the eyeball being thus pushed downwards and forwards. Haemorrhage is also found sometimes in the loose tissue of the upper and lower eyelids, causing the black eye of which mention will be made. A thin layer of newly-formed osseous material is occasionally found beneath the upraised periosteum, forming a bony sheath round the shaft of the long bones, or a similar formation of delicate bony film under the periosteum of the flat bones, such as the scapula. Haemorrhages also take place, in some cases, into the medullary cavity of the long bones of the limbs and of the ribs, forming masses of blood-clot there; the medulla itself being soft and reddened. When haemorrhage into the central canal of the long bones occurs, the bone suffers also; the compact tissue of its wall becomes absorbed and rarefied, and is reduced to a thin shell. A similar condition is found in the ribs.

Another characteristic feature of the morbid changes in the bones in scurvy is the occurrence of fractures. These take place especially in the rarefied imperfectly ossified portion of the long bones connecting the shafts with the epiphyses, and sometimes a little above this; the two extremities of the femur and the upper end of the tibia are the most frequently affected in this way.; occasionally the upper end of the humerus shews a similar fracture. The ribs again are occasionally broken away from the costal cartilages. The fractures are due in part to the weakening of the shaft by the detachment of the periosteum by the haemorrhage into the medullary canal, and by the extensive absorption of the trabecular structure.

German pathologists, Schmorl and Looser in particular, have laid stress upon the microscopical changes in the structure of the bones, which they regard as pathognomonic of the disease. These changes affect the bone-marrow and the bone formation. In the marrow the place of the lymphoid cells is taken by a reticular tissue containing spindle-cells and a few osteoblasts or marrow cells, and the vascular supply is usually diminished, although there may be haemorrhages. These conditions are most definite at the ends of the long bones in the region of the zones of endochondral ossification. The muscular swellings (Fig. 2, Plate IV.) are due to deep-seated extravasations, especially in the muscles of the lower limbs, which are also sodden by serous effusion, wasted, flabby, and pale. In rare instances haemorrhages have been met with in some of the joints, and under the dura mater of the skull; and the purpuric blotches and bruises which are liable to follow handling are also, of course, haemorrhagic in nature. Similarly, extravasations have been observed in the pleurae, the lungs, spleen, intestines, kidneys, and mesenteric glands. In one fatal case, in addition to the spongy, bleeding gums, there were extensive haemorrhages into the lung, and smaller extravasations and ecchymoses into the intestinal mucous membrane and into the lymphatic glands, the bones and muscles being free. Similar cases have been observed by others.

In the mouth the gums are seen to be spongy, swollen, and sodden

with serum, and perhaps clotted with blood. The teeth, if present, may be loose and on the point of falling out.

The viscera do not shew any morbid changes beyond those caused by the haemorrhages which have been detailed, and the well-marked anaemia. The muscles likewise are anaemic, soft, and wasted, whilst those of the limbs most affected usually shew the local haemorrhages so often alluded to. The blood in most instances shews a diminution in the haemoglobin value, which is out of proportion to the decrease in the number of red blood-corpuscles. In some cases in which there has been much haemorrhage there may be in addition the characters of a secondary anaemia. Dr. R. Hutchison failed to discover any alteration in the coagulability of the blood. In the majority of cases, but not in all, the bone-changes of rickets are found in addition to those of scurvy.

It will be seen that, in like manner with the symptoms observed during life, the morbid changes discovered after death in infantile scurvy, namely, the various haemorrhages and their seat, the rarefaction of bones, the fractures, the formation of bony plates under the periosteum, differ in no respect from the similar changes found in the epidemic scurvy of adults.

Etiology and General Pathology.—The general pathology of infantile scurvy, occurring sporadically, is, in its symptoms and morbid anatomy, in all essential points the same as that of the scurvy of adults. The original view of the earlier observers in Germany that this affection is an acute form of rickets has proved erroneous, and is generally abandoned. It was based upon an imperfect acquaintance with the morbid anatomy of the disease, as well as of the exact dietetic conditions under which it arises. Although, as is stated on pp. 906, 907, a certain degree of rickets is usually present, this is not a constant and invariable accompaniment; there is no relative correspondence or proportion between the degree of rickets and the degree of scurvy, nor indeed between it and the supervention of scurvy at all. In severe and advanced cases of rickets in which the bone-changes are extreme and there is marked cachexia, with head-sweats, laryngismus, and all the signs of severe and progressive disease, the gums are not spongy, there are no subperiosteal haemorrhages, no muscular or subcutaneous extravasations, no haematuria, no haemorrhages elsewhere. Rickets is not in itself haemorrhagic in any degree, so that the scorbutic features are not a mere manifestation of severe or acute rickets. Moreover, signs of rachitic implications may be altogether absent, as in two cases under our observation, and in a similar instance recorded by Northrup, in which no rickety change of any kind could be detected on post-mortem examination.

It had been thought possible that the condition might be one of purpura haemorrhagica, or haemophilia concurring with rickets. The lesions found after death and the course of the disease, however, are widely different, and no family history of haemophilia can be traced. Moreover, as has been shewn above, the underlying basis of rickets is not always present. Again, the disease is not simply the purpuric

state which is liable to supervene in the late stages of wasting disease, for the subjects of it are not merely not marasmic but in some instances fat and full-tissued; nor is it the haemorrhagic stage of leukaemia, for there is no enlargement of lymphatic glands or spleen; nor is it a phase of congenital syphilis, the signs and history of which have been wanting in all the cases seen by ourselves, although some instances have been recorded in which this condition was concurrent. The evidence of the real nature of the disease is completed by the effect of full antiscorbutic treatment, and this, added to that drawn from the dietaries of the children affected, and the pathological changes found after death, is conclusive. There is nothing in the whole range of medicine, not even excepting the effect of thyroid extract in myxoedema, more striking and remarkable than the immediate and rapid recovery which follows the administration of fresh vegetable material and other fresh elements of food in these cases of infantile scurvy. Simple rickets is no doubt influenced by dietetic treatment, but it is not especially influenced by antiscorbutics; moreover, the effect of diet is gradual and follows slowly, in marked contrast to the instant and immediate amelioration which follows in the case of scurvy. Lastly, diet is powerless to arrest the haemorrhages of purpura and haemophilia, or those of leukaemia.

Sporadic infantile scurvy, then, like the epidemic affection, the so-called true or sea scurvy, consists essentially in an altered and depraved condition of blood, which gives rise to an enfeebled and fragile state of the capillaries, so that serum readily transudes and the vascular wall easily ruptures. Hence follow the serous infiltrations, fibrinous exudations, and haemorrhages which have been described. The exact nature of this defect in the blood which is the immediate cause of the softness, permeability, and fragility of the capillary walls, has not been ascertained with certainty. It would appear, however, from the researches of Busk, Garrod, Ralfe, and others, that the alkalinity of the blood is diminished; probably because neutral salts such as the chlorides are increased at the expense of the alkaline salts, or else that the latter are absolutely and not only relatively diminished. Sir A. E. Wright maintains that in adult scurvy the exclusion of green vegetables and fruits produces a condition of acidosis owing to the predominance in such a diet of the mineral acids over the bases, and points out that experiments on animals have demonstrated that feeding with acid salts or injecting acid into the blood produces ecchymoses, blood destruction, and fatty changes. He has found also a definite reduction in the alkalinity of the blood in human scurvy. In our experience, however, severe infantile scurvy may occur without any such alteration.

Whatever the exact changes may be, and at the present time we are not prepared to accept that the condition of the blood is entirely explained by an alteration in its reaction, there has been much discussion as to their precise causation. Three very different explanations have been put forward, to the effect that infantile scurvy is a specific infection, that it is a result of food poisoning, and lastly the view to which we adhere, and in favour

of which we believe the evidence to be overwhelming, that it is the result of a lack of fresh food, and in particular of fresh vegetable food. The evidence in favour of the hypotheses of infection and food poisoning have been already given in the article on "Scurvy" (pp. 884, 885), to which the reader is referred. It does not, however, appear to us that the experimental evidence in their favour is nearly so convincing as that in support of the antiscorbutic contention, and clinical evidence is not in accord with such an explanation.

The third hypothesis, namely, that this disease is the result of a deprivation of the fresh element in food, has recently gained great support from the experimental investigations of Holst and Frölich with a "one-sided" diet. The first series of experiments consisted in feeding sixty-five guinea-pigs exclusively upon unpeeled grain, groats, or bread, with the result that they all died in about thirty days. Necropsies shewed haemorrhages in the muscles, and in the periosteal tissues near the epiphyseal lines of the long bones and at the costo-chondral junctions. There were also subcutaneous haemorrhages, and occasionally petechiae, and bleeding from the stomach, kidneys, and lungs. In 18 per cent the teeth were loose and the gums swollen and hyperaemic. Fragility of the bones resulted, and changes in the bone-marrow were found identical with those described by German pathologists in infantile scurvy. In a second series of experiments guinea-pigs were fed on a diet of fresh cabbage or fresh boiled potatoes only. These animals died of starvation, and the post-mortem changes were different in nature. The teeth were tight in their sockets and the bone-marrow was in the condition found in pure starvation. When, however, dried potatoes were substituted for the fresh many of the signs of scurvy were discovered. In another series of experiments fresh lemon-juice was added to the "one-sided" diet, and when the animals died from inanition the lemon-juice was found to have prevented the scurvy changes. Lastly, if the fresh foods were strongly heated and given in the diet the animals died from scurvy. At the annual meeting of the British Medical Association at Sheffield in August 1908, the same investigators pointed out that the addition of liberal quantities of calcium carbonate and sodium citrate to the water of cereal-fed guinea-pigs did not, in spite of their acid-neutralising properties, prevent the death of these animals from scurvy. They express their belief that the cause of this disease lies in the lack of unidentified nutrient constituents in the food, which are of an easily decomposable nature. These are present in antiscorbutic foods, but are lacking in cereals, such as flour and grain, which are dried. They lay stress upon the probability of the existence of several such bodies, because they found that in some instances, for example cabbage juice, the antiscorbutic property was lost by keeping, whilst, on the other hand, the same property in lime-juice was not destroyed by keeping. These substances, they further suggest, are of the nature of enzymes, because even in small quantities their action is considerable. Apart from the valuable evidence furnished by these experiments, clinical observation has proved

almost conclusively that the source of the defects in the blood in scurvy are the results of lack of fresh food.

Whatsoever the exact nature of the antiscorbutic element, it is clearly supplied by this kind of food, and the lack of it sets up the disease. The scorbutic state arises under conditions of life which involve such privation; as on long voyages, expeditions, shipwrecks, the campaigns of armies, sieges, or famines: and it is intensified and fostered by conditions of bad hygiene, by hardship, exposure, foul air, want of light, and probably also by the prolonged use of salt provisions.

In the case of children the cause has been traced with equal certainty to this deficiency of the fresh element in food. The natural ordinary food of infants is milk alone. Instances of children becoming scorbutic when at the breast are almost limited to epidemic scurvy, and no case of the kind has ever come within our own cognisance, although some have been recorded. With the exception of one or two doubtful cases, of which the details of breast-feeding and diet are imperfectly given, the only instances of scurvy arising in sucklings are those when the nursing mother has been suffering from scurvy at the time, or as in a case reported by Mr. Kellock in ill-health and insufficiently nourished. Similarly no case has come under our observation in which scurvy supervened on an ordinary diet of fresh cows' milk unaltered by peptonisation, or by the prolonged heating of a sterilising process.

Fresh milk must necessarily contain the antiscorbutic element, whatever the exact nature of this element may be; for milk is the source from which it is supplied to the infant organism. A careful examination of the conditions of diet in a large number of cases confirms this inference, and establishes the prime point that the children who become affected with scurvy have been brought up upon a diet deficient in fresh milk. In a series of 37 cases under our immediate observation, in which the details of feeding could be ascertained with exactness, it was found that in the great majority—namely, in 27—no fresh milk at all had been given for a long time before the attack. In the majority of these none had been given at any time; and in the rest only at the commencement of hand-feeding, having been quickly and finally abandoned because it did not agree. In the 10 remaining cases a very small quantity of fresh milk had been given; in 4 of these, however, for a few weeks only, the children having been previously brought up entirely on dried or patent foods. In 2 cases only out of the whole number of 37 had the defect of diet been in any degree compensated by the addition of fresh elements in the form of a small quantity of raw meat juice. In a few cases the food was entirely limited to some dried farinaceous preparation made with water only. In the greater number of instances, however, the scorbutic condition arose upon an exclusive diet of one or other of the proprietary preserved foods, consisting of malted flour mixed with dried animal matter, and prepared by the simple addition of water, without fresh element in any form.

Next to these in frequency come the cases where the diet has been

restricted for a considerable period to one of the predigested foods, more particularly the pancreatised farinaceous foods, in which the milk added is pancreatised in the process of preparation; or upon a prolonged diet of peptonised milk, especially peptonised condensed milk. Simple condensed milk is responsible for a certain number of cases. In a larger number still, however, the disease had arisen after the continued use of the commercial preparation of so-called "humanised" milk—that is, milk deprived of a portion of its casein and sterilised by heat or other methods to make it keep.

It is clear that the process of peptonisation or pancreatisation of milk greatly impairs its antiscorbutic property; and this is also the unmistakable result of prolonged heating at high temperatures, as in the process of preparing condensed or desiccated milk. Although no cases of scurvy arising upon a diet of simple sterilised milk have actually come under our notice, it is highly probable that its antiscorbutic virtue is lessened by the process; and leading physicians both in Germany and America, where it is more largely used than in this country, deprecate on this ground permanent feeding on milk sterilised in this way. The mere raising of milk to the boiling-point for a few moments appears to have no serious deteriorating influence, although it is probable that its antiscorbutic power is lessened in some small degree by this minor process.

The antiscorbutic power even of fresh untreated milk is comparatively feeble, far less than that of fresh vegetables; and it probably varies to some extent according as the animal from which it is drawn is fed on dry food, or grass or roots. The imperfect power of milk in this respect was long ago noted by Dr. Parkes, who investigated the point; his conclusion was generally that in the case of adults one pint to one pint and a half was not always sufficient to prevent scurvy in the absence of fresh vegetable food.

The relatively slight antiscorbutic virtue of milk is further exemplified by its slow and imperfect curative power when used as an antiscorbutic agent in the treatment of scurvy. To be effective it must be given in large quantity. This fact seems to explain the occasional occurrence of the disease in children who have milk in small amount, and the deleterious effect of any impairment of its properties by peptonisation or overheating. It is important to realise that scurvy may sometimes result when an insufficient quantity of milk is given, even if this milk be unboiled, and no patent foods be used. This was well illustrated by a recent case under our observation, in which a child aged ten months was taking 16 parts of unboiled milk, and 18 parts of boiled water and lime-water tea with 3 ounces of cream, and 8 ounces of chicken or veal broth each day. In this case the feeble antiscorbutic power of the milk did not apparently counteract the lack of nutriment combined with the absence of fresh vegetables, fruit juice, and raw meat juice. In addition to the cases which occur in infancy, instances are recorded in older children which throw additional light on the etiology. In five cases of typical scurvy in children after infancy, observed by Sir T. Barlow,

the cause was traced to a curious morbid antipathy to vegetables and to meat.

In accordance with the fact that the majority of cases of scurvy occur in children fed upon patent foods and peptonised and other forms of prepared milk, comes out another curious fact; namely, that the disease is met with chiefly amongst the children of the better classes. Although the children of the poor are by no means exempt, the disease is much less common amongst them than amongst the children of the well-to-do.

Of the 90 cases under immediate observation by one of us (W. B. C.) 84 occurred in private patients, and only six in hospital patients; and the experience of others is in accord with this statement. The unequal incidence is partly explained by the consideration that the artificial foods which are without antiscorbutic properties are chiefly used by the well-to-do. They are too expensive for the poor. The poor, however, use largely condensed milk and farinaceous materials, such as cornflour and other farinaceous preparations; the first is feeble in antiscorbutic power, the latter destitute of it altogether. The reason why scurvy does not follow more frequently on diet of this kind is to be sought in the fact that the children of the poor begin to share the food of their parents at an earlier age than the children of the rich; thus they get a more mixed diet, of which potatoes, one of the most powerful of all antiscorbutics, usually form a chief part. The disease would appear to be growing more prevalent, in response, no doubt, to the more extended use of the dried and peptonised food preparations which now prevails. The experience of the American physicians is to a like effect. It is interesting to observe, in respect of the relation of scurvy to rickets, that this prevalence of scurvy amongst the rich, as compared with the poor, is the exact converse of the position of rickets in this respect; for rickets is most prevalent and most severe amongst the poor. The children of the poor grow rickety, the children of the rich scorbutic. The coexistence of rickets in the majority of cases of infantile scurvy is due to the fact that most of the foods—as notably the farinaceous and dried milk foods—are rickets-producing foods also, deficient in fat and protein and phosphates of animal origin, as well as wanting in the fresh antiscorbutic element. It is possible also that the physiological activity of periosteal bone growth in infancy, and its vascularity, may be another factor in the meeting of scurvy and rickets.

Symptoms.—The occurrence of infantile scurvy is almost limited to the period between 6 and 18 months. In rare instances, under special conditions, it may arise earlier or later; but as a rule it appears within the period stated, and most often towards the middle or end of the first year. The onset of infantile scurvy has been regarded as sudden, because the most characteristic symptoms may be manifested somewhat rapidly. There is, however, an antecedent period of pallor, anaemia, and debility; and, although the child may be sufficiently fat, it is soft, and its muscles flabby and feeble; this muscular feebleness is a significant and marked feature. In the majority of instances there is some evidence

of rickets, often limited to slight enlargement of the epiphyses and beading of ribs; in others there is in addition projecting forehead, thickening or rarefaction of skull bones (craniotabes), large fontanelle, delayed dentition, head-sweats, and attacks of laryngismus. But the degree of rickets is rarely extreme, and in some cases the distinctive signs are entirely absent. The first symptom usually noticed is that the child is curiously fretful and uneasy, and that it cries incessantly and violently when being washed or dressed or handled, although tolerably quiet and contented when left at rest and undisturbed by movement or pressure. The legs especially are tender; the child no longer kicks them about, but keeps them drawn up and still. As the condition advances, the tenderness becomes extreme; the child screams out, not only on the least movement, but on the approach of a hand to touch it; and the lower limbs lie splayed out, and absolutely motionless, as if paralysed. This extreme dread of touch and movement, and this quasi-paralytic stillness of the limbs are together almost diagnostic. On examining the legs, swelling of the periosteum will probably be found along the shaft of one or both tibiae above the ankle; the thigh bones may be affected in the same way, and there may be oedema of the dorsum of the foot. In some instances this periosteal swelling is slight and not apparent at first sight; in others it is palpable and at once attracts observation. With the subperiosteal changes are associated, in severe cases, deep-seated haemorrhages into the muscles themselves, causing puffy swellings and brawny indurations. In certain cases these are so great as to excite the suspicion of abscess, and they have led more than once to surgical exploration, which has, however, revealed nothing but blood-clot. There is no heat or redness of the surface, no sense of fluctuation, and no rise of body temperature: the temperature is normal or subnormal, except in a few instances in which the haemorrhages are large and recent, when it may run up to 100° to 102° F. for a period of a few days.

The upper limbs may be unaffected, but there is often some swelling and tenderness of the forearm above the wrist; and more rarely on the humerus. Occasionally other bones are invaded; similar swellings have been observed on the ribs, on the scapulae, and on the skull. In one instance under our care the chief periosteal swelling was on the malar bone. The joints proper, with rare exceptions, escape, although periosteal changes near the epiphyses cause a fulness just above them, which at first sight appears to be connected with them, and is not infrequently mistaken for that of rheumatoid arthritis. At these joints also, occasionally, crepitus due to separation of the epiphysis from the shaft may be detected; or more rarely fracture of the shaft itself. Among the scanty records of fatal cases in the Hospital for Sick Children, Great Ormond Street, there are observations upon the occurrences of haemorrhages into the joint cavities themselves. In some instances fractures are found close to the juncture of the ribs with the cartilages, giving rise to a curious depression of the sternum and costal cartilages connected with it, as if it had been driven forcibly inwards towards the vertebral column. A

PLATE 111

Infantile Scurvy

Shewing spongy gums, proptosis of right eye, external strabismus due to retro-bulbar haemorrhage, with ecchymosis and oedema of right upper eyelid.

H. D., aet. 9 months. Sole diet for previous six months, condensed milk and malted farinaceous food. Drawn from life, July 26, 1895.

PLATE III.

Bale & Danielsson, Ltd. del. ad. Nat. et Chromolith.

Fig. 1

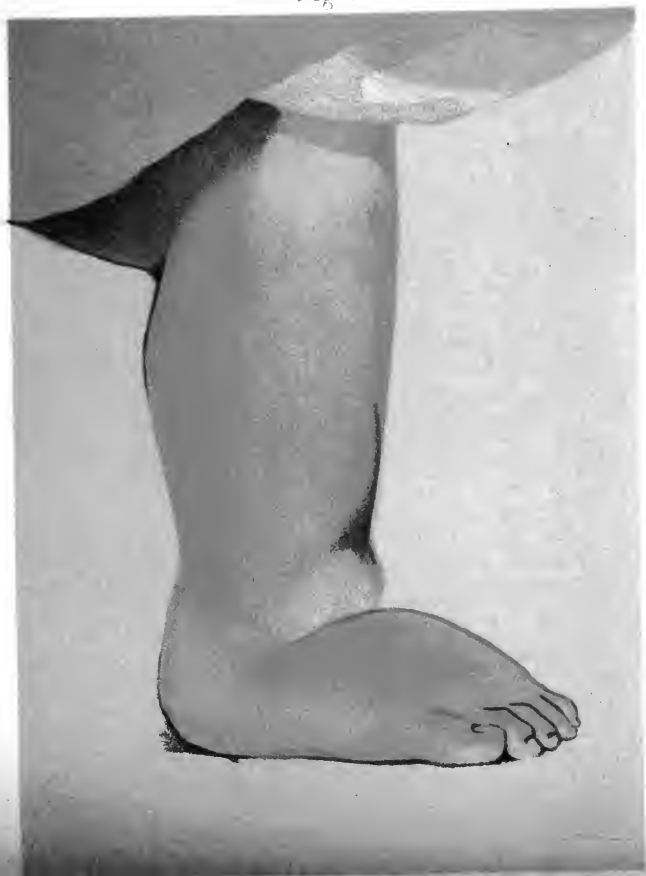

Fig. 2

PLATE IV

Fig. 1

Infantile Scurvy

Shewing swelling on the front aspect of the tibia from subperiosteal haemorrhage, just above the ankle, with oedema of the ankle and foot.

From the same patient as Plate III. Drawn from life, July 26, 1895.

Fig. 2

Post-mortem appearances presented by the femur and surrounding tissues in a fatal case of infantile scurvy, namely, haemorrhages and masses of blood-clot under the periosteum, which is vascular and thickened; haemorrhage and serous infiltration into the deep muscles adjacent; haemorrhage into the central canal of the bone, and fracture of the shaft near the epiphysis.

Sketched from a preparation in the Museum of the Hospital for Sick Children, Great Ormond Street. From a case under the care of Sir. T. Barlow.

similar deformity is sometimes observed in rickets without known scurvy; in such cases there is no fracture of the rib bones, but acute bending only.

As these signs of affections of bones and periosteum are manifested, the anaemia progresses also, and the complexion assumes the sallow earthy hue so characteristic of true scurvy, due probably to diffusion or deposit of altered haemoglobin. With this the debility increases, the patient becomes more limp of body and weak of back, and cardiac power grows more impaired. Other characteristic signs also begin to appear, notably the one which is really pathognomonic; namely, sponginess of the gums.

Spongy gums are swollen, soft, boggy, purple, haemorrhagic. In severe cases, when the teeth have come through, they become so swollen as to protrude between the lips in livid bleeding lobulated masses, sometimes so large as to hide the teeth altogether. These spongy excrescences bleed freely, soon begin to ulcerate, and exhale the horribly putrid odour met with in sea scurvy. The teeth become loose and frequently fall out. In some instances the gums are so tender that a child can only be made to take food with difficulty. The change in the gums is not, however, invariably present. If the incisors have appeared there is almost always some purple discoloration to be seen at their base. If the teeth have not appeared, but are approaching the surface, the same purple colour is found over the gums which cover them, or minute ecchymoses appear there. As Sir T. Barlow has aptly pointed out, the manifestations of this condition of the gums depend not upon the severity of the disease only; it has also a definite relation to the number of the teeth; and that this is strictly analogous to the sea scurvy of adults, in which disease where the teeth have fallen out the portion of gum in relation to them does not become spongy, although in that portion in relation to existing teeth the condition is fully established. To undergo this change the gum must be in functional relation to the teeth. A small haemorrhage may occur at the junction of the hard and soft palate (Still). Another marked and characteristic feature in severe cases of infantile scurvy, as in that of adults, is the supervention of haemorrhages of various kinds into different tissues and organs: in some cases as petechial spots on the skin, occasionally as larger subcutaneous haemorrhages, especially on the trunk and lower extremities; sometimes there is extravasation into the loose areolar tissue below the lower eyelid. In one case under our care the supervention of a well-marked black eye, which suddenly followed a fit of crying, decided a previously doubtful diagnosis. The fragility of the capillaries in these cases is further illustrated by the readiness with which discoloration and bruise marks are produced upon the skin by slight injury; such as the pressure of handling or the blow of a slight fall.

Occasionally a curious phenomenon appears in the shape of sudden proptosis of one eye, with slight discoloration of the upper eyelid and redness of the conjunctiva, due to haemorrhage under the periosteum of

the orbit. Heubner has also directed attention to a blue half-moon discoloration under both eyes, the result of haemorrhages into the subcutaneous tissues. The haemorrhagic tendency of the disease is further marked in some cases by haematuria, which is occasionally the first or the principal sign of the supervention of the scorbutic state, and this haematuria may be associated with nephritis or pyelitis (Still). In addition there may be epistaxis, or haemorrhage from the bowel. Prof. Still records a remarkable case in which a haemorrhage in connexion with the bowel simulated the tumour of an intussusception and gave rise to extreme difficulty in diagnosis; but these occurrences are not common, and the loss of blood is seldom or never very copious. In some of the slighter cases the symptoms of the disease may be limited to one or two signs, the significance of which, when occurring alone, may be overlooked or misinterpreted. In some instances haematuria may be almost the only manifestation in addition to anaemia and muscular debility; in others orbital haemorrhage and proptosis may be the only prominent features. More frequently, perhaps, there is merely slight purple staining over the gums of the erupted or pushing teeth, with some tenderness of the limbs and general anaemia and cachexia.

There are no doubt cases slighter still, in which the only symptoms are pallor, wasting, slight oedema, and tenderness of limbs evidenced by irritability and intolerance of handling, with perhaps some signs of rickets, to which the symptoms are referred. The fact that in many instances these conditions, so closely associated with scurvy, rapidly disappear upon antiscorbutic diet, whilst those more particularly identified with rickets are little affected by it, is highly suggestive of their real nature.

This characteristic group of symptoms, in well-marked examples of infantile scurvy, accurately corresponds, not merely individually but as a composite whole, with the series of phenomena met with in the epidemic form of the disease. The pallid, earthy complexion, the progressive anaemia, the excessive muscular feebleness, the tendency to syncope, the various haemorrhages and their seat, the haematuria and albuminuria, the oedema, the swellings of periosteum and of muscle, the extreme tenderness of limb, the special implication of the lower extremities are the same in both. The fact that the bones suffer somewhat more severely in proportion to other tissues is explained by the great formative activity which pervades these parts in infancy. The symptoms are indeed practically identical with those of the adult with, in most cases, the signs of an underlying rickets, such as beading of the ribs, enlargement of the epiphyses, head-sweats, and laryngismus. In most instances, however, these signs are slight, and in some no indication of rickets can be discovered.

Course of the Disease.—The course of the disease varies according to the degree of its intensity and development, and the conditions under which it arises and under which the patient remains. If the defects of diet in which it has its origin continue unchanged, and the hygienic

surroundings are unfavourable, the patient grows steadily worse, the debility and anaemia increase and become extreme, and the cachexia profound. In this state the child may die suddenly, from haemorrhage into some vital organ, or from syncope, or from more gradual exhaustion; or from some intercurrent affection such as bronchitis or pneumonia, or diarrhoea; or, again, an acute infectious disease may prove rapidly fatal to the enfeebled organism. Occasionally, without special treatment, slow amelioration of the disease takes place after a time; some change of food in the ordinary advance to a wider and more varied dietary, as the child grows older, leads to a gradual improvement in the condition, and the symptoms after some months may disappear. Relapses often occur; and in any case the disease, when uninfluenced by treatment, runs a chronic and protracted course, unless cut short by some fatal accident or complication. If, however, the nature of the affection is recognised, and proper antiscorbutic treatment adopted, improvement is immediate, and recovery so marvellously rapid that the child may be practically well in from two to three weeks. The swelling of the limbs subsides, tenderness and the dread of movement disappear, the child begins to move its limbs again voluntarily and to sit up once more, the haemorrhages cease, and the anaemia and cachexia and asthenia quickly decline. Some wasting of the muscles of the affected limbs remains, and for some time afterwards hard thickening can be felt round the shafts of the affected bones. If fractures have occurred, they are repaired without obvious deformity, except in rare cases, when they take place in the middle of the shaft of a long bone; then much thickening may remain for a time. In the end, however, the recovery is final and complete; although, where accompanying rickets exists, the signs of this condition may long persist. As already observed, however, the rachitic complication in these cases is usually slight, and but rarely severe in degree.

Diagnosis.—The recognition of a case of infantile scurvy is not difficult when the typical signs of periosteal tenderness and swelling, and spongy gums, are present. When the latter sign is wanting, as may be the case in very young subjects in whom the teeth are not yet pushing, and the periosteal affection not pronounced, the condition is apt to be overlooked, or regarded as one of rickets, of rheumatism, or of simple anaemia and debility. Even in severe cases, the tenderness and swelling of the limbs lead not seldom to a mistaken diagnosis of rheumatism, from which, however, scurvy may be distinguished by the facts that the joints are free, and the part affected is the shaft of the bone above it, in addition to the other symptoms of scurvy present. Another common error has its origin in the motionless state of the lower limbs, which the child dreads to move on account of the pain; this inhibition of movement is frequently mistaken for paralysis, so that in many cases infantile scurvy is diagnosed as infantile paralysis. In other instances, again, in which the tenderness and dread of movement attract attention, the condition is regarded as one of tuberculous affection of the hip and knee joint. Syphilitic epiphysitis may also be mistaken, but occurs almost

invariably before the sixth month, and is accompanied by other evidences of the inherited taint. Acute osteomyelitis is distinguished by the high fever and great constitutional disturbance, although in some of the subacute cases care is needed to differentiate these two conditions, and a complete review of the entire history is requisite. In another group of cases, in which haematuria or albuminuria are the symptoms first observed, the affection is regarded as a form of Bright's disease.

Even in cases in which the gums are fungous, swollen, and bleeding, this local symptom has been regarded as the sole ailment, and the case judged to be a severe form of stomatitis. Similarly cases of proptosis due to scorbutic haemorrhage may be regarded as cases of orbital tumour.

Dr. R. Hutchison has drawn particular attention to certain rare cases of suprarenal sarcoma in children with metastases in the skull (30). In these cases, of which Tileston and Wolbach have collected 14, there may be ecchymosis of the eyelids and proptosis, with profound anaemia. The primary tumour in the suprarenal may not be palpable, and thus for a while considerable doubt arises as to the diagnosis. The history of the diet must be carefully investigated, and the failure of antiscorbutic treatment, together with the appearance of metastatic tumours upon the skull, will serve to distinguish the two conditions. Lymphocythaemia, although probably very rare at such an early age, may, as Drs. Forbes and Langmead have shewn, occasionally suggest scurvy by reason of the anaemia and haemorrhages. Examination of the blood at once settles the diagnosis, and suspicion will be aroused by the general enlargement of the superficial lymphatic glands and increase in size of the spleen and possibly kidneys also.

Even if there be no sponginess of gums, the periosteal swelling, the exquisite tenderness of the limbs, the extreme dread of movement, and the earthy pallor and possibly haemorrhages under the skin or elsewhere, added to the diet-history, are sufficiently distinctive of infantile scurvy. If the gums be affected also, the evidence is complete, and the diagnosis may be quickly and finally confirmed by the test of antiscorbutic treatment. All doubtful cases, especially those of rickets in which there is some limb tenderness, should be tested in this way.

E. Fraenkel lays much stress upon the results of skiagraphy, and describes, in the lower extremities particularly, a characteristic shadow in the most recent line of the diaphysis. This shadow is broadest at the centre, and tapers laterally. It is produced by the bony trabeculae, bone debris, and effused blood. This observation was not confirmed by Hamilton, and it is obvious that a remarkably accurate knowledge of the skiagraphy of infants' limbs must be at the disposal of the observer before the sign can be considered pathognomonic.

The prognosis of infantile scurvy is almost uniformly favourable. If the disease is duly treated before extreme symptoms have arisen, recovery is rapid and certain. Before the nature of the disease was generally recognised the rate of mortality ran high. In the first series

of 31 cases collected by Sir T. Barlow 7 proved fatal, or upwards of 22 per cent. Since that time, however, the death-rate has fallen remarkably. It is to be noted that the deaths occur usually in hospital patients of the poorer class, in whom the disease has reached an extreme degree, under unfavourable conditions of life, before they come

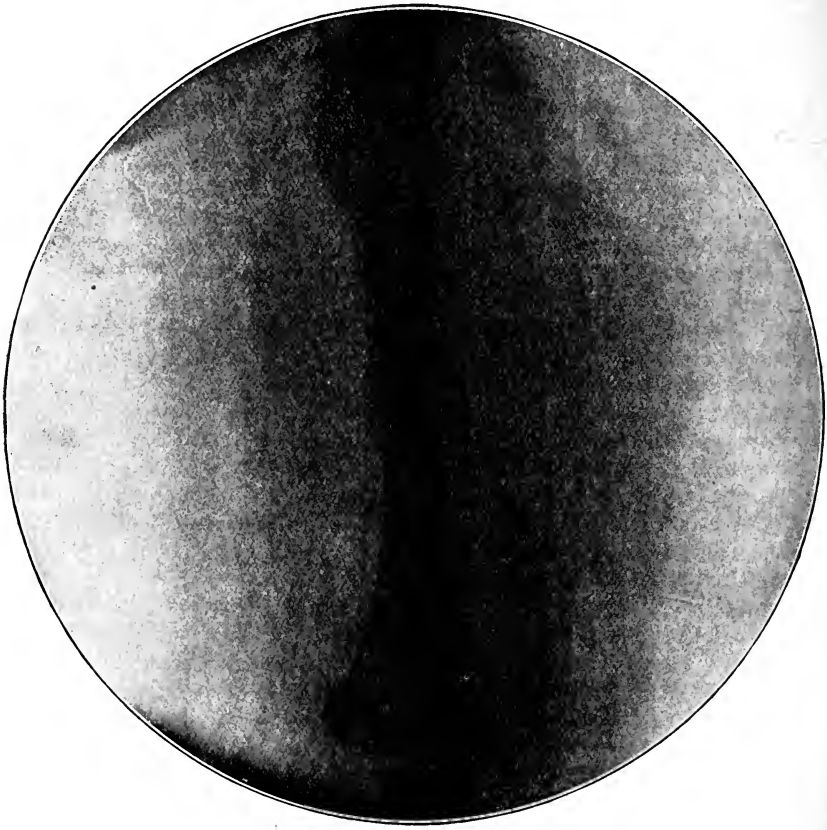

FIG. 38.—Skiagram of the right femur of an infant aged 11 months, suffering from infantile scurvy. The lower end of the bone is surrounded by a dark ovoid shadow occupying almost half the length of the shaft, and extending upwards from the lower epiphysis. This shadow is produced by a subperiosteal haemorrhage which clinically formed a large firm tumour closely resembling a periosteal sarcoma. Fourteen days later antiscorbutic treatment greatly reduced the size of this swelling. The skiagram was kindly taken for us by Dr. G. H. Orton from a patient of Dr. F. G. Bott.

under treatment. In some the difficulty of treatment is greatly enhanced because the curative agent can only be taken sparingly, owing to the extreme prostration of the patient; and death takes place in these circumstances before sufficient time has elapsed for the amelioration of the disease.

Danger to life exists, however, in all cases, both from haemorrhages

and from syncope, until the condition is controlled; and there are exceptional cases in which improvement is curiously slow.

Treatment.—*Prevention.*—Since the disease arises from the persistent use of farinaceous dry foods or prepared foods containing no living or fresh element, or an insufficient amount of it, the obvious means of prevention lies in the avoidance of such foods, and in the use of some aliment of which fresh milk or other fresh material forms at least the chief part. Experience proves further that milk cannot with safety be submitted for any great length of time to predigestion, to prolonged heating at high temperatures, or to the process adopted in preparing preserved "humanised" milk.

If therefore in any case the milk of the mother or of a wet nurse cannot be obtained, and diluted fresh cows' milk cannot be digested, the food in use should be replaced gradually by fresh milk, or some equivalent of fresh living material should be added. If, that is, it should be found absolutely necessary, on account of digestive troubles or other urgent reason, to place a young infant upon peptonised milk, humanised milk, or pancreatised food, or on any patent dried food, this should be regarded as a temporary expedient, and should not be continued for more than a few weeks. The prolonged use of such foods is a fruitful source of impaired nutrition in many ways, and especially of scurvy; its place should be taken by fresh milk by a system of gradual substitution. This can generally be effected by mixing fresh milk with the food used, in small quantity at first, and then slowly increasing it. Should the child be unable to digest a sufficient amount of the fresh milk in the course of a week or two, the lack of fresh elements may be supplied, and disaster averted, by the addition of raw meat juice, or by a small quantity of beef or chicken tea in which potatoes and carrots have been boiled and strained out. Similar precautions should be adopted in the case of older children when from illness or other cause they are placed upon a diet of peptonised or sterilised milk, or predigested food in any form, or upon any dried food to which fresh milk has not been added. In the treatment of this disease, we would emphasise the importance of remembering that the digestion of some of these children is very easily upset, and that a rash change to a diet, though admirable in principle, may introduce even greater dangers in the form of acute vomiting and diarrhoea.

Cure.—The treatment of infantile scurvy consists almost entirely in the administration of fresh foods which possess the antiscorbutic virtue in high degree. The child should, if possible, be placed on fresh milk, which may be raised to the boiling-point, but not sterilised or "humanised." Fresh milk, however, as pointed out previously, possesses only moderate antiscorbutic properties, and is insufficient alone to effect the rapid cure of scurvy; just as it is insufficient to prevent it if given in small quantities.

For effective antiscorbutics we must have recourse to vegetable juices. Fresh green vegetables, more particularly the cruciferae so efficacious in

the scurvy of adults, are not available in the case of young infants of from six to eighteen months old, the period during which the disease usually appears. A most efficient substitute is, however, available in potato, which Baly, in his experience during the epidemics of scurvy at Millbank Penitentiary, proved to possess such remarkable antiscorbutic power. Even young children can usually take potato, properly prepared and administered, without digestive disturbance. It should be well steamed and reduced to light floury powder by rubbing through a fine sieve. This should be well beaten up with boiled milk until it is of the consistence of thin cream, and should be added to the regular food, beginning with a small teaspoonful to each bottle. The quantity may be gradually increased to a dessertspoonful, or even a tablespoonful in the case of children above a year old, if it agrees. Another effective plan, although less rapid than the preceding, is to administer the vegetable juices through the medium of beef tea or chicken tea, in which potatoes and carrots have been boiled and subsequently strained out. A small cup of this may be given once or twice a day.

The fresh element in diet should be further strengthened by the addition of the juice of raw meat, which possesses antiscorbutic power, although, like milk, not in high degree; and similarly it is unequal alone to effect the rapid cure of scurvy, or to prevent it when a small quantity is the sole addition to the otherwise scurvy diet. This comparative feebleness of raw meat juice and milk in antiscorbutic power has sometimes led to erroneous conclusions as to the nature of the disease, when it arises where milk or raw meat juice has formed a small portion of the diet, or has failed quickly to relieve it. Milk and raw meat juice are, in fact, only efficient when given in large quantity, and even then are much less active than vegetable juices. Raw meat juice has, however, a special value in these cases from its haemic virtue. It contains iron in the most assimilable form in its haemoglobin, and is the most powerful of all remedies for the anaemia constantly present and often extreme. The juice should be prepared by macerating the finely-minced pulp of raw beef in an equal quantity of cold water for half an hour, and then expressing all the liquid through fine muslin by twisting it. The straining is necessary to avoid danger of tapeworm by removing possible cysticerci. It should be freshly made at the time of using, for it quickly undergoes decomposition, and, if kept, acquires poisonous properties.

Grape juice, orange juice, lemon juice, baked apples, are useful adjuncts, especially in the case of children above a year old. When potato pulp and raw meat juice are given and well borne, the result is immediate and almost magical. If the gums are spongy and swollen, all sign of this disappears in the course of a few days, the swelling of limbs goes down, tenderness subsides. In the course of a week or ten days the child no longer dreads handling or moving, and in a fortnight or three weeks is practically well—in striking contrast to the slow progress of simple rickets under similar dietetic treatment. In addition to anti-

scorbutic diet, fresh air and sunlight, as in the case of adult scurvy, are useful aids, although diet alone is certainly and rapidly curative. Little local treatment is required beyond wrapping the limbs affected in cotton wool, keeping the child absolutely at rest on a soft pillow, and preventing the movement of the limbs, which causes pain, and therefore wear and tear. The tenderness may be relieved, especially if the limbs are hot and uncomfortable from recent periosteal or muscular extravasation, by the application of warm compresses. As a rule, however, no local applications are required, and such measures as massage or stimulating applications are actively injurious.

Drugs are not required; diet is all-sufficient. Depressing remedies, such as iodide of potassium, often given with the mistaken view of aiding the absorption of the effused material of the subperiosteal swelling, are distinctly harmful; and iodide of iron is little less objectionable. Like all the iodides it is depressant, and if pushed far enough it eventually produces in children a cachectic purpuric condition.

Cod-liver oil and steel wine are useful in the later stages for any underlying rickets which may exist. In the active stage of scurvy they are better omitted, as they are apt to interfere with the ample ingestion of fresh food. In these cases raw meat juice is better than any iron preparation of the Pharmacopoeia, and the cream of fresh milk is more potent than cod-liver oil.

Lactate of sodium has been recently advocated by Sir A. E. Wright in adult scurvy, given in doses of 35-70 grains the day. By this drug he has succeeded in greatly increasing the alkalinity of the blood. One of us has used this drug in infantile scurvy, in 5-grain doses, with good results, but the other precautions in diet have also been insisted upon.

W. B. CHEADLE.
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HAEMOPHILIA

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Definition.—Haemophilia is a disorder depending on a congenital defect in the coagulating power of the blood, and characterised by immoderate spontaneous and traumatic haemorrhages, serous haematomas, and recurrent effusions into the joints.

Incidence.—The disease, as defined above, is restricted to the male sex and is nearly always associated with a family history of bleeding. It is met with in all classes of society and occurs in persons of every kind of physique.

The Symptoms may be most conveniently discussed under the following headings:—

Subcutaneous Haemorrhages and Serous Haematomas.—That a child is

destined to be a "bleeder" is generally first shewn by the occurrence in the subcutaneous tissue of serous haematomas, which appear either as superficial bruises or as deeper diffuse swellings. They may be "spontaneous," or may follow in the train of quite insignificant injuries. The swellings are always tender to the touch, and may, when the effusion has been considerable, be extremely painful. As these serous haematomas are the result not only of an increased transudation of blood fluids through the capillary walls into the tissues, but also of the diapedesis of red blood-corpuscles, a play of colours such as is seen in connexion with ordinary subcutaneous haemorrhages may be seen round them. In those cases in which there has been considerable effusion of all the elements of the blood, a definite blood-clot may form in the tissues. Serous haematomas are not confined to the subcutaneous tissue, but may take place into the sheaths of the muscles, and give rise to very considerable pain. This condition appears to be analogous to the painful intramuscular effusions which were common in "land-" and "sea"-scurvy, and are still seen in infantile scurvy. Like the other active manifestations of the haemorrhagic diathesis, serous haematomas occur pre-eminently in early childhood, and become less frequent as age advances.

Articular Effusions constitute another manifestation of the liability to serous haemorrhages which is characteristic of the bleeder. Effusions into joints occur in practically all cases of haemophilia, generally appearing as soon as active exercise throws a strain upon the joints. These joint-effusions, like the serous haematomas, come on either "spontaneously," or in the train of injuries which in healthy persons would usually be too trifling to attract attention. Judging from the analogy of what occurs in the subcutaneous tissues, the fluid effused into the joints would generally seem to be clear lymph, but sometimes the lymph may contain a large admixture of red blood-corpuscles. As a rule the fluid is only incompletely absorbed, and the joint remains more or less permanently waterlogged with blood-stained lymph. The repeated articular effusions are followed by adhesions and by degenerative changes resembling those in osteo-arthritis (*vide* Vol. III. p. 31). Partial ankylosis often supervenes, and the patient generally becomes more or less seriously crippled. The knees are most generally affected, next in order of frequency come the ankles and elbows. Articular effusions become rarer and rarer as the boy grows up, but they may occur in adult life when the joints are subjected to strain, or when the coagulability of the blood has been seriously reduced by supervening disease. I have, for instance, seen in the case of an adult bleeder both knee-joints spontaneously fill with blood during an attack of malaria.

Spontaneous Haemorrhages from Mucous Membranes. — In addition to these transudations into the tissues the bleeder practically always suffers from immoderate haemorrhages from mucous membranes; of these the commonest is severe epistaxis, and next in frequency haemorrhage from the gums. In other cases blood escapes from the kidney or the bowel. In all these forms of haemorrhage, bleeding may persist as a capillary

oozing until the patient succumbs to loss of blood; but more often—in association with that "haemorrhagic increase of blood-coagulability" to which attention was called by Cohnheim in connexion with bleeding experiments conducted upon animals—the blood-flow ultimately stanches. In the bleeder, however, this may only result after the blood has been oozing away for weeks, at a time when the blood may have become so impoverished in red corpuscles as to leave hardly more than a rusty stain upon the linen.

In connexion with all such haemorrhages continuous headache and racking thirst are prominent symptoms. The cases of bleeding from the nose or mouth are perhaps the most distressing. Here, when after hours or days, the blood commences to clot, coagula collect on the teeth and tongue, and hang down in long strings from the posterior nares, interfering with respiration, and fouling all the food with blood. In addition to blood swallowed with the food, blood here continually trickles into the stomach, and becoming putrid in the intestinal canal, gives rise to a very distressing colic. The clots which adhere to the teeth and obtrude from the nostrils also putrefy, and poison the patient with their stench. It is little wonder that, after going through all this repeatedly, the bleeder should, as he so often does, fall into marasmus and succumb.

Traumatic Haemorrhages.—The bleedings following injuries—and these injuries may be such as would in healthy persons not be of the slightest moment—differ from the spontaneous haemorrhages just described, only in being more serious. The gravest are perhaps those in which a boy cuts his lip or bites his tongue as the result of a fall. Small skin abrasions are seldom of much account: vaccination, for instance, is said to be comparatively free from danger. Deeper cuts, of course, and surgical incisions are perilous. The opening of abscesses, or haematomas, and the major operations of surgery have often been followed by fatal results. Among minor operations the extraction of a tooth is perhaps the most dangerous. It has time and again been followed by death. There is, however, no risk in drawing blood from an ordinary finger-prick. It would seem that the elasticity of the skin here arrests the bleeding. Blood may also, it would seem, be drawn with impunity from a prick in a vein.

Very noticeable in connexion with all these haemorrhages of the bleeder is their nocturnal incidence. Subcutaneous haemorrhages often come on at night during sleep. The same applies in connexion with traumatic haemorrhages. Here it is the rule for the bleeding which supervenes immediately after the infliction of the wound to be comparatively trifling. But it will often break out again as soon as the patient has fallen asleep. In such a case if the boy sleeps on uninterrupted, and no one watches over him, the bed may be soaked with the blood until it drips upon the floor. The perfectly desperate condition that things get into in the houses of the poor when such bleeding as this occurs is more easily imagined than described. I have seen a room look like a shambles; and know a case where a mother, finding her boy bleeding in his sleep,

had to wrap him in the blood-soaked blanket, and to wheel him on a coster's hand-cart, in the middle of the night, bleeding, all the way from a suburb to one of the London hospitals.

Periodic Exacerbation of the Symptoms and the Question whether the Bleedings are preceded by Prodromal Symptoms.—I see no room to doubt that the serous haematomas, and the spontaneous haemorrhages from mucous membranes are only the most conspicuous manifestations of some periodical change in the condition of the blood. I have satisfied myself by repeated blood examinations, and by observation and inquiry from the patient's relatives, that there are in the life of every bleeder recurring periods, during which the coagulability of his blood is reduced far below its mean value, and during which all the symptoms of his disorder are aggravated. The clinical manifestations of such a blood-change, if noticed before the onset of spontaneous haemorrhage, would not improperly be described as "prodromal symptoms." These may be little more than slight puffiness of the face, a feeling of lassitude, and an increased fulness in the joints. Or again the blood-change may induce hysterical irritability, persistent headache, or, as in a case which I had under observation, a quasi-comatose condition. The periodical attacks to which the bleeder boy in question suffered were described by the relatives as "fits." All these nervous symptoms may perhaps be provisionally referred to serous haemorrhages into the nervous system. The headache may be classed with the type of headache described by Dr. G. W. Ross (7), in chlorotic girls who have a diminished blood-coagulability; and the hysterical symptoms and fits may be paralleled with those met with in some aggravated cases of urticaria, in which again there is generally a diminished coagulability of the blood.

Further Points in connexion with the Symptomatology of Haemophilia.—A few other points in connexion with the symptomatology of haemophilia deserve attention either because they are of cardinal importance to the haemophilic patient, or because they may ultimately serve to illuminate the obscure pathology of the disease. The first of these is the very frequent association of early and extensive dental caries with the haemorrhagic diathesis. Seeing the risk attached to the extraction of teeth this disposition to dental caries constitutes a serious calamity. Of less direct practical interest is the frequency with which a depraved appetite, as shewn by the eating of grit and chalk, has been observed in haemophilia; this was specially noted by Dr. Wickham Legg (4), and I have seen notable instances of it. In one case when questioning the mother of a bleeder on the subject I was, for answer, conducted through the front room to the kitchen, the wall of which had been completely cleared of its plaster —and it was very thick plaster—over an area of about three feet by one foot. This had been done by the bleeder boy of three years old, who could not be prevented from picking off and eating the plaster. When in order to prevent this, the boy was shut out into the yard, he set to work upon the mortar between the bricks, which he picked out and ate. His mother saw in this morbid craving something uncanny, but his uncle,

also a bleeder, told me that he had behaved in the same way when a boy. One cannot help suspecting that there may be at work in these cases an imperious craving for calcium. I have very frequently met with chilblains and urticaria in connexion with bleeders; both these disorders occur, as I have pointed out, in direct connexion with diminished blood-coagulability (20-23). Inasmuch as physiological albuminuria is also, as I have shewn in association with Dr. Ross (28), a disorder which occurs in connexion with diminished coagulability of the blood, it would be interesting to see whether it occurs frequently in bleeders; but I have not investigated this point.

Differential Diagnosis.—When the appearance of some one or more of the symptoms enumerated above calls for a decision of the question whether we have to deal with the congenital defect which is properly described as haemophilia, or with some other non-congenital disorder which favours immoderate haemorrhage, the following points, in addition to the history, should be taken into consideration: the subcutaneous haemorrhages of haemophilia may be distinguished from ordinary ecchymosis and purpura by their generally being associated with a certain amount of swelling and by not being of the same deep inky purple as purpuric eruptions. This is in consonance with the idea that we have in haemophilia to deal with haemorrhages *per transudationem et diapedesin* as distinguished from haemorrhages *per rhexin*. The less superficial haematomas may be distinguished from those of infantile scurvy by generally occurring in the subcutaneous tissue, and not specially in connexion with the periosteum, and by the absence of any general tenderness or any implication of the gums. Nor are they, if we may generalise from an observation by Sahli and a similar one by myself, associated with that defect of blood-alkalinity which is in my experience a characteristic feature of scurvy (24-26).

Prognosis.—The outlook for the bleeder would seem to be specially unfavourable when the disorder appears in early infancy. But even in these—the worst cases—the danger to life is not by any means so serious as was once supposed; for we have now, as will be shewn in discussing the treatment of haemophilia, methods for the arrest of haemorrhage which will practically always prove successful. It must also be borne in mind that the risk of fatal haemorrhage diminishes as the bleeder boy grows up, not only because, as he learns caution, injury is carefully avoided, but also because, as it would seem, the coagulability of the blood improves as age advances, with the result that when adult life is reached the spontaneous haemorrhages generally cease, and the traumatic haemorrhages become less formidable. A similar improvement is seen as regards the serous haemorrhages, which can also be held in check by the measures available for increasing the coagulability of the blood.

But when every possible allowance has been made for these more hopeful elements in the clinical picture it must be recognised that the outlook in haemophilia is very depressing. Quite apart from all con-

siderations of the serious risk to life from haemorrhage, and of the miseries which are associated with such haemorrhage (both for the patient and his relatives), the recurrence of serous haemorrhages into the joints means constant invalidism, and almost inevitably goes on to partial ankylosis, which incapacitates the patient for many kinds of work.

Data with regard to the Manifestation of the Bleeding Diathesis in the Female Members of Bleeder Families and Exceptional Fertility of the Women in such Families.—The female members of bleeder families do not shew the symptoms of the disorder; they never suffer from serous haematomas, from the characteristic effusions into the joints, and only very rarely from immoderate spontaneous or traumatic haemorrhages. Nor as a rule do they lose an excessive amount of blood at the menstrual periods or at their confinements. Epistaxis, flooding after labour, and menorrhagia at the menopause, however, are not infrequently recorded. I have myself seen severe recurrent epistaxis in a young woman, the daughter of a bleeder; and in a girl of eight or nine, the sister of a bleeder, serious haemorrhage occurred after the extirpation of a nasal polypus. Although, as I have just insisted, manifestations of the bleeding diathesis are exceptional in the women of bleeder families, some of the anomalous features which are found in the blood of their bleeder sons may be also detected in their blood (*vide* p. 926).

A characteristic point about bleeder women is their exceptional fertility. The family tree of the bleeder family Mampel which has been published by Lossen furnishes, as he points out, striking instances of such fertility. The pedigree shews 4 families with 19 children each, 2 with 13 children each, 2 with 11 children each, and several with 10, 9, and 8 children each. The genealogies of the three bleeder stocks which are given on pp. 932-934, also supply evidence of this fertility. The *first* genealogy shews in the first generation a family of 9, and in the second generation one of 6. The third generation cannot be considered from this point of view, for limitation of the family is continually present to the minds of its female members—one of the sisters absolutely refusing to marry and become the mother of bleeders. In the *second* genealogy there is in the first generation a family of 13, in the next generation families of 9 and of 11, and in the third generation one family of 7 which has been numerously added to since the pedigree was compiled. The *third* genealogy shews in the older generation a family of 18, and in the present generation a family of 7. The nature of the nexus between descent from a bleeder stock and exceptional fertility in the female is an unsolved and perhaps an insoluble problem. And yet when we consider how the discovery of this nexus might throw a light on the complicated phenomena of inheritance through an apparently unaffected parent, and further how the elucidation of this problem of exceptional susceptibility to impregnation might assist in the treatment of sterility, it becomes clear that it is a problem which might fittingly attract attention. Consideration will, I think, lead to the conviction that it is wholly gratuitous to suppose that a woman of bleeder stock would, as compared

with a normal woman, be less liable to suffer from mechanical hindrances to impregnation, or that her blood-fluids would contain less of those products of immunisation (spermato-tropic elements) which from analogy must probably be produced in the organism by the absorption into it of the sexual products of the male. The cause of the exceptional fertility of the woman of bleeder stock might more reasonably be sought for in those features of the blood which are special to haemophilia. Now the special characters of the blood of bleeder families, so far as is at present known are, as we shall see in more detail in a subsequent section, a diminished content in leucocytes, a relatively diminished number of polymorphonuclear leucocytes, and diminished blood-coagulability. The diminished number of leucocytes, and of polymorphonuclear leucocytes in particular, might at first appear not to possess any special significance; it may, however, have a bearing on the question of fertility, for spermatozoa when brought in contact with leucocytes in the presence of the blood-fluids are actively phagocytosed. It would seem, therefore, that spermatozoa in the course of their passage along the uterine and tubal mucous membranes may have to run the gauntlet of the leucocytes before they can effect a junction with the ovum, and it is just conceivable that there may be fewer phagocytes to evade when there are fewer leucocytes in the blood-stream. In like manner the diminished blood-coagulability and correspondingly increased transudation of fluid from the blood-vessels into the mucous membrane of the genital passages, which would accompany it, might quite well be a factor of dominating importance for the successful passage of the spermatozoa along the mucous membranes. When we call up a mental picture of the muscular, nearly amenorrhoeic woman, whose blood is highly coagulable, and whose tissues are correspondingly dry and parchmenty, and contrast her with the muscularly lax type of woman, whose blood is somewhat deficient in coagulability, and whose tissues are correspondingly lymphatic and succulent, we immediately recognise that the latter is incomparably the more fertile type. Now the woman of bleeder stock, to my mind, belongs eminently to this latter type. Is there not perhaps here a hint that it might be reasonable in the case in which we desire to facilitate impregnation in the former type of woman—the type of the sterile virago—to administer citric acid (19, 29), with a view to diminishing the coagulability and viscidity of her blood?

Pathology.—Although consideration of the problem of haemophilia would suggest that there must be some defect in the coagulating power of the blood in this disease, this view has not been universally accepted.

Since blood-clots are in haemophilia, after free and persistent bleeding, a very striking feature in the clinical picture, it has often been contended that there cannot possibly be any fault in the coagulating power of the blood. The supporters of this argument, being obliged to provide an explanation for the excessive haemorrhages of the bleeder, have relied on Virchow's report of hypoplasia of the aorta and arterial system in the necropsy of a bleeder, and on the described occurrence of enlargement of the left side of the

heart in bleeders, to justify the hypothesis that the excessive haemorrhages depend on increased arterial blood-pressure, or the hypothesis that they depend on a defect in the coats of the blood-vessels. To my mind these hypotheses do not rest upon a sufficient logical basis to deserve serious refutation; in the first place, it does not follow from the fact that the blood of bleeders clots that its clotting proceeds in normal time; in the second place, the data invoked to prove that the defect must lie in the mechanics of the circulation or in some abnormality in the walls of the blood-vessels are isolated observations; and lastly, the slow capillary oozing which is the characteristic feature of haemophilia is not explained by the thinning out of the walls of the arteries, and no one, I imagine, would be prepared to contend that the capillary walls of the bleeder can be thinner than they are in a normal man. Still as Sahli (8) in his careful study of haemophilia, and subsequently Morawitz and Lossen (6), have thought it worth while to refute these speculative views, it may in passing be noted that Sahli brings forward evidence from his four cases to shew that a low arterial pressure obtains in bleeders, and that Morawitz and Lossen adduce a comparative experiment made with dry cupping respectively on a bleeder and on a normal person to prove that the capillary walls are not more permeable in the haemophilic than they are in the normal person. It will thus be clear that we may with advantage turn our attention to the blood and more especially to its coagulability, bearing in mind that for the arrest of haemorrhage it is essential that blood-clot should form in the orifice of the cut blood-vessel, and that it is, so far as the arrest of haemorrhage is concerned, a matter of indifference whether the blood clots, or does not clot, after it has flowed away from the bleeding point.

Coagulation-time.—The first measurements of the coagulation-time in bleeders were published by me in 1893 and 1894 (17 and 19), and shewed that the coagulation-times in three bleeders were 60, 20, and 10 minutes respectively, as compared with about 5 minutes, which is the coagulation-time of the normal blood when drawn up into capillary tubes of similar calibre and maintained under the same conditions of temperature. My note-books for the years 1893-1896 contain records of five other bleeders—all belonging to bleeder stock No. 1 (*vide* p. 926)—with coagulation-times of 54 minutes, over 20 minutes, 17 minutes, 17 minutes, and 26 minutes respectively; and also of two unrelated bleeders with coagulation-times of 11 and 70 minutes. Sahli while quoting and confirming, by examination of the bloods of his four bleeders, my published results, insists, and very properly, that during and for some time after haemophilic haemorrhages, coagulation-times are obtained which are as short as or shorter than those of normal blood. The existence of this "haemorrhagic increase of the blood-coagulability" in bleeders I had already reported (19, *vide* footnote 15). More than that, I had pointed out (11) that it was a physiological phenomenon which was already familiar in connexion with blood-letting in animals (2). In order to avoid this fallacy, the blood examinations I reported (and

the same applies to those recorded above) were always made in inter-haemorrhagic periods.

Leucocytes.—In the series of papers just been referred to I drew attention also to the leucocytes in haemophilic blood. The aggregate result of 55 enumerations and of about double that number of differential counts shews that bleeders and the female ascendants of bleeders almost always have a subnormal number of leucocytes, and in particular a subnormal percentage of polymorphonuclear leucocytes. In connexion with the percentage count of polymorphonuclear leucocytes in children, it must be remembered—though unfortunately exact data on this subject are not yet available—that it is the rule for the percentage of polymorphonuclears to be less in early infancy than in childhood, and less in childhood than in adult life—ranging it would seem from perhaps 25 per cent in early infancy to 70 per cent in adult life. The more interesting of my observations, almost all of which date back to the years 1893-1896, on the leucocyte-counts of bleeders are the following :—

(1) *Observations relating to the Leucocytes of Adult Bleeders* :—

	Leucocytes, per c.mm.	Polymorphonuclear Leucocytes	
		per cent.	per c.mm.
No. 1, aged about 25 years . .	6600	56	=3700
No. 2 ,, 45 ,, . .	7400	52	=3850
No. 3 ,, 30 ,, . .	4300	70	=3000

With these may be compared recent observations by Sahli on three bleeders, and by Weil :—

	Leucocytes, per c.mm.	Polymorphonuclear Leucocytes	
		per cent.	per c.mm.
Sahli's cases.—No. 1, aged 17 years .	6200	63	=3800
No. 3, ,, 17 ,, .	6700	55	=3700
No. 4, ,, 21 ,, .	3600	45	=1600
Weil's case.—Aged 45 years . .	2600	57	=1500
,, ,, . . .	4000	60	=2400

(2) *Observations relating to the Leucocytes of entire Bleeder Families.*—My observations on the leucocytes of entire bleeder families are presented below in tabular form. As already indicated above, low leucocyte-counts in haemophilic families are not confined to the bleeders. Evidence bearing on this is furnished in the tables below.

Bleeder Stock No. 1—*Synopsis of Results presented in the Table below.*—The observations tabulated below shew that a subnormal number of leucocytes, and in particular of polymorphonuclear leucocytes, was a constant feature in all the bleeder boys of this stock. It was found also in two of the mothers of bleeder boys (the observation relating to the third bleeder mother may probably be neglected, as the results were obtained in the ninth month of pregnancy). Two of the fathers of bleeders presented a deficiency of polymorphonuclear leucocytes similar to that found in the mothers of bleeders. A

comparison of the bleeder boys with their maternal uncle, also a bleeder, and a comparison of the leucocyte-counts obtained in two of the bleeder boys at an interval of three years, shew that some improvement has taken place with age :—

Name.	Relationship to the Bleeders, H. H. and T. H.	Age.	Number of Leucocytes per c.mm.	Number of Polymorphonuclear Leucocytes per c.mm. or percentage.	Blood Coagulation-times, at 18·5° C. (*circa*).
Henry G. . .	maternal grandfather	72	...	61%	7′ 10″
Jesse H. . .	father	38	8,200	3100	3′ 40″
Emma H. . .	mother	36	4,000	1700	3′ 30″
Jessie H. . .	sister	10½	12,400	7500	2′ 45″; 5′
Harry H.	...	9	6,000	2600	54′; 14′
bleeder		12		47%	
Tommy H.	...	7	5,800	2800	6′ 45″; 9′ 15″;
bleeder		10		54%	over 20′
John G. . . .	maternal uncle	45	7,400	3850	17′
Ellen G. . .	maternal uncle's daughter	19	2,700	1350	9′ 30″
Jane B. . . .	maternal aunt	32	6,400	2900	4′ 45″
Frederick B.	maternal first	5	6,800	2400	7′ 30 ; 17′
bleeder	cousin				
Ethel B. . .	maternal first cousin	3	8,800	4000	7′ 30″
Wilfred K. .	maternal aunt's husband	31	4,970	3000	2′
Kate K. . .	maternal aunt	27	...	78%	3′ 30″
Percy K.	maternal first	3	...	34%	26′
bleeder	cousin				

Bleeder Stock No. 2—*Synopsis of Observations set forth in the Table below.*—The table shews that the mother and grandmother of the bleeder boy, through whom the haemorrhagic diathesis was inherited, present when contrasted with the father and grandfather, who were sound men of non-bleeder stock, a notable inferiority in the number of leucocytes, and in particular in the number of polymorphonuclear leucocytes. The observations which relate to the leucocytes of the bleeder boy himself do not confirm the general rule which applies to bleeder boys. On the other hand, it is to be noted that the leucocytic observations on this boy here tabulated were made at a time when he was just recovering from an alarming haemorrhage which had almost proved fatal. The observations which relate to the three married sisters, the eldest of whom (Esther) had had a family of perfectly healthy sons, whilst the two younger (Caroline and Kate) had had bleeder sons, shew that the first had a normal number of polynuclears, whilst the two latter had a subnormal number. The female children of this bleeder stock shew striking differences with respect to their leucocyte-counts which do not stand in relation with ages, and which recall the conditions found in their maternal aunts :—

Name.	Relationship to Bleeder, G. C.	Age.	Number of Leucocytes per c.mm.	Number of Polymorphonuclear Leucocytes per c.mm.	Blood Coagulation-time.
Peter H. . .	maternal grandfather	70	10,800	6900	5′ 10″ (13° C.)
Caroline H. .	maternal grandmother	68	7,600	4000	11′ 30″ (13° C.)
George C. . .	father	45	12,200	7500	2′ 30″ (14° C.)
Kate C. . . .	mother	28	8,400	4200	6′ 50″ (16° C.)
Esther C. . .	maternal aunt	48	12,300	7400	7′ 30″ (5° C.)
Caroline M. .	maternal aunt	46	9,000	5100	5′ (9° C.)
Eliza G. . . .	maternal aunt	44	8,600	4100	5′ 20″ (5° C.)
Lily C. . . .	sister	10	7,800	2400	11′ 45″ (13° C.)
Ellen C. . .	sister	7	8,300	4000	8′ (15° C.)
Ethel C. . .	sister	6	16,400	7500	6′ (13° C.)
Maysie C. . .	sister	5	12,200	6700	6′ 45″ (13° C.)
George C. *bleeder*	...	3	15,800	6900	25′ (18·5° C.)
Jane C.	sister	1½	9,200	2500	12′ 45″ (13° C.)
Willie C. *not a bleeder*	brother	2½	...	35 %	4′ 20″ (18·5° C.)
Frank H. *not a bleeder*	maternal first cousin	12	10,200	4400	8′ 30″ (13° C.)

Bleeder Stock No. 3—*Synopsis of the Data in the Table below.*—There is a diminished number of leucocytes and of polymorphonuclears in the bleeder and in the mother of the bleeder, and a diminished number of leucocytes in the father. A brother, who has not inherited the tendency to bleed, has a large number of leucocytes and a normal percentage of polymorphonuclear leucocytes. The girls of the bleeder family present striking differences in the leucocytic counts, which do not stand in any relation to the individual ages :—

Name.	Relationship to Bleeder, W. G.	Age.	Number of Leucocytes per c.mm.	Number of Polymorphonuclear Leucocytes per c.mm.	Blood Coagulation-time, at 18·5° C. (*circa*).
W. S. G. . .	father	45	5,800	4200	3′ 50″
Janet G. . .	mother	42	4,400	3100	6′ 45″
Willie G. *bleeder*	...	11½	7,600	2600	4′ 30″
,, . . .	...	14	6,200	3100	20′
Maggie G. . .	sister	10½	4,250	2300	1′ 50″
Mary G. . .	sister	9	8,600	5500	3′ 30″
Thomas G. . .	brother	6	10,200	5500	2′ 30″
do. . . .	,,	8½	7,000	4900	3′ 45″
Florrie G. . .	sister	3½	8,600	2300	2′ 15″

How far does the foregoing account of the pathology of haemophilia furnish an explanation of that disorder? Even if all that has been set down above had been placed beyond the reach of doubt, it could not be con-

tended that anything in the nature of a complete solution of the problem of haemophilia had been arrived at. The ultimate causes of the defect of blood in the bleeder and of the limitation of the manifestations of this disorder to the male sex are left unexplained.

There are two ways of viewing this situation. There is the point of view of the man who is always concerned about getting down to the very foundation of things. A theory of haemophilia such as he asks for will no doubt be forthcoming when we have completely solved the general problem of blood-coagulation, and when we have discovered how it is that differences of sex are correlated not only with profound intellectual differences but with such completely mysterious differences as are encountered here and in connexion with the inheritance of colour-blindness. But there is also the point of view of the man who has no ambition to go out of his depth, who can acquiesce in a knowledge of proximate as distinguished from ultimate causes, provided only there follows from a knowledge of proximate causes a power of controlling events, and who can in connexion with a disease content himself with a provisional theory provided it calls up before the mind the essential clinical features of the disorder, and suggests at the same time a useful line of treatment.

Now the hypothesis that haemophilia depends upon a defect in the coagulability of the blood—and the existence of this defective coagulation in haemophilia is, as we have seen, attested by a considerable body of observations—supplies the mental picture the practical man requires. It explains the persistent and excessive haemorrhages of haemophilia. It explains also the articular effusions of the bleeder. For, as I have pointed out, defective blood-coagulability—presumably because a blood which is deficient in coagulability is deficient also in viscidity—goes hand in hand with a tendency to serous haemorrhages. The nocturnal incidence and aggravation of the haemorrhages which is such a striking feature in haemophilia also fits in with this conception. Since the coagulability of the blood increases when CO_2 accumulates in the blood, and diminishes when the CO_2 diminishes, it might on a priori grounds alone be expected that an existing defect of blood-coagulability would be exaggerated when the patient is at rest in bed and the output of CO_2 from the tissues is diminished.

Two further points must now be considered The first is the question whether the subnormal number of leucocytes, and especially of the polymorphonuclears, is or is not related to the defect in the coagulability of the blood. It would appear that such a connexion exists; for generally speaking pathological conditions associated with a polymorphonuclear leucocytosis are characterised by an increase in the coagulability of the blood, and, vice versa, conditions characterised by a diminution in the number of the polymorphonuclear leucocytes are associated with a diminished blood-coagulability. The reason of this is unknown, but it has often been surmised that destruction of the white blood-corpuscles—and I would suggest more especially of the polymorphonuclear leucocytes—supplies the blood with a fibrino-plastic element. There remains a point

which has been considered both by Sahli and after him by Morawitz and Lossen. This is the oozing which takes place from under the clot in haemophilic wounds, and the persistence of this oozing when as the result of the haemorrhagic increase of blood-coagulability the blood coagulates in normal time or less than normal time. In explanation of this it is suggested by Sahli that the tissues and the vascular wall may, in the case of the bleeder, fail to contribute to the blood some element which is essential to the effective plugging of the vessel. This may well be; for Delezenne's observations shew that the coagulability of avian blood is accelerated in an extraordinary way when, as it flows from the blood-vessel, it comes in contact with the tissues; and working on the same lines I have found that "Delezenne's phenomenon," if I may so denote it, manifests itself also in a marked manner in connexion with mammalian blood, and that an equally marked acceleration of coagulation is obtained when a trace of lymph is added to blood, shewing that admixture with lymph is probably here the operative factor (27). It is therefore conceivable that this factor which contributes to the thrombogenetic power of the blood may in some way fail to come into operation in the case of the bleeder. But the oozing which persists after the haemorrhage has been arrested by clotting can be even more simply explained. Since the wound does not become sealed with clot until bleeding has continued for many hours or days, when the volume of red blood-corpuscles in the blood has been seriously reduced, and since the clot shrinks more and more as the blood becomes impoverished in corpuscles, until in extreme anaemia it floats as a mere thread in the serum, it is not surprising that in the case of the exsanguine bleeder the clot contracts upon itself in such a way as to reopen the mouths of the cut vessels.

Whatever the explanation, it is clear that the problem of the failure of haemophilic blood to furnish an effective plug for the bleeding vessels, must not be allowed to divert attention from the means at our disposal for arresting the haemorrhage by increasing the coagulability of the blood and at the same time diminishing the retractibility of the clot (14). These means will be discussed on p. 937.

Problems for Consideration in Connexion with the Inheritance of the Haemophilic Diathesis.—The well-known law that the haemorrhagic diathesis is handed down through a female, who does not herself suffer, to her male offspring is strikingly exemplified in the pedigree of the Mampel bleeder stock already referred to (5). This remarkable family tree, published by Lossen in 1905, covers one hundred years, and embraces five generations with a total of 212 persons. From this pedigree and the three bleeder pedigrees given below, pp. 932-934, we may endeavour to elucidate certain further points in connexion with the law of haemophilic inheritance. The following questions may with advantage be asked: (*a*) Does every female who comes of a bleeder stock transmit the diathesis to her offspring, and do mothers who transmit the diathesis present a different blood-picture when compared with the mothers who do not transmit this diathesis? (*b*) Does a transmitting mother convey

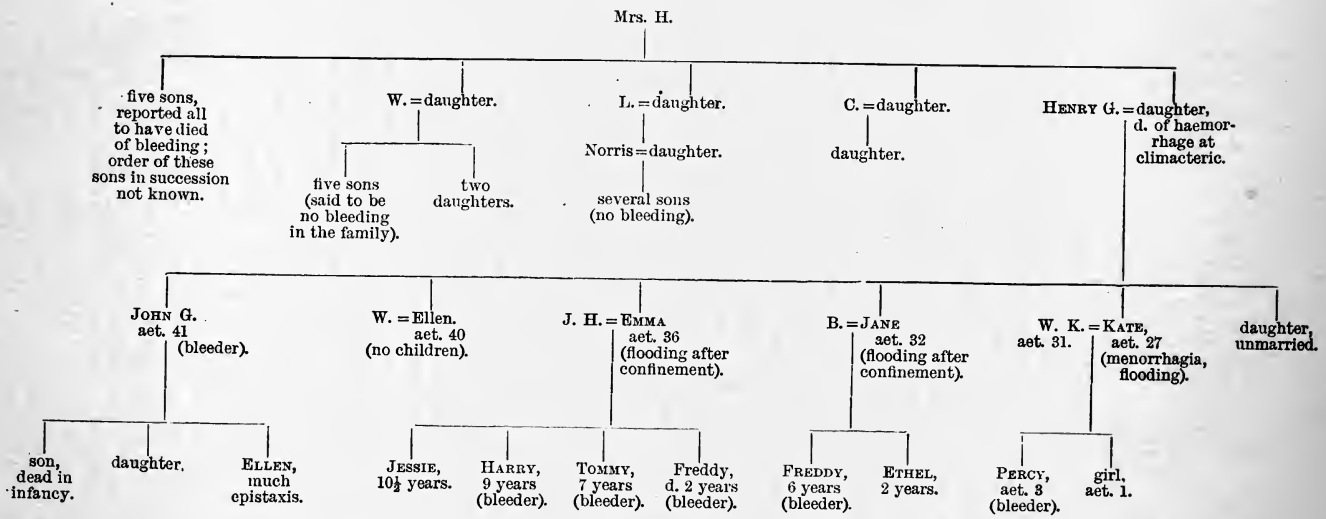
the diathesis in an overt form to all or to some only of her sons, and does she transmit the inheritance in a latent form to all or to some only of her daughters? (*c*) Do the males who inherit the bleeder diathesis transmit the disease to their descendants, and do the males who do not shew any sign of the disease hand it down? (*d*) Have the characters of the blood of the male who mates with a female of bleeder stock any bearing on the transmission of the diathesis, and apart from a bleeder heredity can the disease arise *de novo* in the offspring of a male and female who have a predisposition to bleeding? These questions will now be considered seriatim.

(*a*) *Is the haemorrhagic diathesis transmitted by every mother who comes of bleeder stock?* Analysis of the pedigree of the Mampel bleeder stock shews that the haemorrhagic diathesis was there transmitted by 11 out of a total of 16 women of bleeder stock who became mothers of male children. In *pedigree* 1 (*vide* p. 932), in the first generation reckoned in the ascending line from the bleeder boys, 3 out of 3 mothers transmitted the diathesis to their sons. In the previous generation, if the records can be trusted, only 1 of the 3 mothers transmitted the diathesis. In *pedigree* 2, again going up in an ascending line from the bleeders, 2 out of 3, and in the foregoing generation 3 out of 3 mothers of sons transmitted the diathesis. Adding all these together we find that 20 out of 28 mothers of sons transmitted the diathesis. Whether, as I have suggested on p. 927, the mothers who transmit the diathesis differ in their blood-pictures from the mothers who do not transmit is a question upon which we are still very ill-informed.

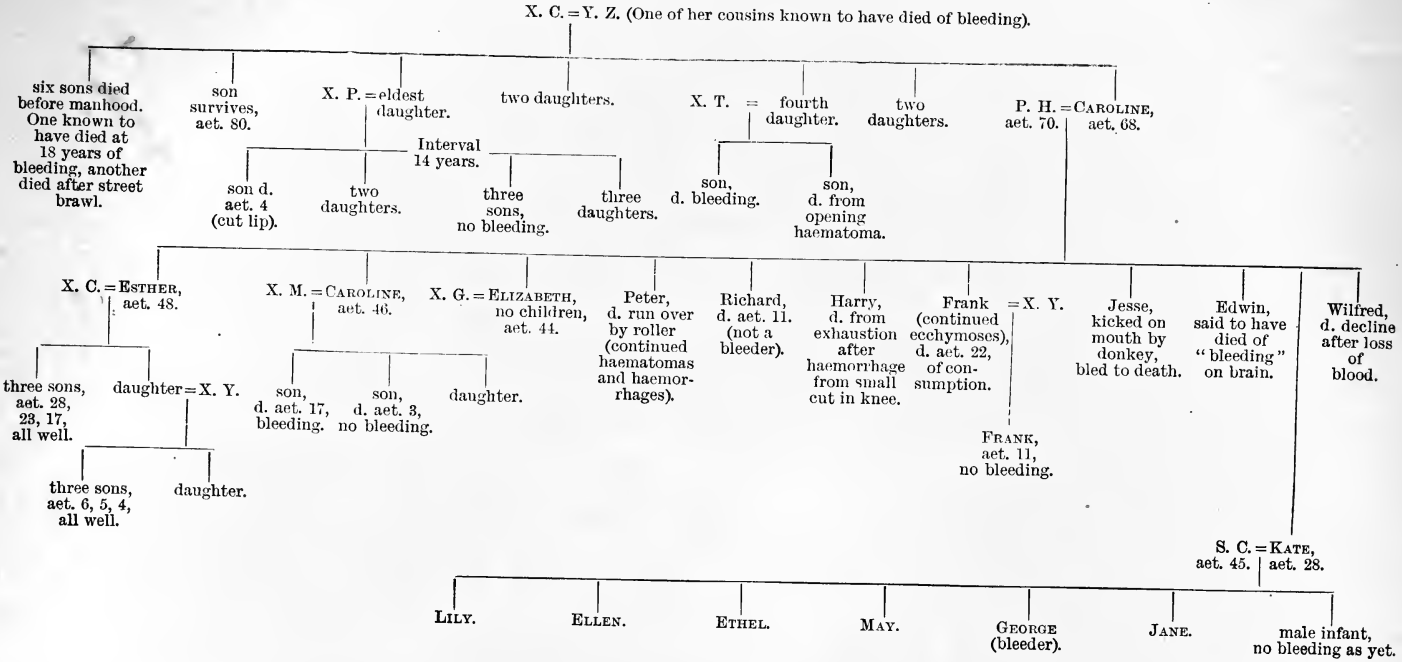
(*b*) *Does a transmitting mother transmit the bleeder diathesis to all or to some only of her sons?* In relation to this question we find that in the Mampel stock only 37 of 82 sons of mothers who transmitted the haemophilic diathesis were bleeders. In *pedigree* 1 (*vide* p. 932) we find that in the present generation of 5 boys all are bleeders, that in the next older generation again there were 5 males all bleeders. In *pedigree* 2 we have, in the youngest generation among the offspring of the mothers who transmitted the disease, 4 boys, of whom 2 inherited the disease. In the previous generation we have in one family 6 out of 7 sons bleeders, in another family 2 out of 2 sons bleeders, and in the third family 1 out of 4 sons a bleeder. In *pedigree* 3, out of 3 sons 2 were bleeders. By adding together the figures relating to these three bleeder stocks we find that 24 out of 31 sons were bleeders, as compared with 37 out of 82 sons in the Mampel bleeder stock.

(*c*) *Is the haemophilic diathesis transmitted through the male?* The Mampel stock contains 7 instances of (male) bleeders marrying and producing male offspring, none of whom was a bleeder. In an 8th instance a bleeder married his first cousin of bleeder stock and had a bleeder son. In estimating the weight of this evidence it is, however, important to note that a scrutiny of the clinical details set forth by Lossen shews that 1 only out of the 8 bleeders in the Mampel stock could be classed as a severe bleeder. *Pedigree* 1 shews an instance of a bleeder transmitting

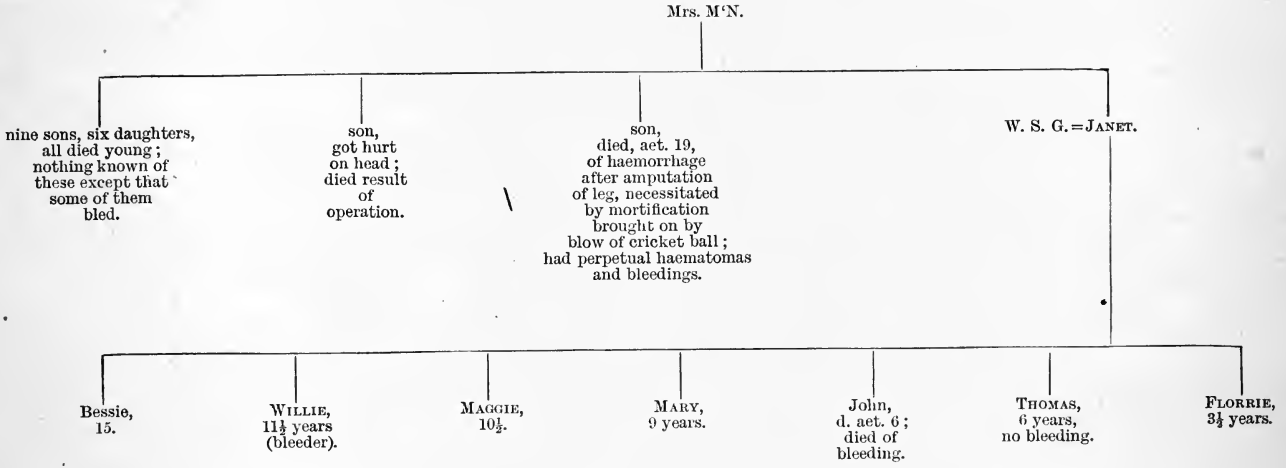
Bleeder Stock, No. 1.



Bleeder Stock, No. 2.



Bleeder Stock, No. 3.



a bleeding diathesis to one of his daughters, and *pedigree* 2 an instance of a bleeder who had one son who is not a bleeder. The inference from the data would therefore appear to be—and here as elsewhere it is probably advisable to discard incompletely reported cases—that the bleeding diathesis is seldom inherited through the male even when he is himself a bleeder. In other words, that with respect to those properties of the blood which come into consideration in connexion with bleeding, the influence exerted upon the blood of the offspring by the father is quite subordinate to that exerted by the mother. It would be extremely interesting to determine whether this inference also holds good with respect to the inheritance of chilblains, urticaria, and physiological albuminuria, all of which are, as I have shewn, correlated with a condition of diminished coagulability of the blood (23; 20, 21, 22; and 28).

(*d*) *Do the blood-characters of the male influence the transmission of the bleeding diathesis to the offspring, and does the disease arise* de novo *from the conjunction of male and female when both have a predisposition to bleeding?* The possibility thus formulated as a question is suggested by the following data. In *pedigree* 1 (*vide* p. 932), 3 out of 3 male ascendants examined (*i.e.* the fathers of two of the families of bleeders, and the maternal grandfather common to these two families) gave in each case a strikingly subnormal count of polymorphonuclear leucocytes; in *pedigree* 2 a similar subnormal count of polymorphonuclear leucocytes was obtained in the father of the bleeder boy, but not in the maternal grandfather; and in *pedigree* 3 exactly the same holds good in connexion with the father of the bleeder family. These data obviously suggest that the influence of the father, even though it would seem to be quite subordinate to that of the mother, may still be a factor of some moment in connexion with the inheritance of haemophilia. Continuing this line of thought we naturally inquire whether in the absence of a definitely haemophilic ancestry the disease may not originate *de novo* from the conjunction of a male and a female both predisposed to bleeding, whose blood has in each case the characters associated with the haemophilic predisposition. Cases of haemophilia without any haemophilic ancestry are not rare; 4 have come under my personal observation. In the case of 2 of these families—and in each of these there had been 1 case of fatal haemophilic bleeding, with evidence of haemophilia in other members—I investigated, in addition to the surviving bleeder members of the family, the bloods of the father, mother, sisters, and brothers. In the one family, that of a tanner whose eldest son, a guardsman, died of bleeding after the extraction of a tooth, the blood of the father gave a total leucocytic count of only 3100 with 1700 polymorphonuclear leucocytes, whilst the mother, who suffered from menorrhagia, gave a leucocytic count of 7200 with only 3900 polymorphonuclear leucocytes. In the other family, that of a London policeman who had lost a son from bleeding at the age of eight and who had another bleeder son, the father had a leucocyte count of 5800 and the mother, who suffered from menorrhagia, one of 5400 with 3800 polymorphonuclear leucocytes.

Question as to the Practical and Theoretical Consequences which may be deduced from the Evidence reviewed above.—The data considered above have a direct practical bearing on the question of the restrictions the male and female members of a bleeder stock might with advantage impose upon themselves as regards marriage, or rather reproduction. It is obvious that in the absence of any proof to the contrary, every woman of bleeder stock should be regarded as a potential mother of bleeders. In future, however, it may be possible by examining the blood to distinguish between the women likely to become mothers of bleeders, and those who would be likely to bear healthy children. As it is probable that the male parent exerts some influence on the disposition of the offspring with respect to bleeding, it would further be desirable, if this were practicable, that women of bleeder stock should mate only with men whose blood is free from any sign of bleeder predisposition. As regards the men of bleeder stock the history of the Mampel family would suggest that male bleeders do not transmit the disease. But this history cannot be regarded as conclusively settling what would happen in the case of a conspicuous bleeder, since only 1 out of the 8 male bleeders in that stock who married and had male offspring, could be classified as such. It would, probably, be a counsel of perfection that in the case of both the partners in a marriage, the male no less than the female, the blood should be irreproachable as regards its coagulability and its leucocytic content.

Passing from matters of direct practical importance to those of speculative interest, we may now inquire whether these data do or do not support the Mendelian theory of inheritance, and whether they throw any light on the general question of genetics. In connexion with the first question it may be pointed out that whilst the Mendelian terms "recessive" and "dominant" may be convenient formulas for expressing the rule that in haemophilic stocks the males become bleeders and the females transmit the disease, it is not by any means certain that the particular properties of the blood which determine the tendency to bleed are really, in the female, recessive in the sense of being present only in the germ-cells. Inasmuch as the females of bleeder stocks appear to have the same character of blood as their bleeder descendants, it would seem that the disease in females was not really recessive, but only masked. Again the figures with respect to the inheritance of the haemophilic diathesis shew that it is largely in excess of the Mendelian expectation. We have seen that in the offspring there is among males a large excess of bleeders over non-bleeders, and among the females a large excess of mothers who transmit, over those who do not transmit the disorder.

Treatment.—Had not modern medicine been evolved, as it has been almost exclusively, by the method of random trial and empiricism, or had it disengaged itself from these, I might have stated as a self-evident proposition that no effective system of therapeutics could be expected in any branch of medicine except as the outcome of experimental research or of personal familiarity with, as distinguished from a purely literary study of,

the results of such research. And in particular I might have laid it down as an axiom that the treatment of haemophilia must be based on a study of the physiology of the blood and blood-coagulation as a whole, supplemented by experimental research undertaken upon bleeders. As it is, I find in the literature of haemophilia, instead of an assertion of this principle, much random trial, many purely empirical judgments, only very little evidence of a personal study of the physiology of the coagulation of the blood, much neglect of the generalisations already arrived at, much rediscovery of and much insistance upon details which are covered by those generalisations. All the more must I reiterate that the treatment of haemophilia can only be successfully attacked from the standpoint of the physiological laboratory.

The three issues to be considered in connexion with the treatment of haemophilia are:—(1) Are there any means of amending the congenital defect which lies at the root of the haemophilic diathesis? (2) Failing these, are there any other therapeutic agents which when given internally will restrain the haemorrhages and serous haemorrhages of the bleeder, and which can be given as a prophylactic measure to patients before surgical operations? (3) Are there any therapeutic agents which when applied locally to the bleeding point will arrest haemophilic haemorrhage?

Under (1) two suggestions will be briefly referred to. The first of these is that it might be worth while to administer ovarian extract to male bleeders with a view of endowing them with the mysterious physiological advantages which, in bleeder families, attach to the female sex. As one who toyed with this speculation long before encountering it in print I may perhaps insist that, although such ideas may have a certain fascination for the intellect, the practical man would do well to treat them, until they have been controlled by serious experimental work, as mere will-o'-the-wisps.

The second suggestion is that nucleo-albumin, its derivative nuclein, or substances which contain nucleo-albumin—and these last are available in the form of thymus tabloids, and various preparations of yeast—should be administered to bleeders with a view to remedying directly that deficiency of leucocytes, and indirectly the associated defective coagulability, which characterise the blood of the bleeder. This suggestion, whatever its value may prove to be, is not without some experimental support. I have satisfied myself both that the number of leucocytes can be increased in haemophilia by the ingestion of nuclein (17) and thymus tabloids, and that the tendency both to serous haemorrhages and actual haemorrhages is often held in check by the administration of these remedies.

(2) Passing now to consider whether there are any other available therapeutic agents which can be employed to increase the coagulability of the blood, it will perhaps be advantageous to retrace the road originally followed in the search for such remedies. We may consider here (*a*) the administration of the salts of calcium and magnesium, (*b*) the administration of CO_2, and (*c*) the inoculation of serum.

(*a*) As soon as Arthus and Pagès proved that the coagulability of the

blood could be abolished by decalcification and that its coagulability could be restored by the addition of calcium salts, it became obvious that the next step for the physician was to investigate the effects of making graduated additions of calcium salts (11, 13, 15, and 17) to blood *in vitro*, to study upon animals (11) the effect of the internal administration of calcium salts upon the rapidity of coagulation, and finally, after devising a clinical method of measuring the coagulation-time of human blood (17), to investigate the effect of the administration of calcium salts to the normal man and to the haemophilic (17 and 19). Confining myself here to what has direct relation to haemophilia, I extract from my published papers and from my notebooks the following illustrations of the effects produced by the administration of calcium chloride to bleeders :—

Serial.	Patient's Initials.	Age.	Date.	Treatment.	Coagulation-time at 18·5° C.
1.	S. W.	11	June 1, 1893.	Nil	10½ minutes.
				1 gram $CaCl_2$ cryst. at bed-time.	
			June 2, 1893.	1 gram $CaCl_2$ cryst. t.i.d.	5½ ,,
			June 3, 1893.	1 gram $CaCl_2$ cryst. b.i.d.	5½ ,,
			June 5, 1893.	1 gram $CaCl_2$ cryst. b.i.d.	Over 1 hour.
2.	H. H.	9	April 13, 1894.	Nil	54 minutes.
				2 grams $CaCl_2$ cryst. at bed-time.	
			April 14, 1894.	2 grams $CaCl_2$ cryst. on rising.	27 ,,
			April 15, 1894.	2 grams $CaCl_2$ cryst. on rising.	13 ,,
3.	Do.		Sept. 28, 1894.	Nil	14 ,,
				0·6 gram $CaCl_2$ cryst. at bed-time.	
			Sept. 29, 1894.	Two doses of 0·6 gram	6¾ ,,
			Sept. 30, 1894.	$CaCl_2$ cryst. at bed-time.	25 ,,
4.	T. H.	7	April 14, 1894.	Nil	6¾ ,,
				2 grams $CaCl_2$ cryst. at bed-time.	
			April 15, 1894.	2 grams $CaCl_2$ cryst. this morning.	4 ,,
5.	Do,		Sept. 28, 1894.	Nil	9¼ ,,
			Sept. 29, 1894.	Two doses of 0·6 gram $CaCl_2$ since Sept. 28.	5¾ ,,
6.	N. R.	26	Mar. 22, 1894.	Nil	7½ ,,
				2 grams $CaCl_2$ cryst. at bed-time.	
			Mar. 23, 1894.	2 grams $CaCl_2$ cryst.	5¾ ,,

These observations, which are in complete accordance with many others made on normal blood, shew that the coagulability of the blood of the bleeder can be increased by the administration of calcium salts. These experimental results are in harmony with the fact that calcium salts have approved themselves to be a mainstay in many cases of haemophilia, both in checking serous haemorrhage and in rendering the blood coagulable and so arresting actual haemorrhage. Calcium salts, however, are not invariably helpful. Nor indeed could they be. For we have in calcium salts not a directly fibrinoplastic element, but only a chemical agent which acts upon the fibrinoplastic elements of the plasma in such a way as both to promote coagulation, and to increase the viscidity of the blood. Moreover, these effects will be exerted (*a*) only when the drug is absorbed, (*b*) only when the patient has not already in his blood the optimum of calcium salts, and (*c*) only so long as the blood is not overloaded with calcium salts. A few words may be devoted to each of these questions. Estimations of the coagulation-time and of the combined calcium and magnesium content of the blood before and after the administration of calcium salts, shew that in some normal persons calcium salts are only very indifferently absorbed (30). This condition is also present in a bleeder whom I have had under observation for years for recurrent haemorrhages from the gums—haemorrhages which have often lasted for weeks, leaving the patient completely blanched. The characteristic features of this bleeder's case are that his haemorrhage is confined to the gums, that he has never suffered from articular swellings, that no heredity can be traced, and that his blood does not shew any conspicuous defect of coagulability—although he suffers from a deficiency in "thrombogenetic" power which seems to depend on a deficiency of fibrinogen in his plasma. The following observations refer to this patient:—

Observation 1. H. G., a man suffering from haemophilia. February 8, 3 P.M.: Coagulation-time, 2 minutes 15 seconds. 3.10 P.M.: 4 grams of calcium lactate were given by the mouth. 3.50 P.M.: Coagulation-time, 2 minutes 15 seconds. No effect was exerted upon the haemorrhage. *Observation* 2. February 17, 2.30 P.M: Coagulation-time, 2 minutes 50 seconds. 2.40 P.M.: 4 grams of calcium lactate were administered. 3.25 P.M.: Coagulation-time, 2 minutes 45 seconds. No effect was exerted upon the haemorrhage. *Observation* 3. February 24, 4 P.M.: Coagulation-time, 2 minutes 50 seconds. 4.10 P.M.: Subcutaneous injection of 0·5 gram of calcium lactate in 10 c.c. of water. 4.55 P.M.: Coagulation-time, 2 minutes 10 seconds. No marked effect was exerted on the haemorrhage.—*Observation* 4. March 3, 2.10 P.M.: Coagulation-time, 2 minutes 5 seconds. There was continuous haemorrhage from the gums. 2.30 P.M.: Hypodermic injection of 0·6 gram of calcium lactate. 2.45 P.M.: Haemorrhage from the gums has ceased. 3.30 P.M.: Coagulation-time, 40 seconds. 4.30 P.M.: Coagulation-time, 35 seconds. March 6: Coagulation-time, 50 seconds. March 16: Coagulation-time, 2 minutes 10 seconds. (The Coagulation-times here were measured at 37° C.)

When the power of absorbing calcium salts is so defective as it was in this patient, no result can be anticipated from moderate doses, and at the most we can expect but slight results from large doses. But in such cases, as I have shewn in conjunction with Dr. Paramore (30), salts of magnesium (the carbonate and the lactate were employed) may be well absorbed, and may have quite as good an effect as the calcium salts, as was shewn in a striking fashion by the case of the bleeder just mentioned. His haemorrhages, which previously were never controlled by calcium salts, are now almost invariably checked by the magnesium salts. In order to guard against possible failure due to deficient absorption of calcium salts, it would, therefore, be advisable to prescribe as a routine measure in every case of haemophilic haemorrhage a mixture of calcium and magnesium salts.

It may be here incidentally noted that the subcutaneous inoculation of calcium chloride is quite inadmissible. I have seen extensive sloughing follow upon its subcutaneous injection into a dog, and know of a case in which it was directly tried on a bleeder with a like result. The injection of calcium lactate on man must also be very cautiously resorted to, for although the lactate has no escharotic properties, very severe pain may follow upon its injection in too concentrated a form.

We must now consider the risk of overloading the blood with calcium salts. It is to be noted here that a retardation of coagulation similar to that which is observed *in vitro* (15) when an excess of calcium salts is added to the blood also appears *in vivo* after excessive doses of calcium (*vide* Table, p. 938). Where, as in haemophilic haemorrhage, a question of life or death may hang in the balance, it would therefore be well before persisting in the administration of large doses of calcium and magnesium salts, first to determine upon the patient's blood *in vitro* whether an addition of calcium salts will accelerate or retard the coagulation-time. In connexion with Experiment 1 in the Table on p. 938, it had been determined before administering the calcium chloride that the coagulation-time of the blood drawn from the finger was diminished by half by additions of 0·2 to 0·1 per cent of calcium chloride to the blood *in vitro*.

Conclusions with Respect to Administration and Dosage of Calcium and Magnesium Salts.—When it has been clearly realised that it is impossible in any particular case to tell, apart from experiment, either that magnesium and calcium will be absorbed from the alimentary canal, or that the patient's blood may not already contain the optimum of calcium and magnesium, it becomes obvious that in connexion with these drugs no absolute rule can be laid down as to dosage, the interspacing of the doses, nor as to what number of doses should be administered. The following, however, may serve as general indications. Where, as in the presence of active haemorrhage, it is desired to obtain the most rapid and marked effect upon blood-coagulation, an initial dose of 1 gram or somewhat less of calcium chloride *cryst.* or lactate, or of a mixture of magnesium carbonate or lactate with calcium chloride or lactate, may be

administered to young children, and fully 4 grams to an adult. In order to keep up the effect of the initial dose, 2 grams daily may be administered to adults, and proportionately smaller doses to children.

(*b*) *Administration of CO_2.*—As in the case of the administration of calcium salts, in order to increase the coagulability of the blood, so also here with regard to the administration of CO_2 with the same object, the rationale of the proposed treatment will be most clearly brought out by explaining the origin of the suggestion. In researches undertaken in connexion with the study of the intravascular coagulation, which is obtained when a solution of nucleo-albumin (Wooldridge's tissue-fibrinogen) is injected into the circulating blood, I found (12) that it was possible to increase or diminish the amount of intravascular thrombosis by increasing or diminishing the venosity of the blood in the general circulation, and that thrombosis could be induced in any particular vascular area by increasing the venosity of blood there. I suggested in connexion with these results that the accumulation of CO_2 in the blood would probably prove to be the causal factor.

The hypothesis that an accumulation of CO_2 in the blood would act in the direction of increasing the coagulability of the blood was afterwards examined by me in a research which was published in March 1894 (18). I shewed there—and these results tallied with those obtained by Mathieu and Urbain with other methods—that when animals are made to breathe out of a reservoir containing a mixture of 80 per cent of CO_2 and 20 per cent of O_2, a very notable increase in the coagulability of the blood is induced. The next and obvious step was to turn these physiological results to therapeutic uses. In addition to utilising them in the treatment of aneurysm and epistaxis I made my first trial of CO_2 (19) in haemophilic haemorrhage on the bleeder boy G. C., whose pedigree is on page 933. The details of the case and the result of the administration of the CO_2 are described in the following extract from my paper :—

The child is at present nearly four years old, and has suffered from an almost continuous succession of subcutaneous haematomas. In September 1893 haemorrhage set in as a result of a fall upon the forehead, which left a scar which was visible for months after. The haemorrhage was treated by ordinary palliative measures, and finally ceased after lasting some six weeks. The blood is said to have shewn no tendency whatever to clot, except when the wound had been tightly bandaged up for several days at a time. The coagulation-time of this child (taken at temperatures ranging between 42° and 57° F.) oscillated between 45 minutes and 1 hour. On February 2, 1894, the child had another fall against a chair, and hurt the fraenum of his upper lip, and bled a little at the time. Haemorrhage came on profusely at night, and his pillow was soaked with blood and a great deal of blood was swallowed. When this was discovered the parents, according to directions previously left by me, administered 0·6 gram of calcium chloride, and they state that the blood, which had previously shewn no sign whatever of clotting, began to clot firmly in two or three hours after the administration of the lime. Bleeding recurred the next day, and in the evening, after the child had fallen asleep, his mouth was found quite filled

with blood-clot. On February 4, 5, and 6, bleeding recurred at intervals (probably owing to the frequent dislodgment of the clot). Calcium chloride had been administered all this time in 0·6 gram doses twice daily. The child was seen by me on February 6, and I found on the fraenum of the upper lip a scratch about one-eighth of an inch long, covered over by coagulated blood. There was no oozing from the wound. A drop of blood was drawn off from the child's finger, and coagulation-time (determined at 37° C.) was found to be 2 minutes 25 seconds, and the addition of calcium chloride to the extravascular blood was found not to effect any acceleration of coagulation-time. The calcium chloride already taken appears, therefore, to have done all that could have been expected of it, and yet there had been frequent recurrences of the haemorrhage when the clot became dislodged. In view of these facts I determined to administer carbonic acid gas in order still further to increase blood-coagulability. I hoped in this way to cause the blood to clot, not only on the surface of the wound, but also some distance up the lumina of the ruptured vessels. Guided by these considerations I inserted a soft india-rubber tube into the child's mouth, and connected it with a Kipp's gas apparatus which I had brought with me. I determined the coagulation-time of the child's blood while the carbonic acid was being administered to him, and found that it was accelerated to 1 minute 40 seconds (determined at 37° C.).

The child was not seen by me again till February 12, when I received another urgent summons saying that the haemorrhage, which had ceased for 24 hours after the inhalation of the carbonic acid, had broken out afresh and had continued ever since. Calcium chloride had been administered twice daily in 0·6 gram doses from the 7th to the 11th, when the child vomited and refused to take it. On arrival I found the child absolutely blanched, and tetchy to a painful degree. Determinations of coagulability were, therefore, out of the question. Blood was found to be oozing from the fraenum of the upper lip, and there was a trace, but only a trace, of clot around the wound. Carbonic acid was immediately administered in the same manner as before, and under its influence bleeding broke out copiously. When, however, the child came more under the influence of the gas, and his struggles ceased, the blood clotted instantaneously, so that even the film of blood which was drawn out between the upper and the lower lip when the mouth was opened instantly congealed into a clot. I proceeded to remove the large clot of blood which had formed round the gum, and found it to be of extraordinary firm texture. A small clot instantly reformed round the wound, the haemorrhage ceased, and the child fell asleep. The administration of the gas was continued for half an hour. The gasogene was then recharged and was left under the parents' charge. Haemorrhage recurred two or three times in the course of the night, when the clots became dislodged, but clotting is reported to have taken place as soon as the inhalation of the gas was renewed. After this there was no further return of haemorrhage, and convalescence took place.

Suggestions with regard to the Administration of CO_2.—A Kipp's apparatus filled in with marble and hydrochloric acid, and fitted with a wash-bottle and a length of rubber tubing to serve as a delivery tube, is all that is necessary for the production and administration of CO_2. In default of a Kipp's apparatus a gasogene can be extemporised by knocking a hole in the bottom of a Winchester quart bottle, filling it in with

pieces of chalk, stretching muslin over the hole to serve as a false bottom and then lowering the bottle into a large jug containing vinegar or any other weak acid, after fitting into the neck a cork perforated by a glass tube with a length of rubber tubing attached. The output of gas can then be regulated by compressing the rubber tube. In administering the gas care must be taken to deliver it only in a small stream so as to avoid the acceleration and deepening of the respiratory movements which is produced by excess of CO_2.

(*c*) *Inoculation with Serum.*—P. Emile Weil suggested injection of serum with the object of increasing the coagulability of the blood in haemophilia. In the course of investigations on a non-hereditary, and in many respects a very atypical, bleeder he recounts that the addition of normal serum made the blood clot more rapidly *in vitro*. In order to determine whether this same effect could be obtained by an intravascular injection of serum, he injected his patient on three successive occasions with serum; and on withdrawing blood from a vein at intervals of several days he found that his expectations were realised. These observations are extremely interesting and suggestive, and his therapeutical proposal has since been repeatedly acted upon. But I do not see in the published results, or in Weil's original experiments—for the shortest interval between the injection of serum and his subsequent examination of the blood was 48 hours—any proof that an injection of serum will effect that rapid increase in the coagulability of the blood which would be desirable in haemophilic haemorrhage. This point can only be settled by clinical observations undertaken in conjunction with estimations of the coagulation-time of the blood. Until such data are available it is important to note that, although Weil's work is distinctly suggestive, its therapeutic bearing has not been placed upon a sound scientific basis. Limiting his outlook as Weil has done to his own particular experiments and the narrow subject matter of haemophilia, he has failed to appreciate that the phenomenon of the acceleration of coagulation by an admixture of lymph or serum to blood *in vitro* (27) is not peculiar to haemophilia, and that the increased coagulability which he observed after injections of serum, although it may prove to be a constant phenomenon and of therapeutic value, is in reality only one of a complicated series of effects produced by the incorporation of a foreign serum. We must remember that injections of a foreign serum may give rise to diminished blood-coagulability, a phenomenon which is associated with the manifestations of the "serum-disease" (20, 21, and 22). Furthermore, in connexion with the suggestion that the bleeder should be periodically inoculated with serum the possible production of anaphylaxis or hypersensibility must be borne in mind.

(3) *Is there any Local Treatment for the Arrest of Haemophilic Haemorrhage?*—Since direct surgical means for the arrest of haemorrhage, such as the use of ligatures and compresses, are in haemophilic haemorrhage nearly always inapplicable, ineffective, or dangerous, and since ergot and adrenalin are of doubtful or temporary utility only, the

question of the arrest of haemorrhage by local treatment is narrowed down to a discussion of what can be done by styptic applications. I must now revert to the distinction, which I emphasised many years ago (11 and 16), between an *escharotic* and a *physiological* styptic. An escharotic styptic, like the red-hot iron of the Middle Ages, produces its effect by charring the tissues in the neighbourhood of the bleeding point and by forming a plug out of the eschar. This form of styptic is an obvious anachronism in any civilised system of therapeutics, and, it may be noted, is specially unsuitable in haemophilia, for in this disease the falling off of the eschar would generally be followed by an outbreak of bleeding from a larger area of denuded surface.

Physiological Styptics, which exert their effect by accelerating the coagulation of the blood upon the bleeding wound, are, in contrast to escharotic styptics, quite painless in application, and are free from the risks which attach to the use of escharotic styptics in bleeders. The only points which arise in connexion with physiological styptics are (*a*) as to the rapidity with which the blood can be made to clot, (*b*) as to the preparation and keeping properties of the styptic agents, and (*c*) as to the liability of the clot to be brushed off or loosened in such a way as to furnish opportunity for fresh haemorrhage.

Preparation of Physiological Styptics and Data with regard to their Potency.—So far as I know the idea of turning to account, for the arrest of haemorrhage, the knowledge which had been won of the process of blood-coagulation occurred first to Wooldridge. I remember his meditating, shortly before his premature death, the problem of injecting a solution of his "tissue-fibrinogens" into an aneurysm which was pointing through the thoracic wall and was threatening to give way. Whilst this particular application of a physiological styptic—though it is ideally effective, if I may judge from an isolated case on which I tried it—promises only very little advantage, the general conception which underlay Wooldridge's suggestion has borne fruit in many directions, and is, if I mistake not, destined to bear further fruit.

When I first set about making a physiological styptic (this was in 1891; (11)), I used a watery extract of fibrin (such extracts were, and perhaps still are, spoken of as solutions of fibrin ferment), reinforced by 1 per cent of calcium chloride. This was, except in respect to the calcium chloride, an example of regressive invention, for, in contrast with that which Wooldridge had proposed to use, this styptic contained no fibrinoplastic element. This defect, however, was soon afterwards rectified by substituting a much more potent extract of thymus gland for the watery extract of fibrin (16). The styptic thus obtained is so powerful that it can arrest the haemorrhage from the cut femoral artery of a dog, provided that the cut artery is compressed for the minute or two to allow of the consolidation of the clot. This styptic is capable of rendering conspicuous services in connexion with haemophilic blood; by its means I have formed round the cut finger of a bleeder boy a clot so dense and hard as to resemble the ball of clay which a gardener

binds round a branch when he is fixing a graft in position. As this preparation acts both by accelerating the rate of blood-coagulation, and by increasing the density of the clot, it is, I believe, beyond all comparison the most potent physiological styptic at present available.

Recently the idea of adding fibrinoplastic elements to the blood with a view to checking haemorrhage has suggested itself also to medical practitioners on the Continent. It has been proposed that human blood should be applied to the wound in haemophilic haemorrhage and should be allowed to clot there. It has also been proposed—and this proposal appears to have been made first by Weil—that serum should be applied to the wound. I have no personal experience of these methods, but I can hardly imagine any one who has had experience of the physiological styptic described above accepting them as substitutes for it. It may perhaps be well to subjoin some details as to the preparation of this physiological styptic.

The Preparation of the Physiological Styptic.—Take a thymus gland (known to butchers in England as the chest-sweetbread) of a calf or lamb, carefully remove all the fat and comminute it on a chopping-board, or pass it through a sausage-machine, then place it in a jar and cover it over with a 0·5 to 1·0 per cent saline solution to which a mere trace of sodium carbonate has been added, using about 10 parts of the solution to 1 part of comminuted gland substance. If time presses, filter off immediately through fine calico and complete by adding 0·25-0·5 per cent of calcium chloride (weighed as crystals) and 1 per cent of carbolic acid. When time does not press the extraction may be continued for 12 to 24 hours, the 1 per cent of carbolic acid being added *ab initio*, the calcium being introduced as before, only after filtering. If a thymus gland cannot be procured, a testis will serve the purpose equally well, but a pancreas should not be used. When neither a thymus gland nor a testis is available an efficient styptic can be made from the epithelial cells of the gastric mucous membrane.

Suggestions with regard to the Employment of Physiological Styptics.—As has already been pointed out incidentally, there is the drawback in connexion with all physiological styptics that the clot thus formed is liable to be brushed away or loosened, with the result that bleeding breaks out afresh. In other words, invaluable as are physiological styptics, the control of haemorrhage thus obtained is only a temporary arrest. What is wanted is a clot extending into the lumina of the open vessels. With this object in view it is always advisable to supplement the action of the styptic by measures which increase the coagulability of the intravascular blood.

Another important point is that even with the most potent physiological styptic we cannot hope to obtain the instantaneous arrest of haemorrhage which is provided by an escharotic styptic. It follows that if the styptic be merely poured upon the bleeding point without being kept in constant contact with it, the blood will clot where it falls and the wound will remain free from clot, and the bleeding will continue.

We must, therefore, always plug the wound with wool or lint soaked in the styptic, or apply pressure when the wound is superficial.

Thirdly, since an excess of calcium salts diminishes the coagulability of the blood it is advisable, when using a styptic which contains 0·5 per cent of $CaCl_2$, to regulate the quantity of styptic, using it in the proportion of 1 part of the styptic to about 2 to 3 parts of blood.

Summary of the Methods of Treatment available for the Control of Haemophilic Haemorrhage.—We have thus seen that, excluding from consideration the method of inoculating serum until it has been scientifically tested, there are four methods which may be employed to control haemophilic haemorrhage; it is, indeed, often necessary to call all four to our aid. Tabloids of thymus gland (B. W. & Co., 5 grains each), administered up to 20 a day will supply the blood with the nucleo-albuminous element which it probably needs. A mixture of calcium and magnesium salts, administered in appropriate doses, will increase the coagulability of the intravascular blood and will favour thrombosis inside the open blood-vessels; and carbonic acid will serve to reinforce this action. The physiological styptic described above applied locally in the manner indicated will at least temporarily obstruct the mouths of the blood-vessels. With these methods at disposal all cases of haemophilic haemorrhage should prove controllable.

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