BY THE SAME AUTHOR

HANDBOOK OF PHYSIOLOGY

HALLIBURTON AND MCDOWALL

An up-to-date text-book for students and practitioners of medicine. 19th edition. Completely revised.

THE SCIENCE OF SIGNS AND SYMPTOMS

IN RELATION TO MODERN DIAGNOSIS AND TREATMENT

A TEXTBOOK FOR GENERAL PRACTITIONERS OF MEDICINE

BY

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PREFACE TO THIRD EDITION

WHEN I first wrote this book I did so because it seemed there was a need for such a volume, but I had scarcely anticipated that within two years I should be asked to prepare two more editions. Once again I express my gratitude to reviewers who must have done much to contribute to its success. Fortunately most of them were aware of the limit of human capacity and of the difficulty of collecting material. With the assistance of my clinical colleague, Dr. Hugh Dunlop, I have been able to extend the scale to many points hitherto omitted. Many chapters have also been remodelled. This has necessitated a slight increase in size, but makes the book much more complete.

The book was originally intended for practitioners and this end is still kept in view, but it appears that the book has had an appeal to teachers and to students preparing for higher examinations. I trust, however, that in the years to come it will help to impress those responsible for medical curricula that there exists a science of Symptomatology as clearly defined and as valuable as its sister sciences Pharmacology and Pathology in its present accepted sense. It may be remarked that the word "symptom," although commonly used in a subjective sense, may from its derivation be held to include objective signs.

In its preparation the book owes much to the publishers, who have done all possible to assist me. In addition to those mentioned in previous editions, the following have been good enough to give me much advice and help: Dr. C. R. Boland, Professor Clarke Kennedy, Dr. J. W. Linnell, Dr. W. Robson, and Professor O. de Wesselow. To those I owe my best thanks.

The Table on p. 110 is reprinted from Dr. Traquair's paper on "Fields of Vision in Intracranial Lesions" (*British Medical Journal*, August 5th, 1933, p. 230) with permission.

EXTRACT FROM PREFACE TO SECOND EDITION

In addition to those previously thanked, I am specially grateful in this respect to Sir Farquhar Buzzard, Professor Stanley Davidson, Dr. Geoffrey Evans, Professor Gulland, Professor Hay, Dr. A. F. Hurst and Dr. K. D. Wilkinson. Many others, especially Dr. A. E. Barclay, Professor Morison, and Dr. H. T. Flint, have answered specific questions on special points. It has, unfortunately, not been possible for me to incorporate the views of all because of consideration of space and of the debatable nature of some of the points. I should, however, like to take this opportunity of asking readers not to hesitate to draw my attention to matters which they think ought to be inserted, for it is obviously impossible for any single person to have a full knowledge of modern Medicine, Surgery, Pathology, and Physiology. It should perhaps be said that the book is not intended to give every disease in which any symptom occurs, but rather to give examples of diseases in relation to symptom production.

PREFACE TO FIRST EDITION

SOME years ago it was my fortune to take an active part in the teaching of clinical medicine, and during that period it was firmly impressed upon me that if medicine and surgery are to progress as they ought some definite attempt should be made to bring clinical work and the sciences closer together. This is done spasmodically by some clinical teachers, but for the most part they have not time to teach how signs and symptoms are produced as well as the essentials of diagnosis and treatment. This book is intended to fill the gap, but in such a way that it will be understood by those who have long since forgotten their sciences, but who wish a more intimate knowledge of the more scientific side of medicine.

The book is based on an earlier work, " Clinical Physiology," of which two editions, one British and one American, have become exhausted. The appreciation which it has received suggested that the scope of the book might be extended, but with the extension a new title was necessary to indicate more clearly the aim of the book.

It is difficult to survey such a wide and ever-enlarging field and it is almost inevitable that the book contains many statements which workers in special fields may criticise, but their criticism will I trust be outweighed by the many kind letters I have received from general practitioners quite unknown to me who found that " Clinical Physiology " had added greatly to the interest of their daily toil.

The volume generally adheres to the title, but as there are many other matters of great interest and importance which are relevant, these have been included at suitable places.

In the preparation of the book I owe much to many friends. In addition to those previously thanked I have received much

personal assistance from Professor Hartridge and Dr. E. P. Poulton. The reading of the proofs was kindly undertaken in part by Dr. Marjory Gillespie and Dr. Hewitt, and systematically by Dr. G. A. Clark, Miss A. Shore, and Margaret Watson, whose suggestions and corrections have been invaluable. The last named also prepared the work for the press.

LIST OF ILLUSTRATIONS

THE SCIENCE OF SIGNS AND SYMPTOMS

CHAPTER I

LIFE AS A CLINICAL ENTITY

You never know what life is till you die.
BROWNING.

LIFE is the most treasured possession of man. Its prolongation and amelioration must ever be the great purpose of the clinician. Its origin and nature are the greatest problems of medical science. Life may be identified with the power of doing something. Before the full power of doing external work is attained, the human organism passes through a series of stages during which this power of doing something is very limited. Although these stages merge into each other, some of them are of more interest than others to the clinician. At first the organism is capable only of growth, but as it becomes differentiated its capacity for work develops. Of special interest is the commencement of movement in muscle, particularly that of the heart, whose beat may be appreciated at the fourth month of intra-uterine life. At this stage, however, the maternal blood supplies all that is required for growth and movement, and takes away metabolic products of the developing organism, whose organs, for the most part, are incapable of such function. At the sixth month the fœtus is legally viable, for it is then capable under suitable conditions of maintaining a separate existence, though in practice this capability is not attained until the seventh month. This stage is so important medico-legally that it may be well to summarize the evidence that it has been reached. The eyelids are separated; the pupillary membrane is disappearing; the face only is free from lanugo; the nails have not quite grown to the ends of the fingers; and there is no cartilage in the ears and nose. From the sixth month onwards the fœtus is increasingly

capable of separate existence, and, by the ninth month, it has attained full fœtal maturity.

At birth, the fœtus, now called a child, becomes responsible for its own digestion, metabolism, and excretion of waste products. In particular, it is responsible for its own respiration, and evidence of air having entered the lungs is of great medico-legal significance as indicating that the child has been born alive. There are, however, certain fallacies in this sign, but for these reference must be made to a medico-legal textbook. In England, if the child is seen to breathe, move its limbs, heard to cry, or if an artery or the heart is seen to pulsate, the child is considered to be alive. In Scotland, evidence of respiration or crying is required. In France, viability is also required. It is a curious anomaly in England, that a child born alive, say, at the fifth month, though it may not be viable, is still capable of inheriting property, and legally transmitting it.

Life, as a clinical entity, must be considered to centre in the circulation and respiration; and in lower animals, such as the frog, the heart is capable of performing external work quite independently of any other organ. It will continue to beat for a considerable period provided it is not allowed to become dry, and its temperature remains that at which metabolism can go on. We believe that this property of contraction is inherent in heart muscle itself, which is also peculiar in that it contains large stores of energy, and, in the frog, is able to obtain oxygen from the air.

The mammalian heart, however, is more specialized. Though it has the same inherent property to beat, it will not do so except under certain conditions. It is essential that it should be supplied, *via* its coronary arteries, with an isotonic fluid at body temperature and at a pressure comparable with that in its aorta. The fluid must also be well oxygenated and neutral, or very slightly alkaline in reaction. It is a fact of scientific interest, that the mere raising of pressure in the coronary arteries is sufficient to start the heart-beat, although the other factors mentioned are essential for longer action. For still more prolonged action, nourishment and hormones to assist metabolism are necessary. A consideration of the above gives an indication of the essentials of mammalian life in its simplest form, and what conditions must be maintained if it is to continue even for a short period. If we apply these facts to the intact animal, we have, for the essentials of life (as a clinical entity): heart action, supported by body heat; blood pressure; adequate respiration; and the maintenance

of blood neutrality. All forms of death are due to failure of one or more of these factors. Thus we see why a decapitated animal or a human being in whom the medullary centres are paralysed, cannot maintain life for more than a few minutes (less than ten) after respiration ceases. Primary failure of the body heat to an extent which will not support heart action, is only seen after prolonged exposure to cold. Failure of respiration is, however, common clinically as an immediate cause of death, and will be dealt with in a later chapter.

If these factors are maintained, the life of the individual will continue, though it is obvious that, to maintain them indefinitely, a large number of additional processes are necessary—for example, those required for digestion, absorption, metabolism, and their control; for the control of the water content and temperature of the body; and for the elimination of waste products. Failure of these mechanisms, however, does not have such immediate effects, although they are needed for a continued existence. The organs on which these mechanisms depend are all subject to disease, which may slowly result in death: the kidney in Bright's disease, the liver in liver atrophy, the suprarenals in Addison's disease, and the pancreas in diabetes. To the list must be added, also, all the undetermined but essential mechanisms which prevent bacterial infection. The higher animals, possessed of all such organs, would yet be incapable of continuing a separate existence unless possessed of the higher parts of the brain, which give them the desire to feed and protect themselves. This may readily be shown in animals by removal of the higher parts of the brain, and is seen in the lowest forms of congenital insanity among human beings. Fortunately, however, there is in the body a considerable store of nourishment which is capable of maintaining the energy requirements for the vital process for at least a month. Even an isolated heart contains sufficient store to enable it to maintain its activity for hours. The supply of nourishment, then, is not of immediate moment in the maintenance of life, although it appears that excessive drain on the reserve may be detrimental to recovery from illness.

When we consider life in a wider sense than the clinical entity, every tissue in the body must be studied. Further, the body, as an integrated whole, appears to be designed for the purpose of carrying out physical work in some form or other. Those mechanisms, such as circulation and respiration which we have pointed out as essential to life, are in reality the servants of the

muscular tissue in so far as their activities are regulated by the requirements of the muscle. This will be more clearly seen later on. Strictly speaking, then, the clinical entity of life, as exemplified by the circulation and respiration, is but evidence of the life of certain vital mechanisms without which complete life would be impossible.

It will be seen therefore how desirable it is to get away from the common conception of the body as a mere collection of mechanisms. The proper integration of these mechanisms is as important as are the mechanisms themselves. We marvel at the variety of physico-chemical processes upon which our life is based and by which our activities are guided. We become painfully aware of how far the paths of civilization lead us from the purpose for which the major part of our bodies was apparently designed. In the development of our higher mental qualities, we should not forget those physical ones which have assisted in our evolution, and which, in our time at least, will not have become wholly adapted to the comparative physical inactivity, and excessive mental activity, which modern life demands. If we forget, too soon we shall be reminded of the words of Massinger : " Death hath a thousand doors by which to usher out Life."

CHAPTER II

CONSCIOUSNESS

In view of the fact that unconsciousness is such an important clinical state, it is a little unfortunate that most textbooks of physiology usually avoid a consideration of consciousness. Consciousness is something which perhaps we are better able to experience than define. It is probably best defined as the appreciation of the stream of afferent impulses which pass to the cerebrum. Although we do not know the exact nature of consciousness, we do know a large number of factors on which it depends. These factors will now be considered.

The Physical Integrity of the Cerebrum.—That the cerebrum is an essential factor is clear when we realize that any injury to this part of the brain, or its experimental removal in a higher animal, brings about an unconscious state. The reason for the unconsciousness which occurs as the result of a sudden blow on the head (known as **concussion**), where there is no obvious damage to the skull and its contents, is not quite clear. Some hold that the mere vibration of the brain may be sufficient to interfere with its function, perhaps, putting it crudely, by a dislocation of the neurones. Others maintain that there must necessarily be damage of a more serious character, as the frequently found petechial hæmorrhages suggest. If this be true, it is difficult to account for those cases in which the symptoms are very evanescent, and the individuals merely feel dazed for a few moments. Still others hold that a wave of cerebro-spinal fluid caused by the blow brings about a cerebral anæmia, from stimulation, according to Duret, of the restiform bodies. It is possible that a cerebral anæmia might be brought about through direct stimulation of the vessels by the cerebro-spinal fluid, but the more detailed explanation of Duret is conjectural.

Balance of Inhibition and Excitation.—These subtle and as yet little understood phenomena are of prime importance in conscious activity. Content with their practical importance, rather than claiming to understand them, we may note certain applications. The unconsciousness of major and minor epilepsy is thought to

result from inhibition of cerebral function (see " Convulsions "). Sleep, according to Pavlov's work, is due to spread of inhibition within the cerebrum. Severe emotional shock may also limit the conscious field in an analogous way, quite apart from fainting.

Maintenance of the Blood Supply of the Cerebrum.—Many of the commoner forms of unconsciousness are due to interference with this blood supply; the interference may be local or general.

Anything which tends to raise the pressure in the cranial cavity above that in the cerebral capillaries and veins will cause circulatory obstruction. This is well seen in the various forms of the condition known as **compression,** whether due to hæmorrhage, abscess or tumour. In the last two the symptoms may be less acute than in the first, as the onset is slower and the tumour may make way for itself by destruction of brain tissue. In compression, the veins are also compressed, as indicated by the cyanosis of those parts of the face, such as the eyelids, which drain into the cranial cavities, and by the venous congestion of the optic disc. Such pressure is not, however, communicated, as might appear at first sight, throughout the cranial cavity, for it is prevented from doing so by the tentorium cerebelli. Thus, immediate death from pressure on the medullary capillaries is prevented. We realize, therefore, why a cerebellar tumour may be very severe, and yet fail to bring about unconsciousness until a late stage—after the characteristic cerebellar symptoms of inco-ordination and postural defect are well marked. This point is important, as it indicates that decompression operations should be done as near the site of the tumour as possible, even if the latter cannot be removed.

The vertebral arteries supply sufficient blood to the medulla to maintain the vital centres. In an animal the carotids may be ligatured with impunity so far as the vital centres are concerned. Indeed, it has been shown by Leonard Hill that even if the vertebral arteries of a dog are ligatured also, an anastomosis which opens up by way of the superior intercostals and anterior spinal arteries is sufficient for the adequate supply of the medulla, though the higher functions of the cerebrum are seriously impaired. The blood supply of the medulla is not interfered with until pressure is actually applied to this region. Here pressure from local causes is rare, and, in the condition mentioned above, it is considered that death is due not to direct transmission of pressure, but to displacement of the brain stalk downwards,

causing the medulla to be compressed against the margins of the foramen magnum. This accounts for the fact that unconsciousness comes on much earlier in cerebral than in cerebellar tumours, for the latter are much less liable to cause downward pressure. Medullary compression is indicated by a slow pulse and respiration, due to stimulation of the vital centres by the anæmia, but it may be noted that this classical stage is often preceded by a stage in which the heart rate is unduly rapid. Respiration is characteristically noisy or stertorous, from paralysis of the soft palate and mouth muscles, due to the effect of the compression on regions responsible for the control of these parts. As the higher parts of the brain cease to function, the respiration may show a prolonged inspiratory phase before the final gasping stage is reached.

General circulatory conditions which affect the amount of blood supplied to the carotids will seriously affect consciousness. Unconsciousness may be brought about by compression of the carotids, and this procedure was not infrequently practised prior to minor operations in pre-anæsthetic days. It is this fact, too, which makes accidental hanging possible. If an individual leans his head over a cord so as to compress the vessels he may become unconscious in that position and strangle himself. For this reason, too, the judicial garroting of Spain, death from cutting the throat, or from rapid strangulation may be looked upon as practically painless.

Similarly, if there be loss of blood, consciousness is eventually lost, but the loss of blood may be relative rather than actual. There may be an enlarged capacity of the vascular system, and the blood may become inadequate in amount "to go round." Thus, if the blood-vessels of the abdomen lose their tone, almost all the blood in the body accumulates there, and the individual faints. It is not, however, to be imagined that the loss of tone is confined to the abdominal vessels. The classical evidence which proves that other vessels are involved is that of John Hunter, who, when bleeding a man from an arm vein, noticed that the issuing blood suddenly became arterial in colour just before the patient fainted. In such instances, the actual **fainting** may be looked upon as a protective measure, for, by becoming unconscious, the individual abandons the upright position, and more blood passes to the head.

On general grounds, the method of production of a faint is of considerable interest and several facts in relation to the effect of

the higher centres on sensation may be significant in this respect. We know, for example, that quite a severe wound may be inflicted under conditions of emotional stress (as during a game of football) without our being aware of the infliction. If a strong stimulation is applied, we know that weaker stimulation in another part of the body is less readily felt.

We can understand, then, that there may be considerable diminution, for various reasons, in the extent to which afferent impulses are appreciated. It seems reasonable to believe that the vascular tone, which is maintained by the vasomotor centre, is really reflex in nature, and depends on the reception of afferent impulses. Under intense sensory or emotional stimulation there may be an " inhibition " of the sympathetic reflexes and consequent loss of tone of the centre. This view is supported by the fact that in unduly emotional individuals similar circumstances may bring about inhibition of other reflex centres, such as those controlling the sphincters.

Recently, Lewis has described such fainting as a vaso-vagal syndrome in which the vasodilatation is associated with cardiac slowing. How far these symptoms are due to increased parasympathetic stimulation and how far to sympathetic inhibition is not certain. Acapnia no doubt often contributes also (see " Shock ").

In some varieties of fainting pooling of the blood may take place as a result of heat opening up vessels in the skin and elsewhere. Fainting in a hot bath, which may have disastrous results, is of this nature, and it is well to warn individuals liable to faint, that on no account must the upright position be assumed if an attack of faintness is felt to be coming on, but that the water must be at once let out and, if possible, the cold tap turned on. Fainting in a hot room is an analogous condition. The emptying of an excessively full bladder has been known to cause similar syncope, as has also the too-sudden removal of a large quantity of fluid from an ascites or pleurisy, or the removal of a large abdominal tumour. In the last two instances, evil results may be guarded against by the use of a binder. If a pleuritic fluid extends above the angle of the scapula, all of it must not be drawn off at once. Here we have also to consider the pooling of the blood in the lung which has been temporarily out of use, and the acute dilatation of the heart and pericardium. Although syncope is usually evanescent, it may be fatal if the heart is insufficiently supplied with blood for any prolonged

period. In all such cases the general pallor so often seen is due to reflex constriction of skin vessels, by which the body makes every effort to maintain arterial pressure.

The **treatment of fainting** and faintness is indicated by the cause. The head must always be lowered, preferably below the level of the body. If the individual is actually unconscious it is well that some gentle pressure should be applied to the abdomen ; this may be done by causing him to lie face downwards.

Faintness, or " swimming of the head " of a very evanescent character, is seen in many conditions, and must be clearly differentiated from true vertigo, for the term " dizziness " is commonly applied to both conditions. In individuals with inelastic arteries, in whom the vasomotor response to the erect posture is necessarily sluggish, faintness on suddenly getting out of bed is a common symptom. Where the arterio-sclerosis is accompanied by aortic incompetence, such faintness is still more liable to occur, and is indeed one of the classical symptoms of aortic disease. Faintness on assuming the erect posture may, however, be experienced by approximately normal people if the change of position is very rapid. Especially is this so after an enforced rest in a recumbent position, as after an illness, when the vasomotor mechanisms have been unused for some time.

The Quality of the Blood.—It will, of course, be obvious that if the blood is incapable of carrying an adequate supply of oxygen, circulatory changes which would not normally cause unconsciousness may readily do so. Thus we see why individuals suffering from anæmia are especially liable to attacks of faintness. The oxygen-carrying power of blood depends on its hæmoglobin content. As pointed out by Haldane, this may readily be arrived at clinically, by a colorimetric estimation of the hæmoglobin content, using a Haldane hæmoglobinometer. The essential principle of this method is that the colour of the blood is compared with that of a standard (laked ox-blood saturated with carbon monoxide). The standard is of a fixed dilution, and the blood to be tested is laked, saturated with coal gas and diluted until the colours match. Should the blood require the same dilution as the ox-blood, the content is said to be normal or 100 per cent. If less dilution is necessary it is expressed as a percentage of normal, and *vice versâ*.

It is marvellous how the circulation can adapt itself even when, as in some of the severe anæmias, the hæmoglobin content of the

blood is reduced to under 30 per cent. of the normal. There is in such circumstances a great increase in the heart and circulatory rates, so that the mass of oxygen required per minute is thus supplied to the tissues. There is, of course, a tendency to syncope if the circulatory adaptation proves inadequate, as when exercise is attempted. That such anæmic patients are conscious at all is very striking, and emphasizes the fact that the actual mass of oxygen required by the brain is very small, and can be readily obtained provided the blood pressure is adequate.

The quality of the blood may also be seriously impaired, if there is present in the inspired air a gas for which hæmoglobin has a greater affinity than for oxygen, as, for example, carbon monoxide, a constituent of coal gas. There is, as a result of the formation of carbon monoxide hæmoglobin, a marked diminution in the amount of functional hæmoglobin, *i.e.*, hæmoglobin capable of transporting oxygen. Not only so, but the carbon monoxide interferes, as shown by J. B. S. Haldane, with the readiness of the oxyhæmoglobin to release its oxygen. There is, then, in gas-poisoning, a marked diminution in the mass of oxygen not only transported by the blood, but also given off to the tissues. The tendency to faintness and unconsciousness is very marked, although breathlessness is not evident because the arterial *plasma* is saturated with oxygen at the proper pressure, and therefore is capable of keeping up the necessary oxygen tension in the respiratory centre. It used to be taught that carbon monoxide hæmoglobin was a particularly stable compound. More recent work shows that dissociation of this compound of hæmoglobin will slowly occur, so that in the event of finding an individual unconscious from gas-poisoning, artificial respiration should at once be begun, if breathing has ceased, as soon as the individual can be removed from the poisonous atmosphere. So long as the heart has not actually stopped there is a chance of recovery.

The opposite state of affairs occurs in ascent to high altitudes. The blood is no longer adequately oxygenated in the alveoli, for the partial pressure of the oxygen inspired is diminished, and for the same reason the respiratory centre no longer receives blood plasma supplied with oxygen at sufficient pressure. The centre therefore becomes increasingly sensitive to carbon dioxide, and breathlessness becomes marked although consciousness is not appreciably affected. On proceeding still higher, or after exercise in such circumstances, the mass of oxygen supplied to the brain

becomes inadequate, and unconsciousness results as in exertion in anæmic states.

A similar result is produced in the unconsciousness of asphyxia, where there is interference with the replacement of the alveolar air, or where the air breathed does not contain its proper constituents. Here, however, the accumulation of carbon dioxide brings about the characteristic respiratory distress which precedes the unconsciousness.

Elimination of Toxic Products.—The normal products of tissue metabolism if allowed to accumulate in the body in conditions of defective excretion by the kidneys may eventually produce unconsciousness such as is found in advanced obstructive anuria ; a similar result may be brought about by the ingestion of toxic substances such as alcohol or by the production of abnormal metabolic products in the tissues as in diabetes. In nephritis the cause of the coma and other manifestations of uræmia is far from clear (*vide infra*). Treatment in such circumstances aims at the elimination of the toxic products. Bleeding the patient, and the substitution of a large amount of intravenous saline for the removed blood, may resuscitate a patient unconscious from uræmia. Every effort should be made to activate the bowel, even if it is not the organ primarily at fault. A drop of croton oil [1] placed on the back of the tongue is most efficacious in this respect. In diabetes, insulin therapy is urgently called for, and the patient may recover. Cases of liver atrophy, however, are hopeless from the first. Recent work on uræmia has emphasized the importance of reducing the pressure of the cerebro-spinal fluid, the withdrawal of which brings about a great amelioration of the symptoms, especially the distressing dyspnœa. It is now fairly certain that uræmia is not always due to an acidosis, as was first supposed, but may, in part at least, result from cerebral œdema. Urea is probably not a factor in the production of uræmia; toxic influences are undoubtedly at work in many cases, but whether excessive retention of normal products or the accumulation of abnormal substances is responsible is uncertain. There are probably different causes in different cases.

Toxic products ingested by the mouth have to be dealt with similarly. Alcohol must be removed from the alimentary canal, and its excretion by the skin hastened by keeping the patient warm. Poisoning by other drugs and toxins calls for

[1] The small amount of croton oil should be dissolved in butter before it is administered, to avoid blistering of the tongue.

action according to the danger of failure of respiration or circulation.

Coma.—From a consideration of the foregoing discussion it will be seen that, clinically, profound and often prolonged total unconsciousness or coma may result from several causes of which the following are the most important: epilepsy, head injuries, cerebral vascular lesions, uræmia, diabetic coma and poisons, such as opium, veronal and coal gas. Alcohol is chiefly of importance in confusing the diagnosis. A comatose patient who smells of alcohol may be profoundly drunk, or, what is a more likely occurrence, may have taken alcohol to relieve faintness prior to loss of consciousness. Stupor is a term applied to partial loss of consciousness, the patient being still rousable, and often lapses into coma. Whether a transient total loss of consciousness, such as occurs in fainting, should be called coma, is a matter of discussion.

CHAPTER III

DELIRIUM

DELIRIUM is a state of mental confusion due to disorder, usually toxic in origin, of the higher levels of cerebral function. We do not call mental confusion delirium unless it is associated with certain phenomena, viz., the "elation" and "excitement" of psychiatric terminology.[1] Of the three chief modes of consciousness, the cognitive (perception) is specially disturbed, and the patient is disoriented in space and time. He has, moreover, no clear idea of his own identity. As Yellowlees pertinently says, the consciousness is clouded. Externally received sensory stimuli are ineffective or else give rise to illusions. The mind is left to the influence of irregularly released memories of past experiences which furnish an imaginary world, and delusions result. The delusions are so unstable and fleeting that they hardly justify their name, and hallucinations of the special senses are present, from overaction of the visuo-psychic and psycho-auditory spheres. Affective tone (feeling) and conation (will) are usually in abeyance, the patient being content to exteriorize his mental state in fragmentary speech (*cf.* the low muttering delirium of typhoid fever), or he may be noisy and restless. Occasionally, however, the delusions give rise to a severe emotional reaction, as in delirium tremens, in which the visions of uncouth animals, etc., afflict the sufferer with a deep sense of horror and he repeatedly tries to get out of bed to avoid them. Signs of intoxication—dry tongue and lips, fever, etc.—are usually present in delirium, and incontinence occurs. In the severe form of delirium known as acute delirious mania or acute confusional insanity, which may be due to a recognizable specific fever or arise without a *known* infection being present, the patient is completely sleepless and the temperature is high. Disorientation is complete, the hallucinations are terrifying and very impulsive behaviour may result. Post-mortem, a meningo-encephalitis may be present. Should the patient recover, exhaustion is more profound than that

[1] The reader should consult Yellowlees' "Clinical Lectures on Psychological Medicine."

following less severe grades of delirium, and for a time he may lie stuporose. Mental confusion is to be carefully distinguished from true mania. In mania the patient is not disoriented, and his perception of his environment is abnormally acute. The mental processes are actually too rapid to be effective, and in this way the aimless restlessness results. Ophelia in *Hamlet* is an example of mania. In motor delirium, a condition well seen in belladonna poisoning, the motor cortex is unduly excitable and the patient's thoughts tend to be translated into action. For example, if the patient is dreaming of hunting he may imitate the speech and movements of a rider to hounds.

Clinically, delirium is easily recognized, and from the diagnostic aspect falls naturally under two heads according as to whether fever is present or absent. Pyrexia itself seems potent to cause, or at least facilitate, the occurrence of delirium, as in sunstroke. Febrile delirium is commonly due to the toxins of infection, particularly those of acute specific fevers, *e.g.*, scarlet fever, typhoid, mumps, pneumonia. In delirious pneumonia the inflammation is usually in the upper part of the lung (apical pneumonia), and, further, it may be remarked that both apical pneumonia and mumps are in certain cases complicated by true meningitis, suppurative in the former case. In mumps, even in the absence of meningitis a lymphocytosis is often present in the cerebro-spinal fluid. In certain other infections there is also a recognizable factor which determines the onset of cerebral symptoms. Thus in cerebral malaria the parasites are most numerous in the cerebral capillaries, and in erysipelas delirium is specially likely to ensue when the scalp is involved. Of intracranial diseases, encephalitis and meningitis may be mentioned.

In most diseases headache disappears when delirium begins, but in meningitis the headache persists. The stimulus is so intense and persistent that even in his confusion the patient cannot escape it, and may even cry out with pain, particularly if he is a child (*cf.* the hydrocephalic cry of tuberculous meningitis). The physical signs of meningitis, such as head retraction and the tonic contraction of the hamstrings tested for in the elicitation of Kernig's sign, can be regarded as due to a reflex (? protective) from the inflamed membranes. These signs are also present when meningeal irritation without gross inflammation is present, a condition known as meningismus. Examination of the cerebro-spinal fluid readily differentiates the milder from the graver condition.

Various drugs, hyoscine, atropine, alcohol, can cause delirium. Fever is usually absent, although a mild degree may be present in belladonna poisoning. When the cortical neurones have been long accustomed to the action of a drug, such as morphia, sudden withdrawal of the drug may result in delirium. Similarly, it is believed that sudden withdrawal of alcohol from a chronic drinker is an important factor in the genesis of delirium tremens.

In acute necrosis of the liver, delirium is apparently due to the action of substances normally rendered innocuous (detoxified) by that organ and to hypoglycæmia. In uræmia the nature of the toxin is unknown ; cerebral œdema is often present.

" Cardiac " delirium occurs in congestive heart failure, and is probably due to slowing of the cerebral circulation and œdema of the brain.

Delirium may follow mental trauma, *e.g.*, the terrifying experience of modern warfare. In such a case instability of the nervous system is postulated as the predisposing factor.

It may be considered the aim of psychopathologists to relate the symptoms of the psychoses to lesions of the cerebrum, but apart from certain well-known instances, such as idiocy, general paralysis, senile dementia, tumours of the pre-frontal region and the toxic psychoses, considerable uncertainty exists as to whether there are definite anatomical or histological changes in, or a definite toxic affection of, the brain in cases of mental disease. It seems likely, however, as Yellowlees points out, that the major psychoses, viz., dementia præcox, paranoia and manic depressive insanity, are without anatomical and patho-physiological basis in any known sense of these terms. Much less, beyond the single factor of hereditary predisposition, is known of their pathogenesis than of that of the psychoneuroses, such as hysteria. The latter can at least be understood in terms of psychological mechanisms, *i.e.*, they have a psychopathology in the purest sense of the word, although their relation to physiology is such that, in terms of our present knowledge, physiological changes when present are secondary to the psychological disturbance (see Chapter XLVIII.)

CHAPTER IV

VOLUNTARY MOVEMENT

In this chapter is considered the movement made by a striped muscle as the result of an effort of will, and which has paralysis as a pathological corollary. For such movement to take place, it is evident that the nervous pathway must be intact, that the effector muscle or muscles must be able to contract, and usually that the bones and joints must be capable of being moved.

Nervous Pathway.—All striped muscles, other than those supplied by the cranial nerves, are controlled by motor fibres which have their origin in the cells of the anterior horn of the spinal cord. Each anterior horn cell supplies approximately 150 muscle fibres. These cells are affected by a large variety of stimuli. They may, for example, be stimulated reflexly, but, especially for our present consideration, they may be affected by impulses reaching them from the brain by way of the pyramidal tracts, for it is along these paths that the voluntary impulses pass. In effecting a response through the anterior horn cell, the pyramidal tract competes for the possession of the lower motor neurone with the afferent limb of the reflex arc and with other pathways. Sherrington has termed this arrangement the principle of the final common path. The principle is well seen in the case of the thoracic muscles of respiration which are controlled by the cells of the anterior horn in the spinal segments of the thoracic and cervical regions. These cells are controlled by the pyramidal tract, as is shown by the fact that we can breathe temporarily in a voluntary manner ; and also by motor fibres apparently from the respiratory centre by which breathing is kept up involuntarily. Where there is some form of dual control, there must also be some mechanism for deciding priority. It has been established that the impulse which is most important for the preservation of the animal is always given priority in the final common path. Thus we may voluntarily inhibit the cells controlling the respiratory muscles, but we cannot asphyxiate ourselves voluntarily, as eventually the stimulus from the respiratory centre gains priority over the voluntary impulses, and we are obliged to breathe involuntarily.

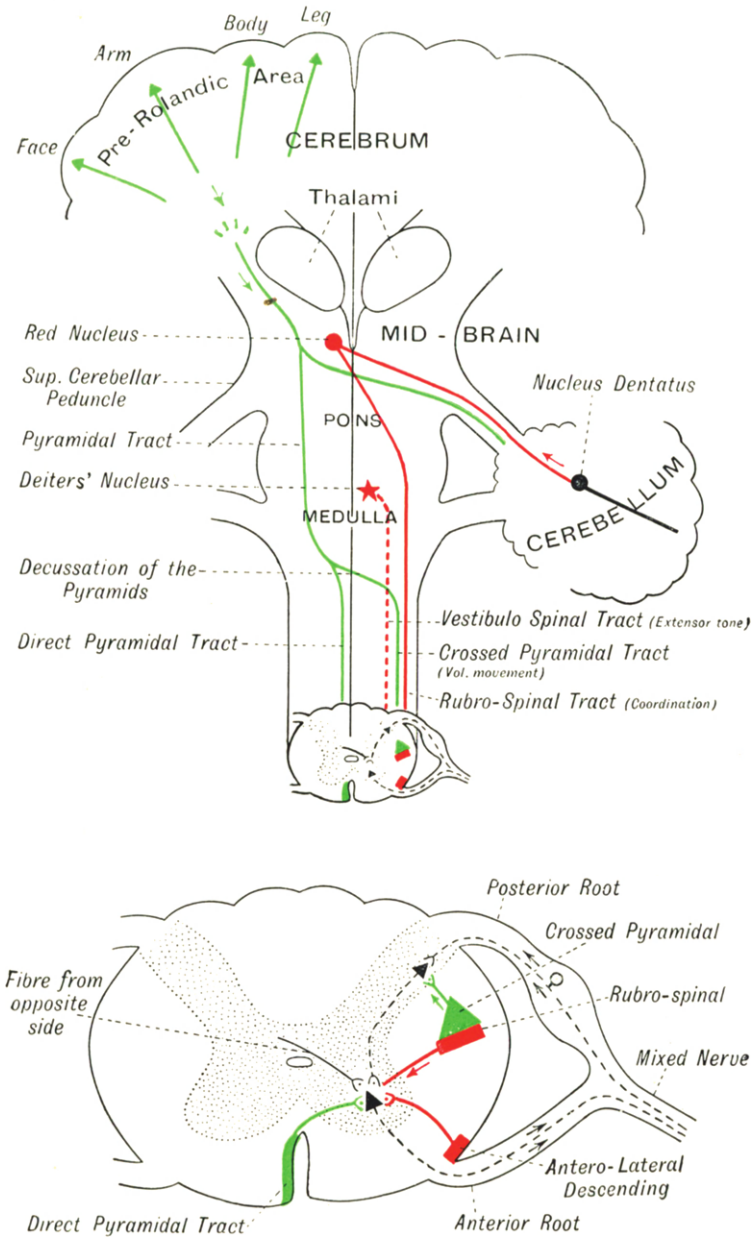


FIG. 1.—THE EFFERENT PATHS OF THE CENTRAL NERVOUS SYSTEM.

Facing p. 17.]

The pyramidal tract arises in the giant cells of Betz in the motor area of the cerebrum, situated in the ascending convolution immediately in front of the fissure of Rolando. Thence it passes through the corona radiata and internal capsule in the cerebrum, mid-brain and pons to the medulla, where it crosses (for the most part) to the other side at the decussation of the pyramids. During its passage through the brain stem the tract gives off branches to the motor nuclei of the cranial nerves of the opposite side. From the medulla it is continued downwards in the lateral column of the spinal cord, and gives off branches to the anterior horn cells of the various spinal segments through which it passes.[1] The neurone composed of a Betz cell and its axon was described by Wyllie as the upper motor neurone, as distinct from the lower motor neurone, which consists of a cell of the anterior horn of the spinal cord with its axon to the muscle.

There is, in addition, a subsidiary tract, known as the direct pyramidal tract, which does not cross in the medulla but passes down the spinal cord in its anterior and medial aspects. The fibres cross to the other side at intervals to end round anterior horn cells.

These tracts have been made out by studying the spinal cord at different stages in its development, and noting the different times at which the various groups of fibres have developed their myelin sheaths. More detailed information has been obtained by section of the tracts at different levels, and subsequent study of the differential staining of the areas which have become degenerated. The motor fibres which have been cut off from their parent cells degenerate distally.

Any interference with the motor pathway, either in the upper or lower motor neurone, must result in paralysis. Paralysis of the lower motor neurone occurs most commonly, other than from polyneuritis, injury, or neoplasm, in the condition of acute anterior poliomyelitis or in the more chronic state of progressive muscular atrophy, in both of which there is degeneration of the cells of the anterior horn. Lesions of the upper motor neurone may occur at any level throughout its course. It will be noted that any interference with the tracts below the level of the decussation in the medulla will bring about paralysis on the same side of the body, while if the interference is above that level the paralysis will be on the other side of the body. Thus, in pontine lesions, although

[1] Strictly, the pyramidal fibres end round the posterior horn cells of the spina grey matter from which intermediary neurones axons reach the anterior horn cells.

the face is paralysed on the same side as the lesion the limbs are affected on the opposite side. A similar though rarer form of crossed paralysis may occur if the lesion is in the region of the crus cerebri, and here the paralysed oculomotor nerve is on the same side as the lesion, the face, arm and leg on the opposite side.

One of the commonest forms of injury to the pyramidal tract is seen in apoplexy, in which the tract is pressed upon by hæmorrhage in the region of the internal capsule. This is commonly the result of rupture of the lenticulostriate artery (a branch of the middle cerebral), whose walls obtain little support from the surrounding nervous tissue in this region. If

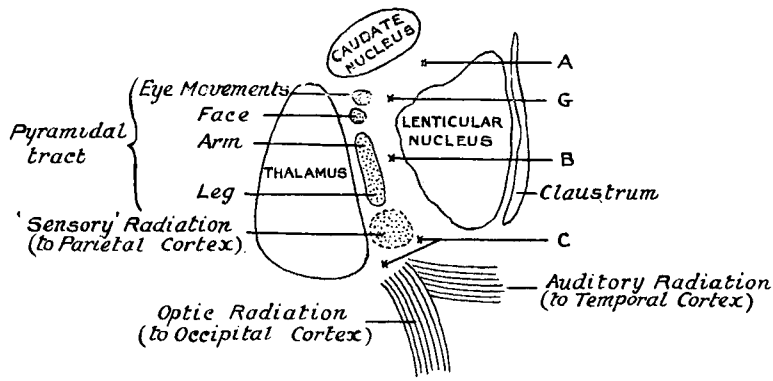


Fig. 2.—Diagram of the Internal Capsule (modified from Elliott Smith). The Right Internal Capsule is represented in horizontal section.
A. Anterior Limb of Capsule.
G. Genu.
B and C. Lenticular and Post-lenticular parts respectively of Posterior Limb.

the hæmorrhage is not enough to raise the cerebral pressure sufficiently to paralyse the vital centres in the medulla, then, when the clot contracts and the individual recovers consciousness, the interference with the path of the voluntary impulses becomes evident.[1] The degree to which the paralysis may affect the fibres in the different areas depends on the anatomical arrangements of the internal capsule and the size of the hæmorrhage. The fibres for the face which pass down from the lower part of the Rolandic area lie anteriorly, and are therefore most liable to be pressed upon (and next come those of the arms, see diagram). Thus a small hæmorrhage may leave little permanent effect other than some slight interference with facial movements or speech.

[1] Many of the non-fatal cases of apoplexy, formerly regarded as instances of hæmorrhage, are now considered to be cases of thrombosis.

The effect of lesions of the motor cortex depends on the exact part of the area affected. As the result of extirpation, electrical stimulation and disease, it has been shown that the region is strictly limited, as already noted, to the convolution immediately in front of the fissure of Rolando. The area for the leg is uppermost and most mesial, while, in order downwards, come the areas for the body, arms and face. It is to be noted, too, that the area concerned with arm movements is very large compared with that for the body. This is not surprising when we compare the many complicated movements which the arm carries out with

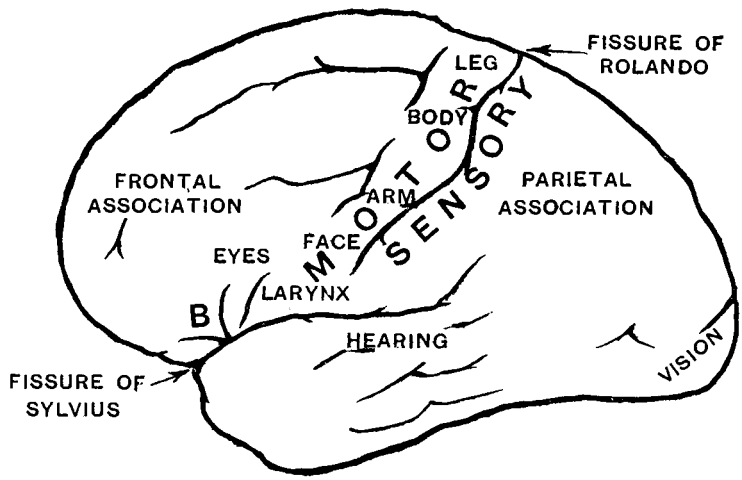


FIG. 3.—Diagram indicating the chief functions of the Cerebral Cortex.

the more limited body movements. The anatomical sequence in which these areas occur is of importance in relation to the blood supply, a branch of the middle cerebral artery which passes upwards in the fissure of Rolando. This artery, like most of the cortical arteries, is terminal : that is, it does not anastomose with others. Any condition of blockage, due to embolism or thrombosis, is liable then to shut off the blood supply completely from certain areas, and is more likely to affect the artery towards its termination. Thus we may get paralysis of the legs only, although at first quite commonly the lesion is more widespread. Again, the clot may block any of the branches of the artery in this region, and the area paralysed will be strictly localized. Apparently the area responsible for the motor action in relation to speech is unilateral. It is situated on the left side in right-

handed persons, in the inferior frontal convolution, and is known as Broca's area. This is dealt with further under "Aphasia" (page 90), which we now know to be a less simple condition than was formerly thought. On the other hand, movements of the trunk are seldom markedly affected. It would seem that these have a bilateral representation in the cortex. In embolism the source of the embolus is usually evident, and is generally the left auricular appendage in mitral stenosis, or the friable vegetations of ulcerative endocarditis. Clots from the venous side are more likely to be held up in the lung. In thrombosis, in which there is local clotting from disease of the vessels, the result of syphilitic or atheromatous changes in the wall or pressure from without, the onset is often more gradual than in embolism. The effect in the brain tissue is an infarct which soon softens. Extensive cerebral thrombosis with mental impairment is commonly called "softening of the brain." As would be expected from the nature of the lesion, in embolism and thrombosis (where localized) there is not necessarily any great interference with the blood supply of the cerebrum as a whole, and consciousness is not always lost.

For convenience it is desirable to consider motor movement as starting in the Betz cells, but it will, of course, be realized that this is but an arbitrary point of commencement. The stimulus which results in motor movement reaches the Betz cells from some other area of the brain. It may be held that no movement can occur except as the result of a stimulus from the outside world, usually immediate, but remote in the case of stimuli, such as pain, arising within the body itself. As Noël Paton has pointed out: "It is unnecessary and gratuitous to invoke the conception of automatic action on the part of any parts of the central nervous system."

Kinnier Wilson emphasizes the possible importance of the frontal lobes as constituting a higher motor area, and points out the many association fibres which connect them with the thalami. He suggests that, since the movements of chorea are obviously of a higher type than those of Jacksonian epilepsy, the source of the former may possibly be in this physiologically superior motor area.

We must also consider what are known as the *extra-pyramidal tracts*, that is, motor tracts other than the pyramidal, which affect the movement of ordinary voluntary muscle. We shall see later that when the cerebrum is removed the muscles pass

into a state of excessive tone, the result of impulses passing down from the region of the brain-stem. We shall also see that the postural reflexes do not depend on the cerebrum, but on the existence of an arc through the mid-brain, pons and upper part of the medulla. It is obvious that there must be a motor path which can be activated from the region of the mid-brain. The best known extra-pyramidal tracts are the rubro-spinal from the red nucleus in the mid-brain, and the vestibulo-spinal from Deiters' nucleus in the medulla. The efferent impulses concerned in the co-ordination of voluntary movements and in the reflexes of posture pass down these paths. More and more evidence has accumulated that many of the primitive movements of voluntary muscle are not solely controlled by the pyramidal tract. Thus we find that, in conditions in which there is complete loss of voluntary power of a limb, yet its muscles will still respond to some of the primitive movements associated with posture, such as standing and walking. It is said that very young children can move their limbs before the pyramidal tracts are functional. How far this may be due to reflex action at a lower level is difficult to say. Further, evidence has been brought forward by Graham Brown, showing that stimulation of the red nucleus brings about purposive movement, such as that of walking. The fact that in lower animals, such as fishes, the optic thalamus is a motor as well as a sensory area, further emphasizes this possibility. In lenticular degeneration, increased tone is a marked feature, while the facial expression, which is one suggesting chronic laughter, may reasonably be considered as an exaggeration of a primitive movement. More recently the condition of paralysis agitans has been described by Ramsay Hunt as being due to degeneration in this region, especially in the globus pallidus of the lenticular nucleus. In this instance there is loss of the primitive auxiliary movement, such as that of the arms in walking. Interference with the postural reflexes in walking brings about the characteristic festination, in which the individual is described as chasing his centre of gravity. This worker goes on to suggest that the impulses passing down from the basal ganglia do not use the final common path, but follow a separate path throughout to the muscle. So far, however, the attractiveness of the possibility is its chief claim for notice, since our knowledge of this subject is still in its infancy. Kinnier Wilson remarks that it is ridiculous to assume that such a simple histological structure as is found in the corpus striatum could be responsible

for the vast number of functions which have recently been attributed to it. He puts forward much evidence to show that many of the oft-quoted signs and symptoms of striatal disease may readily be due to disorder in other parts of the brain. It is one of the subjects on which accurate clinical observation, together with detailed post-mortem examination of the tissues possibly concerned, may throw much light.

The Muscles.—In voluntary movement the muscles are seldom, except in actual injury or in rare conditions, the primary cause of paralysis. In the muscular dystrophies, however, for no apparent reason, the muscles, especially certain groups, degenerate. In pseudo-hypertrophic paralysis the muscles although degenerated may appear large because of the deposition of fat which eventually replaces the fibres. In this condition the paralysis occurs in early life, is slow in onset, and is therefore readily distinguished from the more rapid acute poliomyelitis. Further, in dystrophies the reflexes are not affected until the disease is sufficiently advanced to affect muscle tone ; nor is there a reaction of degeneration. Why certain muscles, *e.g.*, the shoulder girdle and upper arm in Erb's type, or the face and later the shoulder and arm in the Landouzy-Déjerine type, are affected, is as yet unexplained. The muscular dystrophies are differentiated clinically from progressive muscular atrophy, not only by the distribution of the wasting, but also by the absence of the fine fibrillary twitchings which are so frequent a feature in progressive muscular atrophy. The twitchings which are generally a sign of slow death, one by one, of the anterior horn cells, also occur in syringomyelia, when the disease invades the anterior horn. They may, however, occur when the peripheral nerves are irritated by inflammation of their sheaths, as in sciatica. They must be carefully distinguished from the coarse twitchings of fatigue, neurasthenia and enteritis.

The muscles, however, may be at fault secondarily if the motor path is interfered with, since in such circumstances the muscles supplied may degenerate or may not develop. In the latter instance the bones also fail to grow properly, no doubt partly because they are not used. This condition is seen in meningeal hæmorrhage which causes the more usual " birth palsies."

More generally, degeneration occurs as a result of disease of the spinal cord or of injury to the spinal nerves, and such degeneration may be of importance in estimating prospects of

recovery. When a muscle degenerates, there is first a brief period of increased excitability to all forms of direct stimulation. This is followed by a period in which the muscle shows a marked reduction of excitability or increased chronaxie (Lapicque). As a result of this change the muscle does not respond to currents of short duration. It therefore no longer responds to a faradic (rapidly alternating current such as produced by an ordinary transformer or induction coil), but it will respond to a galvanic stimulus, even to a weaker current than on the healthy side, although it reacts more sluggishly. Further, in degenerate muscle the contraction obtained is greater when the circuit is made and the anode is on the affected muscle (A.C.C.), while a stronger current is necessary if the kathode is on the muscle (K.C.C.).[1] This condition of affairs is the reverse of that found in healthy muscle, where K.C.C. is greater than A.C.C. It is, however, generally admitted that these reactions are often far from clear and they merge gradually into a condition in which the muscles fail to respond to any stimulus.

The muscle may become the seat of spasm and rigidity, which occur when there is a lesion of the upper motor neurone with exaggerated reflexes and increased tone. On the other hand, when the lower motor neurone is destroyed, the muscle is quite flaccid and toneless, and this, like the state of the reflexes, assists in the determination of the site of a lesion causing a paralysis or loss of muscular movement. The condition of the muscle also necessarily affects the position of the limbs. Thus, after an anterior poliomyelitis the affected limb is loose and flail-like, as is commonly also found after neuritis, which may bring about dropped-wrist or dropped-foot. On the other hand, the rigid limbs of a spastic paraplegia are also characteristic and, when affecting the leg, lead to a typical spastic gait.

Bones and Joints.—It is obvious that in order to perform the majority of muscular movements it is necessary that the bones and joints themselves should be acting properly, a fact which can be tested as a rule by passive movement. If this is forgotten, a congenital dislocation of the hip may easily be mistaken for some sort of paralysis, or a patient with an ankylosed knee may unwittingly be requested to flex the knee joint.

Finally, voluntary movement may be appreciably affected by pain, but this is usually made clear by the patient.

[1] The anode is the positive pole and the kathode the negative pole. A.C.C. is anodal closing contraction, and K.C.C. is kathodal closing contraction.

Hysterical Paralysis offers a strange and, as yet, an inexplicable problem. The individual is convinced that *she* (for the condition is usually met with in women) cannot make certain movements and she simply does not make them. There may be complete trance or the condition may be local. For example, she may be unable to speak, yet may be capable of saying "Ah" if a show is made of inspecting the larynx. Again, she may claim that she has lost the power of moving her eyes, so that when she looks about she has to move her whole head. The paralysis is quite genuine and is maintained, even though the patient does not know she is under observation. Yet, if she is asked to maintain a fixed gaze on an object, she can do so while the head is moved, which indicates that there is no paralysis of the ocular muscles except in her mentality. Cure by persuasion, suggestion, or trickery, which often requires a very keen wit, is usually possible. Such paralysis must clearly be distinguished from organic paralysis which is usually accompanied by either wasting or spasticity and a typical change in the reflexes. Functional paralysis is also important, in that it may be grafted upon a real organic paralysis. Indeed, it is commonly so. This is often seen, for example, in disseminated sclerosis, which is almost invariably improved by a short stay in hospital without any treatment, but when the functional impairment is removed the progressive organic impairment still remains.

Hysterical disturbance may, on the other hand, take the form of a contracture of a limb or, in the case of the abdomen, may have the appearance of a phantom tumour. It may also be convulsive and simulate epilepsy, but is distinguished from the latter by the fact that it is usually purposive, and the patient never hurts herself. It must, however, be realized that these patients are not feigning; they suffer from a genuine mental disturbance which is not dependent, so far as we know, on any pathological change in tissue, but has rather an emotional basis. The sensory aspect of the condition is dealt with later.

The Movements of the Face.—Although these movements are in no wise different from other muscular movements in so far as they depend on the functional efficiency of certain muscles and nerves, they have a special importance in relation to medicine and surgery, in that they are largely responsible for the expression of the individual and are often influenced by general and nervous lesions.

We are all familiar with the extent to which the expression

may be " the tablet of unutterable thought " (Byron), although we are at the same time fully aware how often it may be far from an index of the feelings in those accustomed to conceal their emotions. Usually, however, the habitual expression of an individual does give a general idea of his outlook on life. The melancholic and the hypochondriac often proclaim themselves by their expressions, as do the self-satisfied beings of this world. Pain, fear, and anxiety each has its facies more difficult to describe than to appreciate.

The eyes may be largely responsible for an expression, and this is well seen in the surprised or fearful aspect of exophthalmic goitre. Any sympathetic stimulation, such as fear, brings about dilated pupils, widened palpebral fissures, and a similar expression. But in exophthalmic goitre there is a definite exophthalmos, the exact cause of which is not quite clear. It is commonly said to be due to the contraction of Muller's muscle at the back of the orbit. In animals exophthalmos may be produced by the injection of ephedrine, the great sympathetic stimulant. The fact that recovery from hyperthyroidism may not result in recovery from the exophthalmos however, suggests a more permanent cause.

The part played by the tone of the muscles of the face is made evident by its absence at death, or its approach. The so-called facies Hippocratica, first described by the Father of Medicine, in which the face is hollow, the eyes glazed and sunken, and the jaw dropped, is commonest in acute general peritonitis, cholera and at the end of wasting diseases where the patient dies of exhaustion. Dehydration is probably as important as loss of muscle tone in the production of the Hippocratic facies. The expression, on the other hand, will be affected by excessive muscle tone, as in tetanus, where the corners of the mouth are drawn up, and produce the risus sardonicus or fixed sarcastic aspect. Every attempt to open the mouth is accompanied by a contraction, instead of the normal inhibition, of the more powerful muscles which close it.

The normal tone of the facial muscles depends on the facial nerve, and the exact path of the sensory side of the arc presents an interesting anatomical and physiological problem, for it is to be presumed that the tone of these muscles, like that of others, has a reflex arc. The fifth nerve, which is sensory to the face, would be an obvious path, but excision of the Gasserian ganglion does not usually appear to interfere with facial tone nor with deep pressure sensation.

It would seem, therefore, probable, that sensory impulses from

the facial muscles pass centrally by way of the facial nerve, although this nerve is not usually considered to be sensory except in so far as the chorda tympani is concerned. The geniculate ganglion on the facial nerve appears to contain the parent cells not only of taste fibres but also of the sensory fibres from the facial muscles. That such fibres exist has been shown by Wakeley and Edgeworth, who find that after section of the facial nerve proximal to the ganglion, 7 per cent of the fibres contained in the nerve at the stylomastoid foramen fail to degenerate.

The tone of the facial muscles is profoundly altered, not only by lesions of the facial nerve, but also by lesions at or above its nucleus and of the motor area of the cerebral cortex responsible for facial movement. Should the whole facial nerve be involved, outside the skull, as it may be from neuritis (due to exposure to cold), or in the aqueduct of Fallopius (commonly as an extension from middle ear disease), or, more rarely, between this point and the nucleus, typical Bell's paralysis is seen in which the muscles of the whole of one side of the face are immobile and toneless. At first, the healthy muscle pulls away the skin from the affected side, but later, should contracture of the affected muscle set in, it produces the stronger pull. The diagnosis of the site of the lesion depends on the associated symptoms, especially those affecting hearing and taste. Taste is involved only when the facial nerve is affected at the part where it is accompanied by the chorda tympani—for practical purposes in the aqueduct. Hearing may be reduced by disease in the ear, or, if the auditory apparatus is not otherwise affected, hearing may actually become more acute for low tones, from paralysis of the stapedius muscle, which is supplied by the facial nerve as it passes through the bone.

Lesions affecting the tract between the cortex and the nucleus of the seventh nerve, the so-called supra-nuclear lesions, are commonly seen in hemiplegia. In this instance the upper part of the face escapes, and the patient can close his eyes. This may be taken to indicate either that the pyramidal fibres concerned with the upper part of the face are supplied from both sides of the cortex, or else that they are indirectly supplied to the facial nucleus *via* the oculomotor nucleus and posterior longitudinal bundle. A crossed paralysis is not infrequently seen when the lesion is in the pons, and affects the fibres to the seventh nerve nucleus after they have crossed. At this point the pyramidal fibres to the limbs have not yet crossed. Hence the limb paralysis is on the opposite side to that of the face.

Emotional expression, however, persists on the affected side, and may even be present in an exaggerated form. It is suggested (Spencer) that there exists an emotional pathway (cortico-thalamo-mesencephalic) from the cortex to the facial-respiratory nuclei which bring about crying and laughing. Normally this system is, as we know, only partially under voluntary control which is lost in extensive bilateral pyramidal injuries, when the patient may laugh or cry on the slightest provocation. Such an individual, unable to move his face voluntarily, may laugh immoderately at his being unable to do so.

Some neurologists believe that the corpus striatum and the substantia nigra are also related to emotional expression. In paralysis agitans in which lesions are found in these regions the face wears an expressionless mask, described by some as a reptilian stare. The individual has not really lost the power of expression. He can laugh or cry, but he does not easily pass from one expression to another. The condition is, according to Wilson, a general one in which there is a reduction of all unnecessary movements on the part of the patients.

The expression of the face in progressive lenticular degeneration is one which suggests chronic laughter, but how this is produced is not clear.

The tone of the muscles which move the jaw and which are to some extent responsible for the symmetry of the face, depends on the motor division of the fifth nerve, which, if damaged, leads to paralysis of the masseters and pterygoids. The result of this is that if the mouth is open, the jaw is pushed over to the diseased side by the healthy muscles of the other. There is also loss of perception of the high notes in hearing, from paralysis of the tensor tympani.

The Nature of Voluntary Paralysis.—The persistence of emotional expression in facial paralysis emphasizes the fact, pointed out by Farquhar Buzzard, that voluntary paralysis when due to a pyramidal lesion is essentially a paralysis of movement but not of muscle. A hemiplegic patient may, for example, be unable to lift his arm voluntarily, but when he yawns the arm may rise, indicating that the lower motor neurones concerned with the arm movements may still be thrown into action by impulses which reach them by tracts other than the voluntary tracts which are thrown out of action. We shall see later that when, in similar circumstances, the power to make a spoken reply to a question is lost, automatic speech such as an exclamation may still be possible.

CHAPTER V

SENSATION

ALL sensations of whatever kind are in the first instance received by receptor organs adapted for the variety of stimulus they are intended to receive. The receptors which exist in the so-called special sense organs such as the eye, are but nerve endings of a highly specialized kind. We have, for example, quite definitely, a number of organs which respond to vibrations in the air and the ether. Some waves we appreciate as sound by the auditory apparatus ; the spectrum we appreciate as various colours by our visual apparatus, the longer infra-red waves we appreciate as heat. The very short rays, on the other hand, we cannot appreciate directly, although (as many X-ray workers know to their cost) we may become aware of their effects later. Whether all kinds of sensation will some day be shown to be due to vibrations, possibly intra-molecular, forms a most fascinating speculation, more within the realms of modern physics and chemistry, however, than of physiology.

When we remember that each nerve fibre is apparently insulated from the other, it is easy to see that direct excitation of the fibre requires a strong stimulus—as pointed out by Bayliss, the sense of touch may be brought about by a stimulus which would not be sufficient to stimulate the trunk of a nerve. The essential function, then, of special nerve endings is to produce an impulse by a degree of excitation which would not otherwise be effective. It seems probable that all the sensory nerve endings which exist in the skin have a specific function, but our knowledge is as yet not very accurate on this point.

In the skin we have the sensations of touch, pain, heat and cold. The sense of pressure depends on the deeper structures, and, like muscle sense, is served by the muscular, rather than by the cutaneous nerves. The cutaneous sensations of man have been made a subject of special study in the Clinical Institute at St. Andrews, where it has been shown by Herring and Waterston that the heat and cold spots (long known to exist) fluctuate, that is, the exact situations of the spots vary as if to give certain

regions a rest. This fluctuation may be related to the formation of certain rashes and blotches. As yet, however, it has not been ascertained on what special nerve endings these sensations depend. Touch is known to be dependent to a large extent on Meissner's corpuscles, which are found especially in the palmar surface of the fingers. But apart from this little definite is known.

The sense of pain is of special clinical interest. How far it depends on special nerve endings has been a matter of some discussion. Von Frey described separate pain spots like those for heat and cold, while in some areas, *e.g.*, the cornea, pain is practically the only sensation experienced. Further, Head, Rivers, and later Stopford, have put forward evidence that pain is phylogenetically more primitive, distinct from touch and intimately connected with the protection of the animal. Ransom has claimed that the pain fibres may be non-medullated. The view that pain has special receptors is still further supported by the fact, discovered by Adrian, that the currents of action set up by stimulation calculated to be painful (*i.e.*, the sticking of a needle into the pad of the foot of an anæsthetized cat) are not excessive in frequency. If pain was due to excessive stimulation of various nerve endings it might be expected that painful stimuli would set up currents of action much greater in frequency than do non-painful stimuli. One characteristic, however, of pain is that a certain minimum degree of stimulation is necessary before it is produced, and Adrian suggests that some of the naked axis cylinders which act as pain receptors may also serve for signalling milder forms of stimulation which do not give rise to pain.

It must, however, be agreed that these conclusions are by no means final. Why excessive heat or cold, if they do not cause pain by excessive stimulation of heat and cold spots, should produce pain is unexplained, unless extremes of temperature stimulate the pain spots. Herring also has pointed out that it would not be reasonable to assume that structures like the ureter and other viscera are provided with special receptors and special nerve fibres to meet a pathological event which may not occur for a generation. It may be that the mechanism of the production of pain is different in the internal organs and in the skin.

The study of impulses set up by sensory stimulation was investigated by Holmgren in 1866, and subsequently by Einthoven, Gotch, and Waller; of recent years the work has been greatly extended by the use of wireless valves and a modern rapidly recording oscillometer, especially by Adrian and Mathews

who have shown each stimulus sets up not isolated impulses but bursts or groups of impulses. As shown by Gotch in relation to the retina, Adrian has found that sensory end organs rapidly become adapted to certain stimuli which then cease to be effective. At first there is a rapid discharge of impulses from the end organ, but the rate gradually falls off. This falling off is, however, less marked in the nerve endings of muscle which appear to be specially designed to send out a regular series of discharges over a longer period of time than ordinary sense organs.

Closely allied to adaptation is the degree of stimulation necessary to evoke a sensation. It can readily be shown that this is proportional to the previous degree of stimulation (Weber's Law). For example, a single candle causes a considerable stimulation if lit in a dark room but not in daylight. These facts play a much greater part in the sensations experienced by patients than has been yet appreciated, and offer a wide field for investigation.

In certain circumstances, such as after a very superficial burn, or if the normal covering of the nerve endings be removed, as by a blister or removal of the finger-nail, a heat stimulus which is just warm on normal skin becomes exquisitely painful. Similarly, an irritant readily abolishes the sense of heat, cold and touch, leaving only pain, while again we have in central irritation, as at the upper level of the anæsthetic area in paralysis, a zone of hyperæsthesia in which pain is very easily elicited. With such increased sensitivity of the skin as occurs after the application of an irritant, there is also a considerable loss of exact power of localization.

The cause of pain in muscle presents a special difficulty. Muscle is not sensitive to any ordinary sensation. In striped muscle the only sensation experienced, apart from ordinary muscle sense, is pain which results from spasmodic contraction, as in cramp or from distension of the muscle. When fatigue products accumulate in a muscle they attract water and the muscle becomes larger. The nerve endings become compressed. This has long been looked upon as the cause of the pain which follows unaccustomed exercise, and Lewis has brought forward evidence that the pain of ordinary fatigue is probably produced in the same way. Intermittent claudication (Latin *claudicare*, to be lame) occurs in cases of arterio-sclerosis and thrombo-angeitis obliterans. The patient at rest is free from pain, but on exertion he experiences pain, sometimes severe, in the calves, because the blood supply is inadequate for actively contracting muscle. The

dorsalis pedis and posterior tibial arteries are often found to be pulseless. The shutting off of the blood supply by an embolus also causes pain. The embolus may bring about a spasm of the muscle itself, or may allow the accumulation of metabolic products. Lewis suggests that the pain of coronary thrombosis is of this nature, but whether all anginal pain is of this nature is a subject of much discussion. Mere vascular spasm, when it occurs elsewhere in the body, as in the fingers or retina, is not necessarily associated with pain.

However excited, whether directly or by way of the nerve ending, each fibre gives rise to its own special sensation and, to some extent, has a local sign. Thus pinching of the retina or section of the optic nerve in surgical removal of the eye gives rise to a flash of light, as does also a blow on the occipital region, where lies the visual area of the cerebral cortex. Similarly, electrical or mechanical stimulation of the chorda tympani gives rise to a sense of taste.

The **significance of the sensation** depends on the analysis which takes place in the central nervous system. Crude sensation may be appreciated in the optic thalamus, from which it is distributed to the cerebral cortex, where a more refined analysis takes place. To certain areas are allotted special functions in this respect: for example, the visual area in the occipital lobe; the auditory area in the temporal lobe; the post-Rolandic area for general sensation (Fig. 3). Past experience is of great importance in the appreciation of sensation. A new sensation, such as that due to section of the vomer in resection of the nasal septum, cannot be localized accurately at all. We rapidly form associations round objects of a certain size and shape, *e.g.*, from experience, we expect a large key to be heavy. A small object, which requires a certain muscular effort to lift it, which is cold to the touch and hard, although it may be disguised in appearance, we know from past experience is probably metal. This association expresses itself further in the local sign. Thus there is a time-honoured experiment of Aristotle in which an object, placed between the crossed fore and middle fingers, is appreciated as two objects. The stimulation of certain fibres we appreciate as something touching the foot. Even when the leg is amputated, stimulation of these fibres in the stump will give rise to pain referred to the lost foot. Clinically, too, it is important to remember that pain may be experienced in regions remote from the lesion. Pain in the leg, simulating sciatica or disease of the

knee joint, may be the first indication of a tumour pressing on the nerve roots higher up. This is not infrequently seen as the result of cancer of the rectum with associated enlarged glands. When the pain is of an obscure origin and is not associated with any obvious local abnormality, the whole pathway from the seat of the pain, at least theoretically, to the cortex of the cerebrum has to be considered. The various crises of tabes, in which the posterior roots are diseased, may be looked upon as produced in this way. Experimentally in animals, the painting of the sensory area of the cortex with strychnine will, as shown by Dusser de Barenne, bring about sensations of pain referred to the periphery by the animal.

Pain in Visceral Disease.—Pain arising in the body wall has a local sign, *i.e.*, it is projected by the brain to approximately the site at which the impulses of pain (nociceptive impulses) are generated. Perhaps it would be more correct to say that the pain calls forth a judgment of locality. The frequently associated sensation of pressure increases the accuracy of the localization. Touch and pressure sense have a more accurate local sign than has pain. If the pain is severe, radiation may occur. Pain due to a lesion of the body wall is said to be " somatic " as opposed to " visceral " in origin. If any part of the sensory pathway, viz., peripheral nerves, posterior nerve roots, or central pain tracts, is stimulated, pain is projected to the periphery. Thus the root pains in spinal compression are felt in the part of the body wall supplied by the affected spinal segments, and are, after a time, accompanied by blunting of tactile sensation (anæsthesia dolorosa). Nerve trunks are locally painful and tender only when their connective tissue sheaths are inflamed, for these are supplied by the nervi nervorum.

The accompanying figure illustrates the cutaneous distribution of the sensory spinal roots. In the head region the fifth cranial nerve replaces the spinal nerves, except for an area innervated from the second and third cervical segments.

The local signature of somatic sensation, innate in the structural arrangement of the nervous system, is brought out and greatly reinforced by the manifold sensory experience of the individual, particularly by the correlation which he effects between touch and vision. When pain arises in a structure somewhat less familiar than the skin is to the mind's eye, localization is less perfect. Thus, toothache of a molar often radiates along the gums, to the cheek, and to the ear, and it is often only by experimental stimula-

tion of the cavity with the tip of the tongue or by inspection in a mirror that the victim learns which tooth is at fault. Radiation of toothache has been vividly described in poetry by Burns. It is customary to X-ray the teeth in cases of neuralgia of any branch

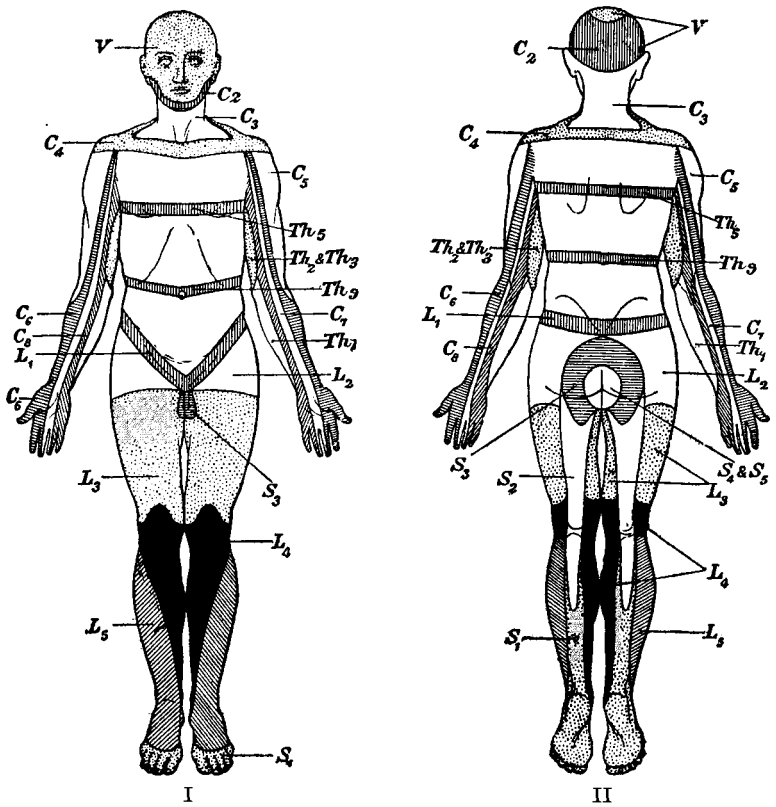


FIG. 4.—DIAGRAM OF CUTANEOUS AREAS OF POSTERIOR NERVE ROOTS.

(Reproduced by the courtesy of Messrs. E. Arnold's from Sir James Purves Stewart's "Diagnosis of Nervous Diseases.")

I, anterior; II, posterior aspect.

V = area supplied by fifth cranial nerve. C, cervical; Th, thoracic; L, lumbar; and S, sacral segments. The numbers refer to the numerical segments of these various groups of segments. The segmental innervation of the trunk is not shown in detail, a few segments at intervals only being indicated.

of the fifth cranial nerve, but in this connection we must remember that teeth have often been needlessly sacrificed in cases of true trigeminal neuralgia (tic douloureux). Further examples of referred pain in this nerve's territory are the supra-orbital pain of iritis and pain in the ear in certain cases of cancer of the tongue.

When we come to consider the pain of visceral disease, we find that much controversy has arisen concerning the way in which it is appreciated. The viscera, if we except the œsophagus, which is endowed with some degree of pressure and thermal sensibility, the stomach, which is the source of impulses of hunger and the bladder (or posterior urethra) and rectum, which, when full, excite appropriate sensations, are in health outside the field of consciousness. Nevertheless, the viscera have afferent nerve fibres, which enter appropriate spinal segments, probably by way of the posterior nerve roots. Thus Langley noted a rise of arterial blood pressure and reflex movements when the central ends of the autonomic nerves of various organs were stimulated, and found that the exact levels at which the nerves of a particular organ entered the cord could be determined by section of nerve roots and noticing which must be intact for the reflex effects to occur. The author has introduced a more sensitive index of afferent impulses than Langley's, viz., the dilatation of the pupil in the chloralosed cat, which occurs when the viscera are stimulated.

In disease of the solid organs pain and tenderness may be present, *e.g.*, the tender pulsating liver of congestive heart failure. In these cases the capsule is possibly the source of the pain impulses, but whether these are to be regarded as " felt in " the liver (or other organ) or in the body wall is not certain. The parenchyma of the solid organs is certainly insensitive. Pain is a more prominent feature of splenic than of renal infarction, for in the latter the necrosis does not reach the surface of the organ on account of the collateral capsular circulation. In the case of infarction, however, irritation of the overlying parietal peritoneum is the probable cause of the pain.

In the hollow abdominal viscera, pain arises through spasm, irregular peristalsis, or stretching of the muscle coat. The exact mechanism by which the receptors are stimulated is discussed later under " Gastric Pain." In the case of the gut, including the appendix, pain excited in this way is felt about the middle line of the abdomen, deep in and not sharply localized. Morley believes that the foregoing is a true visceral pain, felt in the gut itself, but most authors have regarded it as a pain referred to the abdominal wall.

The conception of **referred pain** was originally due to Ross, and has been made the basis of extensive study by Head, by Mackenzie, and by Morley. Head believes that referred pain is an example of a general law, that when a sensation is excited from

an area of low excitability it is projected by the brain to a neurologically intimate area of high sensibility : in the case of a viscus, to the skin supplied by the corresponding spinal segment. Mackenzie's view was somewhat different from Head's. He held that the nociceptive impulses from the viscera impinged on the brainward pathway for somatic pain, and that in this way visceral disorder could cause a pain in the body wall. The impulses might also be reflected into the anterior horn cells of the segment concerned, and so cause muscular rigidity—a " viscero-motor reflex "—and also produce an " irritable focus " in the cord with resulting cutaneous and muscular hyperalgesia. The views of these two authors, which differ chiefly in the mechanism whereby the pain arises once the impulses have entered the central nervous system, well explain the radiation of pain in angina pectoris and in intestinal, renal and biliary colic.

It is well known that peritonitis and the irritation of the parietal peritoneum by contents which have escaped from a perforated hollow viscus cause pain and muscular rigidity, which may be diffuse or local according to the extent of the peritoneal involvement. This fact was fully recognized by Head and by Mackenzie. Morley has recently stressed the importance of the " somatic " nerve endings in the parietal peritoneum and basal part of the mesenteries in the genesis of pain and rigidity not only in gross degrees of peritonitis, but also in visceral inflammation. This author claims that the old statement of Lennander, that local pain and rigidity in such conditions as appendicitis and cholecystitis depend always on local irritation of the overlying parietal peritoneum, is true, with the proviso that visceral pain due to violent or irregular peristalsis can also occur. It should be noted that Lennander entirely denied the existence of visceral pain. Thus, in many cases of acute appendicitis, the pain begins as a bellyache near the umbilicus, and Morley says this is a visceral pain (referred pain of most authors) due to violent peristalsis of the obstructed appendix and that it is unaccompanied by rigidity. The later localization of the pain in the right iliac fossa and local rigidity are due to irritation of the somatic nerve endings in the peritoneum or adjacent connective tissue. Cutaneous hyperalgesia is due to a radiation to the afferent fibres from the skin, probably as these enter the grey matter of the cord—" peritoneo-cutaneous radiation." A good example of this is the occasional shoulder-tip pain and hyperalgesia in cases of perforated gastric ulcer ; the shoulder pain is explained by the fact that the phrenic nerve is

connected with the fourth cervical from which the supra-acromial also receives a contribution. The hyperalgesia of the skin of the abdomen in gastric perforation is also due to peritoneo-cutaneous radiation. It will be seen that Morley believes in radiation within the somatic sensory system, but not from the visceral to the somatic, at any rate where the abdomen is concerned. In denying utterly the existence of referred pain from the viscera, he has probably gone too far, but he has rendered a valuable service in stressing the importance of the parietal peritoneum.

We must remember also that, in the case of an abdominal lesion, repeated palpation by enthusiastic students may help to focus a patient's attention on the site of the organ supposedly diseased, and so lead to a sharper localization of the pain than would otherwise occur ; hence the importance of a proper method of abdominal palpation in which the region likely to be tender or rigid is examined last of all. It is evident also that the way to a correct diagnosis of an acute abdominal disease is to consider not only pain, rigidity and tenderness, but also the mode of onset, the presence or absence of vomiting and the general condition of the patient, especially in regard to temperature and pulse rate.

In biliary colic the pain is referred to the epigastrium, right hypochondrium, back of the chest, and occasionally, right shoulder, *i.e.*, to the territory of the seventh, eighth and ninth thoracic and, occasionally, fourth cervical nerves. The explanation of the occasional radiation to the fourth cervical segment is to be found in the fact that the phrenic sometimes furnishes a twig to the gall bladder. In renal colic the pain is ureteric in origin, and, commencing in the loin of the affected side, radiates to the groin, inner part of the anterior surface of the thigh and the testicle. The afferent fibres from the ureter enter the eleventh and twelfth dorsal and first lumbar segments of the cord and from the last are derived the inguinal and part of the genito-crural nerves which supply the skin of the upper and inner region of the thigh and the tunica vaginalis. The main bulk of the scrotum is not tender as this is supplied from the sacral plexus.

In acute epididymitis the patient is usually sufficiently aware that the testicle is swollen and tender. Occasionally a misleading reference of the pain to Scarpa's triangle and the right iliac fossa has been observed, and depends on the innervation just described. The sickening sensation experienced when the normal testicle is firmly compressed is believed to depend on the tunica vaginalis.

Abdominal pain in diaphragmatic pleurisy is explained by the fact that the lower intercostal nerves furnish sensory twigs to the diaphragm as well as to the abdominal wall. It is because of this confusing abdominal reference of the pain in diaphragmatic pleurisy that laparatomy has occasionally been carried out in early pneumonia.

In the early stages of thoracic aneurysm, true aneurysmal pain occurs due to stretching of the aortic wall. This pain is referred to special sites according to the site of the aneurysm, and should be separated clearly from pain due to pressure on adjacent thoracic structures such as bones and nerves. True aneurysmal pain is reflected to the first four dorsal and certain cervical segmental areas, when the ascending portion and arch of the aorta are concerned. Thus, when the sinuses of Valsalva at the root of the aorta are involved, the distribution of the pain is that of angina pectoris,[1] while pain from the ascending aorta is referred to the right side of the chest as low as the nipple, to the back of the head (causing occipital headache) and to the inner side of the right upper limb. In the case of the arch proper (transverse arch of text-books on Medicine) the area of pain is chiefly the left shoulder, occipital region and left arm. In early aneurysm of the descending aorta the pain is referred to the fifth, sixth and seventh thoracic segments, *i.e.*, below the left breast, between the left scapula and vertebral column, and the uppermost part of the epigastrium.

In angina pectoris the exact cause of the pain is in dispute. Allbutt believed the root of the aorta to be the receptive field, while MacKenzie favoured the theory of exhaustion of the heart muscle. More recent work has stressed the importance of the myocardium, and particularly the importance of an adequate supply of oxygenated blood. Thus angina occurs in coronary arteriosclerosis, aortic regurgitation and occasionally in severe anæmia. Exertion would tend to excite the attack by increasing the need of the heart muscle for blood. Amyl nitrite relieves the pain not merely by lowering the arterial pressure but rather by dilating the coronary vessels, for relief is obtained even if the pressure does not fall. The pain is chiefly substernal and tends to radiate to the inner side of the left arm and occasionally to the neck. The radiation to the arm corresponds to the first and second dorsal roots, to the neck to the cervical nerves. The

[1] Angina in aneurysm of the sinuses of Valsalva may, however, be due to interference with the coronary blood flow.

predominantly leftward distribution is due to the fact that the left ventricle, which is connected principally with left-sided afferent nerves, is the chief source of the pain. Nociceptive impulses from the heart, as experimentally shown by Langley and also by McDowall, travel chiefly by the sympathetic nerves and enter the upper thoracic rami communicantes. These observers found no good evidence of impulses of pain in the cardiac vagus supply, and Langley concluded that the operation devised for section of the depressor nerve could not be expected to relieve pain. Langley advocated section of the upper thoracic rami communicantes as the logical operation, but section of the depressor nerve has to be considered from another aspect, viz., the retarding effect which depressor impulses exert on the coronary blood flow in virtue of the reflex coronary vasoconstriction they produce. In any case nitroglycerine, which the patient can take not only to relieve an attack (and for this purpose amyl nitrite is equally effective) but also when he finds himself in circumstances conducive to an attack, still seems to be the most generally useful and effective agent of treatment. The crushing nature of anginal pain is probably due to spasm of the intercostal muscles (viscero-motor reflex of MacKenzie).

In coronary thrombosis the pain, also chiefly substernal, tends to radiate more widely than in angina. A striking feature is the frequent spread to the epigastrium, and the prominence of nausea and vomiting. The pain, as might be expected, because of the gross structural disturbance of the heart wall, lasts much longer than that of angina, which probably is due to inability of an ischæmic heart muscle to function easily in moments of additional but normal stress. Further, the patient is restless in coronary thrombosis, probably because the sudden insult to the myocardium is so rude that a protective inhibition of general muscular movement no longer occurs as in angina, when the patient keeps quite still. Lastly, as might be expected, amyl nitrite does not relieve the pain, for it obviously cannot dilate occluded vessels, and the administration of morphia is imperative.

The Pathways of Sensation

The impulses which cause sensation pass into the central nervous system by way of the afferent nerve fibres to the cells of the spinal ganglia, and thence to the posterior horns of the grey matter of the cord. These fibres may be concentrated in one nerve, as in the fifth cranial, but more commonly they form part of a mixed

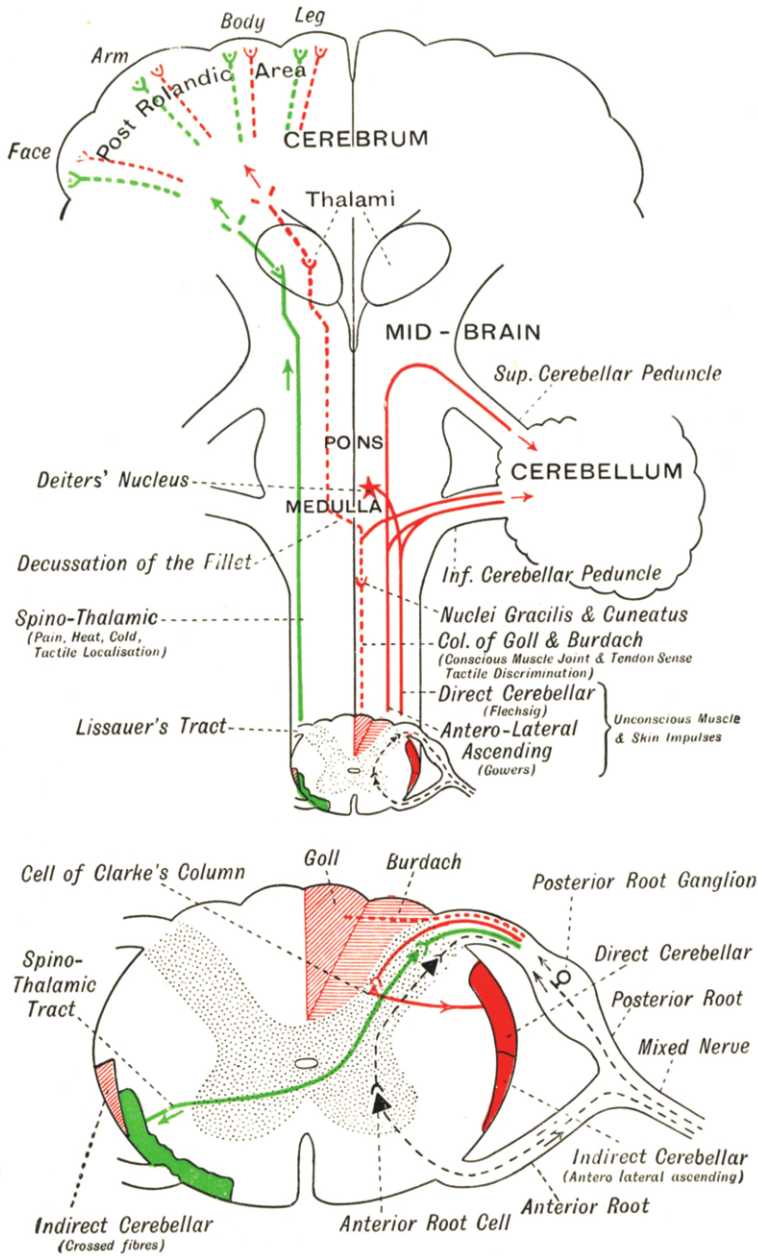


FIG. 5.—THE AFFERENT PATHS OF THE CENTRAL NERVOUS SYSTEM.

Facing p. 39.]

nerve. The impulses responsible for **pain, temperature, and tactile localization** cross immediately, or soon after entering the spinal cord, to the opposite side. We know this is so because in the condition of syringomyelia (in which there is gliosis and excavation round the spinal canal in the centre of the cord) there is a loss of these sensations in the segments affected, usually at first in the cervical region. In such circumstances severe injury, such as burning the fingers by cigarettes, may readily occur, unknown to the patient. Joint and muscle sense and tactile discrimination, however, are intact, and sensory loss of this type is often called dissociated anæsthesia.

The impulses then pass up the spino-thalamic tract (part of that of Gowers) to the thalamus. At this point there is evidence that they become appreciated in consciousness as crude sensation, further refinement taking place in the cerebral cortex, to which the impulse is relayed from the thalamus. Thus if the cortex is removed, an animal or a person knows when he is hurt but is unable to localize the pain. Similarly, he cannot distinguish between different grades of temperature. The area actually responsible for the more detailed appreciation and localization is known definitely to be the post-central convolution—immediately behind the fissure of Rolando and on the other side of the fissure from the corresponding motor areas. This localization has been determined from the fact that in man injury or stimulation (Cushing) causes numbness or other sensation in the appropriate part. Similarly in animals, painting a part of the sensory area (not necessarily post-central in lower forms) with strychnine (Barenne) causes the animal to have all the appearance of suffering pain in the corresponding part of the body. Tumours cause impairment of fine sensibility and sensory Jacksonian epilepsy.

Muscle and Joint Sense.—With this sense, for purposes of convenience, is discussed also the path of impulses conducting the sensation of **tactile discrimination,** that is the sense by which we can distinguish between two or more points placed on the skin. By muscle and joint sense we appreciate the position in which our limbs may be placed, either by ourselves or passively. The afferent impulses from the muscles and joints are partly conscious and partly unconscious, and are set up in sensory nerve endings (muscle spindles and organs of Golgi) in the joints, tendons, and muscles. The unconscious impulses are those which, in the main, are responsible by reflex action for the maintenance

of posture, equilibrium, and muscle tone, including that of certain organs, such as the bladder.

The pathways of such impulses are quite distinct from those which carry the other forms of sensation. The impulses pass into the cord through the posterior nerve roots. Here the *conscious* and *unconscious* impulses take a different course. The former continue up the cord on the side they enter, by the axons of the cells of the spinal ganglia, running in the posterior columns of Goll and Burdach to the nucleus gracilis and cuneatus respectively. From this point they are again relayed by the fillet to the optic thalamus of the opposite side. The actual crossing occurs at the decussation of the fillet, in the upper part of the medulla. From the thalamus there is a further relay to the cerebral cortex, like that of ordinary sensation. The thalamus acts, then, as the distributing centre for all sensory impulses to the appropriate part of the cerebrum. (Fig. 5.)

The pathway which is responsible for carrying the *unconscious* muscle impulses which are so important in relation to posture is as follows: A number of fibres from the posterior roots do not pass directly up the cord, but arborize around the cells in Clarke's column. From these cells arise the cerebellar tracts, which lie in the postero-lateral part of the cord. These tracts are uncrossed, and pass by way of the peduncles to the cerebellum.[1] The afferents are very distinct, and may be traced by the fact that they degenerate if cut off from the cells from which they originate.

The size of the tracts in the upper parts of the cord indicates the enormous number of afferent impulses from muscle which are conducted to regions not concerned with consciousness, and their importance for the animal. An interesting explanation of why the fibres for conscious muscle sense do not cross until they reach the medulla was given by Halliburton. He pointed out that the cerebellar tracts arise from collaterals from the fibres carrying similar muscle and joint impulses upwards in the columns of Goll and Burdach. If these fibres were to cross immediately on entering the cord, they would have to recross in order to join or give rise to the cerebellar tracts of the proper side.

On the tracts conveying muscle and joint sense depend not only posture and co-ordination, but also the senses by which we appreciate size and shape (the stereognostic sense) and weight of bodies. In using these senses we rely on the results of the associations which have been made around tactile discrimination and

[1] A few fibres also pass to the cerebellum from the columns of Goll and Burdach.

muscle sense. The clinical symptom of astereognosis or inability to recognize the qualities of an object by touch, is the result, in cerebral cases, of limited lesions of the superior parietal lobule (Kinnier Wilson) of the cerebrum. Lesions of the tracts leading to this region will obviously have the same effect. Evidence that stereognostic power depends on association may be seen in the fact that if two fingers are crossed, and a thin pencil placed between them, two objects will be appreciated instead of one. This is due to the fact that normally the outsides of the two fingers are not stimulated by a single object. Similarly in judging weight we compare it with the amount of muscular movement which we remember was necessary to sustain a known weight. The same principle is used when we estimate blood pressure by obliterating the radial artery with the finger and we use as a comparison the amount of pressure necessary to obliterate our own presumably normal pressure. A similar mechanism is at work in the estimation of the size of an object. We are all familiar with the various optical illusions which may result if the associations around a given movement are upset, or if the standard objects with which we normally compare unknown sizes have been altered.

Vibration sense of bone appears to have the same afferent pathway as joint- and muscle-sense.

From a consideration of the above, it will be evident that sensations may be interfered with in a very large variety of conditions, and that any lesion on the pathway between the periphery and the sensory cortex may cause a reduction in one or more senses. Advantage is taken of the fact in some forms of surgical anæsthesia.

Considerable success has been achieved of late by anæsthetizing with a local anæsthetic the posterior roots by the so-called paravertebral anæsthesia, in which the results are much more localized than in the better known spinal anæsthesia where the anæsthetic is injected into the spinal theca.

The *sensory nerve endings themselves may be paralysed,* and this is brought about intentionally when we inject local anæsthetics subcutaneously. The nerve endings may also be paralysed by cold, or their excitability impaired if the part is insufficiently supplied with blood.

The nerve paths themselves may be interfered with in their passage to the spinal cord. Thus, numbness after neuritis is common, and total anæsthesia will result from nerve section. We commonly experience such numbness if we chance to keep up pressure

on a nerve trunk such as the popliteal when we develop a temporary numbness of the foot. The anæsthesia of beri-beri is considered to be neuritic in origin.

The posterior roots are markedly affected in tabes dorsalis. The degeneration may affect the spinal ganglia and the roots degenerate secondarily or may themselves be involved at their entrance into the membranes of the cord. The posterior columns of the cord are secondarily degenerated as a result of the disease of the posterior roots. Muscle and joint sense is markedly affected and there are consequently disturbances of equilibrium. If a limb is placed in a certain position the patient has difficulty in placing the other limb in a similar position or he is unable to describe accurately the position into which the limb or, for example, the big toe has been put. It must, however, be noted that purely voluntary movement is unaffected, and by the use of his eyes the patient may succeed in placing the two limbs in similar positions. At the same time considerable destruction of tissue may occur without any appreciable sensation. In this condition perforating ulcers of the foot and Charcot's joints, in which a joint may be entirely disorganized, are strikingly painless. At the same time there is a loss of trophic influences, normally dependent on the existence of the reflex arc, which is interrupted. It is seen, too, that in spite of structural change, the normal accompaniments, such as heat, redness, and swelling, are absent. Similar atrophic conditions may occur in the nails and gums. Perforating ulcers also occur in diabetic neuritis which seems to affect the sensory fibres to a greater extent than the motor.

The exact nature of the lesion in tabes determines the sensation affected. As the result of loss of general sensation the patient may experience the feeling of walking on cotton-wool. What is still more strange, in the " masque tabetique " of Duchenne, in which the fifth nerve is affected, the patient may experience the sensation of having no face. The disorders of co-ordination which may result are considered in the chapter on " Equilibrium." Lightning pains are frequent, and with loss of ankle jerk and Argyll-Robertson pupils constitute the early features of the disease. Gross ataxia is a late sign.

Interference with the sensory pathways in the spinal cord produces a varied result in virtue of the fact that the fibres for pain and temperature cross immediately on entering the cord, while those for muscle sense do not. We have seen that at the actual point of crossing the former may be involved in lesions

near the central canal as in syringomyelia. Here, however, the effect is, for a time at least, limited to those areas, the pain and temperature impulses from which cross at the level of the lesion. Impulses from a lower level are not affected; they are, however, affected by a new growth or anything which interferes with the conduction of the cord. It will be obvious, however, that should the lesion be limited to one side of the cord, the pain and temperature impulses from the same side, which have crossed below the level of the lesion, will not be affected, although those of ordinary sensation, which do not cross until they reach the medulla, will be lost. Sensory impulses of pain, which have crossed from the opposite side, below the level of the lesion, will be interrupted (see Fig. 5). These changes are characteristic of the Brown-Séquard syndrome discussed on p. 44.

It is to be noted, too, that at the upper level of the zone of cutaneous anæsthesia, on the opposite side from the lesion, there is a zone of hyperæsthesia presumably due to a reaction at this level. This fact tends to demarcate the level of the lesion more clearly for diagnostic purposes.

In some diseases, certain of the afferent paths appear to be more liable to suffer than others. Thus, in postero-lateral sclerosis, *e.g.* in certain rather rare cases of disseminated sclerosis, there is no cutaneous anæsthesia because the spino-thalamic tract, lying more anteriorly, escapes, while there is destruction of the more posterior, such as those of Goll and Burdach, and of the cerebellar tracts, with loss of conduction of muscle and joint sense. From the loss of the latter, muscular inco-ordination is a marked feature, and the term ataxic paraplegia has been given to the condition. Ataxic paraplegia also occurs in the middle stage of subacute combined degeneration, but here cutaneous sensory changes soon develop. The pyramidal tracts also suffer, giving the characteristic motor effects with exaggerated reflexes. Similarly, in amyotrophic lateral sclerosis, although there may be some disturbance of sensation, there is no actual anæsthesia, the lesion being chiefly confined to the pyramidal tracts and anterior horn cells; the lower motor neurone lesion is most marked in the cervical region of the cord, giving a characteristic combination of wasting and weakness of the muscles in the hand, with spastic weakness of the legs. In Friedreich's disease or hereditary ataxia sensory loss is not a prominent feature, but in the later stages partial loss of vibration-, joint- and muscle-sense occurs. It may be that the paths of ordinary sensation which pass upwards depend on some-

what variable and less well-defined tracts, while those on which muscle sense depends are more rigidly fixed.

In disseminated sclerosis, paræsthesiæ, such as numbness and tingling, are liable to occur, though usually the interference with movement and inco-ordination are the most marked features. Sensory loss is slight or absent. Hemisection of the cord such as may result from a bayonet wound, causes Brown-Séquard's syndrome, in which, in addition to upper motor neurone palsy and loss of joint and muscle sense below the level of the lesion on the same side, there is loss of pain and temperature sensibility on the opposite side below the lesion. A segment or two just below and on the same side as the lesion lose temperature sense and pain, while the corresponding segments on the opposite side escape, because the impulses do not cross immediately, especially the temperature impulses. Intra-medullary tumours may cause incomplete Brown-Séquard syndromes.

In total transverse lesions, such as the inflammation in acute transverse myelitis, the anæsthesia is complete below the lesion.

The sensory change in hysteria we do not yet understand, and it offers the best possible field for enthusiastic research. Lack of sensation may be complained of by the patient or anæsthesia of the palate or cornea may be discovered by the physician. There is evidence that these latter are actually produced by suggestion during the examination, as the palate and cornea at other times act normally. The patient is frequently anæsthetic in a given region, such as the hand as a whole, and there is no correspondence with any definite nerve supply. The disability may persist or may be rapidly evanescent. Any of the special senses may be affected, and many of the cures are dramatic. In the cures suggestion plays the chief part, although all manner of physical aids, *e.g.*, a faradic current, may be used to reinforce the suggestion. An interesting collection of cases has been published by Hurst.

It is certain that hysteria is closely related to the hypnotic state in which anæsthesia or any anomaly of sensation may be suggested, such as that a pebble is too heavy to hold or actually burns. The anæsthesia of hysteria may even be made to disappear in hypnosis.

Physiologically, hysteria is of interest, since it emphasizes the importance of the mental attitude in sensation.

What is possibly of more consequence is the opposite condition,

in which there is hyperæsthesia. When this is local it may be extremely difficult to differentiate from pain due to organic cause. Here again we find that the functional element is not infrequently grafted on an organic condition. It is obvious that the occurrence of such a condition may have very dire results, since operations and the like may be performed in an attempt at relief.

CHAPTER VI

HEADACHE

THE mechanism whereby headache, one of the commonest of symptoms, is produced, is obscure, and appears to vary in different groups of cases ; but for convenience we may differentiate headache into that which is persistent, due to anatomical lesions, and that which is temporary, but there is no hard and fast dividing line between the two varieties.

Persistent Headache.—In the more or less localized headache of disease of the bony sinuses, such as the frontal or sphenoidal, the production of a vacuum as the result of obstruction of the outlet into the nose, plays a part. This mechanism explains the effect of change of atmospheric pressure in altering the intensity of the pain, as when the subject ascends a steep hill in a motor car. Distension of the sinus with mucus or pus will cause local pain, called in its less intense degrees headache by the patient. The pain in sphenoidal sinusitis is deeply situated along the base of the skull and is often referred to the eyes and occiput.

Inflammatory conditions in the skull, such as syphilitic osteitis, cause headache. The dura mater is probably involved as well as the bony substance itself.

In various disorders headache appears to be due to impulses which arise in the nerve endings of the dura. Collier states that after one Gasserian ganglion has been excised, headache is no longer experienced on the corresponding side, but may occur on the opposite. The operation has interrupted the sensory fibres of the meningeal branches of the trigeminal nerve which supply a wide area of the dura. The dura may be irritated by an increased intracranial pressure as in cases of cerebral tumour. If the tumour is pedunculated and situated near one or other of the foramina of Munro, sudden headache may arise in certain positions of the skull from transient blockage of the opening.

The headache which follows lumbar puncture is due to undue lowering of the pressure and is particularly liable to occur when a large needle has been used and a hole left in the theca through which cerebro-spinal fluid escapes into the epidural tissue.

Probably the abnormally low pressure allows of displacement and stretching of the processes of the dura. Pituitrin is said to relieve lumbar puncture headache by increasing the pressure of cerebro-spinal fluid. An intracranial aneurysm may cause headache localized always to one side, but not sharply limited to the site of the lesion, for dural sensations, like protopathic cutaneous sensations, tend to radiate. In meningitis headache is due to a combination of pressure and inflammation. Pain may be referred to the head from various sources, *e.g.*, from the ocular muscles in eyestrain or from an impacted wisdom tooth. In these instances the branches of the fifth nerve are usually responsible. In the case of an impacted wisdom in the lower jaw the nervus spinosus (recurrent meningeal branch of the mandibular division) is specially concerned and severe unilateral headaches resembling migraine may occur.

Temporary Headache.—Fortunate are those who have never suffered from headache. Yet occasionally we meet those who have no personal experience of it. The temporary headaches which occur in the majority of persons are conveniently called toxic, but their mode of production is far from clear. It may be suggested that the toxins modify the intracranial tension and so affect the nerve endings of the dura. This is suggested by the fact that increased body temperature or the inhalation of amyl nitrite may cause intense headache and that in many cases the headache is relieved by the administration of a concentrated saline purge calculated to deprive the body of water. The headache produced by certain alcoholic liquors appears to be due not to the alcohol but to the other substances associated with it. Whether these substances act directly or, by irritation of the alimentary canal, permit of toxic absorption, has not yet been decided. The headache of uræmia may be the result of increased intracranial pressure which is a common accompaniment. A stuffy room, a hot motor car, a too warm bed or the approach of thunder may cause headache by increased body temperature, but, on the other hand, mere increased temperature without absence of skin stimulation due to lack of air movement does not necessarily cause headache. So far as I can discover, no attempt has been made to differentiate accurately between the causes of frontal, parietal and occipital headache. They may be due to excessive use of these regions. Excessive use of the eyes or excessive noise may produce headache.

It has been shown that if animals are subjected to intense

olfactory stimuli, a post-mortem examination of their brains shows a marked vascular dilatation of the olfactory lobes compared with other regions and with the olfactory lobes of control animals not subjected to such stimuli. It may be suggested, therefore, that similar local increases in cerebral volume may be responsible for the headache due to excessive stimulation of the ears or eyes, but no doubt also the headache is but a convenient excuse for avoiding certain circumstances which have become disagreeable, for such excessive stimulation does not always cause headache. In those accustomed to such excessive stimulation there is presumably a large amount of adaptation and failure of the receptors to be stimulated, and possibly, as in boilermakers' disease, degeneration of the receptor. In the case of the eyes, however, we must differentiate between excessive stimulation such as may occur from bright lights or flickering such as occurs with worn or antique cinematograph films and actual strain of ocular muscles from excessive focusing. The latter is particularly liable to occur in attempting to compensate for errors in refraction, and the pain, which is essentially that of fatigue of the ocular muscles, may be referred to the head.

Migraine.—Paroxysms of headache, often unilateral, are a prominent feature in this condition. They tend to be accompanied by vertigo, vomiting, and to be preceded by peculiar visual disturbances such as spectra and scintillating scotomata. Occasionally a "sensory" aura precedes the attack. Vasomotor phenomena such as pallor, and spasm of the temporal and retinal vessels are frequently observed. Any theory of migraine must be adequate to account for the foregoing phenomena and also for the occasional paralysis of the sixth, third, or fourth cranial nerve, which may last several weeks. The theory must also explain certain other phenomena which may accompany the headache, such as aphasia and facial palsy, or occur between attacks, such as hemiplegia.

According to Spitzner, intermittent occlusion of the foramen of Munro by an abnormal choroid plexus with resulting distension of the lateral ventricle is the cause of the attacks; his theory is based on anatomical evidence and would account for most of the phenomena of migraine. The fact that during the migrainous paroxysm the pressure of the cerebro-spinal fluid is low does not necessarily contradict the hypothesis; the theory, moreover, is the only one adequate to account for third nerve paralysis which Spitzner would explain in terms of pressure of the distended

ventricle on the third nerve as the latter enters the dura mater. It is difficult to visualize, however, how the sixth nerve can become paralysed in this way, unless the general intracranial pressure rises, and exactly the opposite condition is believed to obtain during the attack. Further, Spitzner's post-mortem specimens were admittedly obtained from cases of severe and unilateral migraine, and, it may be, represent a special group of cases which we may call " mechanical migraine."

The metabolic theories bring migraine into line with epilepsy with which, according to various authors, it bears affinities. One of these theories takes acidosis as the fundamental cause. On this special theory, however, it would be difficult to relate migraine to epilepsy (*q.v.*). Acidosis is found particularly in *status hemicranicus* in which recurrent attacks over a period of a month or more greatly exhaust the patient and is revealed biochemically by a diminution of the alkali reserve of the blood plasma. In status hemicranicus the acidosis, however, is usually attributed to the prolonged attack, rather than being the cause thereof. Between migrainous attacks, however, the alkali reserve is often found to be diminished (Osman), an observation which we have been able to confirm. Moreover, alkalis in the form of effervescent alkaline mixtures may afford relief. Such relief is frequently temporary (Dunlop), and may last for a period varying in length from a few weeks to two years. Migraine bears some relationship to cyclical vomiting ; children the subjects of the latter condition not infrequently develop the former as they reach adult life. In both conditions acidosis is present and plays a part, even if only a secondary one, in the production of symptoms. Hepatic deficiency may be the cause of cyclical vomiting, and certain cases of migraine may depend on the same metabolic disturbances. In a number of cases a positive indirect van den Bergh reaction in the blood serum is found.

Migraine has also been attributed to a state of allergy (see below).

The theory of local spasm of the cerebral vessels is based largely on the observation of constriction of the temporal and retinal vessels during the attacks. The vasomotor theory would explain the visual phenomena and headache and also the occasional occurrence of hemiplegia and aphasia ; it fails, however, to account for paralysis of the nerves to the eye muscles, and, further, the cause of the spasm would still need elucidation.

Menstrual Migraine.—That migrainous attacks may disappear

at the menopause is well known and has suggested some relationship with the endocrine glands. Migrainous attacks may occur only during the menstrual period, and the suggestion has been made that they are then due to menstrual swelling of the pituitary body within an abnormally confined sella turcica. X-ray pictures have shown that in some at least of these cases the interclinoid ligaments are ossified. Relief is said to be afforded by the administration of pituitary gland.

Migraine and Allergy.—Balyeat believes that the hereditary factor in migraine consists in a liability to become sensitive, not that a specific sensitivity is transmitted. He believes that the basis of the attack is localised cerebral œdema. Eyestrain may act as a precipitating factor, but never as a sole cause.

CHAPTER VII

REFLEXES

REFLEXES are movements which we make without any effort of will and, quite apart from their great physiological interest, their study is of the utmost value in the localization of nervous disease. Reflexes are amongst the most primitive movements of the body. They are primarily designed for protection, the maintenance of posture, the supply of food, and the adaptation of the animal to its environment.

The axon reflex is the simplest form of reflex known, and is best exemplified by the fifth nerve, as shown by Ninian Bruce. If a blister is applied to the cheek a reddening of the skin results from dilatation of blood-vessels. This is not due to direct action on the blood-vessels, because, when the nerves supplying the part are cut, the dilatation is only obtained for a short time, and once the nerve has degenerated the reaction disappears entirely. Such section is not infrequently carried out in the treatment of obstinate neuralgia. As excision of the Gasserian ganglion does not affect the reaction, provided the nerves have not had time to degenerate, it must be assumed that the reflex depends entirely on the distal portion of the nervous connection. We know, however, that vaso-dilator nerve fibres pass out with the sensory nerves, and we may assume, then, that these have been stimulated and the impulse has passed over to the efferent vaso-dilators in the nerve trunk. The value of such a mechanism to the animal, for the protection of its skin, is obvious. The Lovén reflexes, which are probably of the nature of axon reflexes and are of importance in relation to the blood supply of organs in general, are referred to later.

The spinal reflex, on the other hand, depends on the integrity of the reflex arc through the spinal cord. By means of such a reflex, sensory stimulation brings about a movement of voluntary muscle. Spinal reflexes are of two kinds : the superficial reflexes which are brought about by stimulation of the skin, and the deep reflexes, brought about either by a blow or by sudden stretching of the sensory nerve endings in muscle or tendon.

The organic reflexes, on which depends the evacuation of the

bladder and the bowels, are probably brought about by a variety of axon reflex, which, however, is supplemented by a spinal reflex control. This is evident from the effect of injury to the spinal cord, and, in adults, from the voluntary control of micturition.

A reflex arc consists of a sensory nerve ending or receptor; an afferent neurone to the posterior root ganglion, and from there to the spinal cord; in the case of some reflexes an intermediate neurone in the cord; an efferent neurone; a motor nerve ending; and an effector organ, usually a muscle or gland.

Absence of a spinal reflex is an indication of interference with this arc at one point or another, and such interference may result from disease of any part of the arc. The muscle itself is seldom at fault, although this may occur in later stages of the muscular dystrophies. The nerve trunks, too, are occasionally the site of disease, as in neuritis. Usually, however, the cells of the arc are affected. This occurs in progressive muscular atrophy, and acute anterior poliomyelitis. In both conditions the motor cells of the anterior horn are affected, and the absence of the reflexes is associated with impairment of movement and degeneration of muscle; the essential difference is that in the former the onset is gradual and the course of the disease progressive, while the latter is an acute disease, as the name indicates, and its effects remain local.

A similar state of affairs occurs in the sensory side of the arc in tabes dorsalis, where there is degeneration of the posterior nerve roots, often of the cells of the posterior horn of the spinal cord and the posterior root ganglia. Here the absence of reflexes is associated with sensory impairment, and, although movement as such is unaffected, ataxy results, through faulty conduction of the proprioceptive impulses from the muscle, upon which impulses co-ordination largely depends.

In some areas, such as the arm, where the normal reflexes are no longer required to any great extent for the maintenance of posture, it is often extremely difficult to elicit deep reflexes. In skin reflexes, too, the sensory nerve endings are appreciably altered by local conditions, such as cold, or excessive stimulation. In other areas, such as the leg, the reflexes are normally more active, and their absence is therefore of more significance. In some individuals, however, the normal reflexes, as, for instance, the **knee jerks**, are by no means easy to elicit without reinforcement, such as getting the patient to concentrate on some other act, *e.g.*, pulling apart the clasped hands. The reflex arc, in general, may be depressed by conditions affecting the nervous

system, as by drugs, *e.g.*, bromides, which appear to reduce the conduction across the synapses between the neurones of which the reflex arc is composed. Similarly, conditions of low blood pressure, seen in shock for instance, bring about a marked depression of the arc.

The spinal reflex is of itself a complete mechanism, capable of independent action and activity. It is, as we shall see later, part of the mechanism for the maintenance of posture, and the protection of the animal. It is, however, greatly influenced by the higher centres. This is shown by the experimental removal of the cerebral hemispheres. By this procedure the reflexes are exaggerated, and, as seen below, some may be elicited which it is not possible to obtain normally. Widespread or mass rigidity occurs occasionally in disease, but more commonly, for reasons given below, the rigidity is local.

The motor impulses from the cerebral cortex, as we have stated, make use of the same paths as the spinal reflexes, and it is easy to see that impulses passing down from the higher centres affect the reflexes markedly, sometimes reinforcing, and sometimes inhibiting them. If, however, the stimulus is a harmful one, it may be extremely difficult, as in stimulation of the cornea, to inhibit the reflex by volition.

Clinically, if there is any separation of the higher centres from injury to the pyramidal tracts, there is marked **exaggeration of the reflexes** below the level of the lesion. This feature is made use of as a clinical means of localization. For example, exaggeration of the reflexes of the leg (and not those of the arms) indicates a lesion, usually a sclerosis or tumour below the level of the cervical segments responsible for the arm reflexes and above the level of the lumbar segments responsible for the leg reflexes. On the other hand, if both the arm and leg reflexes are exaggerated, the lesion is above the level of the cervical segments concerned in the arm reflexes and is situated commonly in the internal capsule, as in cerebral hæmorrhage, or in the cortex as the result of embolism or thrombosis. It must be borne in mind that if the onset of the lesion is acute, as in the former condition, there is at the time of onset a profound general shock and all reflexes may be temporarily abolished. The same thing occurs in total transverse sections of the cord in which, although there may be considerable recovery of the organic reflexes concerned in the bowel and bladder, tendon reflexes are poorly recovered from below the level of the lesion. It used to be thought that recovery of reflexes

was quite impossible, but during the World War it was demonstrated by Head and Riddoch that cases of complete spinal section are not as hopeless as at first sight they appear, if the urinary tract and the site of the lesion can be prevented from becoming infected. The feebleness of the deep reflexes is regarded as being due to the loss of impulses which pass down by way of Deiters' nucleus and the vestibulo-spinal tract.

Exaggeration of the reflexes may occur in any general irritable state of the nervous system, and its occurrence without any other sign or symptom of disease of the pyramidal tract is of no special significance. This is especially true of the knee jerk. More importance, however, has to be placed on the less easily elicited reflexes, such as **ankle clonus** from sudden stretching of the tendon of Achilles, and the **plantar protective reflex.** The latter, which is associated with the name of Babinski, is almost absent in health, except with a strong stimulus, and its presence is considered pathognomonic of disease of the pyramidal tract. There are really two distinct plantar reflexes (Walshe). In one a gentle stimulus such as scratching the sole of the foot with the finger-nail tends to cause the toes to bend downwards, as if to grasp the stimulating object. In the other, a severe stimulation applied to the foot causes it to be withdrawn, as occurs normally when we step accidentally on a sharp object. If the two kinds of stimuli be applied at the same time, the latter, being more powerful, predominates. When there is a pyramidal lesion, this latter reflex becomes exaggerated and a gentle stimulus to the sole of the foot which normally causes a grasping movement now causes a withdrawal, as indicated by the extension of the toes (especially the great-toe, which is the first movement seen). It will be evident that although both the flexor and extensor reflexes may be exaggerated, as usual the more important protective one predominates.

Pyramidal disease is not, however, the sole cause of the extensor plantar response, nor does the absence of such a response exclude disease of the pyramidal tracts. The extensor response, as emphasized by Hawthorne, is commonly present in coma from a variety of causes and even in deep sleep. It will be evident that when the cerebrum is thrown out of use, the extensor reflex is of no physiological value and the protective mechanism predominates.

The same is also to be said of the **jaw jerk,** in which, by a tap on the chin, the jaw is jerked forward. When jaw clonus can be

obtained there is almost certainly a lesion of the motor fibres between the cortex and the motor nucleus of the fifth nerve.

An ankle clonus, brought about by jerking the foot upwards to extend the calf muscles when the patient is lying down, is occasionally obtainable in functional nervous disease, but it is characterized by not being maintained like a true ankle clonus if the pressure on the foot is kept up.

Exaggeration of the reflexes may also be brought about by the therapeutic use of strychnine which diminishes the resistance in the synapses. A similar condition is brought about in the early stage of tetanus, and, as was emphasized in the Great War, increased tone of the muscles is seen in the immediate vicinity of the lesion before the onset of the more severe symptoms indicated below.

In the spinal cord, the more severe and diffuse the disease, the more likely is the hypertonus to affect the flexors. Unfortunately these facts are as yet unexplained, but they are of considerable value as an indication of the severity and possibly the progress of the condition.

The Nature of the Tendon Reflex.—When a tendon is tapped the muscle is stretched and impulses are set up by the tendon organs which lie in the fibrous part of the muscles, and pass into the central nervous system. The response in a flexor muscle is shorter lived and is not sustained, but that obtained from extensor muscles, such as the gastrocnemii, extensors of the thigh or elbow, is sustained and is really part of the mechanism of posture. Normally, when the weight of the body tends to bend the legs, the limbs are maintained in the rigid position by such stretch reflexes, the arcs of which include afferent and efferent fibres to Deiters' nucleus in the upper part of the medulla; but in order to permit of free movement and co-ordination the reflex arc concerned is under the influence of the cerebral cortex, red nucleus, and cerebellum. If section is made through the mid-brain below the red nucleus the animal passes into a state of exaggerated reflex standing known as decerebrate rigidity.

The character of a tendon reflex may change appreciably. This is well seen in the case of the knee jerk, and here we are reminded that, although this reflex is spinal, the normal jerk consists of several components. The knee jerk of a spinal animal (see page 63) is a transient contraction of the quadriceps; in cerebellar disease, too, the knee falls limply after the contraction (the pendulum knee jerk); but in the decerebrate animal and in

disease of the pyramidal tract in man, the contraction is sustained *i.e.*, the relaxation is prolonged. The controlling influence of the higher centres causes the normal knee jerk, which consists of a sharp contraction and a deliberate but not unduly prolonged relaxation which allows the limb to come slowly to rest.

Reflexes have the important characteristic that they are improved by repetition, a process which Sherrington has called *facilitation*. The passage of the impulse through the synapse from one neurone to another is made easier by the passage of a previous impulse in the same direction. An easier path apparently becomes formed, and the response becomes more immediate. As the rate of nerve impulse does not vary, we may assume there is diminution in the normal resistance at the synapse. There is, however, evidence which suggests that the diminished resistance is brought about by chemical changes in the synapse. That such a resistance exists is clear, since the time between the stimulus and the response is longer than can be accounted for by the time the impulse takes to travel along the nerve tract. The latter time can readily be measured by comparing the time of arrival of the current of action at two points a known distance apart, in a stimulated nerve. In the mammal, the rate has been shown to be 120 metres per second. Facilitation can be imitated by causing water to run through a box of hay from which there are two openings. If flow is allowed from one exit only, the hay gradually offers less and less resistance to the flow of the water and its strands ultimately lie in the direction of the flow. What is just as important, however, is that by adjusting themselves to suit one direction of flow, they offer more resistance than normal to flow from the other exit from the box. The importance of this canalization process in the region of the synapse is obvious in relation to habit formation, which is discussed below.

We also look upon the spread of reflexes as being influenced by the same principle. If the stimulus is strong, the response may involve the efferent neurones at several levels as the result of spread upwards and downwards in the spinal cord. If the stimulus is weak, the response remains localized. Strychnine, however, by diminishing the synaptic resistance, may cause an appreciable spreading of reflexes, from stimuli which otherwise would cause only a local response.

The spinal reflex is really twofold in action, as indeed is any voluntary movement. Not only does the stimulus bring about contraction of one set of muscles but it must necessarily inhibit

the antagonistic set. We owe our knowledge of this subject to the work of Sherrington, who has established the principle of *reciprocal innervation*. This refers to the fact that when one muscle shortens, a reciprocal lengthening occurs in the opposing muscle as the result of diminution in its tone. Death from strychnine poisoning, or tetanus, is the result of upset of the reciprocal mechanism in which the opposing muscle, instead of being inhibited, is stimulated. Any attempt at movement, therefore, brings about a contraction of the muscles acting in opposite directions on a joint, with the result that fixation occurs. As the extensor muscles are the more powerful, the fixation of the limbs is in extension. When this fixation occurs in the muscles responsible for respiration, death results from asphyxia.

What has been said of the spinal reflex is also true of other reflexes in which there is involved normally a large number of efferent neurones. Thus, in sneezing and coughing, the sensory path is comparatively simple. In the former the fifth nerve and in the latter usually the superior laryngeal or vagus are the afferent nerves, but the efferent ones are all concerned with respiration. In this respect, the sensory cranial nerves may be looked upon as corresponding to the afferent routes in a spinal reflex.

Of a similar nature, too, are those reflexes which bring about rigidity of the abdominal wall in internal inflammatory conditions. Here they are obviously designed for the protection of the underlying inflamed parts, and the existence of rigidity may be of great diagnostic value. In peritonitis, for example, the whole of the anterior abdominal wall may become immobile and abdominal respiration disappear. In such a reflex, the afferent impulses go by way of the sensory nerves supplying the parietal peritoneum and the sensory sympathetic fibres from the viscera, while the efferent paths are the ordinary spinal nerves supplying the abdominal muscles.

Conditioned Reflexes.—These reflexes are still more elaborate. The impulse passes to the spinal cord, but before the response is given it passes up to the higher centres where it is compared with the memory of past sensation, and the result is influenced or conditioned by past experience. In the first instance the process is in part conscious, but later on it requires no conscious effort.

We owe the beginning of our knowledge of this subject to the work of Pavlov, the Russian physiologist. We are all familiar with the fact that if a hungry dog is shown food it salivates freely

or, as we say, its mouth waters. Pavlov showed that if a bell is habitually rung at the time of feeding, after a time salivation is produced at the ringing of the bell although the food is not forthcoming. It is possible, indeed, so to train a dog that it will salivate on a specific note of the piano being struck, and the animal can be taught in this way to distinguish between half-tones. Moreover, by ringing the bell half an hour before feeding, the dog may be made to salivate automatically, as it were, half an hour after the bell has been rung. In this instance Pavlov took the normal involuntary act of secreting saliva as the response and the sensory path as that of the sense of hearing. Any sensation, however, may similarly be made to become the stimulus of salivation. This will be dealt with in a later chapter, in which we shall see the relationship of psychical influences to salivary and gastric secretion. A reflex of a similar nature may be produced where the effector organ is a voluntary muscle. Anyone who has been fortunate enough to be behind the scenes at a fire station in the old days of horse-drawn engines could not but be impressed by the way the horses responded to the ringing of the alarm. They would rise to attention and, on the opening of the stable doors, hasten, unguided, to their appointed places. The training of performing animals depends on similar principles, each movement of the trainer having its associated memory, usually that of food or punishment.

We must realize that a large number of our daily actions are of a purely reflex character. At the same time it is evident that many actions of the lower animals are acquired by training, for we see the mother animals training their young. A bear, for example, is taught by its mother to walk a tree-trunk. We can, to some extent, appreciate how many of our normal actions are reflex if we compare ourselves with a child or attempt to use our knife and fork in the unaccustomed hands. Learning to drive a motor-car, to ride a horse or bicycle, depend on the formation of reflexes. Once the reflex is formed, the movement ceases to be the result of conscious effort, and at the critical moment the appropriate response is made with a minimum of delay. What, however, is most important is that even the sensory stimulus does not affect consciousness until we realize that a response has taken place. We are familiar with the fact that we fail to appreciate a repeated stimulus. Once we are in a hot bath we cease to appreciate the heat of the water. A good example of the uncertain relationship of stimulus and response to consciousness is to be

seen in a person who habitually travels by bus or train. His ticket is received and put in a particular place quite reflexly and without any conscious effort. Both the stimulus and the action are oft repeated and he expects to find the ticket in its proper place when needed. What has been said on an earlier page in relation to facilitation and the analogy of the water flowing through a box of hay may be held to apply equally to a conditioned reflex. Repetition is the important factor in its normal formation, and we recognize this in the formation of habit. The Duke of Wellington is credited with having said that habit was merely something done twelve times. Once the habit is formed, however, we know how difficult it is to alter it. Indeed, it may be easier to break it altogether. Habitual smoking and chronic alcoholism present special difficulties in this respect, and are closely allied to conditioned reflexes, but in these instances the failure to repeat in itself causes a stimulus to repetition, and a vicious circle is the result.

When the reflex is established it is extremely difficult to get the impulse to flow in another channel. Thus, if a dog has established a reflex by which it salivates on the sounding of a certain note of a piano, it is no easy matter to get salivation on any other note. Indeed, the dog has to be taught all over again. In the formation of the conditioned reflex, then, consciousness has been required in the first instance, but gradually as the stimulus is repeated the conscious memory is no longer needed, the sensation is not clearly appreciated, and the final reflex has the appearance of a short-circuited edition of the mechanism by which the original movement was brought about.

The final product is an activity, the result of a stimulus, but neither the activity nor the stimulus may affect consciousness.

Many suggestions have been made regarding the exact nervous mechanism by which conditioned reflexes are formed, but anything which is said on this subject must be considered hypothetical. The suggestion that new short circuit paths are formed is negatived by the fact that the cerebrum continues to be necessary for the reflexes. Removal of the appropriate part of the cortex causes a disappearance of the reflex.

The most probable hypothesis is that the impulses concerned pass through the higher centres too rapidly to be appreciated in consciousness. This might result from a diminution in resistance of the pathways such as occurs in the lower reflex arcs. Such a view is but a convenient structure on which to hang our facts, and

in view of the increasing importance of psychology (which can no longer be denied a place in scientific medicine), some such structure is necessary if the proven facts of physiology and psychology are to be correlated.

The action of drugs is of considerable clinical importance in relation to reflexes. As we have seen above, bromides have been stated to depress and strychnine to augment reflex action. At first sight these drugs are physiological antagonists, yet it is agreed that in cases of neurasthenia, for example, the giving of both drugs together is of undoubted value (Bramwell). We have seen that strychnine in small doses facilitates reflex action by reduction of the synaptic resistance, and it is only in large doses that there is reversal of reciprocal innervation. It has now been shown that bromides have a special action in inhibitory processes, and that under their influence it becomes easier than usual to extinguish conditioned reflexes. In pharmacological doses, therefore, these drugs are not so antagonistic as at first sight appears, and no doubt in this fact lies the value of the clinical evidence referred to.

Extinction of Reflexes.—When undesirable reflexes have become established their extinction may become an important therapeutic consideration, and it must be remembered that the longer the reflex persists the more difficult it is to eradicate. Coughs, sucking the fingers, and various habits and tics are examples of such reflexes. Idcally, the stimulus should be removed. If this is not possible, drug treatment, *e.g.*, opium derivatives in cough, may be necessary. Otherwise the methods used may be based on those used by Pavlov to cause extinction of conditioned reflexes in dogs. A permanent extinction is brought about by causing the stimulus to be associated with a noxious stimulus. This has been extensively used in the elimination of the cough whoop after the fever has subsided in whooping cough and is the basis of various cures, *e.g.*, the whipping cure extensively used in Germany or holding of the child upside down. The putting of mustard on the fingers to prevent sucking is a similar treatment. Often a severe scolding is sufficient, but the repetition of the scolding is physiologically as important as its severity.

Conditioned Pain.[1]—The reflexes with which we have just dealt are those in which the reception of a sensory stimulus results in some

[1] This conception of the formation of sensory reflexes analogous to motor reflexes is a purely personal view which appears to go a long way in explaining what are undoubted facts. Similar phenomena may also be observed in pet animals which have been injured. So far as the author is aware the view has not been put forward elsewhere.

form of activity. Knowing what we do of the formation of reflexes, the possibility that motor movement may in certain circumstances result in sensations of an analogous conditioned nature can no longer be ignored. For example, a patient has a lesion, *e.g.*, fibrositis, which causes pain on movement. The lesion clears up, but pain on movement remains. That this pain is often quite genuine there is little doubt. Yet the fact that it may often be made to disappear with amazing rapidity by treatments which can have no possible influence on the local condition indicates the possibility of its reflex nature. Clinically such cases abound, although of course they cannot easily be reproduced artificially in animals. Here we are on the borderline of psychology, and at this borderland lie a valuable province of medicine, and, also, a realm of unscrupulous quackery. For our present purposes, it must be realized that no amount of verbal persuasion will convince the sufferer that there is no pain. Often a show of violent treatment, such as that commonly adopted by osteopaths and chiropractors, some of whom claim that they reduce a dislocated spine (in itself an alarming diagnosis), is often strikingly efficacious and suggests the value of methods which we know to be necessary in altering conditioned reflexes or even habits. It remains for clinicians to work out more carefully this aspect of the subject. It is impossible to have seen the effect of a pilgrimage to Lourdes, or the collection of crutches, bandages, and splints at an Eastern shrine, and not have been impressed with this aspect of the curative art. The fact that so many successful cults, such as chiropractic, osteopathy (using the term in its original American sense), faith healing, Christian Science, and Couéism flourish in our midst indicates the necessity for serious study of the subject. Medical psychology, the scientific counterpart of these cults, meantime struggles for recognition. Its acceptance is undoubtedly hindered by its unfortunate tendency to alienate itself, especially in its language, rather than to ally itself with what is straightforward physiology, when so much could be gained by co-operation. It is hoped that in time medical psychology and physiology will learn to understand one another.

The physical effect of fear is closely related to this subject. It may, for example, be shown that a prick with a pin results in diminution of the volume of a limb (Mosso), or a fall in the electrical resistance of the skin (the psychogalvanic reflex), but the mere threat to hurt results in a similar response. Mental effort alone produces a similar effect.

In a more exaggerated form these are the signs of general increased sympathetic activity seen in exophthalmic goitre. This opens up the possibility that the effect of many irritations in life may depend on a similar process of conditioning and that many minor circumstances may, by a process of association, produce, if continued, harmful effects on the organism as a whole, leading to upset not only of the circulation and alimentary canal (see Blood Pressure and Digestion), but of the general mental outlook.

The whole problem is intimately bound up with the phenomena of hysteria in which suggestion plays such an important part; indeed, there is no dividing line between the two. The attitude of some pseudo-scientific doctors, and still more of the patient's friends, in describing certain symptoms as " functional " and as if they could be avoided, is unfortunate and seldom does the patient any good. Undue severity and lack of sympathy may merely suggest to the patient that she must prove her case by not getting better. Undue sympathy may also cause the symptoms to persist. Here the successful doctor is he who calls to his aid the cult of Aesculapius rather than the science of Hippocrates and treats the patient rather than her disease.

These facts are already well known to the good physician, and still better to the good general practitioner who takes the trouble to understand the circumstances of life of his patients, and they are already made use of. It is only when an attempt is made to arrange them in the cold light of science and when the language used bears little or no relation to existing knowledge that difficulties arise.

CHAPTER VIII

MUSCLE TONE AND POSTURE

MUSCLE tone may be described as the state of partial contraction maintained by a muscle and depending on the integrity of reflex arcs. If the tone of a limb is exaggerated it is difficult to move the part which may take up an abnormal position of flexion or extension; this state is found in the muscles of the limbs when the pyramidal tracts are injured or diseased. If, on the other hand, the reflex arc is destroyed, not only are the tendon reflexes of the part lost but all tone in the muscle is lost and the limb becomes flaccid and flail-like. This we see in anterior poliomyelitis, in which the cells of the anterior horn are diseased, or when the posterior roots are destroyed. To understand the clinical changes which may be found in man, it is desirable to consider briefly the phenomenon of muscle tone in animals whose central nervous systems have been cut at different levels.

If the spinal cord has been transected in the cervical region[1] the position assumed, after the stage of "spinal shock" has passed away, is one of general flexion as if protective, the tone of the flexor muscles being exaggerated. If, on the other hand, the section is made between Deiters' nucleus in the upper part of the medulla and the red nucleus in the mid-brain, the animal passes into a state of **decerebrate rigidity** which is characterised by a sustained exaggerated tone of the extensor or anti-gravity muscles (Sherrington). This tone may easily be shown to depend on a reflex arc, the apex of which is Deiters' nucleus, the afferent path in the spinal cord being the antero-lateral tract and the efferent the vestibulo-spinal tract. This we know because section of any part of the arc causes the rigidity to disappear. The impulses are set up by the stretching of the extensor muscles.

Although the *decerebrate animal* is rigid, it is found that the position of the rigid limbs can be altered by various procedures. For example, if the head is bent forward the forelegs lose their extensor tone, while, on the other hand, if the head is bent backward the forelegs extend. We can well imagine that these changes in the posture of the fore-limbs normally take place when the animal is attempting to reach anything on the floor or on a

[1] For convenience this animal is often known as a **spinal animal.**

shelf respectively. A large number of similar changes in tone can be brought about by movement of different parts of the body.

The contraction of the calf and quadriceps extensor muscles, which occurs when an attempt is made to bend the leg, is often referred to as the extensor thrust. This is no doubt a reflex normally used in walking; it is more readily appreciated in skating that by its means we propel ourselves forward.

If the section of the brain is made above the red nucleus the tone of the muscles is normal and the animal is able to right itself from any abnormal position in which it is placed. The exact mechanisms concerned have been worked out largely by Magnus. He has shown that normal posture is maintained by impulses which arise from the muscles like those just described, from the skin in contact with the surface on which the animal is resting, from the eyes, and from the otolithic cavities, the utricle and saccule. In the latter cavities are maculæ, the cells covering which have hair-like processes, to which are attached by mucin granules of chalk which cause stimulation of the hairs according to the position of the head. The calcareous granules are called otoliths and stimulate the hair cells by pulling on them, when the position of the head is such that the otolith comes to lie beneath its particular macula.

The utricle is continuous with the semicircular canals, and the impulses from both otolithic cavities and utricle are transmitted by the vestibular nerve. The otolithic cavities are static in function, the semicircular canals kinetic, the one reacting to simple changes in posture, the other to progressive movement of the head.

The afferent postural impulses are correlated in the mid-brain and the upper part of the medulla. The cerebellum and the cerebral cortex are apparently not much concerned in posture. The occipital cortex is of importance, however, in visual righting reflexes.

It can be shown, moreover, that the cerebral cortex is not entirely inactive in relation to posture, for in recovery from cerebral anæmia or anæsthesia, especially with ether and avertin, a position of flexion of all four limbs is obtained prior to return to sensibility. It has been found also that there is a difference between the hind and fore-limbs in their speed of recovery, the fore-limbs recovering before the hind. There is then obtained a position of flexion of the fore-limbs with extension of the hind limbs (Blair and McDowall).

If, now, the cerebral cortex is removed the extension returns. Since section experiments indicate that the production of extensor rigidity requires destruction of the red nucleus we must presume that in the flexor stage the red nucleus has not recovered from the anæsthesia.

These facts throw considerable light on the various postures assumed by man in disease. In spastic hemiplegia the limbs commonly assume a characteristic position, the paralysed arm being flexed and the leg extended. In some cases the flexion is converted into extension by causing the patient to bend forward. It has been said that these states are produced by similar interference with the region of the corpus striatum (of which we know the rubrospinal tract from the red nucleus is ultimately the efferent pathway) leaving the flexor activity of the cortex unopposed. The cause of difference in posture between the arm and leg in hemiplegia is difficult to explain. Walshe suggests that it is due to the difference in function between the arm and leg ; and Brain suggests that the flexed arm is really the standing position in those animals which walk on their hind legs, while if they return to the horizontal position the arms may extend. This argument is, however, not so applicable to cats, for example, in which a similar state may be produced by anæsthesia.

The view that the impairment of function of the corpus striatum is concerned in hemiplegia is at first sight supported by the symptoms of striatal disease in which muscular rigidity is also present, but both the extensors and flexors are affected, and the rigidity is most marked in the flexors. This state may be the result of release of the cortex and of Deiters' nucleus. The rigidity of striatal disease also differs from that of pyramidal tract lesions in quality as well as distribution. In upper motor neurone lesions the spastic quadriceps yields reluctantly when the knee-joint is forcibly flexed, but once it has yielded, it surrenders fully—the so-called " clasp-knife " rigidity. In striatal disease, on the other hand, when the rigid muscles are stretched, they yield bit by bit, and the rigidity is therefore spoken of as being " cogwheel " in type.

More common is the spasticity of muscle occurring in lesions of the upper motor neurone. This occurs in disease of the motor cortex or pyramidal tracts. It may also result from tumours or injury to the spinal cord in the thoracic region. Immediately after an injury there is a stage of complete flaccidity with a loss of reflexes, but gradually the tone and the reflexes return. When

the tone is established the legs are extended with the toes pointing downwards. This is commonly known as paraplegia in extension and is associated with exaggerated reflexes, ankle clonus, a positive Babinski's sign, and a thrust reflex. The condition indeed resembles that found in decerebrate rigidity. Spastic hemiplegia is an analogous unilateral condition.

Complete transection of the cord, on the other hand, by destroying all connections with the brain, produces, after the initial flaccidity due to shock has passed off, a state like that of the spinal animal—the so-called paraplegia in flexion in which flexor reflexes only are present. Even the flexors, however, have here less than normal tone, although they are strong enough to overcome the still weaker extensors.

We are now in a position to realize that the tendon reflexes are part of the mechanism of posture, and that the knee jerk of a spinal animal is really a fractionated postural reflex.

CHAPTER IX

CONVULSIONS

CONVULSIONS are usually either epileptiform or spinal, although other varieties are recognized, *e.g.*, " bulbar " fits in poisoning with picrotoxin.

Epileptiform fits are due to abnormal processes occurring in the cerebral hemispheres. They are often heralded by an aura, which may be a simple sensory or motor phenomenon, or, on the other hand, may be a complicated visual or auditory experience, even a " vision." The simple auræ are apparently due to a local action on the corresponding cortical area, and are absent in the convulsions due to heart block. Loss of consciousness, deviation of the eyeballs, and tonic and clonic spasms ensue. The deviation of the globes suggests that the processes underlying the fit are initiated on one side of the cerebrum, and rapidly pass to the other.

In *Jacksonian epilepsy* the convulsion begins locally and travels in an orderly manner until the face, arm and leg are involved on one side. The " march " of the fit is evidently related to spread of disturbance through the motor cortex of the affected side of the brain. The disturbance may not spread, however, and the fit remain sharply localized. Weakness of the affected muscles may follow the convulsion (Todd's paralysis). Consciousness is usually retained, but may be diminished or lost. Sensory varieties of Jacksonian epilepsy may occur. Jacksonian fits are commonly due to local gross lesions, but the stimulus does not act mechanically, for mechanical stimulation is ineffective to excite the motor area ; disturbances of the circulation and œdema and locally produced chemical products may represent the effective agents. Moreover, Jacksonian epilepsy may be a manifestation of so-called " idiopathic " epilepsy, *i.e.*, no lesion, even of histological magnitude can be discovered. Petit mal is epilepsy without convulsions.

The way in which the ætiological factors underlying epilepsy act is not definitely understood. These factors include (1) gross cerebral disease. Generalized as well as local fits may occur in cases of cerebral tumour, etc. ; (2) interference with the cerebral

circulation as in experimental occlusion of the cerebral arteries, cerebral anæmia from Stokes-Adams disease, etc.; (3) hypoglycæmia, particularly in animals; (4) severe asphyxia; (5) toxæmia, *e.g.*, specific fevers, uræmia, etc.; (6) convulsant poisons, such as cocaine, absinthe, etc. In a large group of cases, "idiopathic" or "cryptogenic" epilepsy, the factor is unknown; Purves Stewart speaks of "an explosive cortex together with a metabolic dyscrasia." Some authors regard a disturbed water-balance as the factor concerned, and attribute the beneficial effect of a ketogenic (fatty) diet to dehydration. This benefit certainly occurs. McLaughlin and R. H. Hurst have shown that there is no evidence of alkalosis as a causal factor.

Collier strongly favours the metabolic theory. It has been stated that the blood of epileptics will cause convulsions when injected into animals, whereas normal blood is without this power. Dendy and Miller showed the importance of the influence of a general factor in epilepsy due to gross cerebral disease. Lesions of the brain in experimental animals did not of themselves cause convulsions, but if doses of absinthe, not sufficient to excite epileptic phenomena in normal animals, were now given, convulsions ensued.

At first sight, the convulsion would suggest an excitation of the motor area. Cocaine, for example, renders the motor area more easily excitable by electricity. On the other hand, Hartenberg's view that epilepsy is due to inhibition of higher cortical levels, with resulting overaction of lower ones, has much to support it; the loss of consciousness must surely be an inhibitory phenomenon, so also is the loss of the corneal reflex. The fact that loss of consciousness alone (petit mal) may occur in an individual subject to major fits may be regarded as evidence of inhibition; and here may be placed the fall of blood pressure which commonly precedes the attack. The presence of extensor plantar reflexes immediately the convulsion is over can be regarded as evidence of exhaustion of the pyramidal system from over-excitement, but more likely represents inhibition spreading even to the motor area.

Probably the truth is divided between the two theories and paralysis of higher levels is accompanied by excitement as well as release of lower. By crude analogy certain drugs, *e.g.*, morphia, may depress one region of the central nervous system while exalting others.

In status epilepticus the convulsions recur frequently, and

hyperpyrexia ensues. Death is apt to occur and is due to a combination of exhaustion and toxæmia.

Spinal convulsions are seen particularly in tetanus and in strychnine poisoning. The cranial reflex arcs do not escape, particularly in the former case. Consciousness is not lost until near the end in fatal cases. Although in strychnine poisoning clonic convulsions of the hands are seen, these rapidly give way to tonic spasms, often of great severity. In tetanus there is some rigidity between the convulsions, but in the case of strychnine poisoning the muscles relax between the spasms.

The convulsions are excited by trifling stimuli which would ordinarily have no such effect, and the excitatory process spreads widely throughout the spinal cord so that the mere approach to the patient produces fearsome consequences that are painful to the physician and patient alike. Moreover, opposing groups of muscles may contract together and rupture of muscle fibres may result. Whether strychnine does this by reversing inhibitory processes, making them excitatory, or whether the greatly increased excitatory processes swamp the inhibitory ones is not quite clear ; modern work favours the latter theory, for a number of purely inhibitory actions can be elicited during the action of the drug.

Excitation is also seen in the increased acuity of vision and hearing in the earlier stages of the action of strychnine. Death may occur from asphyxia from fixation of the thorax by the spasms or from exhaustion.

CHAPTER X

EQUILIBRIUM, VERTIGO, ATAXIA, GAIT

THE maintenance of equilibrium depends on a larger number of factors than is generally recognized, and these are reasonably clearly defined. Briefly, they may be summarized as : afferent impulses from the eyes, vestibular apparatus, and organs of muscle and joint sense ; the paths by which these impulses are conducted ; the mechanisms by which they are co-ordinated, especially in the mid-brain and cerebellum ; and the efferent paths by which co-ordination is brought about. The efficiency of the muscle, bones, and joints is presumed. The above factors are dealt with below in so far as they are clinically important. The number of impulses actually passing centrally appears to be an important factor.

The Eyes.—Here the extent to which objects may be focussed is the important factor, and also the regularity with which visual impulses are received, although people vary in the extent to which they use their eyes. In the majority of individuals, however, a reduction in the number or confusion of such impulses brings about a feeling of giddiness. This is experienced if one attempts to cross a plank bridge, look from a height, or to watch movements of a river from a bridge, and, in some people, even to watch a train start. It is not, however, necessarily experienced in an aeroplane where there are numerous near objects which can be focussed. When climbing the Eiffel Tower also one becomes much more giddy on the first platform than further up, where it is more difficult to avoid seeing the understructure. Further evidence that it is the focussing of objects which is concerned is derived from the fact that the instillation of atropine, by paralysing accommodation, is liable to bring about a loss of equilibrium. Patients so treated may find themselves suspected of being under the influence of alcohol. Similarly, in diplopia, due to inco-ordination of the extra-ocular muscles, when the proper convergent movements associated with accommodation are rendered impossible, giddiness is common. The fact that in this condition the giddiness is not abolished by covering the

eyes, suggests that afferent impulses from the eye muscles are concerned.

Muscle Sense.—That muscle sense plays a large part in the maintenance of equilibrium is shown by the fact that if the number of afferent impulses from the muscles is reduced, the eyes become more important for equilibration. Thus, it is usually impossible for a person to stand steadily on one leg, with closed eyes, although there may be no difficulty in doing this when the eyes are open. Advantage is taken of a similar difficulty in Romberg's sign by which is tested the patient's power of standing steady with the feet together and the eyes closed. When the afferent impulses from the motor organs are diminished, as in tabes or after severe peripheral neuritis, unsteadiness results. Similarly in tabes, closure of the eyes when bending forward in washing, may cause the patient to fall forward, and not infrequently damage himself through violent contact with the taps of the lavatory basin. The dizziness experienced by some people in stepping suddenly from a hard pavement to an india-rubber pavement is of a similar nature.

Under conditions in which there is a reduction in the number of ocular sensations equilibrium may be maintained and a feeling of confidence given by the addition of muscle impulses. Thus a man who is quite giddy when looking down from a height is not so if he holds on to something, and will have no difficulty in climbing a ladder or a tree provided he looks at objects he can focus easily.

In the same way ataxic individuals walk reasonably steadily by making more use of their eyes, and it is of course in these persons that the effect of closure of the eyes is most marked. The ataxia is the result of loss of muscle sense, for the patient can no longer adjust the exact extent of his muscular action, and the stamping, or hen gait, is characteristic of many conditions affecting either the posterior roots or the posterior columns. In the treatment of tabes it is possible to re-educate co-ordination by causing the patient to practise walking along a floor on which the positions in which the feet have to be placed are marked.

Vestibular Apparatus.—It is well known that removal of the semicircular canals in animals, first carried out by Flourens, or disease of the canals results in a loss of the power of equilibration. We now know that the otolithic cavities are responsible for our appreciation of the position of the head ; and the work of Breuer and Crum Brown in 1875 showed that the semicircular canals are responsible for the sense of rotation. The canals, three

in number, lie one in each of three mutually orthogonal planes, each with an ampulla or enlargement at the end where it branches off from the common vestibule. In each ampulla is a crista surmounted by sensitive hairs which are stimulated by movement of the endolymph. In each of the otolithic cavities (utricle and saccule) are the maculæ, the hair cells of which are stimulated by the pull of calcareous granules or otoliths. Excessive movement of the endolymph, such as that set up by rapid turning, will upset the normal mechanism, and giddiness from this cause is well known. Impulses pass from the cristæ by way of the vestibular part of the eighth nerve to the pons and thence to the same side of the cerebellum. From Deiters' nucleus which is related to the vestibular nerve in the pons, impulses pass up in the posterior longitudinal bundle to the oculo-motor nuclei and down in the vestibulo-spinal tract to the anterior horn cells.

Labyrinthine disease, or disturbance of the afferent path by a lesion such as an acoustic nerve tumour, will bring about loss of equilibrium with a tendency to fall to the diseased side, for most of the afferent impulses responsible for equilibrium are, so far as we know, uncrossed. Paroxysmal vertigo of a similar nature is seen in Menière's disease, where it is accompanied by vomiting and deafness ; the exact nature of the labyrinthine disease is unknown. Nystagmus (*q.v.*) is also a symptom of labyrinthine disease.

The Cerebellum and Mid-Brain.—It used to be considered that all the afferent impulses were co-ordinated in the cerebellum, but more recent knowledge from the Utrecht School has emphasized the fact that the mid-brain and the brain stem even down to the upper part of the medulla play an important part in equilibrium. Complete clinical equilibrium exists not only in posture, but also during movement. The brain stem appears to be responsible for the former, the cerebellum for the latter, facts of considerable clinical importance, seeing that tumours of the brain stem will simulate tumours of the cerebellum, although in the latter the loss of equilibrium is more marked during movement. Sherrington has described the cerebellum as the chief ganglion of the proprioceptive system. That this is so is evident from the effect of total or partial ablation in animals, or of disease in man. Abscess and tumour are the commonest pathological lesions of that organ. Since impulses passing to the cerebellum do not cross in their upward path, we expect the lesion to be on the same side as the symptoms.

The symptoms of cerebellar disease may conveniently be grouped under two headings: disturbance of posture and disturbance of co-ordination of voluntary movement.

There is a general weakness of muscles, which feel flabby and may be stretched without producing pain. The patient is unable to hold his hands steadily and symmetrically out in front of him, and lying in bed with his eyes closed he is unable to raise his finger exactly to an observer's finger held above the bed although he has previously learnt its exact position (Barany's pointing test). The disturbance of the posture mechanism is also seen in the pendulum knee jerk. After a brief contraction the leg falls limply and may go on swinging backwards and forwards.

Voluntary movement is also affected by the weakness and, in addition, ataxia is present.

The loss of co-ordination and muscular tone leads to a characteristic gait. Cerebellar ataxia, gait and nystagmus are described later under appropriate headings.

It seems likely that the loss of equilibrium which accompanies loss of consciousness, is due to the loss of the functions of the cerebellum and mid-brain, just as the unconsciousness is due to loss of cerebral function.

In alcoholism, probably the commonest cause of loss of equilibrium, the early "light-headedness" suggests a paralysis of higher centres of appreciation of all kinds, although later the drug depresses the activity of all nerve tissue.

It is interesting to note that the functions of the cerebellum may be taken over by other parts of the brain, such as the cerebrum. This would appear to indicate that the cerebellum has been specially developed in relation to the mid-brain for the purpose of co-ordination at a lower level than the cerebrum. If the cerebellum is removed in a dog, the animal loses its power of co-ordination, but eventually it recovers control, and in such circumstances the cerebrum can take over the cerebellar function. This observation is important in relation to the removal of cerebellar tumours, for even if the cerebellum is largely destroyed, the patient may hope to recover his co-ordinating powers.

The results of re-education treatment in tabes and of the experiments on the dog quoted are significant, as indicating that the normal reflexes of co-ordination and, possibly, some of those of posture may be reproduced in the same way as conditioned reflexes.

Similarly, too, we may consider that the performance of special feats of balancing by acrobats depends on such processes. One is tempted to compare what may be called inherited reflexes and powers of co-ordination with the " Ego " (or inherent self, of the psychologist), and the reflexes of posture and co-ordination, produced by training, with the " self " produced by education. It may be that we have a thought mechanism analogous to motor co-ordination, and the effect which inherited mechanisms can have on educated mechanisms and *vice versâ* is strictly comparable.

Vertigo may be a sensation only : the patient feels he is going to fall, or that objects are rotating round him. On the other hand, the disturbance may be more severe, and he may reel or fall to the ground.

Certain fundamental types of vertigo have been discussed in the foregoing paragraphs, viz., visual, and labyrinthine and cerebellar varieties. Labyrinthine vertigo is frequently accompanied by pallor and other evidences of vasomotor disturbance, and by vomiting, as in seasickness.

Certain drugs act through one or other of these channels. For example, vertigo in quinine poisoning is due to an effect on the labyrinth, in alcoholic intoxication to an effect on the cerebellum plus higher centres. Vertigo in pathological conditions is, as a rule, due to some form of cerebellar or labyrinthine disturbance. Amongst these conditions may be instanced various diseases of the ear and Menière's syndrome, cerebellar tumours and abscesses, concussion and increased intracranial pressure. Epilepsy may also cause vertigo which then probably represents a transient disturbance of cerebellar function. Interference with the blood supply, either locally produced as in thrombosis of the posterior inferior cerebellar artery, or from lowering of the general arterial pressure as in fainting, is a potent cause. The cause of the vertigo which accompanies high blood pressure is not well understood. Hyperæmia of the labyrinths and spasm of the cerebral vessels are among the explanations which have been adduced. Diminished respiratory capacity of the blood reaching the brain is the effective factor in anæmia. The toxins produced in various infective conditions can disturb the equilibrating mechanism. Mention must be made of the not uncommon alimentary vertigo, but whether this is due to a toxic or reflex disturbance of the equilibratory functions is not clear.

Ataxia signifies defective co-ordination of the muscles during

movement. Clinically it is most easily observed in the limbs. In the upper limbs good tests for ataxia are the finger-to-nose test and the execution of moderately fine movements such as picking up a small object from a flat surface. In the lower limbs the condition is revealed in the gait and by the heel-to-knee test. The two chief causes of ataxia are : (1) loss of afferent impulses from the muscles and joints ; and (2) disturbances of the cerebellum or of its afferent or efferent tracts. In the first group the ataxia is aggravated by closing the eyes, in the second is not appreciably affected thereby. Ataxia also results from an acute labyrinthine disturbance, and from the rare lesions of Deiters' nucleus.

One of the commonest causes of loss of kinæsthetic impulses is disease of the posterior nerve roots in tabes dorsalis, but it must be emphasized that gross ataxia is a late sign of the disease. Damage to any part of the pathway *viâ* the posterior columns of the spinal cord, the fillets in the brain stem, the thalamus and the cerebral cortex will cause loss of muscle sense and ataxia. An example of spinal ataxia is seen in the subacute combined degeneration of the cord in certain cases of pernicious anæmia ; some degree of paraplegia is also present, for the lateral columns are involved as well (ataxic paraplegia). Part of the ataxia is due indeed to involvement of the lateral column where it contains the spino-cerebellar tracts. A lesion of one thalamus causes hemi-ataxy on the opposite side of the body, associated with the characteristic sensory disturbances of such a lesion. The cortex is at fault in the ataxia of finer movements seen in parietal lobe lesions ; the loss of the discriminative aspects of kinæsthetic sensation renders fine movements difficult or impossible and astereognosis is also present.

In cerebellar disease sensation is unaffected and the disturbance of voluntary movement results from loss of the guiding action which the cerebellum exerts over the cerebral cortex as the latter discharges impulses down the pyramidal tracts. This guiding influence the cerebellum is able to exercise in virtue of receipt of proprioceptive impulses from the muscles, etc. (see Fig. 5). Although these afferent impulses do not reach consciousness they are offshoots from the sensory stream. Disturbance of the afferent paths as in Friedreich's ataxia causes symptoms similar to those due to direct damage to the organ itself.

In cerebellar disease slowness of movement is present so that a voluntary act is executed in a series of discrete stages instead

of these being fused together. Moreover, stages that should be simultaneous are performed one after the other. Gordon Holmes has given the apt name of " decomposition of the movement " to this disorder. The force with which the movement is carried out is ill-judged (dysmetria) and often excessive. In the finger-to-nose test the face may be struck with considerable force. Further, asynergia of the muscles is observed, *i.e.*, the proximal muscles which would normally fix the limb during the movement by others of a more distally situated joint fail to contract properly.

Cerebellar ataxy may affect the articulation (ataxic dysarthria). The speech may be slow and each syllable uttered separately in a manner reminiscent of a schoolboy scanning Virgil, or else syllable stumbling occurs. The peculiar speech and the inco-ordination of disseminated sclerosis are probably due to involvement of the cerebellum or its tracts.

The ataxy observed in chorea is probably the result of interference with the efferent pathway from the cerebellum to the cerebral cortex (see page 82). In the mid-brain a lesion of the corpora quadrigemina, which are connected to the spinal cord by the tecto-spinal tracts and which are also in intimate relationship with the oculo-motor nuclei, causes bilateral ataxia together with inability to move the eyes upwards (Nothnagel's syndrome). Disease of the red nucleus causes tremors and inco-ordination of the muscles of the opposite side of the body ; there is also paralysis of the third nerve on the side of the lesion, for the oculo-motor fibres traverse the red nucleus. Attention has already been drawn to the close relationship between the cerebellum and mid-brain. The red nucleus is an important relay station on the cerebello-spinal pathway.

Abnormalities of gait may arise from disorders of the bones and joints, of the muscles and of the nervous system. Among abnormal gaits due to affections of the joints may be mentioned the waddling seen in the subjects of congenital dislocation of the hips. A waddling gait may also be present in myopathy when it is due to weakness of the glutei. Later in this disease when the patient from muscular weakness loses the power of standing, he may in moving from place to place adopt a frog-like attitude in which the hips and knees are fully flexed and the fingers touch the ground. A characteristic high stepping occurs when the dorsiflexors of the ankles are weak, as in alcoholic neuritis, for the leg has to be lifted high in order that the toes may not catch on the ground. In certain cases of peripheral neuritis, ataxia from

loss of muscle sense may complicate the picture and care must then be taken to distinguish the condition from tabes dorsalis.

Spastic weakness of the muscles in bilateral pyramidal tract lesions, *e.g.*, in disseminated sclerosis, causes the characteristic spastic or " dancing " gait, in which the lower limbs move stiffly with short steps, the toes being scraped on the ground. In hemiplegia one foot only is scraped in this way. In the spastic " scissor gait " of cerebral diplegia the tonically contracted adductor muscles cause the legs to cross in front of each other with each step.

Ataxic gaits are seen in the noisy stamping of advanced tabes (see page 71), and in cerebellar disease. In the latter the gait is reeling, although the patient may walk with exaggerated care. He tends to stumble on the affected leg if the lesion is unilateral. The peculiarities of the gait in cerebellar disorders are readily understood, provided that the fundamental disturbances of the muscles, viz., hypotonia, weakness and ataxia are kept in mind. The patient is very easy to push over, for the reflex balancing reactions are diminished or lost, and voluntary efforts to recover his position are apt to be executed too slowly to be effective.

There remains for consideration the gait in paralysis agitans in which the influence of the corpus striatum is in abeyance. Owing to the rigidity of the muscles, both flexor and extensor, the steps are short and shuffling, and, should the foot catch on some projection, they are taken faster and faster. If the patient is pushed forwards or backwards he is apt to run in the same direction (propulsion, retropulsion). The gait in paralysis agitans is often called festinant (Latin, *festinare*, to hasten or accelerate). The explanation of festination is to be found in the muscular rigidity which prevents long strides. If, for any reason, the trunk is thrown forwards, the lower limbs have to take more rapid steps in order to keep up with the trunk's centre of gravity, or the patient would fall.

In hysteria various fantastic gaits are seen. One of the most interesting is the " tight-rope " variety.

In certain of the abnormal gaits described above, the normal swinging of the arms may be interfered with. In spastic hemiplegia the paralysed arm does not swing but is held with the elbow flexed and the forearm pronated in the position of human decerebrate rigidity. In cerebellar disease the arm on the side of the lesion fails to swing and hangs limp ; this is of value in diagnosing the affected side of the cerebellum. The absence of arm swinging

in the gait of paralysis agitans is to be regarded as a result of the muscular rigidity and general poverty of movement which are noteworthy clinical features of this disease.

In a few conditions the patient can run more easily than walk, a condition known as kinesia paradoxa. Particularly is this the case in some cases of paralysis agitans and in moderate cases of cerebral diplegia. Indeed, the fact that Lord Byron was able to run but walked with difficulty has been adduced by Cameron as evidence that the poet was a victim of a mild degree of diplegia.

CHAPTER XI

TREMOR, CHOREA, ATHETOSIS

TREMORS are, from the clinical point of view, divided into toxic, organic and hysterical groups. Another useful clinical classification is into fine and coarse varieties.

The Nature of Tremor.—It is dangerous to prophesy in science, but it may be suggested from the work, especially of Sherrington, of Adrian and of Rijlant, that the tremors are fundamentally fractionated muscular movements or muscle tone, for it has been shown that nerve cells and sensory receptors discharge large numbers of impulses the rate of which may vary in varying circumstances. For example, the reflex tone of muscle is brought about by large numbers of impulses arising from receptors which are stimulated by the stretch applied to the muscle and playing upon cells which have a power of rhythmic discharge of constrictor impulses back to the muscle. On this system plays a further series of impulses from various higher centres. We may assume that when for any reason complete fusion of the muscular response fails to occur, tremor results. A crude imitation of such tremor is seen in the well-known class experiment in which a frog's muscle is stimulated with different rates of stimuli. Or it may be that the muscle is being stimulated by two or more series of rhythmic stimuli and the tremor is due to the occurrence of coincident stimuli like the throbbing produced by the simultaneous sounding of two notes of different pitch. So far as I am aware, this possible explanation has not hitherto been put forward, but it would explain the comparatively slow rate of tremor compared with the rate of discharge of known nervous impulses.

Tremor due to the toxins of infection and to drugs and poisons is usually fine, although an exception is encountered in chronic mercurialism ; the exception may be more apparent than real, for the occasional persistence of tremor for years after the original cause has been removed suggests that organic changes may be present in the nervous system. Of special interest are the fine tremors of Graves' disease which have been attributed by Collip

to disturbances in the parathyroids which are in close anatomical and vascular relationship with the thyroid gland.

Tremor in Organic Nervous Disease.—Apart from general paralysis, in which fine tremors are an important diagnostic sign, tremor in nervous disease is usually of the coarse variety. These coarse varieties can be clinically classified into " static " and " intention " types. In animals from which the cerebrum and thalami have been removed, stimulation of the mid-brain may excite tremor. In view of this and other evidence the condition has been usually regarded as a " release phenomenon " in which certain lower levels of the central nervous system are no longer dominated and kept under control by higher regions. The more deeply inrooted the postural tonus of a given part of the body, the less frequent is the incidence of tremor therein. Thus the upper limbs are much more frequently involved than the lower limbs or trunk and in the upper limbs the hands are more liable to be affected than the shoulders.

Static tremor is well seen in **paralysis agitans** in which rigidity and weakness of the muscles and general " poverty of movement " (Wilson) are present. The term " poverty of movement " applies to all movements other than the tremor which, it may be noted, is often temporarily diminished during volitional use of the affected limb. In post-encephalitic Parkinsonism a similar syndrome is present, although one or other additional sign such as spontaneous sudden movements of the lower jaw, oculo-gyral crisis (attacks in which the eyeballs are deviated upwards), etc., may be superadded.

The post-encephalitic syndrome rests on a secure foundation of morbid anatomy, viz., disease of the substantia nigra, and in this connection it may be noted that certain physiologists have claimed that stimulation of the substantia nigra causes jaw movements (such as may accompany the syndrome). The structural basis of classical paralysis agitans is not definitely proven (C. B. Dunlap), although the general opinion is that the corpus striatum is damaged. In any case the extrapyramidal system is at fault and it can be visualized that loss of function on the part of the globus pallidus or of its henchman the substantia nigra can release lower levels of the system which then produce tremor most marked in restless muscles, such as those which move the fingers and rigidity and sometimes tremor in posturing muscles, such as those of the trunk and lower limbs.

Extrapyramidal Neurones.—These are presided over by the

corpus striatum, the anatomical parts of which (caudate and lenticular nuclei) do not represent a true division of function. From the standpoint of comparative anatomy, and probably of physiological interpretation of symptoms also, the real subdivision is into (1) the palæo-striatum (" ancient striatum ") which comprises the caudate nucleus and putamen of the lenticular nucleus, and (2) neo-striatum (" recent striatum ") composed of the globus pallidus. The palæo-striatum consists in the main of large nerve-cells, the function of which is believed to be to inhibit the activity of lower levels, while the neo-striatum is made up chiefly of small cells which in virtue of the afferent impulses they receive, correlate and control the discharges of impulses from the larger cells.

According to Kinnier Wilson, the corpus striatum has no direct connection with the cerebral cortex, but other authors, notably Monakow, believe that such a connection exists. The afferent impulses of the corpus striatum are received from the thalamus and so, ultimately, from the voluntary muscles. The efferent fibres, which arise in the globus pallidus, pass into the *ansa lenticularis* and eventually reach various groups of nerve cells in the brain stem, particularly the substantia nigra, subthalamic nucleus of Luys, and red nucleus. The substantia nigra receives a liberal accession of fibres from the median fillet ; we must therefore assume that the lower as well as the higher levels of the extrapyramidal system receive proprioceptive impulses.

The " extrapyramidal " tracts include the rubrospinal, pontospinal, vestibulo-spinal, etc., and in virtue of connections with these, direct or indirect, the red nucleus and substantia nigra, and, ultimately, the corpus striatum are enabled to influence the anterior horn cells and so the voluntary muscles. The red nucleus and nucleus of Luys fall under the influence not only of the corpus striatum, but also of the cerebellum, a fact which may in part explain the conflict of opinion with regard to the site of the lesions in chorea and in athetosis (see page 83).

Action of the Atropine Group of Drugs on the Parkinsonian Syndrome.—Of these hyoscine is perhaps the most effective. Rigidity and salivation are mitigated, but tremor is usually unaffected. The mode of action is far from clear. The effect on salivation may represent nothing more than a drying up of secretion by the well-known action of these drugs. Although it has been supposed that rigidity of the muscles of deglutition and diminished swallowing are responsible for salivation, it seems possible that

there is also a true increase of saliva, as salivation, commonly observed in the encephalitic syndrome, is rare in paralysis agitans proper. How the rigidity of the muscles can be relieved by atropine and its allies is not known, but the effect is probably a central one. The patients are abnormally tolerant of the drug.

Cerebellar Tremor.—Static tremor due to loss of postural tone may be present, but the intention or kinetic variety is also frequently seen, as might be expected from the fact that the cerebellum exerts an important influence in phasic contraction of muscle. If the patient is asked to touch the tip of the nose with his finger, the latter part of the movement is broken up into a series of irregular jerks, and he usually ends by striking some other part of the face. Closing the eyes does not materially affect the condition. Asynergia of the muscles is present. The other signs of cerebellar disease have already been discussed (see page 73). The intention tremor of disseminated sclerosis is probably due to involvement of the cerebellum or the cerebellar tracts by which muscular movements are co-ordinated and rendered "smooth."

Fine tremors are common in conditions of emotional excitement and are also frequently seen in hysteria. In the latter condition coarse tremor, often intention in type and not infrequently dramatic in range, is also occasionally present.

Chorea.—Choreic movements are so well known that they need not be described here. They are often spoken of as "quasi-purposive." The essential phenomena of the choreic state have been ably summarized by Collier as consisting of spontaneous, irregular movements, muscular weakness and ataxia and psychical disturbances. Any one of these cardinal features may be exaggerated, *e.g.*, the weakness may be so marked as to justify the term limp or paralytic chorea. In paralytic chorea the movements are often slight. For choreic movements to occur the pyramidal tract must be functioning.

Choreic movements have been produced experimentally in animals by injury of the red nucleus (Economo and Karplus) and Bonhoeffer's opinion that disturbance of any part of the cerebello-cortical pathway *viâ* the red nucleus and subthalamic tegmental region (especially the nucleus of Luys) will cause chorea, has been widely accepted. Certain authorities, however, attribute chorea to a lesion of the small cells of the corpus striatum (Ramsay Hunt).

The majority of cases of chorea (Sydenham's chorea) are

rheumatic in origin and the lesions are vague and are not sharply localized. Probably disturbance of the cortex cerebri plays a part, as shown by the frequency of psychical changes ; moreover, lesions of the ascending parietal gyrus occasionally give rise to choreiform movements. As stated in an earlier chapter, the movements in chorea are of a more complicated type than those which occur when the motor area is stimulated. Probably they are generated in the physiologically superior regions of the brain where the finer pattern of voluntary movements is worked out, to be superimposed on the crude basis which is all that the motor area is able to supply. The effect of lesions of the cerebello-cerebral pathway in causing chorea can be pictured as resulting from a loss of a restraining influence normally exerted on these physiologically superior regions. Hyoscine may cause choreic movements ; this is probably due to an action on some special region of the brain (*cf.* the action of alcohol on equilibration in certain individuals). Probably in different persons different regions of the central nervous system vary in the ease with which they succumb to the influence of a given poison.

Athetosis.—Athetosis occurs usually in cases of old hemiplegia in which the limb, although spastic, is not completely paralysed. The upper limb is affected far more frequently than the lower and the face is involved in bilateral cases only. The movement is due to irregular contractions of muscles and is seen most typically in the hand where purposeless contortions and writhings occur. The mechanism of reciprocal innervation is lost and antagonistic groups may contract together. The condition is increased by voluntary movement whether of the sound or of the disordered side.

Athetosis is probably a further example of a release phenomenon ; it is believed by Ramsay Hunt that the activity of the globus pallidus is uncontrolled owing to damage of the neostriatum, *i.e.*, the small cells found chiefly in the caudate nucleus and putamen. This author believes that these cells are also damaged in chorea ; but in athetosis the movements are modified by the muscular rigidity which is present. Kinnier Wilson has brought forward evidence, however, that lesions of the corpus striatum do not interfere with reciprocal innervation of muscles and believes that disorder of the cerebellar control over the discharges from the motor cortex is the cause of athetosis ; the disturbance is supposed to occur at the thalamic level. On the other hand, Oppenheim and Vogt have described a type of infantile athetosis

associated with structural changes (*état marbré*) in the corpus striatum, especially in the caudate nucleus and putamen.

Experimental physiology has thrown, so far, but little light on the problems of athetosis and chorea, for the shift of function in the cerebral direction which has occurred in man renders the results of animal experiments less relevant than they would otherwise be, although it is surprising how little difference there is.

CHAPTER XII

SPEECH

Of recent years much controversy has raged on the subject of speech and aphasia, but while many of the older conceptions require to be modified, much of the evidence is by no means so contradictory as at first sight appears. In the present chapter speech is considered in its widest sense, namely, as the mode of interchange of ideas between mankind.

Speech may be looked upon as depending on three separate factors—receptor mechanisms, association mechanisms, and effector mechanisms. Failure of any of these will result in impairment of the power to respond to a particular kind of stimulus. A deaf man cannot respond to the stimulus of spoken words, nor can one with a tracheotomy respond by speech.

We must be careful to distinguish dysarthria or difficulty in articulation from aphasia or loss of speech in the higher sense of this term. Dysarthria results whenever there is interference with the proper action of the muscles of articulation. There are three main causes for this, in which the disorder lies in the medullary lower motor neurone, the pyramidal tracts and cerebellum respectively. The first is the ordinary bulbar palsy, and the dysarthria is called flaccid because the muscles are toneless and wasted, the second is called spastic (" pseudo-bulbar palsy "), and results only from *bilateral* lesions of the pyramidal tract, while the third is called ataxic. Aphasia is thus distinguished anatomically from dysarthria in being always cortical in origin.

The Receptor Mechanisms (*Afferent Projection System*).—Although normally the receptor mechanisms are those of hearing and seeing, any kind of sensation may be utilized. We are familiar with the fact that in the education of the blind use is made of the sense of touch. The peripheral mechanisms of hearing and seeing will be described in later chapters, and their nerve paths traced as far as the cerebral cortex in the temporal and occipital lobes respectively. In close association with the visual and auditory areas are association areas wherein appear to be analysed and stored the memories of visual and auditory words.

It must be understood that there is no hard and fast distinction between the receptor and receptive association mechanisms.

Association Mechanisms.—Our knowledge of these mechanisms is still comparatively crude, but while it is not yet possible to define accurately all the anatomical areas in which these functions take place, many facts which have been collected from the study of disease are of great clinical and physiological interest.

We may consider the association mechanisms as being of two kinds : the *receptive* which lead from the receptor mechanisms to conscious understanding, and the *expressive* which lead therefrom to the effector mechanisms. As we shall see, we have indications of the pathways used by some of these two association mechanisms, but unfortunately we have not a glimpse of the nature of conscious understanding although we can appreciate it. When, then, a stimulus of a spoken or written word is received through a receptor mechanism, it is first dealt with by the *receptive mechanisms*, which decide its significance to the person concerned. This significance will obviously depend on the previous associations which he has for the particular stimulus. Language is the expression of conventional association of ideas round certain sounds and symbols which groups of individuals find convenient for the interchange of thought.

When communication with a fellow-creature is desired, use is made in the first instance of the *expressive association* mechanism ; certain sounds, symbols, or movements which have a conventional significance are chosen, the actual speech being carried out by an effector mechanism. This mechanism, on the other hand, is merely a final common path which may be utilized for several purposes. For example, some of the muscles which produce speech may be utilized for mastication and other purposes.

The method by which associations are formed round certain sounds and symbols is of interest as it forms the basis of early education.

In learning to speak, a child at an early age associates certain words with certain objects which he sees. Gradually also he begins to imitate the sounds he hears, without necessarily understanding their meaning, and eventually learns to make the sounds which he associates with certain objects. These sounds are not infrequently, as a result of difficulty in pronunciation, a travesty of the words attempted, and such faults may be retained for a long time even when articulation is fairly complete. The sounds are symbols for the object or desire, and subsequently

they are put together in sentences. Later, through practice and by education, the sentences become more grammatical.

When the child begins to read and write, the symbolic nature of speech becomes still more evident. In the first instance, a written representation of the sound is learned, and subsequently this is imitated. Gradually everything with which the individual has come into contact is found to be capable of similar written symbolic representation, although it may be some time before the proper method of spelling is acquired. Further, as the development of a man in modern civilization is so closely associated with the possession of a facile method of communication with his fellow-men by means of speech, it is impossible to differentiate clearly between the development of speech and of intelligence. It will be evident that if the receptor or effector mechanisms are inadequate for the development of normal speech, the intelligence will tend to suffer. We have seen that in the development of speech, the associations of reading and writing are, as it were, superimposed on those of hearing and speaking. Impairment of the former does not interfere with the latter, since the individual may have a fully-developed mechanism by which he can communicate normally with his fellows. Absence or loss of hearing before intelligence is fully developed will result in loss of the power of speaking, as in the deaf mute, and must seriously interfere therefore with reading and writing, so that the person so afflicted is deficient in all the normal mechanisms of communication. As emphasized by Shaw Bolton, deafness is a much more serious impairment than blindness from the point of view of intellectual development, and it is a familiar fact that those blind from birth are much more intelligent than those congenitally deaf.

The above is a consideration of speech in its simplest form. Associations simultaneously are made round other sensations in relation to speech. A child, for example, may have had certain experiences which have resulted from its neglect to say " Please " or " Thank you."

This outline probably indicates only what we may call elementary intellectual development, since we know that more advanced association may not proceed in such a sequence. We may associate any sensation with an object, and different persons appear to have special facilities for association in relation to different sensations. This is well observed in students of anatomy. Some find dissections most useful ; to some, diagrams are quite

adequate ; to some, descriptions ; some prefer mnemonics to aid memory. On the other hand, some find that repetition aloud or writing down is of most value.

A similar variation is seen in the methods by which different people learn a foreign language, and the effect of a given lesion will depend to some extent on how the language has been learnt. In Chinese, the written symbols do not refer to the spoken language, but to objects or ideas. A localized lesion has been known to blot out completely a foreign language.

It seems reasonable to believe that the extent to which memories of reception or expression are made use of in intellectual development varies appreciably and it cannot be expected that destruction of any particular part of the brain will result in a constant degree of mental impairment.

The degree of association which takes place depends on the stress of the moment and the speed of reply. If time is given, we may bring a whole host of memories to bear on a given question, while the more elaborate mechanisms of speech, such as those concerned with correct grammar and sentence formation, may also have to be consulted. It can indeed with some justification be held that in the power and speed of association of ideas depends the general success of individual members of a civilized community.

There is still some uncertainty as to the anatomical region in which the speech associations take place, but there is general agreement that in right-handed persons it is normally situated on the left side of the cerebrum, within a well-defined cortical region which extends from the posterior part of the lower frontal lobe by the island of Reil to the temporal and lower parietal occipital region (after Kinnier Wilson), *i.e.*, the areas of Broca and of Wernicke. It is also clear that the anterior part of this region is concerned with expression and the posterior with reception.

Of special interest is the situation of the speech association areas on the left side of the brain in right-handed persons. It is believed that the preponderance of the mechanism on the left side does not occur until the child is taught to write, and possibly the process has been facilitated by the custom of previous generations to use their right hand in writing. For the use of the right hand, the left side of the brain is essential, although it is important to note that even in right-handed persons there is evidence that the right side of the brain is also concerned. Never-

theless, Dandy has found that total ablation of the right cerebral hemisphere for tumour does not grossly disturb speech or even intelligence. One of the three cases which this author has described survived the operation for three years; the chief results were hemiplegia, hemianopia and some interference with sensation on the contralateral side.

The regions responsible for the associations of reception occupy a wide area. In front of the visual area in the angular gyrus is the region responsible for the associations of sight, such as reading, and close to the auditory area, in the temporal lobe, are regions responsible for the associations of hearing. Since lesions of this area are fairly common, *e.g.*, abscesses from the ear, it has been possible to localize these associations more accurately. Syllables are dealt with by the first or upper temporal convolution, the posterior part of which is also responsible for grammar and syntax. The names of objects appear to be stored in the second and third temporal convolution, minor lesions of which give rise to paraphasia, in which mistakes are made in the use of words. Such detail suggests that in close association with the regions responsible for sensation generally, are areas in which are stored the associations of such sensation. We have already noted that lesions of the parietal lobe are likely to cause astereognosis (the loss of the power of recognition of form of objects), which is really loss of the associations of tactile and motorial sense. Certain associations are obviously in closer relationship than others, *e.g.*, those concerned with reading and writing, and it is to be expected that a lesion of the visual association area will affect writing and spelling.

In relation to expression, the area of Broca, just in front of the face area in the ascending frontal convolution (*i.e.*, in front of the fissure of Rolando), may be looked upon as being responsible for the associations of spoken speech, although, in view of the work of Marie, it is no longer held to be wholly responsible for speech. Similarly, in front of the arm area is a region responsible for associations connected with writing (Buchan). It was originally considered by Broca that the area associated with his name was wholly responsible for speech, and we owe especially to Marie the recognition of the responsibility of other areas. Few, however, will go as far as Marie or Moutier in denying that Broca's area has a special significance in relation to spoken speech; indeed there seems to be abundant post-mortem evidence to the contrary. It is emphasized by Kinnier Wilson that to

exclude the area of Broca, macroscopic without microscopic evidence is insufficient. This area may be affected secondarily from a lesion elsewhere.

In considering cases it has also to be remembered that although we look upon the left side of the brain as that primarily associated with speech, the right side also has function in this respect. This statement is particularly true of the receptive associations. We can, for example, hear words with the right side, although they are interpreted chiefly by the left.

When the form of expression has been decided upon, the stimulus is passed to the more executive mechanisms in the Rolandic area.

The Effector Mechanisms (*Efferent Projection Mechanism*) are normally those of spoken or written words, but any motor movement may be used. We are familiar with the use of the dumb alphabet, while in certain circumstances an expression of the face or movement of the head is as truly an effort of speech as the spoken word. Normally a shake of the head is accepted as an indication of negation, quite as emphatic as the word "No." Indeed, it may have the added significance on the part of the speaker that it is not audible. Usually, the impulse passes through the cells of the left cerebral cortex, from which fibres pass down to the nuclei of certain cranial nerves governing the movement of certain of the head and neck muscles, or to the anterior horn of the cervical and dorsal regions of the spinal cord which govern the movements of the hand in writing, or those of the chest in speech.

Aphasia.—This is a symptom, not a disease, and during the last few years there has been a tendency to enlarge the significance of the term. For practical purposes it may be taken to refer to impairment of the powers of expression and appreciation of language. From a consideration of what has been said we can deduce the mechanisms which are likely to be at fault in such circumstances.

The *effector mechanism* proper is impaired when there is destruction of pyramidal fibres in the internal capsule or lower, from cerebral hæmorrhage.

The mechanism may be merely disturbed in function as in disseminated sclerosis, in which interference with cerebellar tracts results in staccato, slurring, or stumbling speech, or in Parkinson's disease, facial neuritis, muscular dystrophies, etc., in which a large variety of disorders of speech may be found. Such a

destruction may cause a paralysis of part of the face and tongue and affect *only the actual articulation* of words (anarthria or dysarthria) just as a paralysis of the arm may affect writing. A similar paralysis may occur in the case of destruction of the part of the Rolandic area responsible for movements of articulation as in hemiplegia, due commonly to embolism or thrombosis of the branches of the middle cerebral artery. These lesions usually affect also the associations. Actually a pyramidal tract lesion has usually to be bilateral, before it causes dysarthria (see p. 85).

The *association mechanism of expression* may become impaired from cortical or transcortical lesions causing what in the past has usually been included in motor aphasia. In impairment of these mechanisms there is loss of the power of adequate expression, although there is no appreciable loss of understanding. In loss of voluntary speech, there is not necessarily any interference with the effector mechanism, as is shown by the fact that the patient has obviously full powers and full use of the structures normally employed in articulation. He may also be able to articulate accurately the words he can say, and not infrequently a patient may still be able to speak "reflexly." He may, for example, recite poetry, express sudden emotions by speech, as in swearing, or he may be able to repeat to order. How this is made possible is a very interesting problem, and many of the ideas on the subject are little more than speculations. It has been suggested that for such automatic speech, the right side of the brain is brought into play, that only certain pathways converging on that part of the Rolandic area responsible for speech are affected, or that short cuts have been laid down at a lower level as the result of repetition. With regard to the site of the lesion, it can only be said with due consideration of the evidence of Marie and of Moutier that in a lesion in the region of Broca's area, such expressive aphasia is usually found. A lesion immediately in front of the arm area will similarly be liable to cause loss of the power to write.

Lesions in the Receptive Association Areas result, as would be expected, in loss of the function of the particular region affected. From the diverse nature of receptive associations it is obvious that a large variety of symptoms may be produced. Further, as indicated in relation to the temporal lobe, associations are scattered over a wide area, and it is therefore possible for lesions to be produced which affect certain associations, say, of hearing, leaving others untouched. Word blindness and word deafness are

amongst the better known results of impairment of the regions responsible for the association of vision and hearing, but there may be simply failure of the power to name objects or to speak correct grammar. In this latter connection it is interesting to remark the association of grammar with hearing rather than with expression. In some cases the patients recognize words but do not know their meaning. Their own language in print becomes a foreign one to them.

An interesting condition is " jargon aphasia," in which there is a more or less uninterrupted flow of misshapen words. Jargon aphasia results from deep-seated lesions of the temporal lobe, and seems to depend on interruption of association tracts whereby the higher centres for speech are cut off from the visual and sensory areas, and the patient, although not deaf or blind, is nevertheless unaware of what he is saying, and fails to correct his speech as a normal individual does by listening to his own " backlash " and appreciation of kinæsthetic impulses from the muscles of articulation. Jargon aphasia is thus paraphasia without attempts at correction.

It is impossible to deal with all the results of lesions which may occur. Not only may there be cortical destruction, but any impairment of the transcortical fibres joining different association areas may bring about very diverse symptoms. In different individuals even the same lesion cannot be expected to produce a similar effect. Especially is this true of the intellectual state. Head, however, has succeeded in showing that there may be a considerable degree of mental impairment. No doubt we all develop our more elementary associations in the same order, and Head draws attention to the fact that the most recent associations are most readily lost, or they may cease to be used intelligently. He has differentiated the varieties of aphasia as disorders of symbolic thinking, and has shown that such factors of speech as the appreciation of the meaning of words (apart from the saying of the word), the formation of sentences, grammatical construction, and so on, may all be separated in aphasia of different degrees of severity. It is doubtful if this differentiation has any practical value, although of extreme interest in a study of the mechanism in the formation of speech. It will be generally agreed, with Head, that an aphasic individual is seldom quite normal mentally unless the disease is limited to a small area of the cortex. When we learn to speak, we learn to think and form ideas by a similar mechanism. The effect of a given lesion

on mentality will then depend on how the individual has acquired his knowledge. If, for example, there is a lesion of the association fibres connecting the visual association area with the motor area for the vocal organs not only will the individual be word blind, *i.e.*, be unable to read aloud, but probably other associations and ideas which depend on knowledge acquired by reading will be affected, although he may reply quite well to verbal questions and knowledge acquired by hearing may be unaffected.

It must also be remembered that in diseases affecting speech other motor movements, such as those of the arm, are commonly impaired, and the aphasia may help in localizing the lesion and throw some light on its nature. The degree to which a severe case of aphasia may recover is remarkable. There are indications that in such a recovery the right side of the brain may take over functions which normally belong to the left, and various attempts to re-educate the opposite side of the brain have been made.

Lesions of the receptive mechanisms such as produce deafness or blindness proper need only be mentioned for completeness. The loss of the sensation is obviously the predominating symptom.

CHAPTER XIII

THE CEREBRO-SPINAL FLUID

THE cerebro-spinal fluid, whose limpidity caused Cotugno in the eighteenth century to liken it to spring water, is formed by the choroid plexuses which project into the ventricles of the brain. The fluid escapes through the foramina in the roof of the fourth ventricle into the subarachnoid space. These foramina are the median opening of Magendie, which leads into the cisterna magna, and the two lateral apertures of Luschka, which open one into each cisterna lateralis. Through the foramen of Luschka on each side projects a process, known as the cornucopia, of the choroid plexus of the fourth ventricle, and in this way a small amount of the fluid is poured directly into the cisterna lateralis of the subarachnoid space. If, by plastic meningitis, the cisterna becomes sealed off, the cornucopia continues to produce fluid and a cyst is formed which presses on the adjacent cranial nerves, the eighth included, and symptoms of a tumour of the cerebello-pontine angle, viz., tinnitus, deafness and vertigo, arise.

In the subarachnoid space the cerebro-spinal fluid acts not only mechanically, as a protective water cushion for the brain and spinal cord, and, to a limited extent, as a medium which can be displaced when the bulk of the intracranial contents is increased, but also as a recipient of some of the waste products from the brain. These waste products reach the subarachnoid fluid from the narrow perivascular spaces which surround the vessels as these penetrate the nerve tissue.

The cerebro-spinal fluid is absorbed for the most part into the venous sinuses of the cranial dura mater through the arachnoidal villi ; but small amounts enter the lymphatics of the cranial and spinal nerves.

The normal amount of fluid is probably about 150 c.c. This figure is increased when the brain is wasted, as in general paralysis and senility ; to this mechanical replacement of brain tissue by fluid the rather pompous term *hydrocephalus ex vacuo* is given. Where there is increased formation or diminished absorption, hydrocephalus proper results. In infants when hydrocephalus

develops, the skull bones can separate, and the head distends without at first any gross increase of intracranial pressure. In adults, on the other hand, the rigid skull cannot expand and the pressure rises, and soon reaches a serious degree. In cases of cerebral tumour the development of hydrocephalus is probably a more potent factor in the genesis of increased intracranial tension than the mere bulk of the tumour itself. The tumour causes hydrocephalus, in some cases by preventing the escape of cerebro-spinal fluid from the ventricles by pressure on the aqueduct of Sylvius or by occlusion of the roof-foramina, in others by interfering with the venous return from the choroid plexus. Experimentally, ligature of the great vein of Galen, at a point distal to the entry of the basilar vein—if the ligature is proximal to this point the basilar, offering a wide collateral channel for the escape of blood, frustrates the object of the experiment—causes hydrocephalus by setting up congestion of the choroid plexus. Pathologically, acute ependymitis serosa also results in increased formation of fluid. The adjective *productive* is given to hydrocephalus due to increased formation, as distinct from diminished absorption, of fluid.

In cases of cerebral tumour, the increased intracranial pressure tends to force the medulla and cerebellum downwards, so that they occupy the foramen magnum to a greater extent than normally. This is particularly liable to occur if the tumour is below the tentorium. If fluid is withdrawn too freely from the lumbar sac, the " pressure cone " may be intensified and lead to a fatal paralysis of the bulbar centres.

An important but not invariable clinical sign of increased intracranial pressure, whether due to cerebral tumour or other cause, is choked disc or papillœdema. Papillœdema is by no means pathognomonic of increased intracranial pressure, but occurs also in nephritis, etc. In cerebral tumour the production of papillœdema certainly depends on the transmission of the rise in intracranial pressure to the fluid between the optic nerve and its dural sheath. When the problem is pursued further than this point, a difference of opinion is found to arise, and whether the increased tension of the fluid compresses the central retinal vein as this crosses the subarachnoid space around the optic nerve or whether fluid is actually forced through the lamina cribrosa into the optic disc is not definitely known. Not only may the rise in intracranial pressure cause papillœdema, headache and vomiting, but may also disturb the function of certain intracranial structures

and so produce " false localizing signs " of which the commonest is paralysis of the sixth cranial nerve.

Sudden (apoplectiform) onset of symptoms which occurs in certain cases of cerebral neoplasm is due either to vascular lesions —hæmorrhage into the tumour, or thrombosis of adjacent vessels —or to acute œdema of the surrounding cerebral substance. This œdema is due in turn either to compression of local veins by the growth, or, more probably, is a result of the action of metabolic products of the tumour on the surrounding capillaries.

Obstructive hydrocephalus is an occasional sequela of meningitis which acts by blocking the foramina of exit from the fourth ventricle or by occluding the isthmus of the subarachnoid space between the edge of the incisura tentorii and surface of the mid-brain. A similar condition may be experimentally produced by the injection of lamp black into the cerebro-spinal fluid (Weed, Nañagas). In congenital hydrocephalus the foramina in the roof of the fourth ventricle are usually patent and if a harmless dye is injected into a lateral ventricle it appears in the fluid obtained by lumbar puncture. Hydrocephalus with patent foramina is called communicating, and in the congenital variety the obstruction is probably caused by maldevelopment of the absorptive arachnoidal villi (Cushing). Productive hydrocephalus is naturally of the communicating variety ; so also is hydrocephalus due to adhesions round the mid-brain which prevent the fluid from reaching the great absorptive area of the vault (Dandy).

If one of the foramina of Munro is blocked, the lateral ventricle which it drains distends. A pedunculated tumour of the choroid plexus or septum lucidum may in certain postures of the head fall into and occlude the foramen, and so cause severe paroxysms of headache.

The cerebro-spinal fluid is usually collected by lumbar puncture by which the theca is tapped below the lower end of the spinal cord. Occasionally a cistern puncture is performed, especially in cases of suspected spinal compression, with a view to a comparison of the lumbar and cisternal fluids and to the injection of lipiodol. The descent of the latter is interfered with at the upper level of the obstruction which can thus be accurately located by X-rays. Cisternal puncture should not be too lightly undertaken as there is a danger of wounding the cerebellum or medulla.

The pressure of the fluid is in health 100–200 mm. water ; it is best measured by a manometer which prevents loss of fluid. The rate of escape of the fluid from the needle is not always an

accurate guide, and further, it is to be borne in mind that extreme flexion of the spine, crying, etc., tend to raise the pressure. As a general rule the pressure is high in cases of cerebral tumour, low in thrombosis of the cerebral arteries. Digital compression of the internal jugular veins raises the intracranial pressure and causes an increased flow from the lumbar needle. This phenomenon is absent in cases of spinal compression. When a hypertonic solution of sodium chloride (15 per cent. strength) is injected intravenously the intracranial pressure falls, because of the osmotic action which withdraws tissue fluid from the brain (Weed and McKibben). Hypertonic salt solution has been used in this way to lower excessive intracranial pressures prior to decompression operations.

Examination of the Fluid.—Blood may be present and may be obvious or merely cause a yellowish turbidity. If the presence of blood is due to pricking of a vessel during puncture, it is most abundant in the first drawn sample. If due to cerebral or subarachnoid hæmorrhage, the blood is intimately mixed with the fluid. Sometimes it is impossible to tell which cause is operative, unless the fluid is centrifuged, when, in cases of pathological hæmorrhage, the supernatant layer will be seen to have a yellow tinge.

The fluid drawn from the lumbar region may be yellow but clear. This occurs in cases of recent subarachnoid hæmorrhage after time for hæmolysis has elapsed, and in compression of the spinal cord. In the latter instance there is a marked excess of protein without cellular increase (Froin's syndrome), and, further, the cisternal fluid, *i.e.*, the fluid above the obstruction will be found to be normal. Ayer produced spinal compression experimentally by injection of paraffin wax around the theca in animals, and found that the lumbar fluid contained an excess of protein as in spinal block in man. It is believed that the protein excess in spinal compression is due to transudation into the stagnant fluid from congested vessels and, where there is a tumour near the subarachnoid space, also to exudation from the surface of the growth. A great excess of protein in a cell-free fluid also occurs in certain cases of polyneuritis.

The fluid may be turbid because of the presence of pus. This is due to suppurative meningitis. In tubercular meningitis the fluid is often slightly turbid, and even if the fluid is clear a fine "cobweb" clot, due to coagulation of fibrinogen, appears on standing. In this clot the tubercle bacilli can frequently be

demonstrated. A clot may also form in a clear fluid from a case of acute poliomyelitis.

Normally the fluid contains very few cells, less than six lymphocytes per cubic millimetre, but in inflammatory states is invaded by cells in varying number. In acute suppurative meningitis there is found a very large number of polymorphonuclear cells, *i.e.*, pus is present, and the infecting organisms may be seen. The leucocytes come from the congested meningeal vessels. When the meningococcus is the infecting agent, many of the organisms are seen to be enclosed within the cells. In tubercular meningitis, in the acute stage of poliomyelitis and in acute cerebro-spinal syphilis a mixed leucocytosis is usually present, while in encephalitis lethargica and chronic cerebro-spinal syphilis lymphocytes are the principal cells found. The lymphocytosis in encephalitis is often scanty. Disseminated sclerosis but rarely causes cellular increase. As meningitis passes from the acute to the chronic stage, the polymorphonuclears are gradually replaced by lymphocytes. In meningococcal meningitis a change in this direction is a favourable prognostic sign. In cases of cerebral abscess small numbers of polymorphs are seen ; when the abscess is complicated by meningitis these are much increased.

In most of the various conditions in which the cells are increased the total protein, albumin as well as globulin, is increased. The normal protein content is 0·02–0·04 per cent. An excess of globulin is revealed by the precipitate obtained by addition to the fluid of an equal amount of saturated solution of ammonium sulphate. Excess of globulin without cellular increase occurs in disseminated sclerosis and when a cerebral tumour is " leaking " into the cerebro-spinal fluid.

The colloidal gold reaction of Lange depends probably on the albumin-globulin balance of the fluid. If the gold reagent is diluted in standard series with a normal cerebro-spinal fluid, no change of colloidal state and, therefore, of colour are seen, but in certain conditions characteristic alterations occur, the dilutions effective depending on the condition present. Thus in general paralysis of the insane the " gold curve " is usually characteristic, but the findings are of more value in diagnosing which type of syphilis (whether general paralysis, tabes dorsalis or meningitis) is present, in cases in which the Wassermann reaction is positive than in proving, *per se*, the presence of neuro-syphilis, for conditions other than syphilis may affect the gold curve.

The Wassermann test on the fluid is apparently the most

reliable single test for neuro-syphilis, but it is negative in 20 per cent. of cases of tabes, and in about 50 per cent. of cases of syphilitic hemiplegia (Greenfield). The W.R. in the blood should always be done as well, for in the case of cerebral gumma or arterial thrombosis the blood reaction is occasionally positive while that in the fluid is negative.

The sugar present in cerebro-spinal fluid is dextrose and its concentration varies with that in the blood, but runs at a somewhat lower level. In conditions characterized by hyperglycæmia, *e.g.*, diabetes mellitus, the sugar level in the cerebro-spinal fluid is correspondingly raised. In suppurative and tubercular meningitis the sugar is diminished or absent ; the reason for the disappearance of sugar in these conditions is to be found in the fermentative action which the specific bacteria exert. If in a case of suspected tubercular meningitis, the fluid does not reduce Fehling's solution, the diagnosis is likely to be correct. In acute " sterile " meningitis the fluid is cytologically and chemically similar to that of tubercular meningitis, but the onset of the disease is sudden and tubercle bacilli are absent.

The chlorides are present chiefly as sodium chloride, and, as in lymph, are more abundant than in the blood. They are decreased in amount in fluids from cases of suppurative meningitis. This is due in part to addition of protein from the blood, in part to a diminution in blood chloride, but further work is needed on this subject.

The urea content runs parallel to that of the blood. High values are found in uræmia, especially when this is due to chronic nephritis.

CHAPTER XIV

SIGHT AND THE REFLEXES OF THE EYE

THE sense of sight arises through impulses received by the brain as a result of the action of light upon certain specialized nerve endings in the retina, upon which the light is focussed by the optical mechanism of the eye. Perfect vision, therefore, is dependent on the efficiency of the eye to act as a perfect optical instrument, and on the functional continuity of the nervous paths along which the stimulus must travel from the receptor station, the retina, to the perceiving station, the cerebral cortex.

In regarding the eye as an optical instrument, we must consider its structure, and also any active function it may have by virtue of its being a living entity: wherein it differs from a purely physical optical instrument.

The common simile which compares the eye to a photographic camera is a useful one, conveying as it does the idea of a box containing several different media through which the rays of light must pass before they reach the sensitive plate.

The path of a ray of light through the eye to the retina lies through several different media—cornea, aqueous humour, lens, and vitreous humour.

The cornea consists chiefly of a transparent, white, fibrous tissue, the substantia propria, containing a number of flat, plate-like cells (the corneal corpuscles). These are so arranged that their narrow diameter is at right angles to the entering ray of light, thus diminishing the amount of tissue through which the light has to pass. The cornea is covered on its outer surface by stratified epithelium situated on a homogeneous membrane (Bowman's Membrane). This corneal epithelium is in direct continuity with that of the conjunctiva, and is indeed a modification of it. It is therefore affected by similar pathological conditions to those affecting the conjunctiva.

The substantia propria, likewise, is continuous with and a modification of the sclera, so that again we find that similar pathological conditions affect both, but in the cornea are modified by the avascularity of that structure.

The inner surface of the cornea is lined by a second homogeneous membrane (Descemet's Membrane), and covered by a layer of cubical cells. This membrane is very resistant to ulceration, and often prevents perforation.

Unless the substance of the cornea is clear, its surface smooth and curvature regular, there is an interference with vision. The cornea has no blood-vessels, and is simply nourished by diffusion of lymph, although, when ulcerated or injured, it becomes vascularized. Corneal ulcers, interstitial keratitis (non-ulcerative), and injuries bring about in this way diminution of vision, which may be temporary or permanent.

All corneal ulcers, which have penetrated Bowman's membrane and involved the substantia propria, leave a certain amount of scarring, since repair is by ordinary white fibrous tissue, which causes the appearance of nebulæ (white opaque patches) on the cornea. When very dense (leucomata) they may cause total blindness, and it is evident that a faint diffuse nebula covering the pupillary area causes more interference with vision than a denser one situated peripherally. Some forms of interstitial keratitis may clear up entirely, or may leave diffuse opacities all through the corneal substance, or, as in cyclitis (inflammation of the ciliary body), where numbers of small spots consisting of groups of cells on the back of the cornea (keratitis punctata) are often the only sign that a cyclitis is present, they may be sufficient to bring about diminished vision.

Alteration of the normal curvature of the cornea will also interfere with vision, as in astigmatism and conical cornea. In the latter condition the cornea, instead of being regularly curved like a portion of the surface of a sphere, is pointed and cone-like, and if well developed, results in a defect not remediable by ordinary glasses. Contact glasses have, however, proved beneficial.

In astigmatism, the curvature of the cornea is different in two meridia, which are usually at right angles to each other, *e.g.*, horizontal and vertical, but suitable cylindrical lenses remedy this defect.

Conditions which affect the sclerotic or outer coat of the eyeball only interfere with vision when they involve the cornea. The sclera consists of thick, white fibrous tissue and is subject to inflammation (scleritis) which, when involvement of the cornea (sclerokeratitis) also occurs, may leave permanent scarring.

The aqueous humour is produced by the ciliary body. It fills the anterior and posterior chambers of the eyes and drains away

through the spaces of Fontana, situated at the so-called filtration angle of the anterior chamber, into the venous canal of Schlemm in the sclera at its junction with the cornea.

Its refractive effect on the rays of light is usually included with that of the cornea, and only when it becomes " muddy " through the presence of exuded cells does it interfere with vision.

Intra-ocular Pressure.—Just as the blood within the blood-vessels exerts a certain pressure on their walls, so the contents of the eye exert pressure on its coats known as intra-ocular pressure. It can be tested by getting the patient to look down, and then palpating the eyeball through the eyelid with the tips of the two forefingers, as if testing for fluctuation in an abscess, or by a special instrument called a tonometer. The normal tension is 20–25 mm. of mercury. If the drainage of fluid from the anterior chamber is interfered with, *e.g.*, by blockage from exudate, then the intra-ocular pressure rises, and the condition known as glaucoma is produced; this may lead to complete blindness, owing to interference with the blood supply of the retina and optic nerve fibres. Treatment consists in increasing the filtration from the anterior chamber by the local instillation of a drug, such as eserine or pilocarpine, which, by constricting the pupil, opens out the filtration angle. A similar result is brought about by partial removal of the iris (iridectomy), but it is important to recognize the condition in its early stage before degeneration of the nervous elements has occurred.

Glaucoma may be (1) secondary to conditions such as intra-ocular tumours and occlusion of the filtration angle or of the posterior chamber by adhesions of the iris; and (2) primary, when the cause is unknown. Primary glaucoma especially occurs in eyes with shallow anterior chambers and, therefore, narrow filtration angles. Swelling of the vitreous may play a part. In an acute attack of glaucoma there is usually severe pain round the eye. The patient may speak of the pain as headache, and the frequently accompanying vomiting may lead to an erroneous diagnosis of a bilious attack. The sight of the affected eye suffers rapid impairment, and unless relief is afforded may be irretrievably lost. The cornea is often steamy, and thus prevents an ophthalmoscopic inspection of the fundus oculi. The tension is raised. The cornea is often anæsthetic from pressure on the sensory nerves of the globe. The chief difficulty in the diagnosis is to distinguish the condition from iritis with raised tension. In

iritis the iris pattern is blurred, the iris having a muddy appearance. Moreover, in iritis, the pupil is small, with irregular circumference, because the iris is swollen. In glaucoma the pupil is oval and moderately dilated. The treatment of iritis includes the instillation of atropine. This procedure would be a terrible error in a case of glaucoma, as after atropine the pupil remains dilated for a day or more, even if eserine is instilled, and the dilatation of the pupil means that the base of the iris obstructs the filtration angle ; indeed, in a predisposed subject, the instillation of atropine has been known to precipitate an attack of glaucoma. In a case of doubt, therefore, it is customary to instil homatropine, the action of which can be readily overcome by eserine if necessity arise. If the case is one of iritis relief will be obtained, if one of glaucoma the tension will rise ; eserine is at once instilled, and other therapeutic measures adopted.

The lens consists of a large number of clear epithelial cells modified to form fibres. As the young lens fibres are laid down on the outside, those in the centre become more and more compressed and form a dense nucleus. If an adult lens is cut with a knife, the soft cortex is easily peeled off, leaving the harder nucleus.

The lens is covered with a fibrous membrane, or capsule, which acts as a protective covering.

In old age the lens becomes harder and denser, and less elastic, causing presbyopia. In addition it may show opaque areas known as *cataracts*. These may be in sectors, often worse at the periphery, or the opacities may be central or nuclear. In any case, the entire lens ultimately becomes opaque, and renders vision impossible. The common varieties are senile, diabetic and traumatic. The type of diabetes which is most apt to cause cataract is the mild, chronic form in which the level of the blood-sugar has been moderately raised over a period of years.

In some children in whom there are often other signs of interference with development, the lenses may be congenitally opaque. If for any reason—usually following a perforating wound—the protective capsule is torn, the aqueous humour gains access to the lens substance, the fibres swell and become opaque and a cataract is produced. The interference with vision in cataract varies with the amount of opacity and its position, and in the case of the traumatic form, with the nature of the injury.

The vitreous humour consists of branched connective tissue cells, separated from one another by wide spaces filled with lymph.

It occupies about four-fifths of the eyeball, but plays only a small part in refraction. It only interferes with vision when filled with opacities which may be derived from the cells of the ciliary body, or from a blood clot due to a retinal hæmorrhage.

Refraction.—When a parallel beam of light enters a normal or emmetropic eye, it is so refracted by the media through which it passes that it is brought to a focus on the retina, with the result that the individual is able to see clearly the object looked at. Light rays proceeding from a distance greater than six metres are practically parallel, while if the object is nearer than this distance the rays are divergent. Such divergent rays will not come to a focus on the retina if the normal eye is in the resting position. In order that such rays may be focussed the lens becomes stronger or of shorter focal length by increasing its curvature. Situated behind the root of the iris is the fringe-like ciliary body with its ciliary muscle. It is the muscle of accommodation and is divided into two parts. One is a circular portion [1] situated more internally and when it contracts it approximates the ciliary processes. The other is a radiating portion arising from the corneo-scleral junction and passing back into the chorioid. By its contraction it pulls the chorioid and ciliary processes forward. The suspensory ligament becomes slackened, and the lens increases its curvature owing to its elasticity. This increases its strength, so that it can now focus divergent rays on the retina. In old age this mechanism tends to fail, a condition known as *presbyopia*. The eyes may be assisted by a suitable convex lens.

Abnormal focussing, or errors of refraction, occur when the eyeball is too short antero-posteriorly (hypermetropia), or too long (myopia).

In *hypermetropia* parallel rays come to a focus behind the retina, so that the image is a blurred one. Such an eye, however, can focus a convergent beam. Since parallel rays may be made convergent by the use of a biconvex lens, such a lens is used in the correction of hypermetropia. When a correcting lens is not in use, the defect is corrected by an excessive use of accommodation, with the result that the ciliary muscle is never at rest. When still further accommodation is required for near work, the amount available is insufficient. Further, since accommodation has to be employed without convergence which normally accompanies it, headache and eye strain are common.

In high degrees of refractive error, the two eyes do not work

[1] Not to be confused with the sphincter pupillæ.

together comfortably, with the result that one is thrown out of action. This unused eye squints—in hypermetropia usually inwards (convergent squint) and in myopia outwards (divergent squint). The liability to squint is increased when the refractive power of the two eyes is unequal (anisometropia). Further, the degree of development of the fusion sense, whereby the two images are blended into one, also plays a part. So also may the temperament of the individual, some giving up the struggle more readily than others. A squinting eye has not good vision, owing to disuse and suppression of its image. In alternating strabismus, however, the patient can fix with either eye, first one, then the other image being suppressed, according as to which eye is being used. The squint due to refractive error is called concomitant, in contrast to paralytic, as the eyes, although squinting, have each the same range of movement. An eye blind from any cause always diverges.

In *myopia* the eye finds a means of partially overcoming the difficulty, by a contraction of the eyelids—hence the name myopia. This has the effect of cutting out the peripheral rays, which have a shorter focal length, and only using the central ones, since they have a longer focus. The image is thus made a little clearer but, of course, is often even then quite indistinct. A myope can focus divergent rays, and since parallel rays may be made divergent by a concave lens, this type is used in its correction.

In *astigmatism* the cornea is unequally curved in its horizontal and vertical meridians. It follows that the rays which come from one diameter of an object may be focussed on the retina, while those which come from some other diameter will be focussed in front of or behind the retina. This gives rise to blurring of the object, and can be corrected by wearing suitable cylindrical lenses, which are plane in the normal diameter and curved in the abnormal. Only one example has been given, but all sorts of combinations exist and, moreover, the two meridia may be at any angle, though in regular astigmatism they are always at right angles to each other. Irregular astigmatism occurs when the cornea has been scarred by an injury or ulcer.

The Retina.

As we have said, sight originates in the stimulation of the retinal rods and cones, which are nerve endings specialized for the perception of light. The cones are situated in the more central areas of the retina, and are concerned with accurate vision in a good light; the rods are responsible for vision under

conditions of poor illumination. From these endings afferent impulses pass by way of a chain of two neurones to the ganglionic layer of the retina, whence arise fibres, which when collected together form the optic nerve. At the point where the optic nerve leaves the eye at the back and slightly to the inner side there are no nerve endings. This point is therefore called the blind spot. In medical work it is more commonly known as the optic disc.

By the use of the ophthalmoscope, the **retina** is seen to present several distinct features of importance. Its red colour is the result of the blood supply, but should any area be destroyed it is at once evident by its pallor. A general pallor may result from the occlusion of the central artery, by an embolus, or merely from spasm, a rare condition found occasionally in conditions such as migraine and quinine poisoning. This fact is, however, of some physiological interest, as some hold that the symptoms of migraine are due to a similar spasm of the cerebral arteries.

The retina is also nourished on its outer side by the capillaries of the chorioid, the vascular pigmented layer lying immediately outside it, and supplied by the ciliary arteries. Any disease which affects the chorioid therefore affects the retina also. Should the retina become detached from the chorioid, the separated area becomes markedly paler than the rest of the fundus. In various forms of chorioiditis pale areas due to the sclera showing through the atrophied chorioid may be seen.

On the other hand, dark areas may appear on the retina usually caused by hæmorrhages, which are found in various forms of retinitis and general diseases, such as the anæmias, nephritis, or diabetes.

The optic disc is of special interest as it is normally a clearly defined, easily seen area, often affected in disease. The normal disc looks appreciably paler than the fundus and may often be yellowish in colour. The colour of the disc may, however, approach that of the fundus in inflammation of this region of the retina, or in venous congestion. Such hyperæmia commonly accompanies errors in refraction, but may indicate the beginning of an optic neuritis. In the later stages of optic atrophy a striking pallor of the disc is evident, but it must be remembered that in many normal individuals the very centre of the disc is funnel-shaped and at its edges appears very pale by reflected light.

The vessels of the retina stand out in contrast to the paler disc, from the centre of which is seen to emerge the central

artery and the corresponding veins. The artery is distinguished by its comparative narrowness, and by the fact that it and its branches reflect more light from their surfaces. This reflection becomes especially well marked in arterio-sclerosis, when the arteries may also be tortuous and present a beaded appearance. The arteries are then seen to constrict the veins where they cross them. It is said that narrowing of the veins at the points where the arteries cross them also occurs in cases of high blood pressure, without arterio-sclerosis. An increase in the size of the veins, on the other hand, with distinct tortuosity, is to be taken, with other signs, as evidence of optic neuritis.

The veins may be seen to pulsate normally, but pulsation of the arteries is pathological and may be seen in glaucoma or aortic regurgitation.

The depth of the optic disc can be appreciated only by practice, but with glaucoma there is a distinct cupping, while the vessels are seen to bend sharply at the edge of the cup. If this condition progresses the signs of optic atrophy gradually appear.

The edge of the disc should be clearly defined, but in disease, such as neuro-retinitis, papillitis and papillœdema, this is no longer the case. Such optic neuritis is seen in a large variety of conditions, and it is of special diagnostic significance in cerebral tumour. Strictly, a distinction should be drawn between papillitis and papillœdema, the former being inflammatory in origin, the latter due to transudation. In both the disc is swollen, but the swelling is often greater in papillœdema than in papillitis, and the disc paler. The amount of swelling can be measured with the ophthalmoscope. The observer, relaxing his accommodation fully, focusses by a suitable lens the summit of the swelling, then by a lens of weaker power a retinal vessel. The difference in focal power of the two lenses gives a measure of the swelling in dioptres. Three dioptres correspond to one millimetre of actual swelling.

The actual disturbance of vision which may result from various diseases of the retina and optic nerve, varies from slight loss of visual acuity to complete blindness. The sudden onset may be of value in diagnosis, as in retinal detachment or occlusion of the central artery, but more commonly the onset is gradual, especially so when it is associated with general states of disease. Occasionally the disturbance in vision may lead to the causal disease being suspected. It will be clear that the more the posterior pole of the eye is affected the more likely is vision to be affected,

especially if the lesion is in the macula lutea, which is that retinal area in line with the visual axis where vision is most acute. In tobacco amblyopia, presumably as a result of some selective action on the cones, twilight (rod) vision is often less affected than day (cone) vision.

Moderate lesions of the general fundus, on the other hand, may not be appreciated at all. Various scotomata may be present without the patient's knowledge, and of course we are all unaware of the normal blind spot. It is possible, as in squint, or in microscopic work, to disregard entirely what we see with one eye.

Retrobulbar neuritis is a term applied to inflammation of the optic nerve before it reaches the disc, and occurs in disseminated sclerosis, syphilis, ethmoidal sinusitis, etc. A central scotoma is present, because of the great vulnerability of the macular bundle and the pupil reaction to light is ill-sustained. Optic atrophy may follow later.

The field of vision can be satisfactorily mapped out only by the use of the perimeter, a cheap and simple apparatus. By its use we may detect the typical central scotomata of tobacco poisoning (commonly for red and green); the concentric contraction in tabes; and the typical diminution of the nasal side of the field in glaucoma. This diminution gives very important warning of the necessity for treatment, which may be begun while there is yet time to save vision. A most important use of the perimeter is in the diagnosis of lesions of the optic paths.

The paths by which the impulses reach the cerebral cortex are readily seen from Fig. 6. The fibres from the same side of each eye join together, the fibres from the nasal half of each retina crossing at the optic chiasma. For example, on the right side, the brain receives impulses from the right side of each eye, and therefore from the left side of the visual field. The optic tract is seen to pass to the primary optic ganglia, especially the external geniculate body (although there is some discussion concerning the exact connections in this region), and thence to the occipital lobe of the cerebral cortex in the region of the calcarine fissure.

An interesting observation is that of Brouwer, who has pointed out that the macula has a singularly large representation on the cortex, and that into this area for the macula is a projected part of the area for the periphery, as if to assist us to catch a movement with " the tail of one eye " when we are looking at an object intently and using the macula particularly.

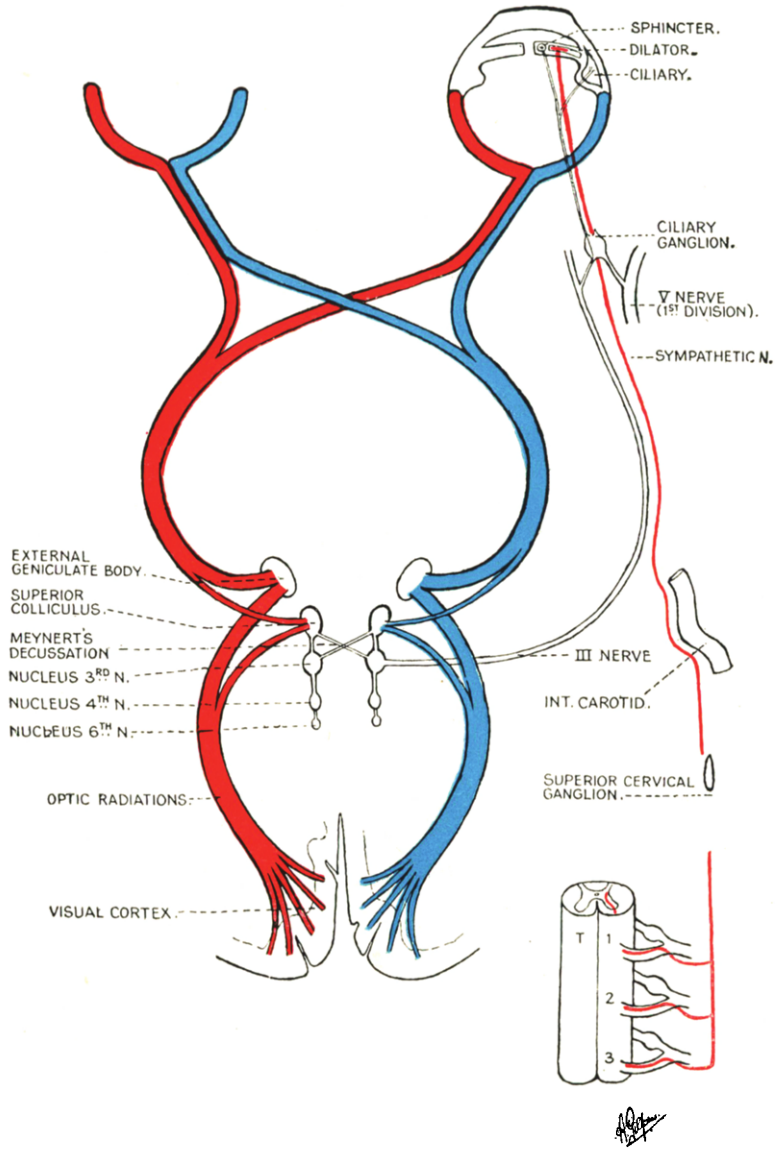


FIG. 6.—THE NERVE PATHS RELATED TO SIGHT.

T 1, 2, 3, first three segments of the thoracic region of the spinal cord.

[*Facing p.* 108.

The effect on vision of any lesion of this path will depend on the part affected. A lesion affecting the optic nerve will cause blindness in one eye, one in the region of the chiasma blindness on the internal side of each eye and therefore bitemporal hemianopia, while a lesion of the optic tract to the cortex will cause loss of vision in the opposite side of the field of each eye (homonymous hemianopia). In each instance it will be evident that the field of vision will be deficient in the side opposite the actual eye blindness. The association of the calcarine region of the occipital lobe with the perception of light is indicated by the flashes of light which are seen if a blow is received on the occiput. In clinical practice the detailed changes in the visual fields are of importance in diagnosing the site and also the nature of an intracranial lesion which happens to involve the visual pathway. These changes must be taken in conjunction with the general clinical picture. The diminution of vision produced by papillœdema and consequent optic atrophy in cases of cerebral tumour may interfere with the localizing value of field changes. Lesions of the optic tract tend to cause incongruous [1] hemianopia, for the crossed and uncrossed fibres from the retinæ lie side by side but separately, whereas lesions above the external geniculate body, *i.e.*, of the radiation and occipital lobe, cause congruous hemianopia. It should be pointed out, however, that the temporal crescent of the field of one eye may be rendered blind by a suprageniculate lesion without a corresponding loss in the nasal part of the field of the other eye. This is merely because the outermost part of the visual field has no nasal homologue, *i.e.*, the field is normally less extensive on the nasal side.

A quadrantic hemianopia, *i.e.*, affecting the upper or lower quadrants of both visual fields, is sometimes produced by lesions of the region of the calcarine fissure on the upper lip of which is represented the superior quadrants of the retina, and on the lower lip the lower quadrants. (In actual clinical practice quadrantic defects are more commonly due to tract lesions, as in tumours of the temporal lobe). Small lesions of the occipital lobe more frequently cause partial loss in the opposite half of the visual field in a different way from the foregoing, viz., the central and peripheral parts of the field may be separately affected, according as to whether lesion is at the posterior or anterior part of the visual cortical area. A total lesion of the visual area on one side,

[1] "Congruous" is a term applied when a homonymous hemianopic defect is simultaneous in onset, co-extensive and equal in intensity in the fields of both eyes (Traquair).

The Visual Pathway and Intracranial Lesions (Traquair).

				Field Defect	Usual Lesions
Extracranial			Optic nerve	Enlargement of blind spot. Concentric contraction. Binasal hemianopia.	Papilloedema due to increased intracranial pressure.
Intracranial	Subgeniculate	Subchiasmal	Optic nerve	Defects unilateral. Central scotoma. Hemianopic and quadrantic defects.	Tumour or abscess of frontal lobe (Foster Kennedy syndrome). Local tumour. Disseminated sclerosis. Trauma.
		Chiasmal	Anterior angle	Quadrantic temporal scotoma (junction scotoma). Unilateral temporal hemianopia, passing into bitemporal hemianopia, or blindness of one eye with contralateral temporal hemianopia.	Local tumour or aneurysm. Disseminated sclerosis.
			Body	Bitemporal hemianopia.	Local tumour. Disseminated sclerosis. Syphilis.
			Posterior angle	Unilateral hemianopia passing into homonymous hemianopia.	Local tumour.
		Suprachiasma	Optic tract	Homonymous hemianopia. Sparing of central area uncommon. Quadrant defects common. Defects frequently incongruous.	Local tumour. Temporal lobe tumour or abscess.
	Suprageniculate		Optic radiation	Homonymous hemianopia. Sparing of central area common. Upper quadrant defects rare. Peripheral defects due to internal lesions. Central defects due to external lesions. Defects may be ill-defined with sloping edges. All defects congruous.	Hæmorrhage (?) Thrombosis. Tumour or abscess. Injury.
			Occipital cortex	Homonymous hemianopia. Sparing of central area common. Upper quadrant defects rare. Homonymous hemianopic scotoma. Double homonymous hemianopia with retention of central field. Peripheral defects due to anterior lesions. Central defects due to posterior lesions. Defects sharp-edged and well-defined All defects congruous.	Thrombosis. Tumour. Injury.

will, of course, result in hemianopia affecting the whole of the opposite half-field, as also does a total lesion of one optic tract. These lesions are diagnosed by the aid of a perimeter.

The quadrantic hemianopia which has been observed in cases of tumour of the temporal lobe is attributed by Traquair to pressure of the tumour on the subjacent optic tract. Cushing, however, believes the defect in the visual field is due, in the earlier stages at least, to pressure not on the tract, but on the radiation. Those fibres of the optic radiation which correspond to the lower quadrants of the retina have been described by Meyer as looping far forwards in the temporal lobe, where they constitute the " temporal knee," before they turn back into the occipital lobe. The problem which is one of great interest, cannot be regarded as finally solved.

The accompanying Table, after Traquair, gives a summary of the field changes in intracranial lesions.

THE REFLEXES OF THE EYE

The reflexes in the region of the eyes are not only of physiological interest, but not infrequently of valuable diagnostic significance. Fig. 6 is a comprehensive diagram of the pathways concerned. The retina is supplied by the optic nerve, and has been dealt with above. The chief motor nerve to the ocular muscles is the third or oculo-motor nerve, which supplies all of them, except the superior oblique and external rectus, which are supplied by the fourth and sixth nerves respectively. The third nerve is also responsible for the innervation of the levator palpebræ superioris, and in the same nerve sheath also pass the parasympathetic fibres, which supply the sphincter of the iris and the ciliary muscle.

Interference with the path of the third nerve between its origin and its termination will bring about an external squint as the result of the unopposed action of the external rectus with inability to move the eye inwards or upwards. If there is a lesion of the sixth nerve, the opposite condition exists, the patient having an internal squint with inability to move the eye outwards. Lesions of the third nerve are usually associated with dilatation of the pupil from paralysis of the parasympathetic fibres, and the power of accommodation is lost. The various positions and movements of the eye in conditions affecting the nerves supplying its muscles make a most fascinating problem, which is, however, outside the scope of this book. Individual paralysis of such

nerves seldom occurs as an isolated sign of disease. All the functions of the third nerve need not, however, be affected at once. Ptosis, for example, may exist without there being any other evidence of oculo-motor deficiency. Where the lesion is cortical or between the motor area and the nucleus, there may be no interference with the parasympathetic fibres. In tabes the ptosis may be looked upon as being due to a paralysis of the fibres which supply the upper lid or perhaps to a degeneration of the sympathetic neurones which innervate *unstriped muscle* in the lid.

When one of the cranial nerves responsible for the eye muscles is paralysed by a lesion of its nucleus, not only does paralysis of the particular muscles supplied by that nerve ensue, but there is also some interference with the associated movements of the opposite globe. This fact helps us to distinguish a nuclear from an infranuclear ophthalmoplegia. Thus in sixth nerve *nuclear* palsy, not only is there paralytic internal squint on the side of the lesion, but there is also a loss of the conjugate inward movement of the opposite eye. Third nerve *nuclear* palsy similarly disturbs the conveyance of the sound eye during accommodation.

Lesions above the oculomotor nucleus if situated in the appropriate place, *e.g.*, in the internal capsule, in the corona radiata or in the visuo-motor area which lies in the second frontal gyrus, can cause conjugate deviation of the eyes. This may be paralytic, towards the side of the lesion, or irritative, away from the side of the lesion. Apart from gross lesions such as cerebral hæmorrhage, conjugate deviation occurs frequently at the beginning of an epileptic fit. Disturbance of vertical conjugate movements is usually due to lesions of the superior corpora quadrigemina.

The Corneal Reflex.—This reflex is designed to protect the cornea from injury and has for its afferent path the fifth nerve and its endings in the conjunctiva. When this path is stimulated the impulse passes backwards to the Gasserian ganglion, and thence to the oculo-motor nucleus and nerve which bring about closure of the eyelid.[1] If the stimulation is sufficiently severe, the nucleus of the seventh nerve is also stimulated, producing contraction of the orbital or circumferential part of the orbicularis palpebrarum as well.

Reflex stimulation also occurs if a blow is seen coming towards

[1] The oculo-motor nucleus supplies the levator palpebræ superioris and inferior rectus which sends a slip to the lower lid. Inhibition of these initiates the closure which is completed by contraction of palpebral part of the orbicularis palpebrarum. The palpebral part, although apparently innervated by the VIIth, probably receives its fibres indirectly *via* VIIth from the third nucleus.

the eye, but in this instance the path must depend on association fibres between the optic tract to which the optic nerve carries impulses and the nuclei of the third and seventh nerves. In paralysis of the latter, the reflex on the diseased side is limited to the eyelids. Even when the eye is closed, as the closure is unsupported by the orbicularis palpebrarum, it is found that it can be opened more easily than that of the other side by pulling up the eyelids. Inability to close the eyelids without tremor is seen in conditions of general nervous states, especially neurasthenia.

Disappearance of the conjunctival reflex is a convenient sign in determination of the depth of anæsthesia which is sufficient for operation. If narcotics are used in conjunction with volatile anæsthesia surgical procedures may be begun before the reflex disappears. Beginners have, however, to be reminded that too frequent stimulation of the cornea will cause the latter to become insensitive, and on no account must a finger wet with an anæsthetic be used. Absence of the conjunctival reflex is occasionally obtained in hysteria and is associated with palatal anæsthesia. More commonly, however, it is retained, and its retention is of value in the differentiation of hysterical and simulated fits from those due to more serious causes, such as epilepsy. Loss of the corneal reflex is often the earliest sign of a lesion of the fifth nerve.

The Light Reflex.—By the light reflex the retina is protected from an excessive or dangerous amount of light. It is a true reflex, the afferent path being the optic nerve and tract to the corpora quadrigemina and thence by Meynert's fibres to the nucleus of the third nerve (see Fig. 6).

It is important to remember the bilateral nature of the stimulus, in any attempt to elicit the reflex. The stimulus for each pupil arises from the retinæ of both eyes. To obtain the reaction, both eyes must be shaded and one suddenly uncovered, when, if the patient has been asked to look towards the light, the pupil is seen to contract. Advantage is taken of this dual nature of the stimulus in Wernicke's method of investigating the integrity of the nerve paths. Thus, if light is shone from a mirror upon one half of one retina only, the reflex will not occur if the lesion is between the optic chiasma and the corpora quadrigemina of the opposite side. If it is above the geniculate body the reflex is unaffected, while if the optic nerve is affected the reaction cannot be obtained by stimulation of the eye on the same side.

In tabes, and general paralysis, the absence of the light reflex with retention of the reaction to accommodation—the so-called

Argyll-Robertson pupil—is often obtained. It will be seen from Fig. 6 that such a condition can be brought about by degeneration of Meynert's fibres which cuts off the efferent from the afferent neurone in the reflex arc. It is clear from the figure that it is necessary to keep the eye not under investigation covered, for the third nerve nucleus may be influenced by stimuli reaching it from both eyes.

Normally the parasympathetic keeps up a reflex tonic action on the **sphincter of the pupil.** This tone varies with the amount of light allowed to fall on the retina. It may readily be manifested by the fact that the administration of atropine which paralyses parasympathetic nerve endings, causes dilatation of the pupil. Indeed, this action of atropine is responsible for the naming of the plant " belladonna," from which the drug is derived. It is used when it is desired to paralyse the sphincter in order to keep the iris out of a corneal wound, or to inspect the interior of the eye carefully. It is important to remember that by this atropine dilatation the mechanism of the reaction to accommodation is paralysed. On the other hand, the use of pilocarpine or of eserine which stimulate parasympathetic nerve endings brings about constriction of the pupil. We therefore use these drugs in the treatment of glaucoma where it is necessary to increase the rate of escape of fluid in the filtration angle.

The iris is also innervated by the sympathetic, which maintains the tone of the dilator pupillæ and increases the size of the pupil. There is a balanced action between this tone and that kept up by the parasympathetic accompanying the third nerve. Whenever there is dilatation or constriction of the pupil there must also be reciprocal action between the parasympathetic and sympathetic nerves. The tone of the sympathetic is seen by the fact that if it is paralysed by section of any part of its pathway, or by paralysis of its nerve endings by ergotoxine, there is marked constriction of the pupil. The dilatation of the pupil on stimulation of the cervical sympathetic was, together with the effect of section noted above, first shown by Claude Bernard. Clinically, paralysis of the sympathetic may occur from a lesion anywhere on its long path. Preganglionic fibres for the supply of the eye pass out at the first and second dorsal segments to the stellate ganglion, and thence to the inferior cervical ganglion ; from which a loop round the subclavian artery known as the ansa subclavii passes to the middle cervical ganglion. They then pass up the neck behind the carotid sheath to the superior cervical ganglion, from which they

are distributed along the internal carotid artery to the Gasserian ganglion. From this point distribution is with the nasal division of the fifth nerve, and finally by its branches, the long ciliary nerves. Some sympathetic fibres instead of taking this route pass from the vessels to the cavernous plexus and on to the ciliary ganglion. They are distributed like those of the parasympathetic, by the short ciliary nerves. The sympathetic fibres, however, all relay in the superior cervical ganglion, none in the ciliary ganglion. (See Fig. 6.)

Lesions of the sympathetic may be the result of a number of diverse conditions which may affect it throughout its course. Further, the lesion may be irritative or paralytic, and will bring about dilatation or constriction of the pupil respectively. Irritation or paralysis may, for example, occur where a cervical rib presses upon the roots at their emergence from the spinal cord, or an aneurysm may press on the nerve in its later passage through the neck. An inequality of the pupils in such conditions often gives the key to the diagnosis. A slight degree of inequality of the pupils may, however, occur in conjunction with errors of refraction.

It is possible to stimulate the sympathetic by pinching the skin of the neck. The afferent path of this so-called cilio-spinal reflex is apparently by way of a sensory nerve, but where exactly the impulse becomes efferent is uncertain. The presence of the reflex is said to be an aid in the diagnosis of alcoholic coma. In actual fact any sensory stimulation brings about dilatation of the pupil just as it causes a rise of blood pressure and an increased rate of the heart, from sympathetic stimulation. As would be expected, dilatation is also produced by the injection of adrenaline. This does not occur on instillation normally, but only when the sympathetic has been previously destroyed. It also occurs in acute pancreatitis, in which it forms the basis of Loewi's test.

Where there is any excessive general sympathetic or diminished vagal activity we find dilatation of the pupil accompanying the increased heart rate and rise of blood pressure due to similar causes. Thus, these signs appear in atropine or alcohol poisoning, in exercise, or in fright. A loss of vagus tone is seen too in deep anæsthesia, in early compression causing cerebral anæmia, and at the point of death. On the other hand, constricted pupils due to the opposite cause are characteristic of cocaine and opium poisoning and hæmorrhage into the pons. In opium poisoning, the marked constriction of the pupil and the smell of the breath,

may be important aids to diagnosis. Constriction of the pupil is also seen in the early stage of chloroform anæsthesia, during which the normal vagus tone of the heart is increased and cardiac stoppage is liable to occur. Later on, at a stage before the conjunctival reflex goes, the pupil becomes of medium size and immobile to light. In many operations an anæsthesia in which the pupillary reflex has disappeared and the corneal reflex is still present is of sufficient depth. Full dilatation of the pupil under anæsthesia is an indication of impending disaster, commonly from respiratory or circulatory failure.

The **reaction to accommodation,** although strictly speaking not a reflex, is commonly investigated with the reflexes of the eye. Fig. 6 shows that it is really a motor movement associated with convergence, and designed to cut off rays through the optical system which are more affected by aberrations. The depth of the focus is also increased and more detailed images are produced by focussing on the macula which is straight behind the centre of the pupil. As the mechanism of accommodation is so closely related to that of refraction, it has been considered in relation to " Sight."

Diphtherial neuritis is remarkable in that it may cause a paralysis of accommodation, occasionally as its sole sign, although the palate is often paralysed as well. In such a case the pupil may fail to contract, simply because the patient cannot accommodate. The pupil may, however, contract on an attempt at accommodation as the contraction occurs also on convergence. The light reflex is of course retained.

NYSTAGMUS

The eyes have a special relationship to the movements of the semicircular canals as pointed out by Ewald and finally elaborated by Bárány, whose eye tests for vestibular function are in general use. This relationship is seen in the production of nystagmus, a short rapid oscillation of the eyeball, with a more rapid movement in one direction than in the other. If an individual with the head erect be rotated to the left, nystagmus to the right results from relative movement of the endolymph in the opposite direction. This can, as a rule, be observed. When the rotation ceases the inertia of the endolymph tends to cause it to continue flowing in the same direction, and causes a so-called after-nystagmus to the left. The existence of this after-nystagmus and its duration are indications of the functional efficiency of the

canals, each of which may be similarly tested by moving the head so that the canal is in the plane of rotation. Nystagmus may also be induced by the injection into the ear of hot or cold water which causes movement of endolymph. In health it should be induced in 20 to 40 seconds, although the period is reduced in hyper-excitable individuals and increased in reduced excitability.

The exact relationship between the canal and the eye is not at first clear, but it seems likely that the nystagmus is evidence of a mechanism by which successive objects may be focussed during movement of the head. As shown by Magnus and de Kleijn of Utrecht, if the head of a decorticated animal is moved from the vertical, the eyes are held in the vertical plane by an automatic mechanism of correction. This has been subtly expressed by Sherrington : " A cat is the right way up because the world is the right way up, and Nature arranged that it must always be so." It is usually considered that if the head is moved, there is a lag of the eyes which is evident in the experiments of Magnus. There is, relatively, a movement of the eyes in the opposite direction, so that the object looked at will remain in view. The sharp movement in the direction of the head rotation is a cerebral correction. It is evident that during movement both processes are automatic, and the purpose of such a mechanism is to enable a series of objects to be seen. Everything seen has to be accurately focussed on the retina for a definite period before it is recognized. When the body is turned round quickly vision would be blurred, but for the fact that certain objects are focussed and others omitted. When we travel in a train which passes rapidly through a station, we are conscious of having seen only a portion of the things on the platform and of having omitted others. In such circumstances there is a rapid jump, as it were, from each focussed object to the next, the period during which the object is focussed being approximately that between the jumps. This form of nystagmus may be seen by observing the eyes of a fellow passenger who is looking out intently from the window. The more rapidly the train moves, the more rapid will be the jumps, provided he is looking intently and is using the cerebral correction to the full. Similarly, the more imperfect the vision or illumination, the longer must the image be focussed on the retina, and the more obvious must be the jump. If the defect is habitual the movement of the eyeballs may persist even when the individual is not moving but is merely attempting to

move his eyes, and the oscillation will be brought out best when he attempts to look to his maximum extent to one side. Miner's nystagmus is probably produced by habitual working in a poor light. In this connection it has been pointed out by Ferguson that portable electric lights are often very inefficient, and the coal face absorbs a great deal of any artificial light supplied. Further we cannot expect that miner's nystagmus, which appears only after twenty or thirty years, will disappear quickly when conditions are improved. At the same time it must not be assumed that light is the only factor concerned, for the nystagmus is often part of a general nervous instability. Mackay points out from his very wide experience that nystagmus shows great local incidence, being absent from Midlothian mines, but very common in mines in Fifeshire. He has been quite unable to relate this to differences in lighting.

In ordinary practice nystagmus may be ocular, cerebellar or labyrinthine in origin. The ocular variety occurs when the vision is defective, and is specially likely to develop when the normal fixation of objects which is acquired by the end of the first six months of extra-uterine life is prevented, *e.g.*, by the development of bilateral central corneal nebulæ following ophthalmia neonatorum. Cerebellar nystagmus is seen in cases of cerebellar tumour, abscess, thrombosis, etc., and the nystagmus so frequently observed in the subjects of disseminated sclerosis is probably also due to a lesion of the cerebellum or its tracts. Degeneration of the afferent cerebellar tracts may cause nystagmus, as in Friedreich's ataxia ; nystagmus in certain cases of disease of the cervical part of the spinal cord has probably a similar anatomical cause. Labyrinthine nystagmus occurs in acute and chronic labyrinthitis and during the paroxysms of labyrinthine vertigo known as Menière's disease.

When there is no gross ocular or occupational cause for nystagmus, this sign is very suggestive of the presence of organic nervous disease, and a thorough examination of the nervous system is imperative.

Since there are three pairs of semicircular canals, oriented in three different planes of space, it might on theoretical grounds be expected that nystagmus could occur separately in each of the three planes. Clinically, however, rotatory and lateral varieties only are encountered, vertical nystagmus being very rare. This limitation is said to be due to the direct communication which exists between the superior and posterior semicircular canals.

CHAPTER XV

HEARING. TASTE

General Considerations

The organ of hearing consists of two main divisions, if it is considered from the clinical aspect. The first is the *Conducting Mechanism*, which consists of the external and middle divisions of the ear ; it is designed to collect and convey sounds from the external atmosphere to the sensitive endings of the auditory nerve. This division of the mechanism takes no part in the perception of sound, nor is it absolutely necessary, for even after its destruction hearing is in many cases fairly good, although diminished in acuity to a variable degree below the normal.

The *Perceiving Mechanism* is supplied by the cochlea ; this is a coiled tube situated in the internal ear, where it is in communication with an organ of orientation, made up of the semicircular canals and the otolith systems of the utricle and saccule.

In the cochlea the effect of sound waves is to cause stimulation of the endings of the auditory nerve, by the fibres of which impulses are carried up to the brain, where they are analysed and appreciated.

The various parts of the conducting and perceiving apparatus will be considered separately.

THE EXTERNAL EAR

The external ear consists of two divisions. The *auricle* projects from the side of the head. In many animals it has the important function of collecting sound waves ; in man it is of little use, for its removal causes almost no change in acuity of hearing in the case of the otherwise normal individual, yet in the case of the deaf it must be of advantage. Indeed they reinforce it with the hand or an artificial device for collecting sound and increasing its intensity at the ear.

The *External Auditory Meatus* is a canal leading from the auricle to the middle ear ; it is separated from the latter by the tympanic membrane, on which sound waves impinge after travelling in from the exterior. The canal is protected near the

surface by a sieve-like arrangement of hairs; in conjunction with sticky cerumen secreted by specialized glands lying in the cartilaginous portion of the tube, they give protection against the entrance of insects and dust.

Any marked interference with the patency of the canal causes deafness, because sound waves are prevented from reaching the tympanic membrane, but the canal may be reduced to very

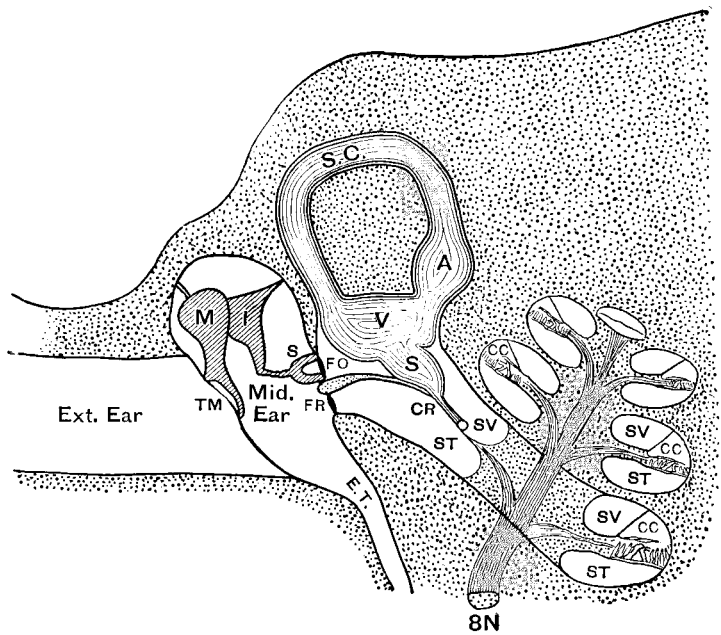


FIG. 7.—Diagram of the Ear, including the semicircular canals. (From Halliburton & McDowall's *Handbook of Physiology*.)

narrow limits, short of being completely occluded, without loss of hearing.

The factors likely to obstruct the canal are large collections of cerumen mixed with dust and soot, swelling of the cutaneous lining caused by a boil or furuncle, and the presence of a foreign body such as a pea.

THE MIDDLE EAR

The middle ear consists of Eustachian tube, tympanic cavity, tympanic membrane, mastoid antrum, and mastoid air cells; it is with the three first-mentioned structures that we are particularly concerned.

The *Eustachian Tube* brings the nasal fossa into communication with the tympanic cavity ; it is only occasionally open, however. It is of importance in that it serves to regulate the air pressure in the middle ear tract, and if it is obstructed serious impairment of hearing may be the result.

Such obstruction is caused by inflammatory swelling associated with rhinitis, blockage by adenoid tissue, or a naso-pharyngeal neoplasm.

After occlusion of the tube, air contained in the tympanic cavity is absorbed to a certain degree, and the pressure falls below that of the atmosphere. The result is that the tympanic membrane is drawn inwards, and presumably the membranes closing the round and oval windows of the inner ear must be drawn outwards. Transmission of sound from the external auditory meatus to the cochlear mechanism is interfered with and deafness is produced.

Violent blowing of the nose may force air through the obstructed Eustachian tube and cause a sensation of bulging of the tympanic membranes. A similar result may be brought about by swallowing with the mouth and nose closed, in which case the raising of the soft palate causes at first an increase of pressure in the nasal fossa, and consequently of that in the tympanic cavity also.

Forced expiration with the nostrils closed brings about the same result, and is a method often adopted by those with obstructed Eustachian tubes ; frequently repeated bulging of the tympanic membrane may, however, cause stretching of its tissues, with deleterious results. A more accurate method of inflation of the middle ear is that in which air is blown into one or other nostril from a Politzer bag. In severe cases the Eustachian catheter is used.

Some consider that in many cases it is not obstruction, but undue patency of the Eustachian tube which is the cause of deafness.

The *Tympanic Membrane* shuts off the middle ear from the external meatus. It consists of a central fibrous layer covered externally by epidermis and internally by mucous membrane.

It can vibrate through a very wide range of pitch and is practically dead beat, without after-vibrations.

The *Tympanic Cavity* is bound partly by bony walls, and partly by the tympanic membrane and the membranes of the round and oval windows ; in it lie the tympanic ossicles. Sound can be conducted across the cavity without the assistance of the

chain of bones, as is found to happen in many individuals who have had middle ear disease ; very often a fair degree of hearing is retained in spite of severe damage.

The *Ossicles* are so arranged that they link the tympanic membrane to the membrane of the oval window. There is a slipping joint between the malleus and incus, so designed that excessive movement of the stapes shall be prevented, as otherwise there would be a danger of rupture of the membrane which attaches the foot of the stapes to the edge of the foramen ovale.

The area of the tympanic membrane is much larger than that of the oval window, so that sound waves coming from the exterior are concentrated to a considerable degree. At the same time the lever action of the ossicles diminishes the amplitude of the sound waves and greatly increases their force.

Middle ear deafness results from any condition which interferes with passage of sound waves from the external to the internal ear.

Conditions producing middle ear deafness are inflammatory changes or perforation of the tympanic membrane, indrawing of the membrane by diminished pressure in the tympanic cavity, arthritis or ankylosis of the ossicles, dislocation or destruction of parts of the malleus or incus, exudation of serous or purulent fluid into the tympanic cavity, and the obstruction of cholesteatomatous collections or granulation tissue.

In the normal individual sound is heard more clearly when it passes through the auditory meatus than when it is conducted through the temporal bone. Thus, if a vibrating tuning-fork be held to the skull behind the ear until its sound is no longer heard, it will again be perceived if held close to the orifice of the auditory meatus, the reason being that the waves entering the meatus are collected and amplified by the tympanic membrane and ossicles.

In cases of middle ear deafness this relation is upset ; the obstruction to passage of sound waves through the conducting mechanism causes a tuning-fork or other sound-producing apparatus to be perceived better when pressed against the bone than when held close to the auditory meatus. This is known as *Rinné's test*, which is positive in the normal individual and negative in those with middle ear deafness.

Not only is sound heard better when conducted through bone than when heard through the air in cases of middle ear deafness, but, furthermore, in such a case a tuning-fork held on the middle

line of the skull is heard better in the unhealthy ear. This is known as *Weber's test*, and may be readily imitated by blocking the auditory canal with the finger. It has been suggested that the tuning-fork is heard better in the impaired ear because of absence of confusion by external sounds, and this is supported by the fact observed by Jenkins that, under conditions of extreme quietness, closure of the auditory canal does not result in better hearing of a tuning-fork in the closed ear. This observation is still further supported by the observation that if both auditory canals are blocked up by the fingers, one's own breathing sounds can be heard, although they are normally inaudible.

The *Action of the Tensor Tympani Muscle.*—The muscle is situated in a bony canal lying alongside the Eustachian tube, and is inserted into the handle of the malleus. It may be observed to contract when sounds fall on the ear. When there is complete absence of sound the muscle is relaxed and the tympanic membrane but slightly stretched. When sounds fall on the ear the tone of the muscle is increased and the tympanic membrane more strongly stretched, thus increasing its ability to respond to the pressure variations which are affecting it. Contraction is said to be greater when high tones are sounded.

The *Stapedius Muscle* issues from a small opening in the Fallopian canal, and is inserted into the neck of the stapes. When it contracts it pulls the neck of the stapes backward and so adjusts the tension at the oval window where the footplate of the ossicle is attached. It causes also a spur of bone below the head of the malleus to engage with the body of the incus and so prevents chattering at the malleo-incudal joint (Hartridge). When the stapedius muscle is paralysed, hyperacousis results.

THE INTERNAL EAR

The internal ear is the receptor organ for sound waves, which normally reach it through the conducting mechanism of the external and middle ear. For details of its structure the reader is referred to a textbook of physiology.

For present purposes it may be considered as a spiral canal divided into three compartments. The upper contains perilymph and receives impressions of sounds transmitted by the movements of the stapes in the oval window. The waves travel through a fine opening into the lowest compartment, which is closed at its basal extremity by the membrane of the round window. Although sound waves are probably transmitted in this way

when the conducting apparatus is normal, yet it seems likely that in cases where disease has destroyed the membrana tympani and ossicles, loud sound waves can travel in the opposite direction, and act most effectively on the round window.

Between the upper and lower compartments of the cochlea there is a third or middle canal filled with endolymph.

This canal is triangular in section, one side being made up of the basilar membrane. This is composed of a series of transverse fibres loosely held together. Each fibre is stretched, and vibrates sympathetically, when sounds of pitch corresponding to its rate of vibration reach the ear and cause waves to travel along the upper compartment, through the narrow communication, and thence along the lower passage. The fibres are shorter, more tense, and of less mass at the base of the cochlea, and are longer, slacker, and more heavily loaded at the apex. Sounds of high pitch bring about vibration by resonance of the basal fibres, while those of low pitch affect the apical fibres.

The vibrations of the fibres are transmitted to hair cells, which form part of the organ of Corti, a structure lying on the basilar membrane. From the hair cells the fibres of the auditory nerve conduct the impulses to the brain.

Internal Ear Deafness.—*Pathological Changes in the Oval Window* occur in many cases of a familial disease known as otosclerosis. Limitation of movement or fixation of the stapes is produced, with a type of loss of hearing showing most of the signs of middle ear deafness. The process may spread to the capsule of the cochlea, and will then give rise to signs of internal ear deafness. There is one peculiar feature in all cases of otosclerosis, namely, paracusis or the ability to hear better with the affected ear in a noisy than in a quiet place. It is thought to be due to abnormal inertia of the stapes caused by its limitation of movement. If sounds of powerful intensity are brought to bear, they will overcome this abnormal inertia of the stapes, and enable other sounds of feeble intensity to be transmitted to the cochlea.

Pathological Changes in the Canals of the Cochlea produce characteristic signs. The changes may be due to inflammation, to effusion of blood, or to injury. Sounds—such as those of a tuning-fork—are heard better by air conduction through the external auditory meatus than by bone conduction through the skull; Rinné's test is therefore positive. The reason is that in the former case the intensity of sound is greatly magnified by the

agency of the tympanic membrane and chain of ossicles, if they be healthy.

Hearing may be partly or completely lost, and it is to sounds of high pitch that perception is first diminished, but why this should be so is by no means clear. Recent pathological findings appear to call for a reconsideration of the generally accepted reasons.

Since the sensitivity of the receptor apparatus is diminished, sounds conducted directly by bone are not perceived so well as in the normal individual. A comparison between the affected person and the normal observer is known as Schwabach's test. Since the affected ear does not hear sounds so well by bone conduction, if, as in Weber's test, a tuning-fork is held on the mid-line of the skull, it is heard better on the good side.

Pathological changes in localized regions of the cochlea have been observed in boilermaker's deafness, and the loss of hearing in these cases has been demonstrated by Ritchie Rodger to affect that part of the cochlea concerned in hearing the particular sounds among which the men work.

Senile deafness is of the internal ear type ; the fact that hearing of tones of high pitch is the first to be diminished may be due to the loss of elasticity which must be the fate of fibres of the basilar membrane in old age. This loss leads to diminished power of rapid resonant movement, and must affect most severely the fibres of most rapid rate of vibration, namely, those responding to high tones.

The nervous paths from the basilar membrane to the brain consist of the hair cells, the fibres of the auditory nerve, the nuclei and striæ acusticæ and corpus trapezoides in the pons, and the tracts up to the temporal lobe *via* the lateral fillet, internal geniculate body and auditory radiation. Fibres from each cochlea are thus relayed to both temporal lobes.

In going to the brain the nerve passes by other important structures, so it is possible to localize a lesion by associated signs.

Thus, lesions in the internal auditory meatus or along the course of the eighth nerve, are usually accompanied by changes in the vestibular or facial nerves. The most common cause of trouble in this situation is an auditory nerve tumour, of which the earliest signs are loss of hearing of tones of very low pitch. The lower tone limit is gradually raised, until in the end deafness becomes complete. Vestibular disturbances are associated with the deafness, and facial paralysis often appears as a late sign,

together with signs of raised intracranial pressure such as headache, vomiting, and optic neuritis.

Since each ear is represented in both temporal lobes, lesions of the central auditory pathway within the brain stem rarely cause deafness. A lesion of one temporal lobe (the left) may cause word deafness but not true deafness. Pineal tumours may press on both lateral fillets in the mid-brain and cause a degree of *bilateral* deafness. Schilder's disease, a demyelinizing encephalitis, which spreads gradually and usually symmetrically through the cerebral hemispheres, may pick out both temporal lobes and so cause bilateral deafness which is, however, but a subsidiary part of a striking clinical picture.

Tinnitus is the term used to describe noises heard in the ears without external cause. It is probable that the sounds are produced by various normal processes in the body, such as the rushing of blood along arteries, or of air through the trachea.

If an observer listens through a stethoscope, of which the chest piece is attached to that of a second stethoscope, and if the ear pieces of the second instrument are placed in the ears of any individual, obvious sounds will be heard. The reason why the individual does not hear the sounds of his own body is because of purposive lack of attention, or a psychological ignoring of them. In those with deafness, especially of the type of otosclerosis or internal ear deafness, external sounds are less well heard, but those of internal origin become distinct, and in many cases give rise to great distress.

Taste.—In the popular use of the word taste includes flavour, which depends, however, on the sense of smell. When during the course of a common cold, food seems insipid, the sense of smell is what is deficient, not the sense of taste in the proper meaning of the word.

The receptors for taste in the mucous membrane of the tongue and palate are the taste buds. These are specially abundant in the lingual papillæ of which the circumvallate are a specially developed group. The various fundamental sensations of taste predominate in different degrees in different regions of the tongue. The sense of saltness is diffuse, but sweetness is appreciated particularly by the tip, sourness or acidity by the sides and bitterness by the base of the organ. Whether the metallic and alkaline tastes exist as separate entities is uncertain. It is to be remembered that substances which excite taste, particularly acids, have some effect upon touch, and that this effect may have been

responsible in part for the confusion which formerly existed with regard to the precise nerves which carry the taste impulses centrally. These nerves are now known to be the chorda tympani of the facial for the anterior two-thirds of the tongue, the glosso-pharyngeal for the posterior third. The lingual is the nerve of touch, and is only a taste nerve in the distal part of its course where it carries the chorda tympani with it. Lesions of the lingual nerve below the pterygoid region—and the nerve from its superficial position behind the last molar tooth is liable to injury during operations on the wisdom—cause loss of taste over the same side of the anterior part of the tongue. Operative removal of the Gasserian ganglion, however, causes no permanent impairment of taste in any region of the tongue, although during the period in which the trigeminal fibres in the lingual are degenerating they may compress or otherwise paralyse those of the chorda which are bound up in the same sheath, and so cause a transient loss of taste on the same side of the tongue (Cushing).

The glosso-pharyngeal nerve as it traverses the base of the skull furnishes a secretory twig, the nerve of Jacobson ; after a devious course in which the otic ganglion acts as a relay station the secretory fibres reach the parotid gland. The chorda tympani supplies fibres to the submaxillary and sublingual glands *via* Langley's ganglion and the submaxillary ganglion respectively. In the medulla the taste fibres are collected into a compact bundle, the fasciculus solitarius, which is in close relationship with the salivary nuclei, and the intimate relation between taste and salivation is thus seen to have an anatomical basis. The sucking of " acid drops " when the mouth is dry, as in fevers and after operations, reflexly stimulates the salivary glands and the flushing of their ducts thereby induced helps to prevent the development of septic parotitis.

The cortical region for taste, as for smell, is the anterior end of the hippocampal gyrus. When a tumour develops near this region, uncinate fits may result, characterized by unpleasant sensations of smell and taste and by smacking movements of the mouth and sniffing. Some degree of impairment of consciousness or a major epileptiform fit may follow. Uncinate fits are thus seen to be a variety of sensory Jacksonian epilepsy, and like Jacksonian epilepsy generated in other regions of the cerebral hemisphere are suggestive of a local gross lesion (temporal lobe tumour), but can also arise as a manifestation of " idiopathic " epilepsy. In every-day medical practice an evil taste is most frequently due to

some local cause in the mouth or adjoining cavities, *e.g.*, dental sepsis, and a metallic taste is not uncommon in metallic poisoning, *e.g.*, mercurialism. Often, however, no cause can be found, and the patient seeks relief in vain. In certain cases of mental disease hallucinations of taste occur.

Local loss of taste, rarely, if ever, noticed by the patient, occurs as a subsidiary sign in lesions of the facial nerve (caries of the temporal bone, Bell's palsy, etc.), and of the glosso-pharyngeal nerve. Total or partial loss of taste may be found when the taste buds have been destroyed by previous taking of a corrosive poison and also in hysteria. A rare but interesting hysterical " syndrome " is loss of smell and taste with cutaneous anæsthesia and motor paralysis, all of which occur on the same side of the body !

CHAPTER XVI

THE RATE OF THE HEART BEAT

In this consideration of the rate of the heart it is assumed that the organ itself is in a normal state and that all its chambers respond in a physiological sequence. Conditions under which different parts of the heart vary in rate are considered in a succeeding chapter.

The frequency of the heart beat, although conveniently elicited by an examination of the pulse, is more accurately determined by auscultation. In most individuals it beats at a rate of 65 to 75 per minute, but it must be remembered that many normal people have a cardiac rate considerably more or less than the average. In infancy, the rate is about 120, and this may be maintained for several years. Napoleon is credited with a pulse rate of from 40 to 50. The physician, then, must be wary before reaching a conclusive opinion about the significance of the pulse rate in a case he has not seen before.

The rate is set by that part of the heart called, by Erlanger, the pace-maker, which is synonymous anatomically with the sino-auricular node of Keith and Flack. It lies in the right auricle near the entrance of the great veins. The circulation is, however, but the servant of the body. This was originally emphasized by Broadbent and others of the old Edinburgh school and, more recently, by their pupils Haldane and Mackenzie. The rate of the heart as set by the pace-maker serves the body at rest, and, were the rate fixed, body function would be extremely limited. The circulation is under both nervous and chemical control, and, as we shall see in relation to the respiratory system, is adjusted so that it can respond with the utmost delicacy and rapidity to the varying requirements of the body.

An increase in rate may not necessarily increase the output of the heart per minute, since, by increasing the rate, the diastole rather than the systole is shortened. This is important in prolonged paroxysmal tachycardia and in hæmorrhage when the heart has less time to fill between its contractions, and the output per beat is reduced. Similarly, within physiological limits, the

resistance to the outflow from the heart may be considerably increased without causing any diminution of outflow. This is of great advantage at the beginning of exercise when there is an appreciable rise in peripheral resistance and in blood pressure. The increase of blood pressure is brought about by the constriction of, probably, all blood-vessels, especially in those areas not affected at the commencement of exercise, such as the skin (McDowall) and alimentary canal. The spleen and the large intestine may be seen to become pale (Barcroft).

The essential factor governing the output of the heart is the inflow, a fact which was called by Starling the Law of the Heart. This law states that within physiological limits the force of the heart's contraction depends on the extent to which the heart muscle has been stretched by the blood—a law which really applies not only to the heart but to all muscular tissue. Normally, however, as pointed out by Yandell Henderson, and as can readily be demonstrated, the height of the venous pressure is such that the heart can fill in less time than that of the normal diastole. Still more is this true when the venous pressure is increased, as in exercise, when a shortening of diastole does not diminish the filling and the output per beat. Normally, in exercise there is not only an increase in the number of beats but also an increase in output per beat and per minute.

Increased Heart Rate, Tachycardia

Various mechanisms are concerned when an increase in the heart rate is brought about. The heart is governed by two sets of nerves from the autonomic nervous system : the sympathetic, whose effect is accelerative, and the vagus, whose effect is inhibitory. The sympathetic fibres arise from the upper thoracic roots, and reach the heart by way of the inferior cervical ganglion, and also, according to some, the superior cervical ganglion. Normally there is a balance between these two, being slightly in favour of the vagus, whose tone is the stronger. This vagus restraint and its development depend greatly on the requirements of the individual. Pet animals have appreciably less restraint than more active field animals, as may be shown by cutting the vagi. Similarly, the effect of atropine in persons of different ages suggests that vagus restraint is greatest at the most active periods of life (Crawford). An increase in the rate of the heart is produced by diminution in vagus restraint, or an increase in the activity of the sympathetic, or both. In exercise, both are

brought about, as shown by Bainbridge, by a rise in venous pressure. This rise of pressure in the large veins of the thorax, and in the right auricle, is caused by many factors. First, the carbon dioxide produced by the exercise constricts the veins both directly and by central action, for we know, from the work of Donegan and others, that the veins are supplied by vaso-motor nerves. Further, there is an increased blood flow to the thorax, owing to the increased respiratory movements which occur at the same time (L. Hill), while the movements of the muscles themselves, in virtue of the valves in the veins of the limbs, hasten the return of the venous blood. Over-filling is prevented by the pericardium. The increased flow of venous blood to the heart would, from its direct effect on the heart, be sufficient by itself to increase the output—both per beat and per minute—without necessarily a change in rate. A further increase, however, is brought about by Bainbridge's reflex, which still further augments the output by affecting, as we have said, the nervous control of the heart.

The sympathetic is also stimulated by oxygen want and the accumulation of carbon dioxide in the blood. These have been shown by McDowall to act through stimulation of higher centres the exact locations of which have not been ascertained.

Recently, also, Cannon has found that the contraction of smooth muscle of blood-vessels causes to be thrown into the circulation a substance, sympathin, which accelerates the heart like adrenaline.

It will be evident, therefore, that for the most part the muscles, in virtue of the carbon dioxide they produce, control their own blood supply—although indirectly—by means of the nervous mechanisms which control the heart and vaso-motor system.

The existence of a nervous mechanism to control the heart makes its response more immediate, and this is facilitated by the existence of a balance between the vagus and sympathetic which may be directly altered by higher cerebral centres. The heart rate of a sprinter at the starting-post is already increased before the race begins. The same may be said of the respiratory rate. There is consequently no lag and the heart is ready to deal with the effects of the anticipated exercise. The mechanism is really a primitive one intended to prepare for such an emergency as a fight or the seizure of food—the successful issue of which was an essential of primitive existence. Pain also increases[1] the heart rate, as does stimulation of any sensory nerve, and these increases

[1] See also p. 8 in relation to fainting during which the heart may be slowed.

presumably depend on the same mechanism. Even examination of the patient by the physician may be sufficient to cause an undue hastening of the heart. The pulse rate should therefore not be taken until the confidence of the patient has been obtained, Several other concomitants of exercise facilitate an increased cardiac rate. During exercise, the venous blood from the exercised part is noticeably hotter than normal, and heat stimulates the pace-maker.

In **fever** the rate of the heart may be increased by a variety of causes—the pain, the temperature of the blood, and the toxin responsible for the fever. The mechanism by which the toxin affects the heart rate is as follows : as soon as the heart is poisoned and fails to drive out its full contents, the venous pressure tends to rise and to increase the cardiac rate by direct and reflex effect on the pace-maker. The output of the heart, although reduced per beat, is, in view of the increased rate, not reduced per minute and the blood pressure is maintained. The increased heart rate, where it is not associated with any other symptoms such as fever or pain, is often most important clinically. For example, in appendix abscess, when the acute symptoms have passed off, the temperature may fall and the pain disappear and one may be tempted to imagine that the attack has subsided. The increased cardiac rate together with local signs is then of primary diagnostic significance. Obscure conditions, such as early tuberculosis, are often suspected as the result of a frequent pulse.

In pathological conditions not associated with toxæmia, but in which there is a breakdown of some part of the mechanism for the conveyance of oxygen or carbon dioxide from and to the lungs respectively, the increased cardiac rate indicates that the circulation is influenced thereby and is probably attempting to make up to some extent for the breakdown. The mechanism of the acceleration of the heart may vary slightly in individual cases, but usually the action is by means of a raised venous pressure affecting the pace-maker. This is well seen in chlorosis, in which the increased rate of the heart is often the most striking symptom. In this case the increased volume of blood, as found by Lorrain Smith, will lead to an increase in venous pressure, and, indeed, the fact that the heart rate is increased may be taken as supporting the conception that in this condition there is dilution of the blood. The only other possibility is that somehow the heart is quickened by the low hæmoglobin or oxygen content of the blood.

The well-known tendency to œdema of the lower extremities in chlorosis may be looked upon as due to this dilution and to the rise in venous pressure which increases the capillary pressure (see Œdema). A further factor which may also play a part in the production of excessive heart rate is the inefficiency of the blood as a carbon dioxide and lactic acid carrier. We know that the corpuscles indirectly affect considerably the amount of carbon dioxide which can be carried by the plasma (see Appendix) without affecting the H-ion concentration of the blood. As will be seen in relation to "Breathing," there will tend to be an accumulation of carbon dioxide in the medulla. Such an accumulation, like oxygen want, will, as we have noted, cause a diminution in vagus activity and sympathetic stimulation. This action must not be confused with the deleterious effect of larger degrees of asphyxia on the heart. In heart cases also, the venous pressure may be raised by the same means as have been referred to above in relation to the effect of toxin, that is, the banking up of blood on the venous side may be largely responsible for the acceleration.

In general it should be realized that, in a person whose normal heart rate under definite conditions is known, an increase in the rate may be of very appreciable significance, as it may be the first indication of approaching cardiac enfeeblement or the effect of toxæmia. According to Mathew, this warning increase is often seen in cases of high blood pressure in which the rate is usually slow, because the high pressure in the aorta and the carotid sinus (at the bifurcation of the carotid) brings about reflex stimulation of the vagus.

The enormously increased heart rate which is so important in exophthalmic goitre is most likely brought about in several ways. The excessive secretion of the thyroid has probably a direct hastening action on the heart metabolism, as it has on other tissues. This may be further increased by its general stimulating action on the sympathetic. Since there is a markedly increased metabolism, there must be an increased carbon dioxide production which will act as in exercise. This explains why dyspnœa is also a common symptom.

In relation to the thyroid (page 286) the heart rate may be taken as a general indication of the state of the patient. Thus in exophthalmic goitre the heart rate is excessive, and in myxœdema notably slow. In the latter the rate can be taken as an indication of the effect of treatment by thyroid. It is usually considered safe to give the extract in increasing doses so long as

the rate does not exceed a hundred per minute. The diagnosis of certain cases of hyperthyroidism without exophthalmos from anxiety states in which also there are tremors, tachycardia and sweating may be difficult. Even determinations of the basal metabolic rate may leave the question undecided, as such determinations are subject to an error of $\pm$ 15 per cent. Nervous tachycardia, however, usually abates during sleep, and estimations of the "sleeping pulse rate" may prove of the greatest service.

The heart may also be stimulated by specific substances ingested, *e.g.*, tea, coffee; and after the average meal there is a normal increase in the heart rate. The accelerating effect of alcohol in concentrated spirits, such as brandy, is considered due to the sensory stimulation of the mucous membranes, but other factors are probably also concerned.

Tachycardia, produced by excessive use of tobacco, depends, however, on the effect of the nicotine on the nerve supply of the heart. Nicotine, as shown by Langley, paralyses the synapses in the ganglia of the autonomic system. In the case of the heart both vagus and sympathetic ganglia are probably affected. Since the balance is on the vagus side, the result of the paralysis is usually an increase in the heart rate. Atropine and belladonna preparations, on the other hand, increase the rate by paralysis of the vagal endings, thus removing the normal inhibitory mechanism. These facts, besides being seen in man, can also be readily demonstrated in animals.

Where the tachycardia is paroxysmal and auricular in origin it may promptly be arrested by digital compression on the vagus nerve or the adjacent carotid sinus in the neck which brings about stimulation of the vagus centre. In some patients regular administration of quinidine may ward off attacks of auricular tachycardia (Ritchie).

Palpitation.—This is a symptom not specifically cardiac. It is the cardiac action perceived by the patient and, although often the result of forcible or irregular and possibly rapid action of the heart, may be the result of the accumulation of gas in the stomach. The heart itself may be normal. The removal of the cause and of the anxiety from the patient's mind are the primary consideration.

In considering the rate of the heart, then, many factors are concerned. They are all comparatively straightforward to deal with, if the general mechanism of heart control is kept in mind.

The study of individual cases in the light of modern knowledge offers an excellent field for clinical investigation.

It will be noticed that the mechanisms used in disease are those normally developed for exercise, a fact which serves to emphasize the value of exercise in keeping the vascular reflexes and heart efficient and, therefore, the better able to cope with a sudden emergency, normal or pathological.

One note of warning in relation to the significance of an increased heart rate is necessary. It is commonly assumed that drugs (*e.g.*, amyl nitrite, alcohol) which accelerate the heart are cardiac stimulants, but this may often be a grave error. The heart may be accelerated reflexly in an attempt to maintain arterial pressure should conditions arise which would tend to lower it, *e.g.*, diminished peripheral resistance or increased capacity of the circulation.

A slow heart of 60 and under is peculiar to certain normal persons, and there is a suggestion that the condition is hereditary; but similarity of occupation in families (*e.g.*, those of hill shepherds) may be responsible.

Bradycardia.—It occurs in those who take a large amount of strenuous exercise, and is produced by training, presumably as a result of increased vagus tone (see page 130). When it occurs in others it is commonly found that they have been the subjects of pathological states, *e.g.*, pneumonia and painful conditions, which, like exercise, have previously caused an excessive rate. The subsequent bradycardia may be looked upon as a physiological overcompensation, the mechanism of which is incompletely understood, although there is evidence which suggests that it has a chemical basis.

Such bradycardia must be clearly distinguished from the slow heart which occurs in impairment of the auriculo-ventricular bundle (see "Heart-Block"), or in myxœdema from thyroid deficiency.

The effect of respiration on the heart rate is for convenience dealt with in relation to the pulse. Here it need only be mentioned that normally there is a slight increase in the rate during each inspiration and that in some persons, especially young, this increase may be very considerable. Indeed the variation may in toxæmias, such as the acute fevers, be a valuable indication that the cardiac control has not been seriously impaired.

CHAPTER XVII

THE PULSE AND THE HEART SOUNDS

THE PULSE

THE examination of the radial pulse has been made by physicians from the earliest times, and to-day it is still a clinical observation of the first importance. The significance of the pulse, however, has been only gradually understood. It has long been recognized that its character varied under different conditions, and the old physicians did what they could to interpret it. This was done with more accuracy than is perhaps generally admitted, but, not fully understanding the factors on which it depended, they inevitably classed together many conditions which are really quite separate. The main features of the pulse are its rate, rhythm, and character.

The Rate of the Pulse.—Physiologically, the pulse rate indicates the rate of the heart, but this is not sufficiently accurate for pathological requirements, as in diseased conditions the beat of the heart itself may be broken up in divers ways. The radial pulse rate indicates essentially the number of beats of the left ventricle of sufficient magnitude to cause a wave to be conducted out to, and felt at, the periphery. The wave passes to the periphery just as a ripple reaches to the edge of a pond, when a stone is thrown into it. If the energy of the wave is too small the pulse is not felt, and if the heart is beating irregularly it is often found, by listening to the organ itself, that the ventricle is beating more rapidly than the radial pulse would indicate, a condition sometimes called " pulse-deficit."

Further, the rate of the left ventricle is not necessarily that of the whole heart, whose auricles may, in certain pathological conditions, be beating appreciably faster. The pulse rate depends on two factors : (1) the number of impulses reaching the auriculo-ventricular node from the right auricle, and (2) the conductivity of the auriculo-ventricular bundle of His. Provided the heart is normal, the ventricle follows the auricle beat for beat, and, except when the bundle is inadequate, the auricular rate determines that of the pulse. Failure of the bundle is, however, compara-

tively rare, and in general the pulse may therefore be considered as giving an indication of the behaviour of the whole heart. Commonly, then, conditions which affect the rate of the auricle will affect that of the whole heart, and the pulse. These have already been fully dealt with in the previous chapter.

Several pathological conditions cause a variation in the number of impulses which reach the auriculo-ventricular node from the auricle and affect both the rate and rhythm of the pulse.

The Conductivity of the Auriculo-ventricular Bundle.—The cardiac impulse commences at the Keith-Flack node (or pacemaker) of the right auricle in the region of the entrance of the great veins. The impulse passes out over the auricle, fanwise according to Lewis, and reaches the auriculo-ventricular node. It passes from auricle to ventricle by a specialized tissue, known as the auriculo-ventricular bundle. This starts from the auriculo-ventricular node, and runs to the inter-ventricular septum near the aortic valve, where it divides into two branches, one for each ventricle. These run down the septal wall and are continued on to the papillary muscles and the Purkinje fibres which lie immediately under the endocardium. The bundle is further specialized in that it permits the passage of the impulse at a great speed, 5,000 mm. per second, as compared with 1,000 per second in the auricular muscle. In this way a minimum of time is lost in the distribution of the impulse to different parts of the ventricle.

The bundle is the only [1] pathway by which impulses can pass from auricle to ventricle, and it is therefore essential that it should be intact. Experimentally, in mammals, it may be severed; while in the frog, by tying a ligature (first Stannius) between the sinus venosus and auricle, a similar condition may be produced. In this latter case, however, it is the muscle which is interfered with, the muscle of the sinus being continuous with that of the auricle and ventricle. This is not so in the mammal. When the conducting path between sinus and ventricle is interfered with, the latter may stop altogether, as it usually does in the frog, or it may continue beating if the tension inside the ventricle is high. It has been noted, for example, that the stoppage is more apt to occur when the first Stannius ligature is tied at the end of systole, the heart being then empty. The tying of a second ligature (around the auriculo-ventricular junction) by increasing the tension in the ventricle, usually restarts the latter, if it has stopped. In the

[1] In a few persons, and especially in children, there is right lateral bundle also joining the auricle and ventricle (Stanley Kent).

mammal the tension kept up by the blood within the ventricle and coronary arteries acts as a stimulus to contraction and prevents the ventricle from stopping. It beats, however, at a much slower rate than the auricle. If the auriculo-ventricular bundle is severed, the auricle continues to beat at its normal rate, but the ventricle takes on a much slower rate. Such a condition is known as *heart-block*, and since the auricles and ventricles beat with independent rhythms, in this instance the heart-block is *complete*.

Recognition of complete heart-block obviously depends on the slow beat of the ventricles (and the consequent infrequent pulse, which must not be mistaken for a simple bradycardia), and the finding of a normal rate in the auricle. This may be evident from the pulsation in the great veins of the neck when the patient is lying down, or from an examination by means of the polygraph or the electro-cardiograph. Moreover, there is usually an increased pulse pressure, for the systolic pressure may be high, but the diastolic normal. Varying degrees of heart-block have been found to occur. There may be only a simple delay in the conduction of the impulse to the bundle, which can only be detected by the polygraph or the electro-cardiograph. Here there may be an undue length of the *a–c*, or P–R intervals. Again, there may be only an occasional failure to conduct, which gives the appearance of missed beats. This rare variety will have to be differentiated from the condition of extra systole, which is dealt with below.

Clinically, heart-block sufficient to cause symptoms is most commonly due to coronary arterial disease with myocardial degeneration. Since in some cases of coronary disease, in which heart-block has been present during life, no histological lesion of the bundle can be demonstrated, it is supposed that ischæmia of the bundle was the cause. Gross degrees of heart-block may be due to syphilis, and then a gumma or gummatous cicatrix is found in the bundle. Minor degrees of block, as shown by prolongation of the P–R interval in the electro-cardiogram, are not uncommon during acute fevers, particularly in rheumatic fever, which, as is well known, is a potent cause of carditis. Certain drugs depress the conductivity of the bundle, the most important being digitalis. Indeed, the beneficial effect which digitalis exerts on the irregular ventricular rhythm in cases of auricular fibrillation can be traced to this action of the drug, for the diminished conduction of impulses down the A.V. bundle allows the ventricle to beat more slowly and regularly. Stokes-Adams syndrome is

heart-block with cerebral symptoms. During the course of a case of heart-block, periods of ventricular asystole may occur, with resulting cerebral anæmia. If asystole lasts up to about seven seconds, loss of consciousness occurs, and if the period is prolonged up to about fifteen seconds, convulsions develop.

The Rhythm of the Pulse.—The impulses initiated by the pace-maker are sent out in a regular rhythm, the interval between the pulse beats being constant, usually, in man, about 0·7 or 0·8 second. Normally the left ventricle beats in a similar rhythm, and the pulse felt at the wrist and elsewhere is regular. When, however, the ventricle does not receive its stimulus regularly, then the pulse must necessarily be irregular. This we have noted as a possible result of intermittent heart-block.

More commonly, the pulse is irregular because the auricle does not pass on impulses at a regular rate, either because the auricular muscle does not contract uniformly, or because abnormal stimuli originate in the auricle. The pace-maker may be slightly irregular in its action, in the common condition, sinus arrhythmia, so-called because the node corresponds to the primitive sinus of the lower animals.

Sinus Arrhythmia.—This is merely an exaggeration of the normal effect of respiration on the heart. It never produces symptoms, nor is it a serious condition, although its existence has to be recognized. The condition is, in toxic states, an important indication that the cardiac mechanism is quite healthy. At each inspiration the negative pressure in the chest is increased, blood is drawn into the thorax, and the descent of the diaphragm drives blood from the abdominal veins upwards. The consequent increased filling of the auricle which results causes a diminution in the vagal, and an increase in the sympathetic tone, as shown by Bainbridge, and an increase in the rate of the heart. At the same time there is also diminished pressure in the pericardium, as pointed out by Lewis, and this still further tends to increase the rate. For the sake of completeness it may be remarked that, as emphasized by Sharpey-Schafer, there is also diminished resistance in the pulmonary circuit. All these factors together tend to produce an increased cardiac output during inspiration, and a rise of arterial pressure. It was also shown by Bainbridge that the hastening of the heart from increased venous filling depends on the integrity of the nervous connections which can be partly thrown out of action by atropine, which paralyses the vagal endings. Hence we find this drug a useful aid in the differential

diagnosis of the condition. It is not, however, an absolute test, for it does not affect the pericardial or sympathetic factors.

Another condition in which the pulse is irregular is that of Extra-systole.

Extra-systole.—By this is meant a premature contraction of the heart, not dependent on an impulse from the pace-maker, but originating from an abnormal stimulus within the auricle or ventricle itself. The contraction may be quite small, as the heart may scarcely have recovered from previous contraction, no pulse wave may be produced or it may be too small to be appreciated at the wrist, although the extra beat may be detected on auscultation of the heart itself. It may sometimes be felt by the patient himself, as a fluttering sensation in the cardiac region,[1] but more often it produces no symptoms. The irregularity usually disappears temporarily after exercise, when the heart beats faster and shortened diastole gives less time for the extra-systole. An analogous condition can be easily produced experimentally. If, when the heart of a frog is in diastole, a stimulus is applied, it replies at once by a second contraction. During contraction, heart muscle is refractory, *i.e.*, it will not respond to a stimulus, and when the normal auricular stimulus arrives, the heart is refractory as the effect of the artificial stimulus. The next normal stimulus is therefore ineffective, and no contraction will occur until the next after that arrives. This unduly long interval simulates a missed beat of the heart or pulse. It may be appreciated by the patient as a cardiac pause, or, since the heart becomes unduly filled and contracts more forcibly after the missed beat, the next contraction may be felt as a thud in the cardiac region. A large number of people have extra-systoles and are unaware of them. Nor is there any evidence that it is of serious import, though a search should be made for a cause amongst the conditions which are known to affect the heart. The condition must be differentiated from the dropped beat of partial heart-block, in which no ventricular contraction can be determined, whether by auscultation, by palpation in the region of the apex beat, or by instrumental means, whereas in extra-systole this is present. The electrocardiographic records of patients suffering from extra-systole have been much studied by Lewis, to whose writings reference may be made for details.

[1] It is specially liable to be felt in bed at night or when sitting quietly, and the alarm it produces may produce tachycardia. As this disappears the extra-systoles recur and the train of symptoms is repeated (Wilkinson).

Auricular Fibrillation.—By far the most serious state in which the pulse is irregular is that of auricular fibrillation. In this condition the auricle contracts in an irregular and disorderly fashion, and, for practical purposes, ceases to act. Here we see quite clearly that the proper function of the auricle is not one necessary to life. The ventricle fills in virtue of its diastole and the slight pressure in the veins. There is no actual suction, for the veins would then be sucked flat, since they have such thin walls. The function of the auricle is subsidiary to a system for the collection of blood. By adding a small quantity to the already filled ventricle, the internal tension of the latter is increased. This makes the ventricle contract more forcibly. Fibrillation appears to be the result of irregular destruction of some of the fibres, as a result of coronary disease, hyperthyroidism, or overstretching, from high internal pressure, as in valvular disease. Auricular fibrillation is specially liable to supervene in certain types of valvular disease, *e.g.*, of the mitral valve, especially mitral stenosis, in which most strain is thrown on the auricular muscle, as shown post-mortem by the great distension of the left auricle. In the majority of cases of mitral stenosis it is the onset of fibrillation which determines the onset of cardiac failure.

It is evident that such irregularity of auricular contraction must lead to irregularity of conduction. The impulses sent out from the pace-maker reach the auriculo-ventricular node irregularly, and the ventricles as a result contract irregularly. The pulse is then characterized by an "irregular irregularity," which distinguishes it from other forms of cardiac irregularity. The degree to which the condition influences the heart depends on the general state of the cardiac musculature. Once established, auricular fibrillation seldom disappears, although the patient may live a moderate life for a long period. More often, cardiac failure is not far distant, and life, if it continues, becomes very restricted. Paroxysms of auricular fibrillation have been described.

Auricular Flutter.—Another condition of interest in relation to the auricle and pulse is auricular flutter, first described clinically by Jolly and Ritchie, although it had been previously demonstrated by MacWilliam. Here we have a condition which is somewhat similar in nature to auricular fibrillation, but much less severe. As a result possibly of local injury, there is a delay when the stimulus reaches certain areas of the auricle, which therefore contract later than the rest of the organ. The late contraction of the localized areas may cause the whole auricle to contract once

or twice or even three times between the normal stimuli sent out by the pace-maker. Lewis has described the condition as a "circus" movement. The auricle then goes on at a greatly increased rate, of usually two or three hundred per minute. All these impulses, however, cannot pass down the auriculo-ventricular bundle, and stimulate the ventricle. There is, then, some degree of heart-block, for only a proportion of the impulses is affected. This yields a three to one, a two to one rhythm, or a varying rhythm between the auricle and ventricle.

The pulse is usually over 150 per minute in such cases, and may be irregular. A simple instrumental examination with the sphygmograph may make it evident that there is a regular irregularity as in sinus arrhythmia, except that the grouping does not correspond to the respiration. Obviously this is due to the fact that the abnormal stimuli which bring about the abnormal rhythmic contractions take a constant time to travel thither, and differ from the normal pace. They, however, coincide occasionally, just as two tuning-forks produce beats, when of slightly different pitch. This occasional coincidence occurs at regular intervals, and so produces a grouping. It must, however, be admitted that it is difficult [1] to make out this rhythm, and often the polygraph or electrocardiograph is necessary.

Ventricular Fibrillation is commonly the prelude of death, for the heart ceases to do its work and the blood pressure falls. The fibrillation may be the result of a large variety of causes such as coronary thrombosis or the action of toxic substances. It is commonly stated that the inhalation of a low concentration of chloroform vapour causes the heart to be particularly liable to fibrillation (Levy). To those accustomed to the administration of chloroform it would seem that this liability has become grossly exaggerated. Levy has claimed that even slight sensory stimulation will bring about the fibrillation. However true this may be of vagus stimulation in experimental animals, the conclusions are erroneous, for chloroform was first introduced by Simpson as a light anæsthetic in midwifery.

Fibrillation is the cause of death in electrocution, and it must be emphasised that such a fibrillating ventricle may recover. Massage is undoubtedly very effective, but the usual cardiac stimulants are valueless. Recently Hooker has advised the injection of potassium chloride followed by calcium chloride.

The action of drugs is of considerable interest in relation to

[1] Sometimes the rapid irregular venous pulse may be present.

cardiac irregularities, notably the time-honoured digitalis. In full doses this drug depresses the conductivity of the bundle of His and gives the ventricle time to fill adequately. The longer diastole rests the heart while the output and force are increased. The dosage of digitalis should be determined by the patient's need and his response ; massive doses (over 20 minims of the tincture) should be reserved for urgent cases with a high ventricular rate (Ritchie). Digitalis is of less value when the rate and rhythm are normal, but it should always be tried in cardiac failure.

The more recently introduced quinidine, in addition to the above, increases the refractory period of the cardiac muscle and thus tends to cut short circus movements. On the other hand, it depresses general conductivity in the heart and the activity of the sino-auricular node, and this somewhat reduces its value as it gives the auricular muscle more time to become responsive to a circus stimulus (see Auricular Flutter).

The Character of the Pulse.—The general character of the pulse is one which can be appreciated only by practice, and even then it must be clearly recognized that clinical observation is very open to fallacy. The normal pulse should rise and fall gradually, and should be fairly well sustained, while there should be no waves appreciable in the falling away. This is to be expected from the driving of a wave of the nature of that produced by the muscular contraction of the heart through an elastic system. Several conditions, however, lend a special character to the pulse wave. If the aortic valve is incompetent the pulse wave may be expected to have certain definite characteristics, and may be seen in the temporal or carotid arteries. The wave is abrupt and a large one, for not only does the heart put out the normal amount of blood, but also that which has regurgitated into the ventricle and, moreover, the resistance to the output is small on account of the low diastolic arterial pressure. The wave is forceful because the ventricle is hypertrophied. The wave falls away extremely rapidly, especially if the arm is help up vertically. This sudden " collapse " of the pulse is due to the abnormally sudden lowering of the pressure in the arteries in diastole. This sudden fall is due to the reflux of blood into the left ventricle, and in this connection Wiggers has pointed out how " regurgitation of pressure " as well as of actual fluid must be taken into account in assessing the importance of this factor. Stewart finds that the falling away of the pulse begins before systole is over, and believes that a sudden reflex vaso-dilatation opens the arterioles to an abnormal extent,

so that the low diastolic pressure is due in part to excessive escape of blood through the peripheral resistance. The pulse in aortic regurgitation has been called the Corrigan pulse, from the physician who first described it, or a water-hammer pulse, from its resemblance to the sensation produced by the well-known scientific toy of that name. The pulse is " rapid " in the strict academic sense of that word, for the whole pulse cycle is rapidly executed, although, since the number of beats per minute is not necessarily increased, the pulse is not necessarily " frequent." In aortic stenosis, on the other hand, in which there is resistance to the outflow of blood from the left ventricle, the pulse has a small amplitude, and is slow in its rise and fall.

When the blood pressure is low there is a rapid rise and fall of the pulse wave, but the amplitude is smaller. A well-marked dicrotic notch on the downward stroke may be seen or appreciated with the fingers. This is due to the fling-back of the aortic valves, and the subsequent wave which is produced as a result of the closure.

The old physicians used to consider that the pulse gave an indication of the cardiac output, but from what we now know of the physiology of the heart, this can no longer be considered to be true. The character of the pulse depends also on the nature of the wave produced, and the state of the system into which it is sent. Thus, in a high blood pressure with rigid arteries, there is an abrupt rise but a comparatively small one, and as the blood does not escape readily from the large arteries there is a very slow falling away. Such a pulse is described as " wiry." On the other hand, relaxed arteries (with a low blood pressure) and a weak heart, yield a very small pulse which may scarcely be appreciated, and which is described as " thready " and " running."

It must be clearly understood that the character of the pulse in no way depends on the rate of propagation of the pulse rate. This latter is dependent on the elasticity of the arterial walls.

THE HEART SOUNDS

The character of the heart sounds has long been recognized as an observation of considerable clinical importance. There are two sounds, which have been aptly compared with that represented by " lūbb-dŭp," the first being long and of low pitch, while the second is sharper and higher. A third sound occasionally occurs, but is of little practical importance (see page 153).

The first cardiac sound is caused by the slamming of the auriculo-ventricular valves and the contraction of the ventricular muscle. The latter is indicated by the fact that the sound may be heard in the empty excised heart (or even in a voluntary muscle) when it contracts. The sound which marks the beginning of ventricular systole is then essentially muscular in nature, for the force of the closure of the auriculo-ventricular valves depends on the ventricles. The valves have already been floated into the position of closure by the accumulation of blood in the ventricles. The manner of its production is of first importance, as it gives a valuable indication, even if the sound is impure, of the state of the musculature of the main chambers of the heart. In fevers, for example, or in myocarditis, faintness of the first sound, *if of recent onset*, is evidence of cardiac impairment, and demands rest in a recumbent position. When, however, the chest is fat or the lungs are voluminous, it may be difficult to hear even normal heart sounds ; indeed it may be possible only by asking the patient to hold his breath in expiration. In such circumstances the relative intensities of the first and second sounds at the cardiac apex are of value. The first sound is best heard in this region where the ventricle abuts against the chest wall, and it may still further be increased by getting the patient to lie over on his left side. Should there be any difficulty in differentiating it from the second sound, this may be overcome by palpating the arterial pulse in the neck, with which it is practically synchronous. In the region of the apex, normally in the fifth intercostal space, $3\frac{1}{2}$ inches from the middle line,[1] the first sound should be louder than the second, and if this is not so, the first sound is weakened or the second exaggerated. Between these two the blood pressure reading will help to differentiate as described below.

When the heart muscle is hypertrophied, the increased muscle and the more forcible closure of the valves cause the first sound to be accentuated, but, as the sound has to pass through more tissue, it assumes the character of a dull muffled thud. On the other hand, when the heart becomes dilated the walls are thinner and the sound, although exaggerated, is clear, sharp, and of higher pitch.

The clearness of the first sound is masked when the auriculo-ventricular valves are at fault. This commonly occurs at the

[1] This is ordinary clinical teaching, but the normal heart really extends beyond this limit, the part beyond being less in contact with the chest wall.

mitral valve. The character of the sound then becomes blowing, and more closely resembles the sound of the word "luff." This alteration constitutes a cardiac murmur or bruit. The commonest auriculo-ventricular murmur is the mitral systolic, which occurs in cardiac systole and is sometimes the result of incompetence of the mitral valve, although it may arise from other causes (*vide infra*). It is best heard in the region of the apex beat. Hence this apical area is often known as the mitral area, though it in no wise corresponds with the actual position of the surface marking of the mitral valve : it is merely the point at which the ventricle comes nearest to the surface. The regurgitation may result from actual valvular disease ("valvular incompetence"), or from imperfect apposition of the cusps from ventricular dilatation ("muscular incompetence"), such as occurs in disease of the aortic valve. In tricuspid regurgitation the murmur is heard best in the tricuspid area, which is over the lower part of the sternum. Here the regurgitation is almost invariably the result of cardiac dilatation and the result of earlier disease elsewhere, *e.g.*, mitral stenosis. In tricuspid regurgitation the force of the right ventricular contractions is directly transmitted to the great veins, and thus systolic pulsation of the veins in the neck, and enlargement and pulsation of the liver are present. Other signs of heart failure, such as breathlessness and œdema, can be observed, and the condition constitutes an important variety of congestive cardiac failure.

The first sound may also be masked by any condition which obstructs the exit of the blood through the aortic valve, or, more commonly, which brings about dilatation of the aorta beyond the valve. This murmur, from the nature of its production, is much rougher than that due to mitral regurgitation and has its point of maximum intensity over the aortic area. Further, it is conducted in the direction of the blood flow and may be heard in the arteries of the neck.

In the consideration of cardiac murmurs it must not be forgotten that in anæmia, debility, or in conditions of excessive heart action, such as exophthalmic goitre, a systolic murmur may accompany the first sound. Apparently these murmurs are due to the decreased viscosity of the blood setting the valves in motion, and possibly to dilatation with subsequent regurgitation, but admittedly the nature of their production is not quite certain. Such murmurs are always systolic in time and of a soft blowing character. They may be produced in any valve, but are more

commonly found in the pulmonary area in the second left intercostal space, where murmurs produced at the pulmonary valve are best heard. They tend to be inconstant, but can be elicited by exercise. Systolic murmurs in the pulmonary region due to actual changes in the valve are seldom found except in congenital stenosis of the valve in which they are associated with patency of the foramen ovale or dilatation of the pulmonary artery.

The loudness of systolic murmurs, like that of the first sound, depends on the state of the cardiac muscle. Hence a faint murmur does not necessarily indicate a small amount of regurgitation, but rather a weak muscle. Confirmation of the diagnosis will depend on evidence of distress produced by exercise.

The second cardiac sound occurs at the beginning of diastole and is due to the closing of the pulmonary and aortic valves. These valves are already in a position of closure as soon as the expulsion of blood from the ventricles ceases and are firmly closed as the result of the elastic recoil of the arteries. In adults the sound is best heard in the aortic area over the second right costal cartilage where the aorta is nearest the surface and, as in the case of systolic murmurs produced at the aortic valve, can be heard, especially if accentuated, in the large arteries of the neck. In children the pulmonary component of the sound is louder than the aortic. The intensity of the second sound, just as we have seen in relation to the first sound, depends on the force with which the valves are closed. An accentuated aortic second sound is to be expected in conditions where the systemic arterial pressure is high and, indeed, is a useful adjunct in the diagnosis of such conditions. Normally, in the aortic area, the two sounds have almost equal intensity and have rather a "tic-tac" or "lubb-dub" rhythm. Accentuation of the pulmonary second sound is found when the pulmonary arterial pressure is raised, as in mitral stenosis and certain pulmonary diseases. It should also be noted that retraction of the upper part of the left lung from fibrosis will cause an apparent accentuation of the sound.

Should, however, the aortic valve be diseased, the character of the second sound is quite changed, and instead of being like the syllable "dŭp," is better imitated by "duff." For practical purposes, only the aortic valve need be considered in this respect, as a pulmonary diastolic murmur is of extremely rare occurrence. It has been described as a result of excessive pressure in the pulmonary artery, as in mitral stenosis. An aortic murmur is produced by regurgitation of blood into the left ventricle during

diastole. It is then propagated in the direction of the flow of regurgitating blood and may be heard all over the præcordia. The heart itself and the sternum may also play a part in its conduction; indeed, the point of maximum intensity of a murmur is often on the left side of the sternum. Like all sounds produced at the aortic valve, it is well heard in the aortic area. There is frequently a systolic bruit as well, so that a "bellows" or to-and-fro murmur is audible. Aortic regurgitation obviously throws great strain on the left ventricle, which has not only to expel more blood, but has to do so in the face of a defective coronary blood flow, due to the low diastolic pressure. If the left ventricle dilates and the mitral valve becomes incompetent, additional work is thrown on the right side of the heart, and a hypertrophy of all the chambers of the organ then takes place. It may, indeed, become so large that the term *cor bovinum* has been applied. Gross hypertrophy of both right and left sides is specially developed when aortic regurgitation and mitral stenosis are present together, and also in the condition known as chronic adhesive mediastino-pericarditis. In these conditions the heart truly merits the appellation "bovine." From the point of view of prognosis, aortic disease, especially aortic regurgitation, is by far the worst form of valvular impairment.

Aortic stenosis is an infrequent condition, and is usually the result of atheroma in elderly men. The left ventricle is hypertrophied, a rough systolic aortic murmur, conducted to the neck-vessels and accompanied by a thrill is present, and the pulse is slow with a systolic plateau. The aortic second sound is weak or a diastolic murmur due to some degree of regurgitation is present.

Another murmur occurs in mitral stenosis. The auricle, it will be remembered, simply drives home the charge, as it were, into an already filled left ventricle, and this occurs just before the ventricle itself contracts. We may consider that in the filling of the ventricle the blood does not flow through the valves sufficiently fast to produce a sound except when the speed is increased as the result of auricular contraction. The sound produced by the blood passing through a stenosed valve is like other obstructive murmurs, extremely rough and purring in character, and is almost fused with the first sound, which becomes exaggerated. An imitation of the sound is produced in the syllable "rupp," or, as is more common, if there is also regurgitation through the impaired valve, by the word "ruff." For this reason the murmur is commonly referred to as being presystolic to

distinguish it from true diastolic murmurs produced at the base of the heart, although less commonly, when the auricle is weak, the murmur is heard only at the time of maximum ventricular dilatation, when it is really diastolic in time. A soft presystolic murmur, known as an Austin-Flint murmur, may be audible at the apex of the heart in cases of aortic disease. It probably results from relative closure of the anterior or aortic cusp of the mitral valve by the regurgitant stream of blood. It is unsafe to diagnose such a murmur in rheumatic aortic regurgitation, as mitral stenosis is often present.

Very often one or more valves are impaired, and is it only by clinical experience and detailed study of the points of maximal intensity, the direction of the propagation of the murmur, the size of the cardiac chambers as elicited by percussion, or more accurately by radiography[1] and the patient's symptoms, that it is possible to decide the exact nature of the lesion present. Thus, for example, a lesion of the aortic valve will be associated with enlargement of the left side of the heart, while a cardinal symptom will be faintness or pain and the patient is usually pallid ; if the lesion affects the mitral (or rarely pulmonary) valve there will be enlargement of the right side of the heart with breathlessness, and later, if the tricuspid valve fails, the signs and symptoms of venous engorgement, *e.g.*, cyanosis, pulsation in the veins, œdema and often gastric symptoms. In obtaining accurate diagnosis of the impairment of individual valves, clinical observation has proved itself to be of the greatest possible value and is not surpassed by any other means. The character of the heart sounds gives, however, only a very limited amount of information regarding the cardiac musculature, and it is now realized that although such accurate diagnosis may be a guide in treatment and in the making of a good prognosis, yet a study of cardiac sounds is of little value in estimating the cardiac efficiency with any degree of accuracy. It may, however, be useful in following the progress of an individual case. For example, the louder the sound due to obstruction the fitter usually is the muscle causing the flow of blood through the stenosed valve.

Precordial sounds are not necessarily endocardial. In peri-

[1] As would be expected in view of the shape of the heart the differences shown by percussion and radiography are often very remarkable. Radiologists suggest that percussion is too inaccurate to be of any value, while a well-trained clinician may rightly claim that time-honoured percussion can still give him all the information he really needs. Percussion is of undoubted value in recognizing the presence of a pericardial effusion.

carditis, there is a rough to-and-fro sound produced by the rubbing of the epicardium upon the parietal pericardium, but the rhythm and roughness taken together with the symptoms are usually sufficient for diagnosis. Similarly, a pleurisy in the region of the heart may be confused with a pericardial rub, but in this instance the sound is related to respiration as well as to the beat of the heart.

Cardiac Pain.—True cardiac pain arises as a result of the blood supply to the cardiac muscle being cut off. Like the pain produced in voluntary muscle by compression of the artery, it is aggravated by effort.

The anoxæmia may be produced by a blood incapable of carrying an adequate supply of oxygen to the heart; but it is more commonly the result of spasm or thrombosis of the coronary arteries, usually part of a more widely spread arterial degeneration. It is probable that there is no hard and fast line between the two conditions, nor is any constant correlation between the pain and the vascular disease found post mortem. Clinically, the important difference is that pain due to spasm is relieved by nitrites and rest, and the prognosis is relatively good; while thrombosis with infarct is an extremely serious condition, commonly accompanied by a marked fall of arterial pressure and restlessness, liable to early fatal recurrence and necessitating prolonged rest in bed. (Parkinson.)

In the acute stage the administration of morphia is an urgent necessity.

CHAPTER XVIII

THE POLYGRAPH. THE ELECTROCARDIOGRAPH

THE VENOUS PULSE

THE venous pulse is found in the great veins of the neck just above the clavicle. Several factors affect the character of the pulse wave. The chief wave is produced by the contraction of the right auricle; hence the reason for taking records of the venous pulse as a help in clinical diagnosis. It gives the rate of the right auricle, and some indication of its force and rhythm, just as the arterial pulse gives information regarding the left ventricle.

Venous pressure is so low that the pulse cannot be palpated, and instrumental methods of recording have to be used, the most practical being the **polygraph,** first introduced by Mackenzie. By its means the venous and arterial pulse may be simultaneously recorded. The writing system consists of two tambours activating two ink-writing levers working at different levels. One tambour is connected by rubber tubing with a lever applied to the wrist to record the radial pulse, and the other similarly to a cup which is applied over the internal jugular vein, just above the inner end of the clavicle, at which point in the veins the valves have not yet commenced. The placing of the patient in a recumbent position increases the pressure in the neck veins and makes the pulse more easy to record. This, however, may not be necessary where there are greatly distended veins and the venous pressure is high. Such a method of recording venous pulsations as compared with optical methods is relatively crude, but, although the records may not be sufficiently accurate for scientific investigation, there can be no doubt that the polygraph is sufficiently accurate for clinical purposes. Characteristic tracings taken by the polygraph are shown in Fig. 8, but although it may be comparatively easy to differentiate the various waves of a normal jugular pulse, difficulty necessarily arises in the interpretation of abnormal or less typical pulses, in which there is doubt regarding the movements of the auricle. A short consideration of the cause of the waves is necessary before the principles of the interpretation

of the polygraph records can be given. The usual nomenclature adopted by Mackenzie is adhered to.

The first wave, known as the *a* wave, is caused by the contraction of the auricle and the cessation of the venous flow into the heart from closure of the venous inlet which is surrounded by auricular fibres. There is some difference of opinion on the way in which auricular contraction causes the wave, but the main fact that it corresponds to auricular systole is not disputed. The latter normally occupies about a tenth of a second, and if it is longer a complicating factor must be sought. The *a* wave is followed after a fifth of a second by the *c* wave.

This second or *c* wave has also been the cause of considerable controversy. Mackenzie held that it was due to transmission of the carotid pulse to the vein. Straub considers it to be due to systole of the right ventricle raising the auricular floor, for a rise in pressure synchronous with ventricular systole is found if the pressure is taken in the right auricle. Starling has found an apparently corresponding wave in the inferior vena cava. The work of Wiggers, who has used very sensitive recording apparatus, appears to show that, although there is a rise in auricular pressure during ventricular systole, the wave produced is not necessarily communicated to the veins, even when it does precede the *c* wave. He concludes that the latter is produced by the pulsation of adjacent arteries, not only in the neck but also in the thorax. This accounts for the corresponding wave found by Starling. Whether the wave is transmitted by the vein or artery does not, fortunately, make any difference to the fact that the *c* wave is produced by ventricular systole. By being so fixed it is the point from which all interpretation of the venous tracing can be made.

The *v* wave is the result of blood collecting in the right auricle while the tricuspid valve is still closed. The subsequent fall is due to the opening of the tricuspid valve and the free passage of blood into the right ventricle. Since the *c* and *v* waves mark approximately the beginning and end of ventricular systole (really the beginning of diastole) the interval between the *c* and *v* waves must be of fixed duration.

The simplest conception of what is occurring in the right auricle is that of a rise and fall of pressure, or a simple wave, brought about by the filling, the contraction, and later the dilatation of the chamber. The fall due to dilatation is interrupted by the *c* wave which corresponds to ventricular systole. The rise in pressure initiated by the filling of the auricle corresponds to the

[*Facing p.* 152.

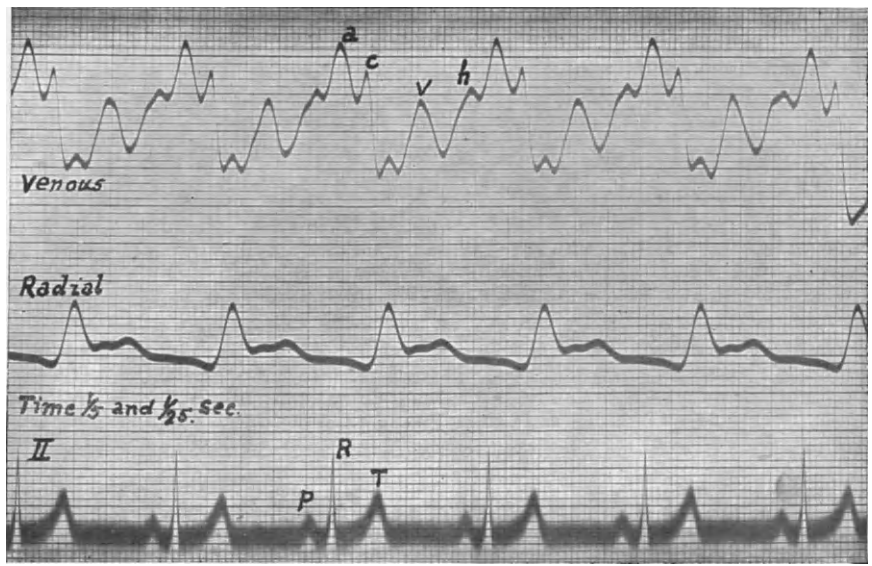


FIG. 8.—COMBINED POLYGRAPHIC AND ELECTROCARDIOGRAPHIC RECORDS.
(Reproduced by permission from "The Heart: Old and New Views." By H. L. Flint. London: H. K. Lewis & Co. Ltd.)

v wave, which, however, is separated from the culmination of the rise or *a* wave due to auricular systole by the notch *y* caused by the opening of the auriculo-ventricular valve.

In such interpretation as mentioned above the starting-point is the *c* wave, which occurs one-tenth of a second before the rise of the wave of the radial pulse. They are of common origin, both being produced by ventricular systole, the difference in time being due to the fact that the pulse wave takes a certain time to reach the wrist. If, then, a point has been marked one-tenth of a second before the rise of the radial pulse, the corresponding point in the auricular tracing is the beginning of the *c* wave. Simultaneous points in the radial and jugular tracings may readily be denoted by stopping the movement of the paper for a moment.

Normally the wave in the jugular tracing which begins a fifth of a second before the *c* wave is the *a* wave, and the space between is known as the *a–c* interval. If the wave begins before this point, then the *a–c* interval is considered to be lengthened. This is taken as an indication that the stimulus has taken longer than normal to pass from the auricle to the ventricle.

Similarly, if a point two-fifths of a second after the *c* wave be measured, the point is approximately the summit of the *v* wave and should fall almost at the bottom of the dicrotic notch in the radial tracing, as the closure of the aortic valve, to which the dicrotic notch is due, occurs approximately at the same time as the tricuspid valve opens, *i.e.*, at the beginning of ventricular diastole. The *v* wave is usually well marked and may, indeed, be the most distinct wave in the auricular tracing. It will be noted, too, that the *c–v* interval is constant for any given heart, as it marks the beginning and end (really the beginning of diastole) of ventricular systole. This period does not vary appreciably whatever the rate of the heart, for any alteration in its rate is for the most part brought about by a difference in the duration of diastole.

Any other waves which occur in the auricular tracing are considered to be due to extra auricular or ventricular contraction. There is, however, one fallacy to be remembered, namely the *h* wave, so called as it was first described by Hirschfelder. Gibson attributed it to the temporary closure of the tricuspid valve by eddies caused in the filling of the right ventricle. To this closure, also, has been attributed the third heart sound, which is occasionally heard. An *h* wave may occur obviously between *a* and *c* during which time the ventricle is filling, but in a rapidly or

slowly-beating heart may add confusion (being taken for an extra beat of the auricle). This may cause a diagnosis of heart-block to be made, while in a real heart-block the *h* wave, if it occurs after auricular contraction, may be taken for a normal *c* wave. More commonly, however, it occurs between *v* and *a*, and here it may obscure the *a* wave itself and cause the *a–c* interval to appear long, but it will be seen that in this case the duration of the auricular wave will be longer than the normal tenth of a second.

Normally, the number of *a* waves should correspond to the number of *c* waves, but in several conditions this is not so. These have already been dealt with in relation to the pulse and need only be summarized. In heart-block the auricular rate is about normal, while the rate of the ventricle is slow, often half or a quarter of the rate, or at an early stage there may be merely an increase in the *a–c* interval beyond a fifth of a second. According to Lewis, one-third of a second definitely indicates a delayed conduction from the auricles to the ventricles. In auricular flutter, on the other hand, there may be an enormous number of *a* waves, and only a proportion of these is followed by *c* waves, while in auricular fibrillation there is no regular *a* wave at all. In auricular extrasystole an auricular contraction, followed by a ventricular contraction, takes place before the normal auricular contraction is due. A ventricular extra-systole causes a premature *c–v* group of waves. The diagnosis of this latter condition, however, may be, as already indicated, sufficiently clear from the examination of the radial pulse, when the compensatory pulse will especially be noted.

THE ELECTROCARDIOGRAPH

In the early days of electro-physiology, it was the fashion in certain quarters to criticize the teaching to medical students of what seemed at the time to be a useless physiological phenomenon, namely the current of action of a muscle. To-day this phenomenon is the basis of electrocardiography.

If two electrodes connected with a galvanometer are placed on a muscle which is made to contract, it will be found that a momentary current passes through the instrument from the normal to the contracting part of the muscle. This is known as the current of action. In electrocardiography we record the current of action of the heart, and from the records are able to obtain evidence of the contraction of its different parts. The

speeds with which the different chambers of the heart contract made it at first very difficult to record the action current. Since the introduction of the string galvanometer by Einthoven in 1901 the matter has become comparatively easy. The galvanometer consists of a string of silvered quartz or in the more modern forms of a gold-spattered glass fibre suspended between the poles of an electro-magnet. A portion of the fibre is so illuminated that the shadow of its movements can be recorded on a moving photographic plate. A typical record is seen in Fig. 8. In man the currents cannot be obtained directly, but may be obtained indirectly by attaching the leads from the galvanometer to the limbs by large non-polarizable electrodes. Three standard leads are commonly used. Lead 1 is from the two hands, lead 2 from the right hand and left leg, and lead 3 from the left hand and left leg. Commonly, the limbs are placed in a bath of saline solution into which dips a porous pot containing zinc sulphate and zinc electrodes which lead to the galvonometer. The accurate interpretation of such records we owe, to a very large extent, to Lewis and his co-workers.

The first wave P of the electrocardiogram is positive and is due to auricular contraction. Following the auricular wave is the ventricular complex of waves Q R S and T, and much discussion has taken place concerning the cause of these. It is generally accepted that the Q wave, when it is seen, is due to the contraction of the papillary muscles, and it has already been noted that the Purkinje fibres in which the bundle of His terminates are specially applied to these muscles. As would be anticipated it is also essential that these muscles should contract at the very commencement of ventricular contraction if they are to prevent the auriculo-ventricular valves from being blown backwards into the auricles. The R wave is due to the contraction of the ventricle, but, when the apex contracts, its stronger negativity opposes the current produced at the base and the S wave is produced. The contraction, however, passes off sooner at the apex than at the base, which again becomes negative to the apex and brings about the T wave.

In the electrocardiograph, as in the polygraph, the main point is the recording of auricular contraction relative to that of the ventricle, and if P be substituted for *a*, and *c* for the R wave, what has already been said in relation to the polygraph applies to the electrocardiograph. It will be evident, then, that the P–R interval in the electrocardiograph corresponds to the *a–c* interval of the polygraph, and normally does not exceed a fifth of a second.

Auricular flutter and fibrillation are clearly revealed by the electrocardiograph, and the tracings are of value in differentiating these conditions from paroxysmal tachycardia and extrasystoles when doubt occurs clinically. In fibrillation of the auricles the P waves are absent in lead 1, and in lead 2 are replaced by rapid rhythmical oscillations of small magnitude.

Hypertrophy of the various chambers of the heart may be deduced from the size of the waves produced, as shown by Lewis, from a study of electrocardiograms taken in animals, in which the auriculo-ventricular bundle has been cut, and the ventricular rates altered. It has thus been found that the left ventricle is chiefly responsible for the R wave in lead 1, and S in lead 3, while the right ventricle accounts for S in lead 1 and R in lead 3. As the production of current depends on the amount of muscle, the size of the waves in the various leads indicates the amounts of musculature at work. For comparative purposes the galvanometer is so standardized that the string moves 1 cm. for each milli-volt potential difference.

Thus in " left ventricular preponderance," often found in cases of aortic regurgitation and high blood pressure, R is large in lead 1, S in lead 3, and *vice versâ* in right-sided preponderance. In " bundle branch block " the right or left branch of the A–V bundle fails to conduct and the ventricle which the affected branch supplies receives its stimulus late, from the opposite ventricle. The Q R S complex is thus unduly prolonged beyond the normal 0·08 sec. Further, the ventricle which contracts first predominates, so that in right bundle branch block, for example, the major deflection is upward in lead 1, downward in lead 3. In each lead the T wave is in the opposite direction to the main deflection. Right bundle branch block is commoner than left. Rheumatic heart disease, syphilis and vascular lesions are the underlying pathological conditions in young, middle-aged and old subjects respectively, rheumatism being the rarest cause. The presence of bundle branch block is proof of myocardial damage.

In coronary thrombosis interference with conduction of the excitatory wave through the ventricular muscle may lead to characteristic electrocardiograms. The most typical feature is the slow return of the R wave to the basal or iso-electric level (Pardee wave). The T wave is also modified. A good account of the electrocardiographic changes in coronary thrombosis is given in East and Bain's book, which should be consulted.

All that has been written regarding the various conditions which

affect the pulse should be read in relation to the electrocardiograph and polygraph. The former instrument has the great advantage over the latter in that, so far as the P wave especially is concerned, it is affected by fewer factors than the *a* wave of the polygraph. It records only the results of muscular contraction, while the polygraph records are influenced appreciably by the cardiac valves. Since the use of the electrocardiograph is so specialised in its practical aspects, only the broadest outlines of the subject are given here. Those who wish for more information are referred to special treatises on the subject, such as those of Lewis. Although the apparatus is costly, there is nothing excessively difficult in its manipulation.

CHAPTER XIX

BLOOD PRESSURE

Arterial Pressure.—The blood pressure determined clinically is usually that in the brachial artery. It is indicative of that in the arteries generally, although it varies from artery to artery. It gives, however, no information about the pressure in the capillaries and veins. Blood pressure as measured clinically bears an approximation to that determined experimentally. Experimentally, the pressure is measured by putting a cannula into an artery and connecting it to a manometer by a tube containing some anticoagulant fluid. In clinical practice we have to be content with finding that pressure which, applied to a limb (usually the arm) by an inflatable rubber armlet, will just obliterate the pulse. The results of such a method can be only approximate, for we have to neglect variations in the wall of the artery and in the nature of the tissues of the compressed arm. The latter we can readily appreciate by finding the difference in the readings shown by applying the armlet to the upper arm and the forearm. Every attempt must then be made to ensure flaccidity of the muscle in making the estimation. It is also necessary to have not only the body but also the mind at rest. The rate of the heart is an important and convenient guide in regard to the latter.

Clinical observation of a large number of persons shows that on an average, in the young adult, there is required an armlet pressure of 110 to 120 mm. of mercury to obliterate the radial pulse. This is the systolic pressure, or the pressure in the brachial artery at the end of cardiac systole. The pressure in the artery during cardiac diastole, known as diastolic pressure, is still more difficult to estimate, as the variety of methods used suggests; but it indicates more accurately the load of the heart. Normally it is 30–50 mm. less than the systolic, and it usually, but apparently not always, varies with it. (See Pulse Pressure.)

The factors upon which blood pressure depends are: the pumping action of the heart; the peripheral resistance offered to the outflow of blood from the arteries together with the

elasticity of the arterial walls; and the volume of the circulating blood.

The Heart.—Experimentally, it is an easy matter to show that the heart plays a part in the maintenance of blood pressure. Stimulation of the vagus, application of cold or heat to the pacemaker, or the injection of any cardiac poison, causes the blood pressure to fall at once. Clinically we should expect to find a low blood pressure for similar reasons when the cardiac musculature is poisoned by the toxins of disease, depressed by cold, or impaired by deficient action of the valves or by fatty degeneration. Actually the blood pressure does not fall in these cases until heart failure is very severe, since the tendency to fall is compensated by increased constriction of arteries and arterioles by the same mechanism as in hæmorrhage. In these conditions the drugs known as cardiac tonics are especially valuable. Rarely, the heart is impaired by the use of drugs for other purposes such as the extensive use of emetine for dysentery. This may bring about a prolonged enfeeblement of the heart.

The Volume of the Blood.—The effect of variations in the volume of the circulating blood is not at first sight apparent, as the addition or removal of small quantities from the blood-stream makes no appreciable difference to blood pressure, even experimentally. In man, fluid is normally added to the blood from the alimentary canal, and is removed by the kidneys, lungs, and skin. The provision of a means of maintaining blood pressure in spite of a moderate degree of hæmorrhage forms one of the primitive protective mechanisms of the animal body. When the blood loss is sufficient to lower blood pressure, it is, unless the hæmorrhage is internal, sufficiently obvious to make the actual taking of the blood pressure unnecessary. The blood volume may, however, be reduced relatively although not actually, as when there is a marked increase in the capacity of the vascular system. This is seen in the condition of histamine shock or in secondary wound shock. The condition of shock is of such great interest and is such a distinct symptom complex that it is dealt with in a special chapter.

The Peripheral Resistance and the Elasticity of the Blood-Vessels.—At each beat of the heart there is expelled into the arterial system a quantity of blood, but if this system were rigid not only would the pressure in the arteries fall to zero between the beats, but the flow from the system would be intermittent. In order to provide a steady outflow from the arteries at a high

pressure, advantage is taken of a mechanism in common use for the same purpose in scent sprays, bagpipes, and fire engines. A resistance is offered to the outflow of blood, so that more is pumped into the system during each beat of the heart than can escape from it in the same time. The extra blood is accommodated because the system is elastic, and the recoil of the walls which are stretched at each systole, maintains the pressure during diastole. The second bulb of the scent spray, the bag of the bagpipe, the compression chamber of the fire engine, together with a nozzle in each instance, provide similar arrangements for maintaining a constant flow at a high pressure. In the body, but for the constant flow, we should be conscious of the pulse at our various nerve endings. Patients with arterio-sclerosis, whose arteries are more rigid than normal, frequently have throbbing sensations which often interfere with sleep. The throbbing of an inflamed part of the body is also partly due to local reduction of the peripheral resistance which permits the pulse to be continued through into the capillaries in the vicinity of the nerve endings. The throbbing in the head which we experience when we inhale amyl nitrite is so produced. In inflammation, the swelling of the tissue may play a part in making the pulse directly transmissible from the artery to the nerve ending. The peripheral resistance is situated for the most part in the small arteries and arterioles, in which the cross-section of the individual vessels is noticeably reduced. That there is a small amount of resistance in the capillaries seems likely, but there are indications that this is appreciable chiefly when the arteries are dilated.

Any constriction of the arterioles will then, by increasing the peripheral resistance, raise the arterial pressure, both systolic and diastolic. This is seen in various pathological states such as nephritis and arterio-sclerosis. In the latter condition, the lumen of the small arteries may become so reduced that little or no blood can pass through, with the result that in extreme cases gangrene or death of the part supplied may set in. In conditions of arterial disease in which the diastolic pressure is high, the heart has to do appreciably more work in evacuating its contents; hence we commonly find in these conditions hypertrophy of the left ventricle, the finding of which may be a useful diagnostic aid in differentiating between a temporarily and a permanently increased blood pressure. The multiple factors in the maintenance of blood pressure are often overlooked in this respect, for should the left ventricle not be equal to the task, there may be a normal or even

a low arterial blood pressure in spite of the greatly increased peripheral resistance, which, as a result, may be overlooked.

In arterial disease too, there is a reduction of the arterial elasticity, and less blood can be accommodated in the arterial system than normal. There is, as a result, a noticeably greater thrust forward of the blood during ventricular systole and greater tendency to an intermittent flow in the capillaries. We are also able to appreciate the characteristics of a high tension pulse. This is a combination in which the increased peripheral resistance and diminished elasticity play a main part, and in which the rise in the up-stroke, as shown by the sphygmograph or felt on careful palpation, is abrupt but small. As the outflow from the arteries is slow, there is a slow down-stroke.

If there is diminished elasticity of the vessels, there is also a marked increase in the velocity of the pulse wave, as shown by Freiberger and by Munzer in 1912, since the velocity of the pulse wave depends on the elasticity of the arteries and the internal pressure. The velocity can easily be calculated from the time of arrival of the pulse wave in the radial and carotid arteries, which is most accurately recorded by the hot wire sphygmograph of A. V. Hill.

The peripheral resistance may also be varied in different parts of the body according to its needs, to allow the part being utilized to receive a large supply of blood. Further, in conditions of blood loss, whether actual or relative, the peripheral resistance is increased in an attempt to maintain the circulation, especially in the coronary arteries and brain.

This indicates that the peripheral resistance is under a certain amount of control, which has been shown to be exerted from the vaso-motor centre in the medulla and subsidiary centres in the spinal cord. The mechanisms by which the peripheral resistance is varied, according to requirements, for the maintenance of blood pressure are now fairly clear and form an important means by which animals can adapt themselves to varying conditions of life, which demand exercise, changes of posture, and the like. These are dealt with in relation to the Integration of the Circulation.

High Blood Pressure.—This occurs normally in physical exercise as a result of increased cardiac output and increased peripheral resistance, especially in those regions (particularly the splanchnic area) which are not required for the exercise. The reduction of the capacity of the abdominal blood-vessels makes more blood available for the active muscles.

In anticipation of exercise the body prepares in advance, by increasing the blood pressure, and thus making the distribution of blood more efficient. This increase of blood pressure is brought about by an increased cardiac output indicated by the increased heart rate, increased peripheral resistance and the throwing of more blood into the active circulation. These changes in turn depend on impulses which descend from the cerebrum to the vaso-motor and cardio-regulatory centres in the medulla. Vaso-constriction occurs particularly in those areas less likely to be required, namely, the alimentary canal, its associated glands, the spleen and the skin. The vaso-constriction in the skin is often evident by pallor, and we talk about an individual being " pale and determined," " pale with fright," or " having the blood run cold." The last-mentioned condition is undoubtedly of the same nature as the sensation of cold experienced at the onset of febrile conditions, and is due to less blood being circulated near the nerve endings of the skin. Many years ago Mosso showed that any kind of mental stress, even light mental effort, results in a diminution of the volume of a limb placed in a phthysmograph. Accompanying any vaso-constriction on the skin is a fall in its electrical resistance. This fact is apparently the physiological explanation of what has been termed by the psychologists the " psycho-galvanic reflex," the presence of which is an indication of the emotive response of the individual to the stimulus. Later in exercise, however, when the sweat glands which are under the influence of the heat-regulating centre (see page 414) become active, the skin vessels dilate. A similar action may be seen experimentally if pilocarpine is injected into an animal. There is at first vaso-constriction, *e.g.*, of the pad of the foot, from direct action of the drug, but later on, when sweating commences, there is dilatation of vessels, no doubt from the effects of the metabolites. In general, once the exercise has commenced, any vaso-constriction in unused parts is counterbalanced by dilatation in other parts.

This response in anticipation of exercise opens up many considerations in relation to the ætiology of high blood pressure as a result of intense mental activity which was shown by Leonard Hill also to cause a raising of the pressure. Habitual over-action of the arterial wall would presumably lead to hypertrophy, and this, if excessive, would bring about permanently increased peripheral resistance. As Dawson puts it, hyperpiesia is " physiology gone wrong."

It is of interest to note how many of the distinguished men of

our time have been the victims of cardio-vascular disease, presumably high blood pressure leading to cerebral hæmorrhage or cardiac failure. Amongst them are Earl Haig, Lord Stevenson the maker of Wembley Exhibition, Stresemann the maker of post-war Germany, Primo de Rivera the Spanish dictator, Lenin the maker of Soviet Russia, Luigi the London restaurateur: all successful men of great energy and subjects of great mental stress. This stress, which is associated with successful effort, must not, however, be confused with anxiety which is the antithesis of successful effort. Anxiety may or may not be associated with a moderate rise in the blood pressure. It is a remarkable fact that in states of psychotic depression, melancholia, the blood pressure does tend to be raised, whereas in mania it is low. On the other hand it has recently been pointed out that amongst the natives of West Africa, leading lives the reverse of physiological in every way, victims of chronic infections and indolence, high blood pressure, like mental stress, is unknown. Similarly it is generally agreed that relaxation from work is the best treatment for high blood pressure. These facts cannot be without significance in the causation of high blood pressure.

That " a man is as old as his arteries " is an old adage attributed to the great John Hunter, but only now, through the medium of physiological experiment, is the full significance of the statement becoming evident. High blood pressure is a disease of civilization, and to escape from it we must escape from civilization, at least temporarily, by arranging systematic relaxation and avoiding *sustained* mental effort so that even if we dream, our dreams will be as much of play as of work.

It would seem that one of the safeguards against high blood pressure produced in the way described is fatigue. When the individual is fatigued the normal response of the circulation to mental stimuli is appreciably reduced.

Dawson has pointed out that sustained blood pressure may be found in schoolboys preparing for examination, and suggests that in some persons there is a greater inherent liability for a high pressure to be produced than in others. After the examination the blood pressure falls.

An interesting treatment which assists diagnosis is suggested by such a nervous view of high blood pressure, namely, putting the patient to bed and placing him under the influence of bromides. A marked fall of the blood pressure indicates that hyperpiesia is functional and not due to permanent arterial change.

High blood pressure from degenerated vessels is not subject to the remissions which characterize high pressure of nervous origin.

It has been suggested that a similar differentiation could be made by causing the patient to over-ventilate. A normal person has sufficient compensating power to maintain the blood pressure in spite of the effect of the loss of carbon dioxide on the vaso-motor centre, but it is said that there is a fall of blood pressure in vascular disease.

High blood pressure may also be produced as a result of primary arterial degeneration, such as occurs in toxic states, but it is probable that this condition is responsible for a relatively small number of cases of high blood pressure.[1] Savill and, later, Dawson have pointed out that commonly the degeneration begins in the middle coat which has become hypertrophied. In the early stages only hypertrophy from over-usage may be seen.

Some authorities, *e.g.*, Rolleston, consider that the chemical element is more important than the nervous in high blood pressure and look with hope towards the discovery of either a pressor substance or the absence of a depressor substance which may be normally circulating in the blood. The literature has many examples of such substances, but none, so far, have stood the test of universal investigation. Rolleston considers that the relative absence of high blood pressure amongst mental workers such as lawyers and its occurrence amongst farmers indicates that the mental factor is not so important as has been suggested. It would be difficult to be sure that the average farmer who is often on the verge of bankruptcy is less free from sustained anxiety than the lawyer who has complete relaxation between his cases.[2]

Low Blood pressure, if severe and causing symptoms of general weariness, is commonly associated with nervous exhaustion. It is best treated by gentle physical exercise, cold baths and sensory stimulation (friction and massage) calculated to tune up the vaso-motor system. In Addison's disease the blood pressure is low, *e.g.*, about 70 mm. Hg. A systolic pressure of over 100 is strong evidence against the presence of this disease. Treadgold points out that in the Air Force, provided the cardiovascular

[1] The high blood pressure of nephritis may be due to an unidentified pressor substance or to a depressor substance which causes the circulation to over-compensate

[2] Many of the most successful barristers suffer from high blood pressure, *e.g.*, the late Marshall Hall.

efficiency is above normal, a systolic pressure of 100 mm. Hg. is compatible with perfect health. Many athletes have low blood pressure.

Pulse Pressure.—Various clinical observers have attempted to draw definite conclusions regarding the exact significance of pulse pressure, or difference between the systolic and **diastolic** pressures, which varies from 160/90 to 100/60 mm. Hg. Formulæ have been devised by which the output of the heart has been said to be estimated by observations made on the pulse pressure and the heart rate. No consensus of opinion has been reached, nor indeed does this seem possible so long as the filling of the heart as indicated by the venous pressure is neglected. If the venous pressure is low, large variations in the rate of the heart may occur and the output remain the same, but since normally the venous pressure is such that the heart is fully filled in a shortened diastole, an increase in the rate of the heart itself affects the output. For example, the increased heart rate which occurs in anticipation of exercise, or in emotion, is associated with an increased cardiac output per minute, and is largely responsible for the raised blood pressure which occurs in such circumstances. Pulse pressure is undoubtedly to some extent directly dependent on heart rate. The faster the heart, the less time the pressure has to fall before the next systole. Account must, however, be taken of the force of the heart, increase of which would tend to raise the systolic pressure more than the diastolic, and since the healthy heart tends to increase its rate and force at the same time, the exact effect on the pulse pressure is difficult to forecast. Moreover, a slow heart rate is associated with a high degree of vascular tone, with the result that the pulse pressure does not materially change with the heart rate but with the systolic pressure, as Treadgold's observations show.

It is usually stated that the high systolic pressures of exercise and emotion are not accompanied by a rise (over 90 mm.) of diastolic pressure such as is seen in arterial disease. Why this is so is not explained, nor does explanation seem possible until accurate instrumental methods are applied.

Difficulty arises, however, in the very cases where information is desired, namely, in those of high blood pressure. A simple increased peripheral resistance, as may readily be shown by a mechanical circulation, results in a high blood pressure together with a small pulse pressure. This is complicated clinically by the fact that, as a rule, in cases of high blood pressure the pulse

is slow, since, as we know, high pressure in the carotid sinus, the aorta, and left side of the heart stimulates reflexly the vagus centre and causes slowing. This slow heart causes the increased pulse pressure commonly seen clinically in cases of high blood pressure. It is probably a good sign in regard to the efficiency of the heart. Later, however, when the heart begins to fail, *e.g.*, from myocardial degeneration, the effect of the increased venous pressure resulting from the weakened heart brings about an increased heart rate (Edwin Mathew) which, as we have seen, now reduces the pulse pressure.

In view of the fact, then, that the heart rate and peripheral resistance are variable and that the blood pressure may be affected by the varying of either, it is difficult to see how any accurate conclusion can be arrived at from a study of pulse pressure. The only significant observation in this direction appears to be that a rapid heart and low pulse pressure, not due to any other obvious cause and accompanied by palpable thickening of arteries, probably indicate an impaired heart. In aortic regurgitation the pulse pressure is high, and the diastolic low, for reasons explained in Chapter XVII. A high pulse pressure with normal diastolic is found in cases of Graves' disease.

The diastolic pressure or the pressure in the arteries during diastole is that pressure against which the left ventricle must force its contents at the beginning of systole, and its importance lies in the fact that there is now a volume of evidence to show that a rise of systolic pressure without a rise of diastolic pressure is of little importance. *Temporary* emotional states, such as are produced by the medical examination may, for example, raise the systolic pressure materially without much rise in diastolic pressure. Presumably there is an increased cardiac output with a reduction in the general peripheral resistance. On the other hand when increased peripheral resistance is masked by cardiac weakness the diastolic pressure may be high, while the systolic pressure may be little altered. Aortic insufficiency, as might be expected, produces a typically high systolic with low diastolic pressure.

In summary it may be said, then, that the diastolic pressure indicates the rate at which the blood can leave the arterial system and, therefore, the total peripheral resistance.

The estimation of diastolic pressure is, unfortunately, not quite so easy as that of systolic pressure. The most used method is

auscultatory and depends on the fact discovered by Korotkow, that when the pressure in the armlet applied for taking systolic pressure is gradually released the silence which occurs when the pressure is above systolic is replaced by a sequence of sounds audible through a stethoscope placed on the brachial artery below the bag. These sounds are as follows : (1) A clear thump which may be preceded in some persons by less clear sounds ; (2) a murmur ; (3) a clear sound which becomes muffled at the beginning of the next phase ; (4) a dull sound. Finally, no sound can be heard. The beginning of 4 is the diastolic pressure and the patient can often assist by stating the exact moment at which the throbbing under the armlet ceases (Treadgold). Between 1 and 2 a silent interval occasionally is present which, unless the determination of the systolic pressure is controlled by palpation, may give rise to a false result. The normal diastolic pressure varies from 60–90, but pressures over 90 demand a thorough investigation of the cardiovascular system.

Venous Pressure.—The value of venous pressure as an indication of the state of the circulation has by no means been adequately studied. Experimentally, it can be shown that the venous pressure gives a very accurate idea of the state of the heart. Any failure of the heart shows itself by a rise in venous pressure long before there is any fall in arterial pressure, as the latter, when due to cardiac conditions, is prevented or reduced by increased peripheral resistance. In moderate hæmorrhage also the fall of venous pressure is much more marked and prolonged than that of the arterial pressure which rapidly recovers as a result of vaso-motor activity. Similarly, any dilatation of vessels, *e.g.*, by alcohol or histamine, is, apart from the transient effect of the latter, indicated by a prolonged fall of venous pressure, although that in the arteries may remain unchanged. Clinically, venous pressure is easily measured by the amount of pressure necessary to compress a vein over which is sealed a glass capsule in which the pressure may be raised (von Recklinghausen), or by the actual putting into the vein of a cannula attached by means of a sterilized non-coagulant fluid to a manometer, preferably aneroid (Bedford and Wright). The second method, no doubt, gives the more accurate value, but is a little inconvenient, and the first gives relative values, especially in a given case. It will be obvious that it is essential when taking such measurements to have the patient always in the same position. There is, as shown by Hooker, some small diurnal

variation and an increase with old age, and more recently Eyster and Meek have emphasized that a rising venous pressure is the first sign of cardiac failure. The writer can certainly support the statement of Eyster and Meek from the experimental standpoint.

CHAPTER XX

HÆMORRHAGE AND SHOCK. THE NATURAL ARREST OF HÆMORRHAGE

THE INTEGRATION OF THE CIRCULATION

In the chapter on Blood Pressure, some of the mechanisms concerned in its maintenance have been described. It has been noted that each of the factors on which it depends is variable. Unfortunately, it has become the custom to consider various parts of the circulation separately, and to study the control of the heart, of the blood-vessels, and of the capillaries somewhat apart. This is the natural result of methods by which the various facts have been isolated. It must, however, be realized that they are but parts of one mechanism for the blood supply of the body and, especially, the muscles. The circulation and respiration (although the central processes of life as a clinical entity) are, in reality, the servants of the rest of the body.

When a muscle is active, lactic acid and carbon dioxide and possibly other substances cause a local dilatation of capillaries. It is possible that metabolites of protein akin to histamine (which has been shown by Dale and Richards to dilate such vessels) may also have a vaso-dilator action. It has been clearly shown by Krogh that in an active muscle very many times the number of capillaries in use in resting muscle are opened up, but tissues vary appreciably in this respect.

In addition, there are reflex mechanisms capable of dilating the vessels in active tissues, and it is probable that the importance of the Lovén reflexes has been overlooked. The stimuli apparently arise within the active organ itself, and bring about reflexly a diminution of the normal arterial tone.

The evidence in relation to adrenaline suggests also that this substance may play a part in dilating the vessels of active parts, *e.g.*, the coronary arteries and the capillaries of muscles.

It will be evident that when certain tissues take more blood in this way, it will become necessary, since the amount of blood in

the body is limited, for those organs which are not required to close down. There seems to be little doubt, from the well-known effect of asphyxia, and from the stimulating effect of carbon dioxide on the vaso-motor centre, that this reduction of the blood supply to inactive tissues is brought about by the carbon dioxide produced by the active tissues. The carbon dioxide not only acts directly on the veins (and the veins of the abdomen can contain about a third of the blood in the body), but also indirectly upon both arteries and veins, by virtue of its action upon the vaso-motor centre in the medulla. The action of this centre is still further enhanced by sensory stimulation, should any occur, and, as we have seen in relation to blood pressure, even by anticipation of exercise.

The impulses from the vaso-motor centre pass down the spinal cord and pass out in the sympathetic outflow in the anterior nerve roots from the 1st thoracic to the 3rd lumbar inclusive. In raising blood pressure experimentally by electrical stimulation of the splanchnic nerves, or by injecting adrenaline, we are but activating some peripheral parts of the mechanism.

We must associate such shutting down of the blood-vessels of inactive tissue with the action of the sympathetic nervous system. As was shown in relation to the " Rate of the Heart," muscular activity accelerates this by raising the venous pressure, reducing vagus restraint by causing the secretion of adrenaline, and centrally stimulating the sympathetic.

Hence we see that the carbon dioxide produced by the muscle during contraction not only dilates local blood-vessels, but closes down those of other tissues not in use. At the same time it hastens the circulation and raises the blood pressure, which still further causes the active tissues to receive more blood. In severe exercise we believe that the action of the whole mechanism is still further enhanced by the action of adrenaline secreted as a result of the stimulation of the splanchnic nerves *via* the vaso-motor centre, while there is increasing evidence that vaso-dilator substances, such as lactic acid and possibly also substances derived from the protein itself may play a part in causing local vaso-dilatation.

Other mechanisms of importance in relation to the integration of circulation are the depressor reflexes, with which are closely associated the action of the vagus. At each beat of the heart impulses apparently pass up from the carotid sinus *via* the glosso-pharyngeal nerve and from the arch of the aorta *via* the depressor

fibres of the vagus to the vagus centre, which is stimulated, and to the vaso-motor centre, which is inhibited. Thus the heart is kept under restraint by the vagus, while the action of the vaso-motor centre on the blood-vessels is reduced. Experimentally, stimulation of the central end of the depressor nerve may be shown to slow the heart by way of the opposite uncut vagus and to cause dilatation of blood-vessels. Conversely, section of the vagus brings about acceleration of the heart and general vaso-constriction.

The depressor mechanism may be looked upon as a means of safety whereby the heart is relieved should the pressure against which the left ventricle has to pump become suddenly excessive, as in strain or arterio-sclerosis. The author, however, recently put forward evidence that this function of the vagus is probably of less importance than the relationship of this nerve to cardiac efficiency. This is discussed later in relation to Exercise.

Just as important, however, is the converse of the depressor reflex : a reduction in the depressor impulses as a result of reduced pressure in the aorta and left ventricle. Such a condition will occur normally on the assumption of the erect from the lying position, and as such may be considered a vasculo-postural reflex, by which vaso-constriction and cardiac acceleration are brought about. This mechanism is also valuable in hæmorrhage.

The Adaptation of Blood Pressure to Posture.—It is important that blood pressure should be reasonably constant in whatever position the body may chance to be. It is common experience that the sudden resumption of the erect posture from the recumbent is associated with dizziness, and a similar but slightly more prolonged state of affairs is experienced after any illness which has confined one to bed. The abdominal muscles and the vaso-motor centre do not constrict the vessels (particularly those of the abdomen) sufficiently rapidly to maintain the pressure in the arteries, and the blood tends to remain in the dependent parts, causing a certain amount of cerebral anæmia. Yandell Henderson has shown that in man the output of the heart per beat is much reduced in the change from the recumbent to the erect posture. A caged rabbit or a snake may actually die if held in the vertical position for a time, as the blood fails to return to the heart. These facts indicate that to be efficient the mechanism must be used. If the blood-vessels are diseased, as

in arterio-sclerosis, the response may be still less adequate and the patient will suffer from giddiness.

At the beginning of a descent in a lift the sensations are probably due to a temporary lack of adaptation on the part of the circulation, although here, no doubt, sensations are also brought about by the labyrinth. There is, however, rapid compensation.

The pallor of some cardiac cases is presumably due to reflex vaso-constriction, the result of a lessening of the impulses which pass up the depressor nerve to the vaso-motor centre. In cardiac failure generally there is often a curious mixture of cyanosis and pallor, the congested veins being rendered more distinct by the pallor. The cause of pallor in aortic regurgitation is not well understood. The vessels of the skin of the face appear to be in a state of constriction in aortic disease. When the forehead is rubbed, the vessels dilate and capillary pulsation becomes evident.

HÆMORRHAGE AND ALLIED CONDITIONS

When blood is lost from the body, provided the loss is not excessive, the blood pressure does not fall except during the actual time of the loss. Further fall is prevented by an increase of the peripheral resistance, the general reduction of the capacity of the vascular system, and an increased cardiac action. These are brought about reflexly. The actual fall of pressure, while it lasts, reduces the depressor impulses which at each heart-beat normally pass up the depressor fibres of the vagus to the cardiac centre. This brings about the increased rate of the heart and increased peripheral resistance. These two processes supplement each other; a certain amount of alteration in the peripheral resistance is therefore possible (should it be necessary) for the redistribution of blood. There is also a direct stimulation of the vaso-motor centre as a result of the temporary fall of pressure in the cerebral arteries. The increased action of the heart and the arterial constriction reduce the amount of blood passing from the arteries to the veins and cause a reduction of venous pressure. This has been shown by the author to cause impulses to pass up the vagus to the vaso-motor centre and thus reflexly maintain the increased peripheral resistance. It seems most likely that the pressor influence of the vaso-motor centre extends not only to the arteries but to the veins and capillaries, whose capacity is reduced thereby, while there is evidence that the liver may

be contracted (Krogh), and also the spleen and intestine (Barcroft).

At the same time there is a passage into the blood-vessels of fluid from the tissues which become dehydrated from reabsorption of lymph (Milroy), giving the face of the patient a shrunken appearance. The reabsorption is probably due to the fall of the blood pressure in the capillaries and the unantagonised effect of the osmotic pressure of the blood which attracts the tissue fluids. This fact and, more particularly, the rapid recovery of blood pressure due to increased activity of the vaso-motor centre have caused the old-fashioned treatment of bleeding to be given up. Records of venous pressure, however, show that this pressure does not recover nearly so rapidly; indeed it remains down until arterial vaso-constriction is no longer present, since the low venous pressure is brought about by the constriction.

This is a fact of considerable practical importance. If a patient is bled sufficiently to reduce the arterial blood pressure 30 mm., it may be taken from experimental findings that the percentage lowering of the venous pressure is relatively three or four times as great. Further, so long as the arterial pressure is below its usual level, it may be rightly assumed that the venous pressure has by no means recovered. The relief which such a procedure will give to an impaired heart is obvious, especially when the cardiac embarrassment is enhanced by an abnormally high venous pressure, as is common in cardiac conditions. In such circumstances some clinicians still recommend bleeding to relieve the right side of the heart. Occasionally, when the administration of digitalis has failed to relieve a case of congestive heart failure, venesection proves of the utmost service.

The tissue fluids contain a greater number of immune bodies than normal blood, so that there may be more justification in bleeding than was thought, even in infective diseases.

If hæmorrhage is very severe or repeated, the yellow marrow of the bones becomes red through increased vascularity and commences to form blood corpuscles. The general effects of oxygen want make themselves apparent on respiration if the hæmorrhage is severe.

In cholera, when the loss of body fluid is excessive, the blood also loses fluid and may become tarry in appearance. The diminution of blood volume causes symptoms resembling those of hæmorrhage.

INCREASED CAPACITY OF THE CIRCULATION. SURGICAL SHOCK

There are few subjects on the borderline between physiology and surgery about which there has been so much controversy as surgical shock. The controversy has been largely the result of attempts to attribute all forms of shock to the same cause, but gradually the position, with a fuller knowledge of the circulation, has become cleared.

The condition of shock is characterized by a marked fall of blood pressure, with all the signs and symptoms of blood loss without there having been an actual hæmorrhage. It is agreed by practically all those who have investigated the subject that there is an increased capacity of the vascular system, which in some instances is associated with increased arterial constriction, brought about as in hæmorrhage. It is also agreed that the heart is not primarily concerned in the circulatory failure.

From what has been said in relation to the integration of the circulation, it will be clear that such a failure may be brought about in two ways: (1) by failure of the *vessels* peripherally to maintain their tone and normal permeability, or (2) by failure of the vaso-motor *centre* to maintain tone generally. It is practically certain that both possibilities may occur.

Peripheral Failure.—Evidence that wound shock, especially when delayed, may be due to substances produced by damaged tissues and capable of dilating the *capillaries* and increasing their permeability, we owe to the work of Bayliss, Cannon, Dale, Laidlaw, Richards, and Wallace. Clinically, it was observed that the degree of shock was closely related to the actual amount of tissue damage; further it was seen that patients suffering from injury to a limb to which a tourniquet had been applied were particularly liable to collapse when the tourniquet was removed, but the collapse did not occur if the limb was amputated before such removal. The fact that, not infrequently, the arteries were found to be markedly constricted indicated clearly that these vessels were not at fault. The final proof, however, that shock could be produced by a chemical substance was given by Dale and Laidlaw, who showed that such a condition could be produced by the injection of histamine. This substance, which is de-

carboxylated histidine, the latter being an amino-acid and a product of protein digestion, is found to occur in tissue extracts generally, is a normal constituent of the intestine, and is produced by *B. coli* even when grown *in vitro*. Histamine has been shown by Dale and Richards to bring about a profound dilatation of the capillaries, and later collaborators have demonstrated the increased permeability of these vessels.

It is not, however, claimed by these workers, as some writers appear to imagine, that all shock is due to the absorption of histamine-like substances; indeed there is ample evidence that shock may occur from other causes.

Central Failure.—As we have seen in previous chapters, the tone of the blood-vessels is kept up by the *vaso-motor centre*, the activity of which Dale and Evans have shown to be dependent on the carbon dioxide content of the blood. It will be clear, then, that any condition which separates the centre from the vessels or which causes the carbon dioxide content of the blood to be reduced must result in a fall in blood pressure not only from an increased capacity of the circulation, but also from a reduction of the peripheral resistance of the arterioles.

Separation of the nervous connections of the vaso-motor centre may occur in spinal injury in which shock is produced by interruption of the vaso-motor paths between the medulla and their points of exit from the spinal cord. Such an injury must, of course, obviously also interfere with impulses other than vaso-motor. The lower limbs may be affected while the upper limbs may be normal so far as voluntary movement is concerned. The effect on the blood pressure will depend on the extent to which the vaso-motor paths have been interfered with.

Porter has pointed out that fat embolism may occur as a result of fracture of long bones, and there are many diverse ways by which the paths of the vaso-motor system may be interrupted. Rendle Short has suggested that the primary condition in shock is loss of muscle tone resulting in lack of support of the blood-vessels. It is true that if a sufficient amount of muscle is rendered flaccid by curare or by nerve section, a fall of blood pressure does take place, but vaso-motor as well as motor fibres are affected by section. While it is agreed, then, that loss of muscle tone may exaggerate the condition of shock and may be produced by spinal injury, it is clear that in other states loss of tone is secondary. This may be shown experimentally by the injection of histamine or by the production

of shock in a decerebrate animal in which there is an excess of tone.

Of special importance in relation to central failure as a cause of surgical shock is sensory stimulation. This factor was first stressed by Crile and Mummery, who noted that shock was produced by excessive sensory stimulation especially if mechanical, as might occur after wounds or during operation under light ether anæsthesia. It was observed that shock could often be prevented by blocking the afferent nerves by local anæsthesia. Crile suggested that there is brought about by the excessive stimulation an exhaustion of the vaso-motor centre ; but it can readily be shown that such exhaustion is not the primary cause, for the centre still responds to sensory stimulation and particularly to the administration of carbon dioxide.

On the other hand it has been suggested by Yandell Henderson that the acapnia or washing-out of carbon dioxide brought about by the hyperpnœa occasioned by the sensory stimulation brings about a reduction in the tone of the vaso-motor centre. That the activity of the vaso-motor centre depends on carbon dioxide has been proved beyond doubt (Dale and Evans). The fact that overventilation in an unanæsthetized man does not necessarily result in a fall of blood pressure does not affect these conclusions. In *unanæsthetized* man and in many animals the alkalinization of the peripheral vessels caused by the washing-out of carbon dioxide leads to constriction of peripheral vessels which compensates for the loss of tone of the centre (McDowall). There is also new evidence that there may be at the same time an active depression of the vaso-motor centre (McDowall). It is extremely easy to produce such shock experimentally by mechanical stimulation in an animal under light anæsthesia, even if respiratory effects are excluded. Whatever the exact method of the production of the shock, it is important to emphasize the fact that the failure of the vaso-motor centre is a consequence of insufficient anæsthesia.

Such considerations are of importance also in local or spinal anæsthesia in which shock may be produced similarly from the hyperpnœa of an excited patient. Too often other possible causes are sought.

Criticism is sometimes expressed by surgeons who are unable to find visual evidence of the " lost blood " at the periphery. The dilatation must be considered of a very general nature, affecting muscles as well as viscera, and even in experimental shock, where the " lost blood " is certainly at the periphery, it is

not visible, and the increased capillary permeability prevents engorgement.

In abdominal operations the mere handling of the intestine may cause the absorption of toxins from the lumen where they exist normally. When the capillaries are dilated by histamine there is, as in hæmorrhage, an attempt by the vaso-motor centre to maintain the blood pressure. The " loss of blood " may even be over-compensated and the blood pressure actually rise in the early stages of shock as it does in normal persons on changing from the horizontal to the erect posture. It is evident therefore that anything which interferes with the reactions of the vaso-motor centre must aggravate shock from histamine. The most important considerations are loss of carbon dioxide from over-ventilation due to pain, and general anæsthesia (Dale and Laidlaw) which acts also directly on the capillaries. The danger of general anæsthesia in strangulated hernia has long been so well recognized that cases of a few days' standing have often been thought hopeless. The use of local anæsthesia with morphine is therefore urged. The detrimental effect of cold on shock was well appreciated in war time. Now we know that cold rapidly exhausts the suprarenals which have now been shown to be so important in the protection of the body against substances such as histamine. It has been shown for example that a dose of histamine which does not affect an unanæsthetized cat is fatal when the suprarenals are removed.

Dale and his co-workers have shown that a poison such as histamine causes adrenaline to be secreted, as would be expected from a compensation on the part of the vaso-motor centre which controls the suprarenals through the splanchnic nerves, while Zackary Cope points out that as soon as the blood pressure has begun to fall it is dangerous to give a general anæsthetic, since by that time all the compensatory mechanisms have been brought into use.

The new treatment of burns by tannic acid is of some interest in relation to shock. The coagulation of the surface fluids prevents the absorption of toxic products, and shock is minimized.

General Considerations.—Whether the failure of the vaso-motor system be due to peripheral or central causes, the practical effect on the circulation is the same, namely, that there is an increased capacity of the vascular system and there is a diminished return of blood to the heart (oligæmia). Experimentally, the fall in venous pressure which occurs is an index of oligæmia.

There is another point over which there has been some difficulty, namely, the actual state of the arteries in shock. It may now be stated that when the shock is due to capillary dilatation as a result of toxins, the arteries are undoubtedly constricted, as has been emphasized by Malcolm. Zackary Cope has also pointed out that the first stage in surgical shock may be a rise of blood pressure. An exactly similar state has been shown by the writer to occur in cats injected with small doses of histamine. To make up for the blood " lost " in the capillaries, there is a compensation by the vaso-motor centre which brings about a constriction of arteries. There is also increased cardiac activity. In many animals there is actually an over-compensation and a rise of blood pressure. A similar over-compensation often occurs to small hæmorrhages, just as it does in the assumption of the erect from the horizontal position.

The SYMPTOMS OF SHOCK from whatever cause are, as would be expected, those of hæmorrhage, pallor being always an outstanding feature as a result of reflex constriction of skin vessels. They are, however, of considerable diagnostic importance where there has been internal hæmorrhage, such as intestinal or tubal. There may be some nausea with a sensation of shivering, and if the hæmorrhage continues there is increased respiration, which becomes an actual air-hunger, and the patient breaks out in a cold sweat. He is frequently restless, and there may be difficulty in keeping him in bed. In the more insidious toxic form the patient is usually apathetic, the skin is cold, grey, and clammy, sensory stimulation awakens little or no response, the limbs are limp and flaccid, the pupil is dilated and responds little, if at all, to light, the heart is rapid, and the pulse is felt with difficulty because of contraction of the artery. Some pulse waves may be so weak that the heart appears slow. The reduced filling of the heart and increased frequency of its beat cause a marked reduction in the pulse pressure, although the systolic pressure may have not yet fallen, the compensatory arterial constriction making up for the capillary dilatation. The temperature is subnormal. The cold grey skin is the result of constriction of the superficial vessels in their attempt to conserve the blood for the more important organs, especially the heart and brain. The difficulty of obtaining a response to sensory stimulation appears to be due to the fact that the conductivity through the synapses is much reduced by the low pressure, for, as has been shown by Pike, the ease with which the spinal reflexes can be elucidated depends on

the blood pressure. The thirst complained of by the patient is the result of deficient secretion of the salivary glands, and expresses the natural call of the body for more fluid to add to the blood volume. The lowered body temperature results from the reduced metabolism.

The TREATMENT is indicated by the obvious attempt of Nature to keep up the blood pressure. The heart is seldom impaired in clinical cases. Whether the fall of blood pressure is due to the diminished volume, actual or relative, or due to diminished peripheral resistance, it is evident that Nature, as the thirst and cold skin indicate, is doing all she can to maintain the blood volume. This, then, is the essence of treatment. As much water as can be taken *by the mouth* is a primary physiological indication, and this refers also to the condition of fever in which excessive water is lost from the skin. Yet it is remarkable how seldom we find an unlimited amount of water available for any patients in hospital. More (but not much more) rapid effects are produced by intravenous injections of 0·9 per cent sodium chloride, or approximately a teaspoonful of salt to a pint of boiled water. The saline, however, is not retained long in the vessels, for even if its osmotic pressure [1] equals that of the plasma, it lacks colloids, the low osmotic pressure of which is, in virtue of their relative indiffusibility, the force which keeps the plasma within the vessels. In cholera, where excessive fluid is got rid of by the intestine, Rogers introduced hypertonic saline treatment to assist in maintaining fluid in the blood-vessels as long as possible. The extra salt, although it attracts water from the tissues, is not retained very long, but is excreted by the kidneys. Transfusion of blood may be used, but care must be taken that the donor belongs to the proper blood group (see page 181). Under conditions of emergency it may be necessary to have recourse to artificial fluids.

We owe to the work of Bayliss, Keith, and others, the provision of a physiological fluid, which in virtue of its osmotic pressure and colloidal nature is retained in the blood-vessels. They found that the addition of 6 per cent of gum to the saline satisfies this requirement. Care must be taken, however, to see that the solution is neutral. Erlanger and Gasser have further elaborated the suggestion of Bayliss. After a great deal of careful work in which the final recovery of the animal, rather than the immediate

[1] Osmotic pressure is so described because of the method by which it may be measured, but physiologically it is the power of a solution to attract water.

recovery of blood pressure, was the criterion of success, they have concluded that it is better to give the concentrated gum slowly, in order to attract fluid from the tissues. Solutions containing 25 per cent of gum arabic, and 18 per cent glucose, infused at the rate of 5 c.c. per kilo per hour, are recommended. This slow rate of infusion is important with all gum solutions, especially strong ones, otherwise sudden death may occur. Simultaneous records (in animals) of the arterial, pulmonary, and venous pressures indicate that not only may rapid injection cause impairment of the heart, but there may be difficulty in getting the gum through the lungs. Neglect of this precaution and faulty preparation (as was inevitable under the hurried conditions of war-time) have done much to detract from the success of such administration. In relation to the red blood corpuscles, reference is made to the value of extract of liver and pig-stomach in assisting in the recovery of the corpuscles of the blood.

A procedure which has not been sufficiently investigated is that of bandaging the patient, especially the abdomen, when the arterial pressure becomes dangerously low. Experimentally it is of great value.

Acapnial and depressor shock are to be prevented rather than treated by a sufficient depth of anæsthesia, and, if necessary, by supplementing the ether with morphia in an excitable patient. Henderson recommends the routine administration of carbon dioxide with anæsthetics, and this is now being done successfully both in this country and in America. The gas mixture used is 5 per cent CO_2 and 95 per cent oxygen, but the addition of 5 per cent CO_2 to air is quite adequate and cheaper. The addition of chloroform to ether undoubtedly lessens the stimulating action of the latter; hence, no doubt, the comparative rareness of shock from operations in Scotland.

Experimentally, the simplest method of preventing acapnia is to cause the animal to breathe through a long tube, and so increase its dead space; and in operations in which stimulation is specially liable to occur, there seems no reason why a similar procedure should not be resorted to by means of a closely-fitting face-piece to which a tube is attached, the anæsthetic being administered at its peripheral end.

Central failure of the vaso-motor centre of a more temporary nature occurs in fainting, in which loss of consciousness is due to cerebral anæmia. The centre may be unable to cope with excessive dilatation of skin vessels, as in fainting in a hot bath, but in

fainting due to emotion the centre appears to fail almost entirely (see " Consciousness "). In some instances this may be due to acapnia, but the suddenness of the onset suggests a more purely nervous cause in many instances.

The conception of the existence of a vaso-motor centre is as yet comparatively crude and depends in the main on the fact that if slices are cut off the brain, the blood pressure does not fall until the region of the medulla has been reached. It is, however, by no means clear that this is not simply an interference with the reflex arc through which pressor impulses are constantly being emitted as a result of afferent nervous impulses and chemical stimuli. Sudden fainting from an intense sensory stimulation, such as great pain in reduction of a dislocation, the incision of a whitlow, or seeing something disagreeable, emphasizes the reflex nature of vaso-motor tone. In such circumstances the higher centres apparently increase the normal inhibitory action over the lower reflex mechanisms, many of which we know to be disturbed under similar conditions of emotional stress. That afferent impulses of a pressor nature are constantly being sent out is undoubted, and is evident from the experiment quoted above, or by isolation of the medulla from its lower nerve connections.

Blood Groups.—The transfusion of blood in the treatment of shock is by no means free from danger, even though actual infection is not transmitted from the donor to the recipient. In choosing a donor, his previous history must be carefully investigated, particularly in relation to diseases of which he may be a carrier. Great care has also to be taken to prevent the transference of clots, the formation of which is commonly prevented in direct transfusion by means of a paraffined cannula or the addition of citrate to the blood after its withdrawal from the donor. Even with all these precautions, however, it has been found that not infrequently patients collapse after transfusion.

Since, of recent years, the danger of allowing a lowered blood pressure to be prolonged has been emphasized, it has become more important to consider carefully the cause of such collapse. The discovery of Landsteiner in 1901, that the serum of one individual might cause agglutination or clumping of the red blood corpuscles of another, has given the key to the cause of such disasters, and it is now recognized that the blood of different people is divisible into four distinct groups according to their compatibility with each other. It has been thought that near relationship between two individuals might indicate that they belong to like groups,

but Skinner has found that the blood of a child is often incompatible with that of its mother.

In determining the blood group to which a person belongs it is necessary to have a sample of serum of groups 2 and 3. The unknown blood is mixed with the known sera in hanging drop preparations, as used in bacteriology. In ten minutes or so the agglutination, if present, is seen with the low power of the microscope, and is even visible to the naked eye. The differentiation is by this means easy. Group 1 (using Moss's classification) is agglutinated by both the known sera, but group 4 by neither. Group 2 corpuscles are agglutinated by 3 but not by 2, while group 3 is the reverse. For completeness it may be added that group 4 serum agglutinates all others, but its corpuscles are not agglutinated by any other serum, while group 1 is the reverse, *i.e.*, its corpuscles are agglutinated by all other groups, but its serum agglutinates no other corpuscles. For this reason group 1 is known as the " universal recipient."

It will be obvious that an individual of a particular group cannot receive corpuscles from any donor whose cells his serum agglutinates.

For example, 4 cannot receive from 1, but as the converse is also true, 4 can always give to 1. These facts find expression in Landsteiner's Law, which states that there are always present in an individual blood agglutinins against the agglutinable substances absent from that blood.

In practice, then, an individual can only take from his own group or from one to which he cannot give, and can only give to his own group or to one from which he cannot take.

Theoretically, the donor's serum might have the effect of agglutinating the recipient's corpuscles, but for practical purposes this can be neglected, partly because the transferred serum becomes so diluted, and for other reasons incompletely understood.

As a source of blood, group 4, the *universal donor*, is of the greatest value in an emergency, as the necessity of typing the recipient is avoided, but it is always best to do a direct typing between the donor's corpuscles and the patient's serum.

The importance of the blood groups is not, however, as emphasized by Swan and by Dykes, confined to transfusion. It is found that in skin grafting it is desirable for the recipient and donor to belong to compatible blood groups, otherwise the grafts may not take. The importance of this fact in other varieties of grafts, such as ductless glands, is no doubt also true.

In medico-legal work, too, it will be evident that the finding of the group to which an unknown blood belongs or does not belong may assist in the elucidation of a crime, and it has been found possible to find the groups even with dry blood. It has been found, too, that if both parents chance to belong to the same group, their children belong either to that group or to that of the universal donor, *i.e.*, group 4, a fact which might be of considerable value in questions of doubtful parentage.

THE NATURAL ARREST OF HÆMORRHAGE

The necessity for the arrest of hæmorrhage has received attention from early times, and is important alike to the surgeon, physician, and obstetrician. Were it always possible to tie the injured vessel, the arrest of hæmorrhage would be a simple matter, but where this is not possible, and, indeed, commonly it is not, the matter is much more serious and a knowledge of the physiological factors concerned in its normal arrest is essential. These factors may be divided conveniently into two classes—the power of closing the blood-vessels, and the coagulation of the blood.

Blood-Vessels.—An artery when cut, or even punctured, at once contracts. This is seen if a main artery be punctured for the purpose of withdrawing blood and it is rapidly realized by a young house surgeon assisting at his first operation. If, however, the artery, even a large artery, be twisted or lacerated when ruptured, the contraction of the vessel is increased and blood loss is prevented. Thus it is possible for an individual to have an arm torn off and yet not suffer from severe hæmorrhage. The arrest is facilitated by the fall of pressure occasioned by the loss of blood. This, together with the other factors, is often sufficient to prevent death even from direct section of a large vessel, such as the radial artery.

Coagulation of the Blood.—Of recent years the general conception of the coagulation of the blood has shown definite signs of simplification along physico-chemical lines, and the conception of Pickering appears to be open to fewer objections than any other. According to his view, there exists in the blood a colloidal clotting complex (fibrinogen-prothrombase) which maintains its fluidity by association with a protective substance. Clotting takes place if the protective substance be disturbed and the clotting complex split up as normally occurs when the blood comes in contact

with any surface which it may wet. If we draw blood through a paraffined cannula and keep it under paraffin it does not clot for hours.

The changes which take place are, we believe, the conversion of prothrombin into thrombin, with the assistance of calcium, and, owing to the subsequent action of the thrombin upon it, the conversion of fibrinogen into the fibrin of the clot. J. Mellanby and others have shown that prothrombase is really an enzyme.

The exact nature of the substances just named is not yet certain and they have been identified rather by their action than their chemical composition. It may therefore be necessary later to subject this conception to some alteration when our knowledge of the physical chemistry of the proteins increases. It seems certain that the final explanation will be along such lines, and for the moment it explains all the facts of the coagulation of the blood.

Several features of blood-clotting are important clinically. It is known, for example, that the clotting of blood is appreciably hastened by heat, and this finds expression in the clinical application of heat to wounds for the prevention of hæmorrhage on bruising and in the use of hot douches for post-partum hæmorrhage. The efficacy of the latter is generally accepted, but their action has more commonly been attributed to the effect on the uterine blood-vessels than on the coagulation of the blood. It has been noted, too, by Pickering that in some varieties of hæmophilia the delayed clotting is a matter of thermo-stability and the application of heat to wounds of some hæmophilics will cause clotting in normal time, a fact probably not taken sufficient advantage of in practice. The putting of a cold object at the back of the neck in the treatment of bleeding from the nose depends in part on the reflex vaso-constriction brought about by the cold.

It is clear that all cases of hæmophilia have not the same ætiology and there is considerable evidence to indicate that the condition should be considered a symptom rather than a disease. Some, but by no means all, hæmophilics respond to treatment with liver extracts (Pickering).

The stasis of blood is also important in relation to blood-clotting, as not only does it allow the thrombin to act locally, but it permits the clot to become firmly adherent and block the ruptured blood-vessels. These facts are taken advantage of in the application of cotton-wool to a cut or in temporarily plugging a bleeding

cavity, such as a wound in the skull, where other treatment may not be possible.

The later contraction of the clot, and its subsequent organization into fibrous tissue, complete the process of natural repair. Advantage of this is taken in the surgical treatment of aneurysm, where the inside wall of the aneurysmal sac is scarified or has passed into it a foreign body such as a silver wire. In the spontaneous cure of varicose veins, also, the question of stasis is important, and, indeed, may be of primary importance. The breaking off of a part of the clot and its subsequent carriage into the circulation may give rise to the formation of an embolus in a vital organ and cause death, which not infrequently occurs when clots become detached from cardiac valves. Sufferers from inflamed varicose veins, especially where "knotting," *i.e.*, clotting, has occurred, must be warned against the use of the limb, since, as we have seen, muscular movement tends to drive the blood, together with the clot, along the blood-vessel by virtue of the valves in the veins.

The treatment of varicose veins by injection depends on the introduction of substances such as quinine which not only cause coagulation of the blood but also fixation of the clot to the wall of the blood-vessel.

Thrombosis.—From time to time, especially after injury, surgical operations, and parturition, aggregation of blood constituents may be found in blood-vessels, particularly the veins of the lower limbs. Similar thrombi are liable to be formed wherever the intima of the blood-vessels or endocardium is damaged or the blood stagnant as in valvular lesions. The actual thrombus may vary appreciably from an aggregation of blood platelets to a typical new blood-clot.

A great many suggestions have been made regarding the causation of thrombi. Some hold that a slowing of the circulation in susceptible persons is liable to allow the blood platelets to leave the centre of the blood stream and aggregate in the walls. Others suggest that there is an alteration in the blood calcium, an upset of hepatic activity, and increased fibrinogen in the blood. The occurrence of thrombosis a week or ten days after the operation is considered to be related to the increase of platelets which reaches its maximum about this time. Full details of the various views are summarized by Pickering.

On the preventive side there is good evidence to suggest that the placing of the patient on carbohydrate diet for a fortnight

after an operation, to reduce the production of fibrinogen which is associated with intake of protein, is of advantage. Undue stagnation of the blood should be prevented by active or passive movement of limbs and massage. Since there is evidence that excessive concentration of plasma may contribute towards thrombosis, any depletion of body fluids liable to be produced by cathartics should be guarded against by ample provision of fluid.

McCann points out that much can be done in surgical operation to avoid thrombosis by using thin material for ligatures and by avoiding the inclusion of "lumps" of tissues within a ligature. Obviously the leaving of blind ends of large veins should also be avoided.

CHAPTER XXI

THE HISTOLOGY OF THE BLOOD

MICROSCOPICAL examination of the blood is now a routine procedure in clinical work. The reader is referred, for details of methods, to the many excellent manuals of clinical and laboratory work.

The Red Blood Corpuscles.—These cells are normally present in the blood to the extent of about five to six million per cubic millimetre. They contain the hæmoglobin upon which depends the oxygen-carrying power of the blood. The extent to which the number of red cells may be diminished during life is quite amazing. In pernicious anæmia, for example, the number per cubic millimetre may be reduced to 600,000. The general condition of the patient, provided he is resting, is often quite good on account of the adaptation of the circulation, although any exercise is impossible.

The adult red cell is the erythrocyte, a non-nucleated cell with an average diameter of 7·5 μ or between 7 and 8 thousandths of a millimetre. In disease many immature forms may appear : the megaloblast, a large nucleated cell with scanty chromatin characteristic of pernicious anæmia ; the erythroblast, nucleated and with a chromatin network ; the normoblast with deeply stained nucleus but no network ; the reticulocyte or young red cell with a network in the cytoplasm which stains with cresyl blue. All the nucleated precursors of the red cell really give this reaction, but as the cell grows older the reticulum becomes less evident. At birth 30–50 per cent of the red cells have a reticulum, but after the first week only 1 per cent. The essential stimulus to corpuscle formation and extrusion appears to be oxygen want, which is dealt with in the chapter on " Anoxæmia." Though oxygen want may lead to an increase in the total number of red corpuscles, yet in some circumstances it does not lead to the appearance of primitive forms in the circulation unless there is a reduction in the number of normal forms, either from actual loss, abnormal destruction, or a deficiency in the mechanisms producing them. Thus, in circulatory disease there may be an

increase in red cells, but these are not the abnormal forms that occur in the anæmias.

Nucleated red cells and cells with reticulæ which can be shown up with a special stain, and abnormally large, small, or deformed erythrocytes occur in the anæmias. A reticulocyte increase is an important indication of active regeneration, and is of special diagnostic importance in hæmolytic anæmias where 20–50 per cent of the red cells may be reticulated. The absence of such cells when the blood count is under two million (Davidson) indicates that the normal regenerative response of the bone marrow is in abeyance. In the severer forms, such as pernicious anæmia or the anæmias brought about by certain intestinal worms (such as ankylostoma), large nucleated megaloblasts make their appearance ; they may be the first indication of the presence of parasites. It is interesting to note that in the secondary anæmias nucleated red cells are rare and the non-nucleated cells, being smaller than normal, contain less than the normal amount of hæmoglobin. This we know because the colour produced by a given number of corpuscles is less than that which would be given by a similar number of normal ones, *i.e.*, the **colour index** is low. In pernicious anæmia, on the other hand, the corpuscles, being on the average larger than normal (megalocytes), the colour index is above unity.

Red blood corpuscles are apparently being constantly removed, and the hæmoglobin broken down in the formation of bile (see page 335). The disintegration seems to take place in the spleen, the hæmolymph glands, in the blood itself, and possibly in the liver, where at least the products of disintegrated corpuscles find their way.

In the adult the **regeneration of new blood corpuscles** takes place in the red marrow, especially of the ribs, vertebræ, and flat bones. In times of stress the yellow marrow of the long bones becomes red and is similarly utilized. The actual site of formation in the bone marrow appears to be the minute vessels and collapsed sinuses. The regeneration of blood corpuscles is of special interest in the anæmias and in hæmorrhage. By a study of the rate of hæmoglobin formation after hæmorrhage in dogs, Whipple found that the addition of liver to the diet greatly increased recovery. Iron in such forms as chlorophyll was not nearly so effective. This led Minot to try out the value of liver in pernicious anæmia. The active principle of liver is soluble in water and efficacious extracts have now been made free from iron, vitamins, and proteins. Intramuscular or intravenous

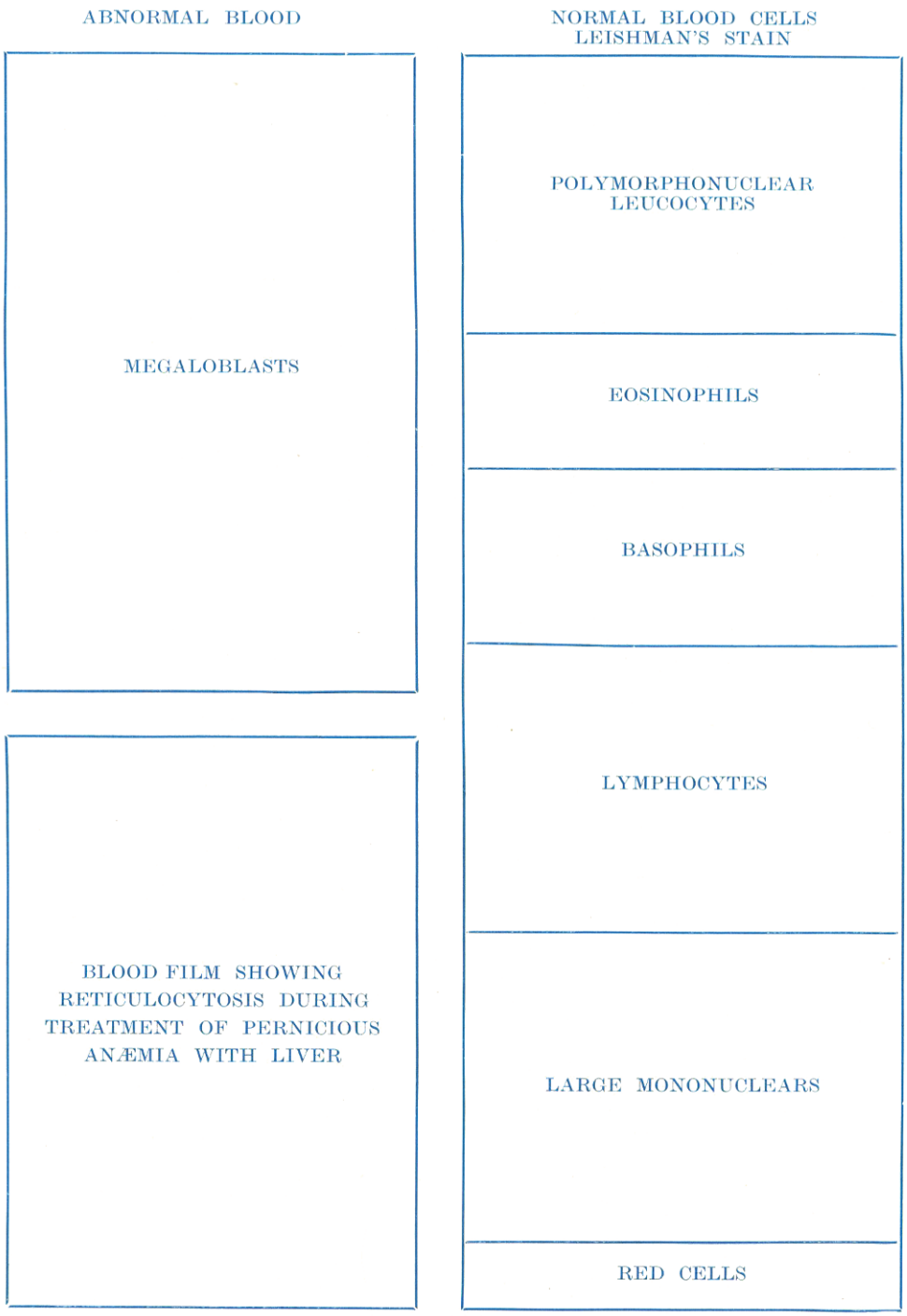
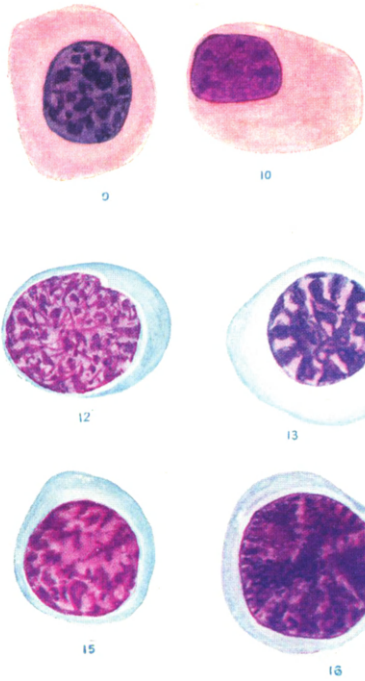
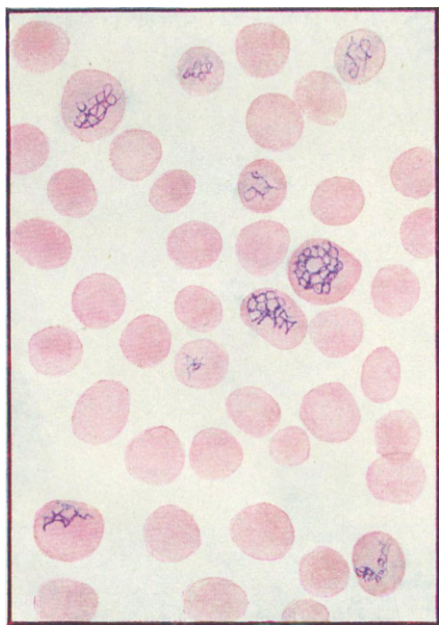
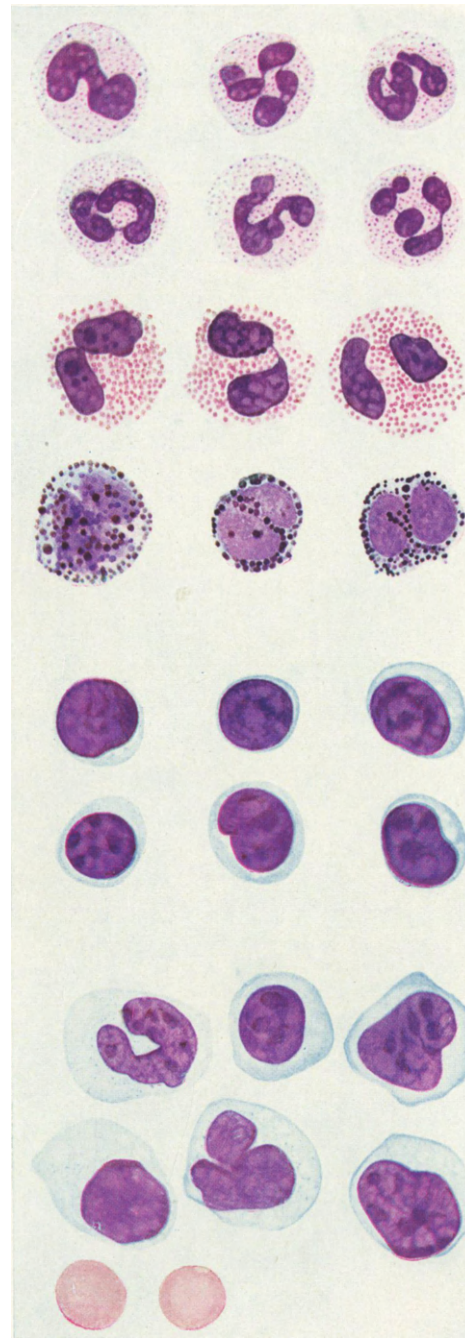


FIG. 9.

A. The right-hand side of the figure shows different types of normal blood cells. (*After Poulton.*)
B. The top left-hand side (*after Piney*) shows six large nucleated red cells.
C. The bottom left-hand side (*after Knott*) shows the reticulocytosis which occurs during the liver treatment of pernicious anæmia. (*Reproduced by courtesy of Messrs. J. & A. Churchill, Ltd., from "Taylor's Medicine" (Poulton).*)







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injection is more efficient than oral administration and is specially valuable when vomiting prevents oral therapy. More recently it has been found that dried stomach wall of the pig, or human gastric juice, especially if incubated with meat, is just as efficacious (Wilkinson). In the treatment of this hitherto fatal condition, pepsin and HCl are, however, valueless. Castle has shown that the gastric juice in health contains an " intrinsic factor " which acts on an " extrinsic factor " in the food, with production of a hæmopoietic substance which is stored in the liver. Pernicious anæmia results when, owing to gastric defect in a predisposed subject, this substance is not formed. Wilkinson has brought forward evidence that the " intrinsic factor " is a thermolabile, enzyme-like substance for which he has proposed the name " hæmopoietin."

Since an excessive bilirubin content of the blood and activity of the marrow can be produced by injecting hæmolytic poisons it has been suggested that a toxin gains entrance because of the achlorhydria which is generally present. Achlorhydria, however, is a common condition, but only a small proportion of achlorhydrics develop pernicious anæmia.

Recent work, however, indicates that the hæmolysis is really secondary to the production of immature red cells which are easily hæmolysed. Moreover, in the early stages hæmolysis is absent. Part of the hæmosiderosis is due to the inability of the bone marrow to re-use the iron which results normally from blood-destruction. A true hæmolytic anæmia such as acholuric jaundice does not respond to liver extracts like pernicious anæmia in which liver treatment causes, in a few days, a cessation of hæmolysis as indicated by a fall in the bilirubin content of the blood. (See " Bile.")

The hæmopoietic substances now believed to be essential for the formation of adequate numbers of mature red blood corpuscles are the liver principle, vitamin C, thyroxine, iron and traces of copper. The first of these, the liver principle, specially influences the production of normoblasts from megaloblasts, and in its scarcity or absence the bone marrow exhibits a " megaloblastic reaction " as in pernicious and allied anæmias. The rate of production of red cells is, nevertheless, slowed down. The red corpuscles turned out vary excessively in size (anisocytosis), but on the average are of larger diameter than in health (megalocytosis). The colour index is high, partly because of the increase in average size of the cells, partly because there is a deficiency of

stroma, but not of hæmoglobin, in the individual cell. Nucleated red cells, including megaloblasts, may escape into the blood stream. The anæmia which results from a deficient supply of iron to the bone marrow is often microcytic in type, and has a low colour index. There is a lack of hæmoglobin but not of stroma in each cell. Nucleated red cells are absent from the blood stream, and there is no secondary hæmolysis. The nutritional anæmia of infants, which is greatly exaggerated by delayed weaning, is due to the relative poverty of milk in iron. Helen Mackay has shown that infection aggravates this anæmia. The Dutch workers showed that copper in small amounts could cure the anæmia which develops in young animals weaned at an unduly late date. Recent work has suggested the possibility that copper may act by enabling the body to use its remaining iron reserves to the uttermost extent. In adults deficient iron absorption is usually secondary to a gastric defect, and anæmia from this cause is specially common in women towards the end of the reproductive period. The strain imposed by menstruation and reproduction is an important accessory factor, and the chronic microcytic anæmia from which women are apt to suffer often improves after the menopause or even after the induction of an artificial menopause (Witts).

Chronic microcytic anæmia is usually associated with achlorhydria. D. T. Davies has shown that a small flow of HCl may be obtained by the subcutaneous injection of histamine in these cases and that pepsin may be present, *i.e.*, there is not usually the complete achylia of pernicious anæmia. Mucus is often excessive in the gastric contents, and some authors regard the achlorhydria as due to gastritis of which, as Hurst has shown, achlorhydria is an early result. Witts believes the achlorhydria is probably congenital and that pepsin is often absent. He has shown, however, in collaboration with Hartfall, that the small flow of juice excited by histamine in cases of simple achlorhydric anæmia contains the intrinsic principle of Castle, for when the juice is incubated with beef, and the resulting material administered to a case of pernicious anæmia, a reticulocytosis occurs. Cases have been described in which simple achlorhydric anæmia gave way subsequently to pernicious anæmia ; the intrinsic factor finally becoming suppressed. Not all cases with achlorhydria develop anæmia, and in any case the onset of anæmia is delayed for years. Pernicious anæmia may develop after the stomach has been partly removed, again, usually after a considerable latent period.

In these cases we must postulate either a " weak " bone marrow, or, as Witts suggests, the " wear and tear " of existence (including, presumably, the effect of gastritis), as a factor.

The simple achlorhydric anæmia already mentioned is characterized by sore tongue, low colour index, chronicity and varying degrees of dyspepsia. The spleen may be enlarged to a very moderate degree. The nails are brittle and may show a spoon-shaped deformity. The dyspepsia leads to an avoidance of meat and other iron-containing foods and the achlorhydria of itself seems to act adversely on the absorption of iron. Even the healthy diet has only a small iron content (see Chapter XXXV), and in simple achlorhydric anæmia the intake is evidently very small. The serum iron content is correspondingly lowered, in contrast to the high values found in pernicious anæmia. The disease is readily cured by the administration of large doses of iron in the form of Blaud's pill ; the scale preparations seem not to be quite so effective as the pill. Dilute hydrochloric acid is a valuable adjunct to the treatment. When the glossitis spreads to the pharynx, dysphagia results. The combination of dysphagia and anæmia is called the Plummer-Vinson syndrome.

Anæmias can be classified into those in which there is a primarily defective production of red cells in the marrow and those in which there is active destruction of circulating red cells and their forbears in the marrow. The former are called anhæmopoietic, the latter hæmolytic. Anhæmopoietic anæmias include those just described as resulting from deficiency, and also aplastic anæmia. Aplastic anæmia is not an entity ; thus it may result from exposure to benzole, it may represent a terminal stage of the hæmorrhagic diathesis or " primary purpura," or may arise without recognizable antecedents. The " primary " anæmias of our student days, *e.g.*, pernicious anæmia, are thus seen to be anhæmopoietic. Some of the " secondary " or " symptomatic " anæmias fall into the same category ; others are hæmolytic. The chief value of the term secondary anæmia nowadays would seem to be to indicate an anæmia which ordinarily occupies a subsidiary part in the natural history of the disease, although becoming prominent in a few instances.

Boycott has suggested that the red cells and the marrow cells which beget them should be grouped together as a single tissue, the erythron. Hæmolytic anæmias are thus properly called erythronoclastic. They result from various infections, poisons and other agents which attack the erythron. One of the most

striking examples of an erythronoclastic anæmia is that described by Lederer in 1925 under the name Acute Hæmolytic Anæmia. Similar cases had previously been included with certain acute leukæmias under the now discarded motley title " Leukanæmia." Lederer's type of acute hæmolytic anæmia is apparently due to an infection of unknown nature with a selective action concentrated on the erythron. Fever and evidences of rapid and enormous blood destruction such as jaundice, urobilinuria or even hæmoglobinuria, accompany a blood picture resembling pernicious anæmia plus leucocytosis. The disease occurs in both adults and children and is mentioned here because of the great value of blood transfusion. A single transfusion often tides the patient over what is a dangerous emergency. The mortality of untreated cases is probably at least 50 per cent (Witts).

The White Blood Corpuscles.—The white blood corpuscles have all the appearance of being active living cells which act as the scavengers of the body, protect it from bacterial injury, form antitoxins, and fix toxins. The method by which they are attracted to the spot of injury or invasion is as yet unknown, but the term chemio-taxis is adopted to suggest that the stimulus is probably a chemical one. The leucocytes can wander in and out of the blood-vessels, while the polymorphonuclear cells have a special power of ingesting and destroying bacteria or other dead matter, the so-called property of phagocytosis. Leucocytes are differentiated according to their histological characteristics.

Polymorphonuclear cells are so called because of their granular lobed nuclei which may vary in shape ; they are phagocytic, and this power is facilitated by amœboid movements. The cytoplasmic granules of the majority of the polymorphs stain with neutral dyes and these so-called neutrophils account for about 70 per cent of the total leucocyte count ; others have coarse granules which stain with eosin (eosinophils = 2.3 per cent), while less than 1 per cent have coarse basophil granules.

The lymphocyte is distinguished by its large round nucleus, almost as large as the corpuscle itself, which is otherwise hyaline and colourless. They vary in size, and form normally 25 per cent of the total white corpuscular count. They are reduced in vitamin B deficiency and exposure to X-rays.

The relative numbers in each group are fairly constant, but in disease the proportions may be much changed and investigation to determine these proportions, the so-called differential count, is

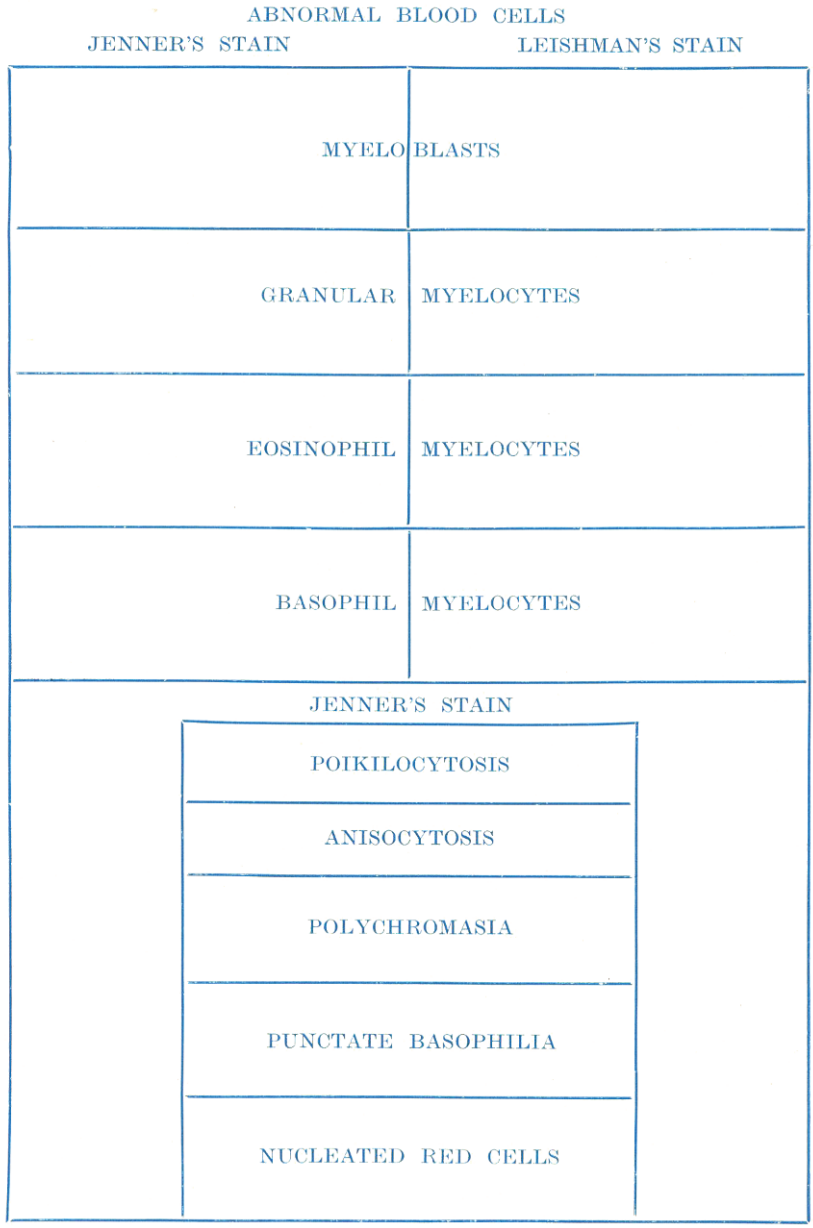

FIG. 10.—ABNORMAL BLOOD CELLS.
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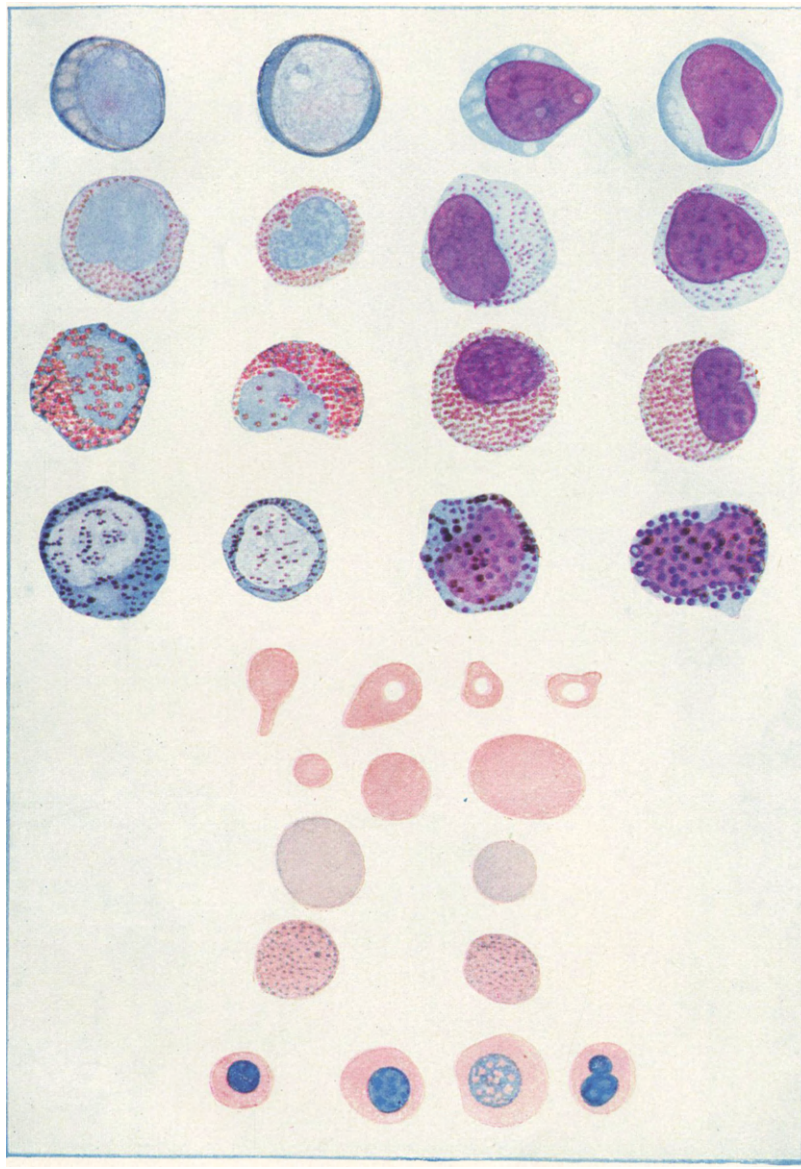

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of considerable clinical value. In acute infective conditions the polymorphs are increased, while in chronic states, such as tuberculosis, the small lymphocytes predominate. Eosinophilia is often associated with the presence of parasites, *e.g.*, ankylostomiasis, and is also found in asthma and in certain skin diseases. The experimental production of eosinophilia in animals by the injection of abnormal protein and in anaphylaxis suggests that when eosinophilia is present clinically a foreign protein has gained access to the blood. An abnormal number of large lymphocytes or monocytes commonly occurs in malaria and other protozoal diseases which suggests that these cells have a special protective power in relation to such parasites. Basophils sometimes appear in large numbers, in leukæmia, polycythæmia, and chronic inflammation of the nasal sinuses.

The total *number* of white corpuscles is very variable. At rest they vary from 6,000 to 10,000 per cubic millimetre. In old age the number tends to diminish. Almost any form of activity, even the taking of food, a cold bath, or exercise, brings about normally a leucocytosis as does also the administration of certain drugs, such as potassium chlorate, thyroid extract, and essential oils. A pyrexia accompanied by a leucocytosis almost invariably indicates an invasion by bacteria and, if associated also with a steady rise in polymorphs, the presence of pus. The one important exception to this is lymphadenoma or Hodgkin's disease, but here the leucocytosis is more often relative than actual. Since a leucocytosis is an indication that the body is responding properly, its absence is an omen of grave significance in acute infective disease, as it shows that the marrow is overwhelmed by the poison. From 20,000 to 100,000 per cubic millimetre may be found when there is a good response. In special instances, such as typhoid and paratyphoid fever and influenza, the absence of leucocytosis may assist the diagnosis, as in these conditions a leucopænia or diminution in the number of leucocytes is constant. The presence of a polymorpho-leucocytosis in conditions where this is not usually present, *e.g.*, enteric fever, is often valuable as indicating the development of some complication.

It has been found by Widal and emphasized by Wilson that the absence of a post-prandial leucocytosis is indicative of liver impairment, as it is considered that this organ can prevent the entrance of substances, especially proteins, into the general circulation. Blood examination, as a test for liver efficiency, is made before and after taking seven ounces of milk instead of breakfast.

Of considerable interest is the *development of the white blood corpuscles*, as in disease more primitive forms than those found normally may be thrown into the circulation. All the blood cells are, like the endothelium of the vessels, developed from the connective tissue or mesenchyme. The general evidence suggests that all the cells are developed from primitive cells which have potentiality to form any variety of blood cell. Considerable difference of opinion exists regarding the details. Some investigators do not accept the monophyletic theory, but there is a general disposition to divide the leucocytes into two great classes. According to Muir, all the leucocytes of the myeloid series are derived from primitive non-granular cells or myeloblasts which have a large single nucleus closely resembling the progenitor of the lymphocytes. The myeloid granular series includes the polymorphs. They all give the indophenol reaction, *i.e.*, give an intense blue with α-naphthol and dimethylparaphenylenediamine. This series may be looked upon as being derived from bone marrow as the result of myeloblastic reaction. The lymphoid non-granular series, which includes the small and large lymphocytes, comes from lymphoid tissue scattered throughout the body, *e.g.*, lymph glands, tonsils, Peyer's patches, and splenic corpuscles. In these structures lymphocyte formation may be seen. Some, *e.g.*, Maximow, differentiate between the large lymphocytes and monocytes. It is believed that the corpuscles are formed extravascularly and find their way into the circulation through the capillary walls. Normally the myelocytes do not leave the bone marrow, but in diseased conditions where the leucocyte-forming tissue appears to proliferate they may be thrown into the circulation. More especially is this so in myelogenous or splenomedullary leukæmia, in which the number of leucocytes (particularly the polymorphonuclear cells and myelocytes) present in the circulation may be over 300,000 per cubic millimetre. In the lymphatic leukæmias, on the other hand, there is an enormous increase in the lymphocytes, either variety predominating. It may also be said that where the leukæmia shows a large proportion (90 per cent) of primitive cells, either lymphoblastic or myeloblastic, the disease is always acute and is soon fatal (Gulland). With a count of 500,000 white cells, consisting mainly of polymorphs and myelocytes, the patient may live for several years. In all forms a certain degree of anæmia with nucleated reds is present, and also enlargement of the spleen. This latter condition is very prominent in spleno-

medullary leukæmia. A moderate leucocytosis may occur after hæmorrhage.

The Blood Platelets.—These small bodies are believed to arise from fragmentation of the giant cells of the bone marrow and number usually some 300,000 per cubic millimetre. Their presence greatly hastens the coagulation of the blood and their reduction is considered to be in part responsible for hæmorrhagic conditions such as purpura. They are reduced in vitamin A deficiency, in anaphylactic shock, in thrombocytopenic purpura (an important diagnostic point in this condition), in agranulocytic anæmia, and in aplastic anæmia. They are few and large in pernicious anæmia. Following hæmorrhage and in trichinosis the platelets increase moderately in number; a large increase occurs in myelogenous leukæmia.

CHAPTER XXII

PHYSIOLOGICAL PRINCIPLES IN RELATION TO CARDIAC EFFICIENCY AND DISEASE

THE physiological aspect of cardiology has been very prominent of recent years, largely owing to the work of Mackenzie, Starling, Lewis, and their pupils. Attention has been particularly focussed on the musculature of the heart. While the state of the valves may, if diseased, be a valuable aid in diagnosis and prognosis, yet it is the power of the muscle to maintain the circulation in spite of the valvular defect, which is the real indication of cardiac efficiency, and which determines the capability of the patient in regard to exercise. Often, the absence of any obvious valvular disease leads to neglect of the condition of the musculature, and to disaster.

Normally, the heart has to deal not only with the blood which reaches it during rest, but also with the greatly increased amount brought to it in exercise.

A heart may be efficient for its resting load, but quite incapable of doing any more work, either in the form of an increased blood-flow from the veins, or an increased resistance to its output. In such a case the muscle is exhausted, indeed some of its fibres may be destroyed by increased intra-cardial tension, or weakened by chemical poisons or the toxins of disease. The most striking example of the latter is seen in diphtheria, in which a patient has been known to fall back dead from cardiac failure on attempting to sit up. Hence, in diphtheria, patients are kept strictly in the recumbent position for several weeks as a routine, for it is quite impossible from the local nature of the lesion to estimate the degree of impairment of the heart. The same applies to all forms of myocarditis and toxæmia, and herein lies the danger of a too vigorous examination of a case of acute pneumonia. In fatty degeneration and infiltration of the heart a similar state of affairs exists, except that in this instance the heart is impaired by the presence of fat which has partly replaced the muscle fibres. In toxæmic cases there is also often superadded the effect of the toxins on the peripheral vessels.

The power of the normal heart to respond to increased demands depends on two factors, namely: that it can increase its rate, and, at the same time, its output per beat. The mechanism whereby the rate is increased has been dealt with. It is obvious that the faster the rate the less is the margin of reserve so far as rate is concerned. Although an increase in rate may deal with the extra load of an increased inflow, what is just as important is load in the form of increased resistance due to contraction of the peripheral vessels or breakdown in a valve. In exercise (see page 131) is added the load of increased inflow. So far as the heart is concerned the effect of both loads is the same. It can be readily shown experimentally that, if the resistance to the circulation is increased within physiological limits, the output of the heart is not affected except for a few beats. The small quantity of blood not expelled is added to the inflowing blood and the cardiac musculature is stretched so that the heart beats more forcibly and overcomes the increased resistance. Similarly, an increased inflow by filling the heart more fully during diastole causes the heart to beat more forcibly. This phenomenon was called by Starling the "Law of the Heart." This law states that the contractile power varies with the length of the fibres. It may, however, be applied to all muscular tissue, since all muscle contracts more forcibly when stretched.

The capacity of the heart, to which there must obviously be a limit, to deal with additional load, is known as the **cardiac reserve,** or power of compensation. On it depends not only the power of the circulation to adapt itself to the increased requirements of exercise, but also, if the reserve is small, the capacity of a person to lead a reasonably normal life. Clinically, therefore, it is important to obtain some idea of the patient's cardiac reserve. To obtain this he must be given some exercise to do, such as bending, hopping, lifting dumb-bells, or stepping on and off a stool. In all such tests the normal habits of the individual must be considered. For example, the lifting of 20-lb. dumb-bells every two seconds for half a minute does not represent much work to a stevedore, but may be a considerable amount for a clerk. Notice should also be taken of any general distress shown by the patient, especially breathlessness. The pulse rate, especially the time taken to return to normal after exercise, is also of value. The physiological value of this observation lies in the fact that the less efficient the heart the more will the blood be banked up on the venous side and the longer will be the time required to get rid of

this venous accumulation which increases the rate of the heart. If one bends down twelve times to touch the toes as nearly as possible, the pulse rate should return to normal in half a minute. If it should not have returned in two minutes, the heart is almost certainly impaired. These tests are somewhat rough, as even such bending may represent a considerable amount of work to a stout person. A variety of exercises should, therefore, be used before arrival at an opinion. These are sometimes known as *Effort Tolerance Tests*.

The 40 mm. Test.—The effect of attempting to maintain by means of expiration a column of mercury at 40 mm. is extensively used in testing air pilots. The test is probably one of the right ventricle, which normally ought to be capable of overcoming easily the obstruction to the passage of blood through the lungs. If the right ventricle is not efficient the venous pressure rises and accelerates the heart.

An Atropine Test.—It seems doubtful if the effects of the administration of atropine have been sufficiently investigated as a means of estimating the cardiac reserve, since there is evidence that vagus tone is closely associated with the power of the heart to adapt itself to the increased venous pressure during exercise. No statistics on this point are available.

The effect of exercise, especially if sudden, is greatly to increase the load on the heart and, if the muscle is in such a state that it cannot deal with this increase, one of two things must happen : the heart may cease to beat and the patient die at once, or it may dilate and evacuate a part of its contents in the reverse direction into the veins instead of the arteries. The dilatation brings about a valvular incompetence, due to disparative size or relative insufficiency, and this may be looked upon as a safety-valve action. This, however, is only temporary, as it obviously throws an additional strain on the chamber behind. In the event of the left ventricle dilating there is an increased resistance in the pulmonary circulation, the right ventricle has to do more work and, as it were, share the burden of what may be disease of the aortic valve. It is important to remember that the pressure in the left ventricle during systole is normally about 40–50 times that in the left auricle. A leak through the mitral valve, although it may have no effect on the arterial pressure, may bring about changes in left auricular pressure amounting to over 200 per cent. That such a condition may produce severe pulmonary symptoms is not then surprising. When, however, it is the tricuspid valve

which becomes enlarged, the extra strain is placed on the right auricle and there is a marked rise in venous pressure with interruption of the venous return to the heart. A patient with such disabilities is considered to be a case of acute heart failure, and if the load is increased beyond the limit of the safety-valve action, the heart, for reasons which will be seen below, may cease to beat. Even if this does not happen, the venous stasis gives rise to all the signs and symptoms of venous engorgement and slowly becomes incompatible with any form of activity. Whether the heart will cease to beat or dilate depends on the state of its musculature and the size of the pericardium, which is primarily designed to prevent sudden stretching.

Function of the Pericardium.—The pericardium is essentially a fibrous sac with all the characteristics of fibrous tissue such as we are familiar with in other parts of the body. Such tissue does not yield to sudden stretching, but it may elongate without rupture to prolonged strain, provided the strain is not excessive. Hence its value in tendons, which do not stretch on rapid muscular contraction, though they may become longer as the result of the growth of bone. This characteristic is realized by the surgeon in the treatment of a torn ligamentum patellæ, and in the formation of scar tissue. The use of the pericardium is also well seen in athletes. Here the load put on the heart is often sudden and excessive. Such persons present many of the features of acute cardiac failure, though there is no failure. The enormous rise in venous pressure is evident from the distension of the veins and the blueness of the face, as after a boat race. But for the pericardium such a high venous pressure would distend the heart during diastole and it might be filled with more blood than it could deal with. The size of the pericardium is such that it does not permit the heart to be filled with more blood than the muscle can evacuate, even in severe exercise. In training for such exercise the cardiac reserve increases sufficiently to deal with the increased blood-flow and resistance.

The above statement does not mean that athletes have enlarged hearts, as is sometimes imagined. The heart of an athlete at rest is not necessarily larger than that of an untrained man, but in exertion the trained heart may enlarge considerably without becoming inefficient. If this were not so it would be impossible to have the enormous increase in the cardiac output not only per minute but per beat, which we know occurs.

The special properties of fibrous tissue indicated above are of

peculiar importance in relation to the heart. They allow the cardiac muscle to hypertrophy and increase in size and yet retain its power of resisting any sudden stretching. It is this property, too, which is taken advantage of when the heart dilates as the result of excessive load. Here we see the difference, however, between what may be called physiological dilatation of the pericardium and dilatation due to disease. If the pressure in the ventricle is frequently above normal the muscle hypertrophies in an attempt to deal with the increased content of blood and the increased tension causes the pericardium to stretch. The hypertrophy, however, may not necessarily keep pace with the increased load on the heart, the increased ventricular pressure continues the dilatation, as we have seen above, and the heart relieves itself by ejecting blood through the inlet valves which become incompetent. There comes a point, then, when, perhaps the heart, and in particular the pericardium, have not dilated sufficiently to permit all the safety-valve incompetence of the auriculo-ventricular valves. If, now, a load is suddenly applied in the form of increased filling or resistance, as in effort, complete heart failure will result, the ventricle failing to drive out its contents. The larger the heart cavity the less is the mechanical advantage at which the cardiac musculature works. Normally, the pericardium maintains the size of the heart, so that its muscle can act at the best mechanical advantage. When it is dilated it is evident that mere increase in the size of its cavities will further increase the mechanical load.

It is the danger of sudden death which has caused it to be stated that digitalis should not be given in disease of the aortic valve unless the mitral valve is incompetent to act as a safety valve. This drug, by prolonging the diastole, might increase the filling to a dangerous extent, but as at the same time it increases the force of the heart the danger is minimized.

Recently the discovery post-mortem that persons who have had reasonably normal health might not have had an intact pericardium has caused the suggestion to be made that its function is merely to prevent the heart from moving about too freely in the chest. Since the absence or rupture of the pericardium cannot be diagnosed during life, it is difficult to find out how far the patient could have withstood great strain. Experimentally animals in which the pericardium is opened are much more liable to acute cardiac dilatation and death from procedures which raise the venous pressure. Further, Heymans has shown that the

capability of the heart to respond to increased filling is reduced if the pericardium of a heart-lung preparation is opened.

Heart Failure.—The COMMON SYMPTOMS AND SIGNS are: breathlessness, the discovery of "a new hill" and palpitation. When the right ventricle fails, cyanosis and venous distension, with, possibly, an obvious venous pulse, become evident.

It might be expected that acute heart failure would be associated with a lowered arterial pressure. This is not necessarily the case, for a fall in blood pressure due to diminished cardiac output is prevented by the action of all the reflex mechanisms which are utilized in hæmorrhage (see page 172). There is, for example, reflex constriction of the vessels of the skin, and this is responsible, no doubt, for the pallor associated with cyanosis in cardiac cases. The engorged veins and venules stand out on a pale background. A falling arterial blood pressure in a cardiac case must be looked upon as an omen of the gravest import.

The palpitation in heart failure is due to the excessive cardiac rate, brought about, as in exercise, by distension of the right auricle. The breathlessness is due to a variety of causes, but principally to pulmonary engorgement and reduction of the vital capacity (see later chapter).

When incompetence of the auriculo-ventricular valves occurs, there is a leak backward into the veins, and the more acute symptoms, such as breathlessness, may disappear from relief of the pulmonary circulation. The signs and symptoms of increased venous pressure continue, such as enlargement of the liver and œdema, while many organs, such as the kidney and stomach, may cease to function properly. Unfortunately, patients do not appreciate the significance of the more chronic signs, such as œdema.

The TREATMENT of acute heart failure, apart from drug therapy, which really is subsidiary, must reduce the amount of work done by the heart to a minimum. The patient is, of course, to be kept in bed and at first to be propped up. This latter procedure is found to add appreciably to his comfort, and it reduces the work of the heart by reducing the venous pressure. Also, by facilitating the descent of the diaphragm, it gives maximum aeration of the lungs.

During the last generation there has been a fashion against the blood-letting which was so common in former days. Its use has been deprecated on the ground that the arterial blood pressure so very rapidly recovered that the blood withdrawal was of no

value. This objection is based on an incomplete knowledge of facts. Although the arterial pressure rapidly recovers, this is mostly due to arterial constriction, but the venous pressure, which also falls, recovers comparatively slowly, as is readily shown experimentally. There may be no diminution in the resistance to the cardiac output, but there can be no doubt that a very large measure of relief must result from the venous fall since the heart is thereby given less blood to force out per beat. The use of blood-letting in properly chosen cardiac cases (which have an obviously raised venous pressure) is certainly indicated on physiological grounds.

If the bleeding (say 30 ounces) is continued until it actually reduces arterial pressure, we may presume that the venous pressure has been very much reduced.

As we have stated, however, as soon as the acute symptoms have passed off, it may be a little difficult for the patient to realize that his movements must still be limited. It may well be made a rule throughout the treatment of cardiac disease in all its stages that the patient should be allowed to do just a little less exercise than will bring about the symptoms of distress mentioned above. For example, he should stop short as soon as he becomes breathless, for any heroic attempt to prolong the exercise would only lead to further impairment due to the strain. So long as there is any indication that the cardiac condition may become worse or there is any œdema, every effort must be made to assist the circulation in the affected parts, and this can be satisfactorily accomplished only by keeping the patient in bed. Since the œdema is due to local anoxæmia and toxæmia, which results from back pressure in the veins, what has been written in regard to blood-letting applies here also, and such treatment must obviously be of value. During the prolonged convalescence it is just as bad for the patient to take too little exercise as to take too much. The heart has to adapt itself to the additional strain thrown on it by increasing the amount and efficiency of its muscle, but, by exercise, this margin of reserve can be appreciably increased. Any increase protects the individual against a strain which may be suddenly thrust upon him in an emergency, and normally we have a considerable degree of cardiac reserve for this purpose. Mental states, such as anxiety and excitement, should be avoided, for they increase the work of the heart and are detrimental to the general well-being of the body, upon which depends adequate hypertrophy. Similarly, in

considering the amount of exercise permitted, due attention has to be paid to the previous habits of the patient, as that to which he is accustomed is less liable to cause strain than a new form. Graduated exercises, provided they are done under supervision, give the patient a certain physical objective, and some spas, such as Nauheim, have specially graduated walks arranged for this purpose. They give the patient something to do, and this is in itself of importance ; otherwise he is apt to become an invalid and introspective. At the same time he must remember that he can no longer live a careless life, and every effort should be made to induce him to lead as simple and as physiological a life as possible.

Massage is often very valuable, as it improves the circulation through and nutrition of the limbs, especially the lower limbs, while putting a minimum strain on the heart.

Drug therapy concerns mostly the more acute cases and here the digitalis series is invaluable. By its use the heart is slowed and the conductivity of the auriculo-ventricular bundle is reduced. It therefore diminishes the number of impulses which can pass down from auricle to ventricle. As is to be expected, the effect of the drug is best seen when the ventricle is receiving an excessive number of impulses from the auricle, as in fibrillation or flutter. The reduction of the number of impulses prevents the heart from having to contract too rapidly, or at irregular intervals ; it therefore becomes more efficient as a pump. Obviously digitalis has to be avoided in a condition of heart-block in which the conductivity of the bundle is already below normal, and a partial heart-block may be converted into a complete heart-block. The use of digitalis has already been discussed on pages 138 and 152.

There is often so much anxiety and fear of death on the part of the patient that small doses of morphia may be necessary, as the mental state itself tends to disorder the cardiac mechanism. An eighth of a *grain* of morphia, with $\frac{1}{100}$ of digitalin or $\frac{1}{250}$ strophanthin, is commonly administered in such an emergency. In this relation hypodermic or intravenous medication is often desirable where there is reason to believe that, secondary to the heart condition, there is impairment of intestinal absorption as the result of venous congestion.

The administration of drugs of the alcohol series is an interesting speculation much adhered to by some physicians. Until lately it was considered that, apart from the sense of confidence given to patients and possibly a little reflex stimulation, they were

of little avail. This view was largely based on experiments on the isolated heart which is not stimulated by therapeutic concentrations of alcohol. It has, however, now been shown that alcohol causes a profound fall of venous pressure which will, if brought about in man, be of considerable relief to the heart. The action of the alcohol is analogous to the effect of blood-letting, which noticeably reduces venous pressure (see page 173). Thus it appears that the older practitioners who have refused to give up alcohol for the relief of the heart are fully justified. Some old physicians used to prescribe intoxicating doses of alcohol as a routine in cases of pneumonia.

The reputation of strychnine in cases of circulatory failure requires some remark, since of recent years the fact that the drug has little effect in the isolated heart has rather led to its disuse. Hale White, on the other hand, goes so far as to say that " patients almost dead from failure of the heart in the course of chronic cardiac disease may sometimes be brought round by a subcutaneous injection of strychnine." This is undoubtedly due to the effect of the drug on the vaso-motor reflexes which are brought into operation in the maintenance of aortic pressure when the cardiac output is reduced. We know that the cardiac contractions depend to a very appreciable extent on the aortic pressure which they maintain. When there is then a mutual failure, the strychnine may just suffice to break the vicious circle.

Adrenaline also is a drug which has been shown to be of immense value experimentally in the treatment of acute heart failure. For reasons discussed later there is reason to believe that its use has not been adequately tested out in cardiac disease, especially in the cardiac emergencies (see " Cardiac Emergencies ").

X-ray Appearances of the Heart.—These afford a valuable aid to diagnosis in certain cases. Considerable experience of the normal is necessary before a sound judgment on the abnormal can be formed. The patient is examined by screening in the antero-posterior and the two oblique positions, note being taken of the form of the shadows and of the degree of pulsation. In certain cases a small quantity of barium sulphate suspension is given to the patient to swallow and the shape of the post-cardiac part of the œsophagus observed, whether it is straight or curved. An enlarged left auricle presses on the gullet, which then curves behind it. Films may be taken if necessary.

In this way the various chambers of the heart can be visualized

to an extent sufficient to reveal any gross alterations in size from the normal. For example, a young subject with a systolic murmur, who has perhaps had rheumatic fever, is suspect of mitral stenosis, although no presystolic bruit is audible. Has this patient a systolic murmur of no importance, or is the murmur evidence of a true *valvular* mitral regurgitation of which stenosis is practically always the accompaniment ? In a number of these cases the left auricle can be demonstrated radiographically to be enlarged. The enlargement is confirmed when the shadow of barium in the œsophagus is curved to an extent abnormal for a young subject, and the presence of such enlargement is strong evidence of mitral stenosis.

In a suspected case of aortic regurgitation there may be a doubtful diastolic murmur only, without clear clinical evidence of enlargement of the left ventricle. The X-rays may then afford some help, for if aortic regurgitation is present there will be observed enlargement of the left ventricle, and excessive pulsation of the aorta. Although the latter also occurs in nervousness and in thyro-toxicosis, these conditions can usually be excluded clinically. The X-ray appearances must, therefore, be considered, in this as in other conditions, in relation to the examination of the patient by what Mackenzie was fond of calling " the unaided senses." Enlargement of the left ventricle, whether due to aortic regurgitation, high blood pressure or other cause, can be readily confirmed (or refuted) by X-ray examination and in a subject with a thick chest wall in whom such enlargement is suspected is a valuable supplement to clinical examination.

Dilatation of the aorta, which results from atheroma with or without high blood pressure, produces a characteristic appearance. In the anteroposterior view, the aortic " knuckle " visible in the left of the superior mediastinum is higher than normal, on account of lengthening and " unfolding " of the vessel which is also widened. In the oblique view the widening and " unfolding " cause the " aortic pedicle " to look very broad and in some cases of high blood pressure the pedicle appears almost as large as the heart. In cases of atheroma, if a plate is taken with the tube placed 6 feet away from the patient, so that a parallel beam of X-rays is obtained, the calcified plaques are often visible.

Aneurysms of the aorta are visible by X-rays, and special stress is laid on the distinct and rounded outline of the abnormal shadow and its continuity with that of the aorta. The chief difficulty in diagnosis is the distinction from mediastinal new growths.

Contrary to what might be expected clinically, the transmitted pulsation in cases of neoplasm is more easily visible on the screen than is the expansile pulsation of aneurysm. The X-ray findings are to be considered in the light of signs and symptoms and of pathological tests, and should not be regarded as infallible.

Pericardial effusion gives rise to a characteristic " boot-shaped " shadow.

CHAPTER XXIII

BREATHING AND FAILURE OF RESPIRATION

Breathing, in its broad sense, is the movement made by the body to change the air in the alveoli of the lungs. As such it may be considered the external expression of the body of its need for the supply of oxygen and the removal of carbon dioxide, which are essential for the maintenance of the full function of any tissue. The blood must therefore be capable of performing this double function in accordance with the needs of the tissues, which may vary enormously according to their activity. To ensure this, the oxygen and carbon dioxide must be maintained at a constant level and provision made for varying requirements. Now the effect of increased tissue activity is to increase the demand for oxygen for oxidation and to cause a greater production of carbon dioxide; if these gases are to be maintained at a constant level in the blood, it follows that there must be better loading of oxygen and unloading of carbon dioxide in the lungs. This is brought about by variations of breathing and must be delicately adjusted to the requirements of the tissues. It is brought about by the activity of the respiratory centre. (Although the term "respiratory centre" is used, the work of Lumsden indicates that respiration depends on a much less localized area than used to be imagined, and it would perhaps be more accurate to use the plural.) The respiratory centres, which lie in the pons and medulla, act as a gauge of the carbon dioxide and are much more delicate than any instrument known to science.

When the carbon dioxide is increased, the respiratory centre is stimulated, the breathing increased, and the extra carbon dioxide is eliminated. In the same way a fall of this gas in the blood causes a cessation of respiration. Excess of carbon dioxide is more important as a stimulant of the respiratory centre than lack of oxygen. The latter, however, has been shown to be effective as a stimulus and in varying the sensitivity of the centre to carbon dioxide, possibly by facilitating the production of lactic acid in the centre itself. In actual fact, except in pathological states and rare conditions which cannot be considered

possible in the life of the primitive animal, deficiency in oxygen and excess of carbon dioxide occur together, and even if the centre reacts only to carbon dioxide, the supply of oxygen is safeguarded. At rest, and still more in sleep, the oxygen requirement is small, but little carbon dioxide is produced, and the breathing is so slight as to be imperceptible to the individual. The more active he is, the greater is the requirement of oxygen and the greater the tendency for carbon dioxide to accumulate in the blood and cause a corresponding increase in breathing. At the end of severe exercise breathing is very laboured. This is physiological dyspnœa or breathlessness in which the body gets rid of the extra carbon dioxide which has been produced during the exercise. We shall see, however, that the body may get rid of carbon dioxide in anticipation of exercise or may utilize the excretion of carbon dioxide by the lungs as a method of removing acid from the body.

To understand breathing thoroughly we must appreciate what is happening in the lungs. There the blood is, as it were, spread out on an enormous surface where it is exposed to the alveolar air with which it rapidly gets into gaseous equilibrium through the extremely thin walls of the blood-vessels, the same cells acting as a wall to the capillaries and to the alveoli.

Such a large surface in the body can be secured only by the anatomical arrangement existing in the lung, comparable to the enormous surface exhibited by the leaves of a tree which, indeed, are developed for a similar purpose. But the anatomical arrangement does not permit the mixture of alveolar air and outside air at a speed sufficient to satisfy the requirements of the blood if that mixture is dependent on diffusion alone. This can only be done by replacing mechanically a large amount of air in the respiratory tract by the process we know as breathing.

Breathlessness.—Breathing, we have seen, depends on a number of factors : the respiratory centre, the replacement of the alveolar air, the circulation of the blood, the quality of the blood, the quality of the air breathed, and all those organs which assist in maintaining the neutrality of the blood. If any of these factors fails, with the exception of the centre itself, breathlessness results, provided the cause is not too acute. If the cause of the breathlessness becomes acute it leads to failure of the respiratory centre from asphyxia, *i.e.*, oxygen-want and the accumulation of carbon dioxide. It is interesting to observe that although small amounts of carbon dioxide stimulate respiration, the sudden breathing of

pure carbon dioxide, such as may occur in descent into a well, results in sudden unconsciousness and almost immediate death: the carbon dioxide acts as a narcotic and cardiac poison.

The Respiratory Centre.—We have already seen that the gaseous content of the blood is the main determining factor in the activity of the respiratory centre. This matter is dealt with further under "Cerebral Circulation."

Variations in the activity of centres other than simple increase are dealt with under "Types of Respiration."

It is well known that the emotions frequently cause great increases in respiration. The respiratory mechanism is, as it were, anticipatory, and we have seen that there is a similar increased activity on the part of the heart. Fear of news which the physician may impart is often a sufficient stimulus, and the practitioner knows that if he wishes to count the respirations it is desirable to hide his intention of so doing.

The increased respiration which occurs on stimulation of sensory nerves is no doubt of a similar nature and part of a primitive defensive mechanism by which the animal is at once made ready for increased activity. As the results of the increased breathing, carbon dioxide is washed out and immediate respiration is not essential. This may be imitated in voluntary forced breathing, after which there is a period of apnœa. Such a period will obviously be of immense value in a sudden emergency as more time will be available before the accumulation of carbon dioxide renders respiration imperative. In muscle work the accumulation of carbon dioxide is more important than oxygen supply, which, although necessary in the recovery process, may not be absolutely essential for muscle contraction. Indeed an oxygen debt may be established: that is, a muscle contracts, but all the oxygen required for its recovery from the contraction is taken up later. This is true, not only for isolated muscle, but for the body as a whole (Hill). Stimulation of respiration may be brought about by stimulation of any sensory nerve: slapping with a towel, rubbing the chest or face, pulling out the tongue, are all methods in frequent use by the anæsthetist and accoucheur when breathing is not satisfactory. In operations on the breast, the effect of such stimulation may be very marked, and care must be taken that the patient does not get an overdose of the anæsthetic as a result.

The breathlessness of some cardiac cases may be due to a similar sensory stimulation within the pulmonary circulation (*q.v.*).

The temperature of the blood has now been shown to affect the sensitivity of the respiratory centre. Bazett and Haldane have shown that the excessive respiration may bring about a marked loss of carbon dioxide, and in order to maintain the body neutrality there is an increased alkali excretion by the kidneys. This will be of value in exercise, and in pyrexia the quickened respiration may be partially caused by the increased temperature.

Failure of the respiratory centre is of serious importance and is a common cause of death, as has been indicated in Chapter I. Not only is it a cause of sudden death, but it is also a method by which death is brought about in many chronic conditions. Failure of the respiration in such conditions occurs by exhaustion of the centre or the loss of neutrality of the blood. Failure is also caused by the extension upwards of spinal disease or downwards of cerebral disease, and also by increased intra-cranial pressure. The complete failure is often preceded by a change in the type of respiration (see " Types of Respiration "). Clinically, failure as the result of the action of poisons is fairly often seen. Opium, anæsthetics, and alcohol are well known to cause death in this way, and the principle of treatment in emergencies will be indicated later. Such failure is the common termination of nervous diseases, such as bulbar paralysis, where the degeneration slowly affects the centre. In such cases the mentality may be good, depending on the nature of the condition, until a few minutes before death. But many normal functions will have already been lost and death will be a merciful release from a pitiful existence ; these cases, though prolonged, are hopeless from the first. Fortunately, many are carried away by inter-current disease at an early stage.

The centre may also fail, as emphasized by Yandell Henderson and his co-workers, from an excessive loss of carbon dioxide (acapnia), and this is specially liable to occur during anæsthesia. In the first instance there is an excessive stimulation of the centre due to the operative procedures—especially if the anæsthesia is light. There results a washing-out of carbon dioxide from the body and a stage is reached when there is insufficient to stimulate the centre, which is already depressed by the anæsthetic. Death ensues from oxygen want unless respiration can be made to recommence by the administration of carbon dioxide and sensory stimulation. A less severe acapnia may result in a variety of surgical shock, as the activity of the vaso-motor centre is also dependent on the carbon dioxide content of the blood.

The partial failure of the respiratory centre may be the result of exhaustion. Such fatigue is seen if respiration is obstructed, and is shown by a shallow respiration (see " Types of Respiration ").

A more chronic form of fatigue may be brought about in conditions such as adenoids and cancerous obstruction of the larynx, with the result that the carbon dioxide finds its exit by channels other than by the respiration, by the kidney, and possibly by the skin ; as the result, however, of the diminished breathing, a very chronic form of anoxæmia is sometimes seen.

In judicial hanging in England, death is really due to failure of the respiratory centre to transmit impulses to the muscles of respiration because of the destruction of the spinal cord, shock rendering the individual immediately unconscious.

Respiratory Surface.—In putting forward a general conception of the nature of respiration in the lung, it has been shown that a minimum surface is necessary, together with additional surface in reserve for increased activity. Actually the internal surface of the lung is much beyond the requirements of the resting organism. One lung would supply sufficient oxygen and remove the necessary carbon dioxide. This is seen experimentally, or in pleurisy with effusion, and is even taken advantage of in the treatment of pulmonary tuberculosis, where one lung is put at rest by an artificial pneumothorax. Normally, a large amount of both lungs is not being used. The extra surface is available in exercise and is used in deep breathing. By increasing the rapidity with which the air in the respiratory tract is changed, aeration of the blood is further benefited. The surface available depends on the individual development of the chest. The simple measurement of its circumference at its widest part gives the clinician an idea of the amount of respiratory surface available, provided there is nothing pathological in the lungs themselves. The average circumference is from 34 inches in expiration to 37 in inspiration, but wide variations occur in persons of different stature and training. The difference between these measurements gives some indication of the spare surface available, but probably only a small part of it, since in men diaphragmatic breathing is so great. It is, however, an indication of the vital capacity, which, as we shall see below, is of very considerable importance.

Certain parts of the lung, as the apices and roots, are normally less used than others, and we know that these parts are very liable to become the seat of tuberculous disease. Limitations of expansion indicate deficiency in the spare surface, but this is not

necessarily to be seen in the depth of respiration. Thus, if one part of the lung is prevented from expanding and normal chest movements occur, the other parts will expand to fill up the space made by the chest on inspiration. In this way we have what is known as compensatory emphysema. Clinically, the finding of such patchy emphysema is often of diagnostic value, as it may indicate local lack of expansion elsewhere, *e.g.*, deep pneumonia or pressure on the lung.

Diminution of the surface is a common clinical condition and may be brought about by affections leading to pressure from without or interference with the surface from within. Typical instances of pressure from without are seen in pleurisy with effusion, empyema, and hydrothorax. In these conditions the residual air, *i.e.*, the 1500 c.c. which cannot normally be forced out of the lung, is slowly driven out and the lung collapses. All conditions such as neoplasm will, of course, have the same effect, and although the pressure, *e.g.*, of fluid, may be removed, the lung does not necessarily expand at once, as it may be prevented from doing so by thickening of the pleura, the result of the inflammatory condition. The sudden withdrawal of the fluid may so increase the negative pressure in the chest that disastrous effects, such as acute dilatation of the heart and displacement of the organs to the side of lesser pressure, may occur. This is guarded against by abstaining from removing too large a quantity of fluid at a time.

A similar condition of lung collapse is brought about when the negative pressure disappears, as in pneumothorax or an injury which admits air into the pleural cavity; but fortunately such conditions are usually unilateral, the wound becomes closed off by adhesions between the visceral and parietal pleura, while the air is rapidly absorbed.

Diminution of surface from internal causes in the lung is common. Should, for example, a bronchus or a bronchial tube be blocked (a fairly common condition in bronchitis and pneumonia in children), the air in the peripheral alveoli rapidly becomes absorbed and collapse of the lung ensues. There is then marked reduction of surface. The symptoms of this collapse are essentially different from those due to external pressure. In the first instance they are referable to the interference with the replacement of the alveolar air, but later, when there is a true surface diminution, the symptoms are, for reasons which will be seen later, considerably diminished.

A functional diminution of surface may be said to occur in pulmonary embolism and infarction. In these conditions the blood-vessels of a part of the lung become blocked and the surface supplied ceases to have a functional value. Later, as the result of the inflammatory condition and contraction of the scar, there may be true surface diminution.

In emphysema we have at first an increased surface, but it has lost many of its respiratory qualities, as the alveolar walls and the blood-vessels they contain suffer from tension and pressure effects. In more advanced cases there is actually destruction of the walls and a diminution of the respiratory surface results, although there may be an actual increase in the volume of the lung. There is then both oxygen want and carbon dioxide retention, which are further increased by the lack of adequate replacement of the alveolar air, the result of deficient expiration. Except in very severe and old-standing cases, cavity formation in pulmonary tuberculosis is not sufficient to reduce the respiratory surface appreciably.

Replacement of Alveolar Air.—In order that the acquisition of oxygen and the elimination of carbon dioxide may be adequately carried out, it is necessary that the alveolar air should be maintained at a reasonably constant composition. If this is not done, an adequate respiratory surface will be valueless. This composition is at about 13 per cent oxygen and 5 to 6 per cent carbon dioxide. At these percentages the hæmoglobin of the blood can take up almost its maximum amount of oxygen, and the blood can get rid of as much carbon dioxide as necessary. The level of the latter in different people is remarkably constant, and is kept so by the activities of the respiratory centre. For these centres to act efficiently the mechanism by which the operation is brought about must be acting properly. When we come to consider the anatomy of the lungs and respiratory passages it will be seen that the replacement of air and the bringing into action of the additional surface when required are dependent on the same two factors, namely, the mechanics of respiration and the patency of the respiratory passages ; the vital capacity indicates their efficiency.

Mechanics of Respiration.—Details concerning the mechanics of respiration may be obtained from any physiological textbook. The main point is that the chest cavity is enlarged by muscular action. The ribs are raised, the sternum pushed forward, and the diaphragm descends or, what would be more accurate in view of

the fact that the central tendon does not move much, becomes more conical and less dome-shaped.

Obviously, then, any external interference with the movement of the chest will interfere with replacement. This is fortunately a rare occurrence, but does sometimes occur in crowds. It is stated that in Moscow, in 1896, fifteen hundred people so perished in the crowds which assembled at the feasts in connection with the coronation. In the same category is death of infants, due to the weight of an arm of the parent during sleep. Exhaustion of the respiratory centre may also play a part. Anything which takes up space in the chest acts similarly by reducing the effectiveness of the respiratory movements. Interference with the nerve supply of the muscles concerned produces a similar condition of affairs. This may occur in injury to the nerves, but is also seen in diphtheria, in which the toxin may affect the phrenic nerves only or the intercostals, or both. Artificial respiration and active treatment of the primary condition by anti-toxins are the only hope.

Death from strychnine poisoning or tetanus is of a similar nature. At each inspiration there is normally a reciprocal inhibition (see page 57) of the expiratory muscles, and at each expiration an inhibition of the inspiratory muscles. Large doses of strychnine, however, reverse the normal inhibition so that both sets of muscles pull at the same time. This renders the ribs almost immobile, and replacement of the alveolar air ceases. A fatal asphyxia is therefore liable to occur during one of the convulsions.

Affections of the respiratory centre may be considered as making themselves effective through the nervous mechanism governing the mechanics of respiration. In the rapid shallow breathing associated with exhaustion of the respiratory centre and exaggeration of the Hering-Breuer reflex, the faulty and incomplete aeration of the blood is really brought about by faulty replacement of the alveolar air (see " Types of Respiration ").

Interference with the movements of the diaphragm as the result of abdominal pressure is fairly common, as in ascites and tympanites. If the patient is already making every effort to make the best use of his respiratory apparatus, even normal abdominal pressure may embarrass respiration. All such individuals, more especially cardiac cases, benefit and are more comfortable when propped up in bed instead of lying down; the sitting position tends to relieve the right side of the heart, while the

keeping up of the legs facilitates the return of blood from parts liable to œdema.

The importance of the movement of the diaphragm has been much emphasized by Briscoe in relation to symptoms other than breathlessness. They are described in the chapter on Protective Respiratory Reflexes.

The Patency of the Respiratory Passages.—This is obviously essential for the adequate replacement of air, and we see the failure of this factor in laryngeal and tracheal obstruction. In these cases, not only is the air inadequately changed, but there is, as noted above, a tendency to fatigue the respiratory centre. This occurs typically, where foreign bodies have entered the respiratory passages, in œdema of the glottis, and in diphtheria. Here the symptoms rapidly become acute if untreated and the asphyxia results in death. Less acute cases fail from central fatigue. More chronic forms are seen in neoplasms causing obstruction of the air passages and in bilateral abductor paralysis. In the chronic cases there appears to be a considerable amount of adaptation to accumulation of carbon dioxide ; this is extremely important should the surgeon decide to do a tracheotomy to relieve the breathlessness. A large number of patients so operated on die shortly after operation. It is to be presumed that such death is the result of lack of oxygen dependent on the inadequate stimulation of the respiratory centre. On relief of the obstruction the carbon dioxide in the alveolar air will be reduced and correspondingly that in the blood. In this way too much carbon dioxide may be removed from the blood, so that the respiratory centre is inadequately stimulated. This condition will be further increased by a lessened sensitivity of the centre to carbon dioxide, which appears to be not improbable. An anoxæmia, then, analogous to that which occurs at low barometric pressures, will result.

In asthma, the obstruction is in the bronchial tubes, and all degrees of severity may be seen up to that of severe asphyxia, although it is very seldom fatal, since the asphyxia itself brings about a dilatation of the bronchi partially by direct action and partially by causing a secretion of adrenaline, which is an intensely active broncho-dilator. The individual is in great distress, due to retention of carbon dioxide, but the symptoms depend on the extent to which the different tubes are affected. In those cases where the asphyxia is marked there are noticeable carbon dioxide retention and oxygen want, and the urine is acid.

An inflammatory lesion of the upper air passages other than diphtheria and œdema of the glottis seldom causes respiratory obstruction, though lower down, as in broncho-pneumonia, this is more likely. Here at first there is an adequate surface, but the air of a large number of alveoli is not replaced. Venous blood, therefore, passes to the arterial side, and great distress and cyanosis are evident. Should the condition progress and the alveoli become filled with exudation, the symptoms may be greatly relieved, provided the total surface reduction is not excessive. This is because the exudation presses on the pulmonary capillaries and prevents the passage of venous blood through alveoli which are not aerated.

VITAL CAPACITY.—Of considerable importance in relation to respiratory surface and to the replacement of alveolar air is the vital capacity, *i.e.*, the amount of air which after deep inspiration is expelled on forced expiration, normally about 3,500 c.c. The greater the vital capacity the less frequently will the air in the lungs require to be replaced, since the more air available the longer will it remain of good respiratory quality, while, on taking a breath, the more will be replaced. Further, with a large vital capacity, there usually, but not necessarily, goes a large respiratory surface and both together increase the possible intake of oxygen and removal of carbon dioxide. There is described in physiological literature the instance of a well-known footballer whose normal rate of breathing was 4 to the minute and whose rate after maximum effort was 9 per minute. This man in the process of training had greatly increased his respiratory surface, his vital capacity, and power of replacement, and as his heart was also fully trained, it was impossible to make him out of breath.

The vital capacity may also be influenced (and this can be shown experimentally) by the amount of engorgement in the pulmonary circulation. Several investigators have shown that in cardiac disease the reduction of the vital capacity is an indication of the cardiac efficiency. Some writers, *e.g.*, Means, hold that such reduction plays an important part in the causation of cardiac dyspnœa. In view of the fact that in pleurisy with effusion there may be a great reduction of vital capacity without much dyspnœa, cardiac dyspnœa may be the result of other factors, such as irritation of the vagus, slowing of the circulation etc. Clearly, dyspnœa from any cause will be made worse by reduction of the vital capacity.

The Circulation.—Even when the lungs are equal in every respect

to all respiratory requirements, if the circulation is inefficient breathlessness occurs, whether due merely to lack of training of the cardiac muscle, the accumulation of fat, or cardiac disease. Breathlessness is indeed a cardinal symptom of cardiac disease.

Failure of the circulation may cause breathlessness in three ways —by interfering with the aeration of the blood in the lungs, by delaying the removal of carbon dioxide from the respiratory centres, and indirectly by increasing metabolism (see below).

Recent investigations, especially on the Continent, suggest that carbon dioxide may also have a stimulating effect on the spinal cord nerve impulses from which stimulate the medulla normally. Experimentally, marked delay of the cerebral circulation does not cause breathlessness.

As we have seen, engorgement of the pulmonary circulation reduces the vital capacity of the chest, reduces the surface available for the aeration of the blood, and interferes with the replacement of the alveolar air.

The speed of **pulmonary circulation** is determined by the right ventricle, whose efficiency depends on the amount of work it has to do. This work is determined by the amount of blood and the resistance against which it has to be pumped. Normally, the right ventricle is able to deal with all the blood reaching it from the veins, and provided the pulmonary resistance is not increased, it can always do so. It has been seen in relation to cardiac failure that if the work of the ventricle has already been increased, by its having to pump against excessive resistance, or if the myocardium is weak, a very little additional work may prove too much for the organ. Frequently the primary cause of failure is increased resistance. This may be of two kinds: (1) actual diminution of the cross-sectional area of the blood-vessels, (2) increased resistance to the onward flow of the blood consequent on impairment on the left side of the heart.

The normal ventricle can without difficulty deal with very much more than the normal amount of work. The response of the heart to effort has been fully dealt with (page 160). It is possible to tie one branch of the pulmonary artery without any failure of the ventricle or without even affecting arterial pressure. This has actually been done in man as an emergency measure in severe pulmonary hæmorrhage. On the other hand, gross obstruction of the *main* pulmonary artery by a large embolus is often fatal. In conditions such as pneumonia, the cardiac failure which may occur is only partly due to increased resist-

ance, although this is a large factor. The heart is already weakened by toxæmia, and we have already seen that the rapid shallow breathing which exists in that condition may lead to anoxæmia, which further weakens the heart. In this way, too, the effect of the increased pulmonary resistance in emphysema is emphasized by the effect of the latter condition on the heart. Here the alveolar walls are no longer fully capable of transmitting gases. They are degenerated and the blood-vessels are reduced, while not infrequently the pressure of the alveoli is continued by the original cause of the condition—coughing, the use of wind instruments, etc. Men of the Edinburgh School are familiar with "the three milestones" of bronchitis, so picturesquely named by Wyllie:

1. Failure of acute bronchitis to pass off, and the inception of chronic bronchitis.
2. The production of emphysema as the result of the constant coughing.
3. Cardiac failure due to the emphysema.

In the final stages of emphysema there is increased breathing from a variety of causes—deficient pulmonary epithelium, inadequate replacement of alveolar air, and deficient action of the right ventricle. All of these tend to increase the amount of carbon dioxide in the arterial blood and stimulate the respiratory centre, which is rendered abnormally sensitive by oxygen deficiency. A certain amount of adaptation does occur, but though this may ameliorate the symptoms for a time, the condition is usually progressive. This condition, at first pulmonary, is, in its final stages, one of cardiac failure.

The myocardium may be the seat of primary disease, such as chronic myocarditis, or fatty degeneration, when the pulmonary and systemic circulations are affected simultaneously.

The heart's action may be interfered with from without as in such conditions as neoplasms or pleurisy with effusion which press on the heart. Interference also occurs after pericarditis, in which the pericardium, having become adherent to the heart and mediastinum, limits the cardiac movements.

One of the commonest causes of interference with the pulmonary circulation is impairment of the mitral valve. It may occur as a stenosis or an incompetence, the result of local disease, or from dilatation of the left ventricle consequent on aortic disease. By simultaneous records of aortic, left auricular, pulmonary, and

venous pressures it has been found possible to study such disease (McDowall). Particularly striking is the fact that in mitral incompetence (a usual accompaniment of stenosis also) the slightest variation of arterial pressure is followed by enormous changes in left auricular pressure. This is easy to understand when we remember that the pressure in the left ventricle is 40 to 50 times that in the left auricle. In exercise there is a double strain on the heart, for not only is there an increased venous return to the right side, but there is an enormously increased resistance in the pulmonary circuit, due to its great congestion. It is therefore easy to see why such patients should be so breathless. The congestion must greatly reduce the vital capacity and prevent adequate ventilation. In some instances, especially in stenosis, the dyspnœa is due to the stimulating effect of the high pulmonary pressure on the sensory nerve endings in the lungs. This is shown by the fact that the carbon dioxide of the arterial blood may be below normal.

It has been shown by Peabody and others that in uncompensated cardiac disease with breathlessness there is usually increased basal metabolism, while those who are not breathless have a normal metabolism. The evidence suggests that the compensation somehow causes, possibly by sympathetic stimulation, an increased metabolism which aggravates the breathlessness or that sensory stimulation, which stimulates the respiratory centre, also stimulates metabolism.

The changes in the **cerebral circulation** really depend on the efficiency of the circulation as a whole and may be due in part to failure of the right side of the heart. The respiratory centre itself requires a very small amount of oxygen in a given time. Short of complete anæmia alterations in the amount of blood passing through the centre have therefore little or no effect on respiration. Thus an individual may have his cerebral circulation so reduced that he faints ; yet there is no breathlessness, as the respiratory centre receives sufficient oxygen from the small amount of blood which passes through the brain. In the same way, in carbon monoxide poisoning there is little or no breathlessness at rest. The respiratory centre requires little oxygen compared with that necessary for consciousness. The latter requires a large amount of oxygen in a given time, and slight alterations in the amount of blood that passes through the brain are therefore extremely liable to cause fainting.

Probably the best way to consider the response of the respira-

tory centre to oxygen is to imagine that it requires to be bathed in lymph which contains a very high percentage of this gas. The respiratory centre uses, however, very little oxygen, and so long as the percentage is kept up little need be supplied. To keep up this percentage the concentration of oxygen in the blood must always be higher than that of the local lymph. Suppose, for example, that the blood has taken up in the lungs oxygen to the extent of 18·5 c.c. per cent and that the respiratory centre is bathed in lymph containing 10 per cent. Then oxygen will be given off by the blood to the centre. If, on the other hand, the blood has taken up 9 per cent of oxygen in the lungs, then none will pass from the blood to the centre, however much blood be supplied, and the centre will be rendered sensitive by its want. Thus we see why it is that breathlessness is a common accompaniment of the faulty replacement of alveolar air and also why there is breathlessness at high altitudes. In the latter circumstance the alveolar air may contain 13 per cent of oxygen at a barometric pressure of 530 mm., which is only the equivalent of 9 per cent at 760 mm. (see "Carriage of Oxygen") and the amount taken up by the blood is reduced.

On the other hand, suppose the amount of *functional* hæmoglobin is very small, as in anæmia and carbon monoxide poisoning (where this gas prevents the hæmoglobin from taking up much oxygen), the concentration of oxygen in the available hæmoglobin is normal, and although the blood will not take up so much oxygen per unit volume, it will give up a small amount of gas if exposed to lymph containing 10 per cent. This small amount will be quite sufficient for the respiratory centre, and so long as it is supplied there is no breathlessness, although the total amount of oxygen supplied in a given time may be so small that consciousness is impossible. Thus we see that it is the concentration of oxygen in the blood to which the respiratory centre responds rather than the amount available in a given time, or, in more scientific language, the partial pressure of the oxygen rather than its mass.

Should, however, the cerebral circulation be inadequate, there will be anoxæmia of the respiratory centre. This is well seen in hæmorrhage, provided it is not too severe, in which respiration may be so stimulated that there is a reduction of the alveolar carbon dioxide, and a consequent reduction in the carbon dioxide in the arterial blood.

Cerebral Injury.—The cerebral circulation plays an important part in the production of respiratory symptoms in which there

is increased intra-cranial pressure, such as in cerebral hæmorrhage, middle meningeal hæmorrhage, neoplasm, or injury. In these cases the effect is really due to anæmia of the medulla, the blood-vessels of which are compressed against the foramen magnum as the result of the brain being displaced downwards ; such symptoms can easily be imitated experimentally and the obvious treatment is by trephining or other decompression operation. It is, however, to be noted that, as pressure is not distributed equally through the different subdivisions of the cranial cavity, the trephine opening should be preferably in the subdivision in which the seat of the lesion is and, of course, should it be possible to remove the compressing agent, all the better. This will indicate that a neoplasm, although a very minute one in the region of the medulla, may produce symptoms out of all proportion to its size.

There is also evidence that the breathlessness of uræmia may be of a similar nature, and it has been found by the Hæmoglobin Committee of the Medical Research Council that in uræmia there is not necessarily acidosis. Pal and also Mayer Bisch have pointed out that in such cases the dyspnœa is much relieved by lumbar puncture and that the cerebro-spinal fluid may be under high pressure. Steps taken to reduce the blood pressure by vaso-dilators, severe purgation, bleeding, and lumbar puncture may be of great value in tiding over the emergency.

The Blood as a Respiratory Tissue.—We have seen that if the respiratory centre is inadequately supplied with oxygen its sensitivity to carbon dioxide is increased. Since the oxygen is carried by the hæmoglobin, then we may expect that any inadequacy in the amount of the latter will produce a deficiency in the oxygen-carrying power of the blood. This is seen in anæmia and after hæmorrhage, where there may be a great diminution. In estimating the degree of anæmia the colour of the skin merely indicates, like the estimation of hæmoglobin, the amount of the latter in a given volume. If the total volume of the blood is increased, as Lorrain Smith has shown, in chlorosis, then the total hæmoglobin will not be much below normal, if at all. In other anæmias a small increase in blood volume is also common. In chlorosis, therefore, where the blood volume is definitely increased, the oxygen supply to the brain does not fail so long as the circulation is capable of supplying the blood. The greatly increased heart rate may make palpitation a most distressing symptom.

Excessive breathing in the anæmias must be brought about by the effect of increased carbon dioxide tension and deficiency of

oxygen on the respiratory centre. An anæmic blood is not only deficient as an oxygen carrier but also as a carrier of carbon dioxide. From the work of Hamburger and of L. J. Henderson we know that the corpuscles by making alkali available are definitely responsible for the carriage of carbon dioxide. Most of this gas is carried to the lungs as sodium bicarbonate, the sodium being made available from the sodium chloride in the plasma by the passage of chlorine ions into the corpuscles. If there is a shortage of corpuscles there must also be a shortage of the immediately available alkali in the blood as a whole, although not necessarily in the alkali reserve of the plasma. At the same time the oxygen deficiency of the blood will lead to an excessive production of lactic acid (formed from glucose during the activity of muscle in the absence of sufficient oxygen), which will still further compete for the alkali.

Although a patient is comfortable at rest, in exercise, when carbon dioxide is produced, not only will there be a diminution in the alkali side of the carbonic acid/sodium bicarbonate ratio, but there will be an extra amount of carbon dioxide in solution compared with that which normally occurs in exercise. The increased circulation, by increasing the number of journeys done as it were by each unit of blood between the lungs and tissues, may succeed in preventing an excess of carbon dioxide in the venous blood. In exercise, however, the circulation is unable to compensate any further, although more carbon dioxide and lactic acid are being added to the blood. The carbon dioxide content thus becomes abnormally high, and respiration is stimulated in excess of what would occur if the circulation rate could increase, as it does normally.

The Reaction of the Blood.—Those who are unfamiliar with the method by which carbon dioxide is carried by the blood and the neutrality of the body tissues maintained are advised to refer to the sections on pages 242-247. For the present purpose it is sufficient to recall that this gas is carried to a small extent in physical solution, but mostly combined with sodium as bicarbonate. That in solution is slightly acid, while that in the form of bicarbonate is faintly alkaline. The reaction of the blood may be looked upon as depending on the ratio

$$\frac{\text{carbon dioxide in solution}}{\text{carbon dioxide as bicarbonate.}}$$

Should there be any impairment of the mechanisms by which acids are normally got rid of, however, or if abnormal acids are

produced, these may compete with the carbon dioxide for the available alkali. More carbon dioxide will be thrown into solution, and will be excreted by stimulation of respiration. The respiratory mechanism plays an important part in the maintenance of body neutrality. Conversely, the factors on which the latter depends help to determine the rate of breathing.

In conditions in which the liver, kidney, or pancreas is diseased there is often an upset of the mechanisms controlling body neutrality, and the characteristic breathlessness is the result.

The Quality of the Air Breathed.—This is included for the sake of completeness, but it is of comparatively little clinical importance, although it is of enormous interest to physiology and hygiene. The air may itself contain an excess of carbon dioxide, but it has now been definitely shown that this possibility has been exaggerated, that carbon dioxide in the most stuffy room rarely exceeds 1 per cent, and no serious effect on respiration is appreciable until it has reached 4 per cent. It is clear that the factor which causes the so-called stuffiness in a room is stagnation of air and that if the air is kept in movement it is no longer disagreeable (Leonard Hill).

The air may contain less oxygen and carbon dioxide than normal, but this only occurs at high altitudes or in special chambers. In these circumstances the relative percentage of oxygen and carbon dioxide may remain the same, but at the lower barometric pressures 21 per cent of oxygen will not represent the same amount of oxygen as it does at sea-level, where the molecules of the gas are closer together.

The air may contain poisonous substances which irritate the respiratory passages (*e.g.*, chlorine) and cause them to secrete to an excessive extent or, by causing bronchial spasm, interfere with the replacement of air.

The inspired substance may be absorbed and cause death by central action (*e.g.*, prussic acid gas) or it may combine with the hæmoglobin and reduce the oxygen-carrying power of the blood, *e.g.*, carbon monoxide in coal gas or exhaust gas. Not only does the carbon monoxide prevent oxygen from being taken up, but it also causes the hæmoglobin to hold on more firmly to its oxygen, producing a severe form of anoxæmia which commonly causes death. Even if death is not caused there are usually serious nerve symptoms. The memory and mental powers may be seriously upset, indeed every organ of the body may be left impaired and in particular the blood supply to the heart.

Partial carbon monoxide poisoning has been mistaken for alcoholism.

The essential of treatment is to remove the patient from the poisonous atmosphere and at the same time to keep him warm, as cold tends to aggravate anoxæmia in the same way as it does shock. At one time the stability of carbon monoxide hæmoglobin led to the belief that it was not dissociable at all. This, however, has been shown not to be true, and indicates that cases of carbon monoxide poisoning are not hopeless until they are dead. Artificial respiration may be necessary and the administration of oxygen is most desirable, as it facilitates the dissociation of the abnormal hæmoglobin compound. For reasons explained later, it is now considered good practice to associate 93 per cent oxygen with 7 per cent carbon dioxide (Henderson and Drinker).

This consideration of the factors on which breathing depends will have demonstrated the truth of what was stated in the first few words of the chapter, namely, that breathing expresses the demand of the body for the supply of oxygen and the elimination of carbon dioxide. The tissues make the demand by the amount of carbon dioxide which is produced in activity. The carbon dioxide message is carried by the blood to the respiratory centre, which in turn activates the necessary mechanisms and answers by sending the required amount of oxygen to the tissues. Certain other interrelations exist. The effect of the higher centres on the respiration may be such that the arrival of the message is anticipated and the breathing, together with the circulation, is hastened in advance.

Respiratory Efficiency.—From what has been said above it is clear that the ultimate evidence of the efficiency of respiration lies in the investigation of the oxygen and carbon dioxide content of samples of blood from an artery. While this may be possible in hospital, it is, of course, quite out of the question in ordinary practice, and, at the best of times, it has to be remembered that, although venous puncture is practically painless, arterial puncture may be exquisitely painful. The general practitioner must rely on the ordinary clinical examination of his patient, but in making such an examination a very large number of factors has to be remembered when a breathless patient is being considered. Fortunately the correlation of clinical and post-mortem findings has resulted in an almost perfect system of diagnosis so far as the pathological condition present is concerned, and we owe much to

the pathologists in this respect, a debt possibly too often forgotten. It is, however, essentially in the treatment that the benefits of our knowledge of the mechanisms of symptom production are best seen and, after all, the symptoms are the complaint of the patient for which he primarily seeks relief.

The best indication of the potential respiration efficiency of the normal person is probably the vital capacity. This has already been dealt with on page 216. The general respiratory efficiency, *i.e.*, the efficiency of all the mechanisms responsible ultimately for the maintenance of general tissue oxidations, is indicated by the effect of exercise. Impairment of any of these mechanisms usually gives rise to breathlessness out of proportion to the exercise taken.

TYPES OF RESPIRATION

Shallow respiration is of two kinds, feeble and forceful. The former is seen in anæsthesia when the anæsthetic is sufficient to affect the centre, or it may be the result of exhaustion of the centre from other causes, such as obstruction of the air passages. Failure succeeds abnormal effort. It is on this account that the tubing of respiratory apparatus such as gas masks of divers' helmets should have a bore of at least one inch. Shallow respiration of feeble type is also seen in lesions of the medulla.

Forceful shallow respiration is seen typically in lobar pneumonia and in conditions which greatly reduce the vital capacity but may be produced by the inhalation of irritant gases or in nervous conditions such as neurasthenia, shock, and hysteria, in which there is a great exaggeration of reflexes generally. It is also present in high temperatures.

Since section of the vagi causes such respiration to cease when it is produced experimentally in animals, it may be considered that this type of respiration is a simple exaggeration of the normal Hering-Breuer reflex (Shaw Dunn).

When the lungs are expanded to a certain extent in inspiration an impulse passes up the vagus which results in the inhibition of inspiration and the commencement of expiration; an impulse with the opposite influence passes up the vagus when expiration has proceeded to a certain extent. According to Lumsden the vagi are also stimulated by the passage of the air along the trachea. Respiration is thereby prevented from being excessive and this vagus action is no doubt important in maintaining the reserve respiratory surface necessary for increased activity. In

the chapter on " Exercise " it will be seen that such mechanisms to maintain a reserve are of common occurrence in the body. This mechanism, known as the Hering-Breuer reflex, may become unduly exaggerated in clinical conditions, and this appears to be partly the cause of the rapid shallow breathing in some cases of cardiac disease, pneumonia, pneumothorax, and possibly also in pleurisy. In the two latter conditions the rapid shallow breathing may be brought about by the patient's knowledge that deeper respiration is liable to cause intense pain.

That in pneumonia the shallow breathing is not due to the toxin is seen by the fact that in pneumococcal conditions in other regions such breathing is not seen. Irritation of the thoracic fibres of the vagus or increased sensitivity of the nerve endings leading to exaggeration of the Hering-Breuer reflex seems then to be the most important cause.

Apneustic and Gasping Respiration.—In hæmorrhage, in cerebral anæmia, or if sections of the brain are made from above downward, it is evident that respiration is very definitely changed in type. The first change which occurs is the excessive maintenance of the inspiratory phase (apneustic respiration). The work of Lumsden indicates that this is produced by removal or death of the brain stem above the lower border of the pons. The loss of a little more of the brain results in the animal breathing only in gasps which in turn cease altogether when the vital node in the floor of the fourth ventricle in the medulla is reached. These types of respiration are not necessarily clearly cut ; gasping respiration may, for example, be superimposed on apneustic respiration.

Clinically the importance of these types of respiration is that their appearance heralds the failure of the respiratory mechanism and " the last gasp." Experimentally, very material improvement can often be brought about by the injection of adrenaline, which, next to carbon dioxide, is the best natural stimulant of the respiratory centre. Among drugs lobeline is powerful in this respect.

Cheyne-Stokes Respiration.—Variation in the depth of the respirations may be a normal characteristic of certain individuals especially during sleep, but when the waxing and waning associated with the names of Cheyne and Stokes occur in disease, it is often of serious importance, as they indicate oxygen want at the respiratory centres (Pembrey). This may result from increased intracranial pressure, toxins, or circulatory failure.

Respirations of the Cheyne-Stokes type may be brought on by overventilation in normal man. After such a procedure there is an apnœa or cessation of respiration from lack of carbon dioxide. During this period the oxygen in the blood becomes used up, and the acute oxygen want so produced, which may cause unconsciousness (Poulton), renders the respiratory centre acutely sensitive, so that as soon as small amounts of carbon dioxide accumulate in the blood the centre is overstimulated, again causes a washing-out of the carbon dioxide, and again an apnœa. The administration of oxygen or of carbon dioxide at once relieves the condition (Pembrey).

CHAPTER XXIV

CYANOSIS AND ITS RELATION TO BREATHLESSNESS. ANOXÆMIA AND OXYGEN THERAPY

FROM what has been written with regard to the factors of respiration it is clear that breathlessness or dyspnœa may result from a variety of causes. It may be made more evident by exercise, as the additional carbon dioxide produced accentuates failure of the respiratory mechanism. Ordinarily a patient complains of shortness of breath, when he is inconvenienced by the rate and depth of his breathing. He may, however, have considerably increased respiration, but become so accustomed to it that he fails to notice it and makes no complaint. We shall see further that he may show every evidence of failure in the respiratory mechanism, *e.g.*, the cyanosis of congenital heart conditions, and yet for reasons given below he may not be short of breath. On the other hand, there may be breathlessness without cyanosis, as in the anæmias. Breathlessness does not necessarily indicate oxygen want or the retention of carbon dioxide, although it usually does, while these conditions may exist without there being breathlessness, as, for example, when the respiratory centre is thrown out of action. Nor need oxygen want and the retention of carbon dioxide exist together when there is breathlessness. Either is sufficient to cause the breathlessness. It is clear, then, that breathlessness, although closely allied to and commonly associated with cyanosis, must be looked upon as quite separate from it.

Cyanosis is due to an excessive amount of *reduced* hæmoglobin as distinct from oxyhæmoglobin circulating through the skin and mucous membranes. It will be noted therefore that cyanosis is not seen in the anæmias in which the blood never contains an excessive amount of reduced hæmoglobin even in asphyxia, although the amount of reduced hæmoglobin *relative* to oxyhæmoglobin is increased. Cyanosis may be due (1) to imperfectly aerated blood circulating in the arteries; (2) to a local stagnation or slowing of the circulation in the vessels concerned so that the

blood passing through these regions loses an excessive amount of oxygen ; (3) to the formation of blood pigments.

The circulation of imperfectly aerated blood will result from any condition in which the aerating mechanism of the lung is inefficient or is short-circuited. In both conditions there is invariably breathlessness except in long-standing cases where a marked degree of adaptation has occurred. The cyanosis becomes apparent in any condition which interferes with the replacement of the alveolar air. This, as we have seen, may be due to a reduction in the patency of the respiratory passages, such as occurs in severe bronchitis, laryngeal abductor paralysis, or in asthma, since the venous blood in passing through the lung, or certain areas of the lung, fails to become oxygenated.

It is, however, very striking what curtailment of respiratory efficiency can occur without there being either cyanosis or appreciable breathlessness, as when the lung becomes consolidated, especially as a result of pressure from without. Thus in the more chronic type of pleurisy with effusion, in which the fluid is slowly produced, collapse of a complete lung may take place with so little respiratory distress that the physician is often surprised when he discovers the extent of the effusion. The absence of symptoms in the latter is due to the fact that in the areas affected not only have the airways been closed but the pulmonary circulation has also been cut off. The blood which does pass through the lung, passes through the walls of fully aerated alveoli and is therefore fully oxygenated until at least more than one lung is thrown out of action and the replacement of alveolar air becomes inadequate. It is now generally agreed that pleurisy with effusion is often, if not invariably, of tuberculous origin and a very curious position has arisen. On the one hand it has become common practice to produce an artificial pneumothorax and so to rest an afflicted lung, while on the other there are few who are prepared to look upon an effusion as having a similar protective function. It should be said, however, that the injection of air is more readily controlled than nature's method.

In **pneumonia** the following sequence of events is often seen. For the first day or two the patient is extremely breathless and often cyanosed, since venous blood passes through to the arterial side unchanged as a result of faulty replacement of alveolar air. This is caused by shallow breathing consequent on exaggeration of the Hering-Breuer reflex and by a blockage of the bronchioles

in the area affected. When, however, the consolidation becomes more complete, the patient obviously becomes easier and of a better colour and continues to be so if all goes well. Sometimes. unfortunately, a severer form of cyanosis may ensue, the patient becoming an ashen grey colour. This is of grave significance, and may be due to several causes. The lesion may have so progressed that now the lung surface and replacement of alveolar air are insufficient for adequate aeration ; this is seen particularly in influenzal pneumonia where, post-mortem, the bronchi are found to be blocked with fluid. The Oxford School have emphasized the importance of continued shallow breathing in such cases and the anoxæmia produced thereby. This breathing is held to be the result of the existing anoxæmia which in itself accentuates the shallow breathing. The irritation of the vagus endings in the lung (see page 226) and the increased sensitivity of the respiratory centre probably contribute. However produced, there can be little doubt, as indicated by Haldane, that such breathing must lead to faulty aeration of the lung alveoli with attendant reduction in the aeration of the blood.

Another common cause of this late cyanosis is right ventricular failure due to the toxæmia and probably anoxæmia of the cardiac muscle with increased pulmonary resistance, and there become superimposed upon the original condition the signs and symptoms of cardiac inefficiency. So important do some physicians consider this factor in pneumonia that at the very beginning they do all they can to relieve or improve the right side of the heart.

Right ventricular failure of any appreciable degree marks the failure not only of the pulmonary circulation but of the circulation in general. A general slowing of the circulation is the result, especially in the capillaries where, by giving more time for reduction of the hæmoglobin, it tends further to produce cyanosis. The cyanosis which accompanies chronic venous congestion of cardiac disease is of this nature.

One of the most severe forms of cyanosis is that of **congenital heart disease** where part of the blood is short-circuited through a patent foramen ovale. The cyanosis will depend on the actual degree to which the blood is short-circuited and all varieties are seen, although the severer cases seldom attain adult life. It is often striking that so severe a cyanosis may exist with little or no breathlessness. This is because the blood which does pass through the lungs is capable of carrying more oxygen per c.c. owing to the increased number of red blood corpuscles, so that although there

is an increased amount of reduced hæmoglobin in the mixed arterial blood, there is not necessarily an appreciable increase in carbon dioxide, as this may be got rid of otherwise, *e.g.*, as carbonate in the urine. There are also certain other adaptive mechanisms which exist in other parts of the body.

Cyanosis and dyspnœa in a somewhat peculiar form are also characteristics of asthma.

In **asthma** there is a bronchial constriction with possibly some swelling of the mucous membrane, but there is ample evidence that the constriction may be produced in a variety of ways.

Recent studies with the bronchoscope and X-rays of the bronchial tree indicate that the function of the bronchi is not merely protective as at first sight might appear. It used to be considered that the primary function of the bronchi was to contract when irritated to keep dust out of the lungs, but the investigations of Negus show that animals which could not normally be exposed to dust have excellent bronchial and tracheal muscles. They are best developed in running animals. Further we know that irritant dusts do find their way into the alveoli.

If the bronchi are observed they are seen to close like the larynx at the very beginning of expiration, and it is well recognized that it is extremely difficult to remove a foreign body from a bronchus during expiration. Experimentally, it is difficult to decide whether the closure of the bronchi is active, or passive and due to the movements of the chest (Negus and McDowall), but it is most unlikely that any active constriction of smooth muscle could take place at the speed of respiration. In asthma the difficulty in expiration makes the patient afraid to take a breath. As a result of the faulty replacement of alveolar air, cyanosis results. It is of interest in this connection that in anaphylactic shock, guinea-pigs die from acute over-distension of the lungs produced by bronchial constriction.

What brings about the bronchial constriction in asthma is a problem, but there seems little doubt that the broncho-spasm may be produced in many ways.

(1) The inhalation of irritant or stimulating substances or their production in the bronchial tract, *e.g.*, histamine by bacteria (Knott). There seems to be little doubt that once the bronchial mucous membrane has been irritated, or injured as in bronchitis, it, like the skin, becomes all the more easily irritated, for there is adequate evidence that asthma may be related in its onset to a severe bronchitis. How far a chronic inflammation set up by

bacteria may produce histamine is unknown, but it has been shown that the lung contains large quantities of histamine or its precursors.

(2) By the circulation in the blood of a foreign substance such as a protein in a sensitive person. It should perhaps be noted that it is most unlikely that the absorption of histamine from the intestine will cause broncho-spasm, for if it is absorbed at all, and that is most unlikely, its activity is probably neutralized by an immediate secretion of adrenaline.

(3) By nervous stimulation *via* the vagus in sensitive individuals. The vagus may be stimulated reflexly from the upper respiratory tract (Brodie and Dixon), or it may be stimulated psychologically. It may be shown, for example, that after a dog has been injected several times with apomorphine to produce vomiting, the mere production of the syringe will bring the vomiting about. Similarly, an individual sensitive to roses may develop an attack of asthma on smelling an artificial rose.

The problem of sensitization is, however, a more general one, and is dealt with in a separate section.

The treatment of asthma comes under four distinct headings, directed against local stimulation, protein sensitization and nervous stimulation, and psychological treatment. Many of the treatments in existence are efficacious because they affect one or more of these possibilities. Many, however, are merely palliative, and produce only sympathetic stimulation and dilatation of the bronchi ; amongst these are adrenaline, ephedrine, X-rays, peptone injection. They may, however, be of the greatest value in getting rid of the asthma habit. It is doubtful whether other forms of sympathetic stimulation such as exercise just as the attack begins, the administration of carbon dioxide by causing the patient to inhale his own expired air (*e.g.*, by placing the head under the bedclothes), or the production of more acid by dietetic or therapeutic means have been sufficiently tried. Recent researches have also suggested the administration of potassium to counteract the action of calcium, which constricts the bronchi in cases where the blood potassium is diminished.

How adrenaline acts is unknown, but it is interesting to remark that d'Silva, working for the Asthma Research Council, has recently demonstrated that it sets free a large amount of potassium in the blood.

Hydrochloric acid (Bray) and pepsin to facilitate protein

digestion have been found of great benefit, as also has been desensitisation, which is discussed under " Hypersensitivity."

Attacks which clinically bear a superficial resemblance to true spasmodic asthma are the nocturnal paroxysms of dyspnœa which occur in cases of hypertensive heart disease. For this reason the paroxysms are often loosely spoken of as " cardiac asthma."

ANOXÆMIA OR OXYGEN WANT

In the preceding pages oxygen want or anoxæmia has been frequently mentioned. It is of the greatest importance in medicine, although it may be looked upon as a pathological condition discovered by the physiologists. We owe the beginnings of our knowledge of the subject to the school of J. S. Haldane, whose words on the condition indicate its seriousness :

" Anoxæmia not only stops the machine but it wrecks the machinery."

At the post-mortem the effect of local anoxæmia has long been observed, but it is only of recent years that the effects of general anoxæmia have been clearly recognized. All tissues suffer as the result of oxygen want, but some tissues more than others, and experience shows that nervous tissues are particularly sensitive.

The types of anoxæmia which are met with may be divided into three groups, and Barcroft in describing them has adopted a homely simile. He compares oxygen supply to milk supply and points out that there are three causes which may conspire to deprive your family of milk :—

(1) There may not be enough milk at the dairy. (2) The milk may be adulterated so that what is sold is not really milk. (3) The milkman from that particular dairy may not call.

These three classes he calls the anoxic, the anæmic, and the stagnant types of anoxæmia.

In the *anoxic* type the blood is normal but cannot get sufficient oxygen in the lungs. There is a deficiency in respiratory surface, in replacement of alveolar air, or the quality of the air is poor. This type will include failure of the respiratory centre. In the anæmic type we have failure of the blood to carry sufficient oxygen because of the deficiency in hæmoglobin; while in the stagnant variety there is faulty transport of normal blood which may contain the normal amount of oxygen.

In anoxæmia we look upon oxygen want from the point of view of the tissues rather than the breathing. It must be

clear that anoxæmia is quite distinct from carbon dioxide retention, with which it may or may not be coincident. Anoxæmia may exist with normal or diminished carbon dioxide in the blood.

An anoxæmia without carbon dioxide retention may readily be produced by forced breathing. This procedure washes out the excess of carbon dioxide from the lungs and that of the blood is similarly reduced, with the result that the respiratory centre loses its normal stimulus and there is a period of apnœa (a period during which there is no desire to breathe). The oxygen in the blood is used up during the apnœic period, and before the carbon dioxide has accumulated in the tissues sufficiently to stimulate the respiratory centre the tissues may be seriously affected by the oxygen want.

A similar anoxæmia without carbon dioxide retention is seen in carbon monoxide poisoning, where the hæmoglobin prefers this gas to oxygen and there is rapid oxygen want. This increases the sensitivity of the respiratory centre and the normal carbon dioxide stimulates the respiratory centre to abnormal activity, so that the carbon dioxide in the blood becomes much reduced. The anoxæmia which is the limiting factor in life at high altitudes is similarly associated with excessive loss of carbon dioxide which results from the low barometric pressure and the earlier hyperpnœa of the oxygen want. The fall of carbon dioxide in the blood which occurs in lobar pneumonia when the severe dyspnœa of the first few days has passed off, is of a similar nature and due to the hyperpnœa which may still persist for several reasons.

In all these conditions the anoxæmia of the tissues is further accentuated by what is known as the Bohr effect. Not only does the reduction of carbon dioxide prevent adequate stimulation of the respiratory centre, but just as we have seen that carbon dioxide assists the dissociation of oxygen, so also does lack of carbon dioxide prevent the hæmoglobin from giving up oxygen. It must, however, be admitted that oxygen want, with, at the same time, a reduction of carbon dioxide, must be considered a circumstance for which the body is not prepared, as the Bohr effect suggests. Such states cannot be considered in any sense physiological. They might be regarded as a result of civilization. It is true that in excessive breathing in emotion there is certainly carbon dioxide loss, but this may be looked upon as a preparation for activity and excessive production of carbon dioxide. Where there is carbon dioxide loss the body attempts to restrain otherwise

its output of acid. Thus we find the urine becomes alkaline as the kidney reduces its excretion of acid sodium phosphate and excretes more of the alkaline salts. In the same way no ammonia is required to assist in the excretion of acids and the ammonium salts in the urine are reduced with a corresponding increase in urea.

The physiological treatment of anoxæmia without CO_2 retention is the administration of oxygen and carbon dioxide, the latter being most easily brought about by the patient's rebreathing a certain amount of expired air to which oxygen has been added. This is exactly the procedure adopted in climbing high mountains.

The type of anoxæmia for which the body is particularly well prepared is that which is accompanied by carbon dioxide retention. This occurs in severe exercise during which the body is capable of considerable muscular activity in an emergency when perhaps breathing is impossible or inadequate. Muscular contraction can take place in the absence of oxygen, which is only required in the recovery process. Such contraction must, however, be considered uneconomical, as the lactic acid formed is incompletely utilised and passed into the blood. It is possible then for the muscles to do more work than oxygen supply can keep pace with during the actual period of activity. There is indeed an oxygen debt which can be paid off, as it were, at a more convenient period. A sprinter may run a hundred yards without taking a single breath. During that period, however, the accumulation of lactic acid raises the hydrogen ion concentration of the blood and causes greatly increased respiration as soon as the sprint is over. The oxygen debt may be looked upon as a physiological anoxæmia, as it is evident that the body is well adapted to deal with it. The lactic acid is rapidly excreted as lactates in the urine and at the same time the various organs responsible for maintaining body neutrality increase their activity; the kidneys excrete more acid phosphate and more acid as ammonium salts with a correspondingly smaller amount of urea; the lungs get rid of more carbon dioxide and the intestines retain more alkaline phosphate.

This is a common type of anoxæmia met with clinically. In this category are those cases of oxygen want which occur from inefficient ventilation, such as failure of the mechanism for replacement of alveolar air and diminution of respiratory surface. The hæmoglobin is unable to take up its full charge of oxygen, insufficiently aerated blood circulates in the arteries, and the

patient is very cyanosed and breathless. So far as the hæmoglobin is concerned, the condition is similar to that seen in life at high altitudes, and, according to Barcroft's classification, is considered of the anoxic type. We may then have two kinds of anoxæmia due to a similar cause so far as the hæmoglobin is concerned, *i.e.*, insufficient saturation in the lung; but in one there is carbon dioxide retention which helps to counteract the oxygen want, and in the other (altitude) the condition is aggravated by the co-existing loss of carbon dioxide. In both there is cyanosis from an increased amount of reduced hæmoglobin.

In the *anœmic* type of anoxæmia there is insufficient functional hæmoglobin in circulation. There may or may not be breathlessness, but there is no cyanosis, as all the blood which passes through the lungs is fully aerated. In carbon monoxide poisoning, as we have seen, there may be diminished carbon dioxide in the blood from the initial hyperpnœa, for as a result of the increased sensitivity of the respiratory centre due to oxygen want the breathing settles down to a new carbon dioxide level which is below normal. In the anæmias, however, as stated in the previous section (page 132), there is considerable adaptation on the part of the circulation and it is not until this becomes inadequate that there is actual anoxæmia. Thus anæmic people may be quite comfortable at rest but quite incapable of even moderate exercise.

That individuals who suffer from severe anæmia retain consciousness is scarcely what at first sight would be expected. It is explained by the fact that, as a result of the adaptation of the circulation, the total amount of oxygen supplied to the cerebrum is sufficient. In carbon monoxide poisoning, on the other hand, the total oxygen available in a given time is reduced, and, further, the carbon monoxide prevents the hæmoglobin from giving up its oxygen to the tissues, including the heart, which therefore fails and causes a fall of blood pressure. This exaggerates the lack of oxygen, and the patient may become unconscious.

The *stagnant* type of anoxæmia is seen typically in cardiac failure where there is marked slowing of the circulation. A similar condition of affairs will occur when the blood volume is reduced, as it may be by hæmorrhage, in which the reduction is actual, or in secondary wound shock where the reduction is relative. If it is due to cardiac failure, the anoxæmia is accompanied by cyanosis as the result of the venous congestion, and breathlessness as the result of the slowing of the circulation. This type of anoxæmia

may result from local stagnation consequent on obstruction of the arterial supply of the part, or to the venous return. When there is loss of blood volume every effort is made by the body to maintain the cerebral and pulmonary circulation even at the expense of the less important parts. It is found that if an animal is bled, the blood pressure does not immediately fall, but the limb vessels are constricted to make up for the loss of blood. At the same time, also, loss of blood prevents activity, little heat is produced and the skin vessels are little required. The pallor of the skin in such cases is very marked.

The Symptoms of General Anoxæmia.—These are as yet so little recognized that it requires no excuse to include them in this volume. Anoxæmia prevents full activity of all tissues, and many symptoms hitherto badly understood are merely those of disguised oxygen want. For example, indigestion, so called, is often the result of a poor gastric circulation. The symptoms discussed here are those which have been demonstrated by physiologists as the result of breathing rarefied atmospheres in evacuated chambers, in climbing mountains, in rebreathing from confined vessels, and in breathing carbon monoxide or observing the results of cases of poisoning.

The effect of sudden anoxæmia may be most dramatic and fatal. This is most frequently seen when attempts have been made to enter disused wells, mines, or pits in which there has been an accumulation of carbon dioxide. Instances have occurred in which a man has suddenly become unconscious and fallen when descending a ladder into such a place, and a similar fate has overtaken several rescuers. In such cases the carbon dioxide may be almost undiluted, and the victim does not apparently suffer from warning symptoms. Experimentally acute cerebral anæmia or the inhalation of a strong concentration of carbon dioxide causes an almost immediate cessation of respiration. More usually the anoxæmia seen in disease is slow in onset. Pulse and respiration are stimulated for reasons explained in the preceding pages, and if, at the same time, there is carbon dioxide retention, as there is most frequently in clinical cases, there is also a marked cyanosis. When, however, there is loss of carbon dioxide, the cyanosis is obviously no guide to the degree of anoxæmia present, and this in the past has frequently been misleading, although fortunately such conditions are not common.

The nervous system is specially apt to be affected even without the knowledge of the patient, although the severity may not be

sufficient to cause actual loss of consciousness. Records of balloon ascents indicate that the senses, memory, and judgment may be seriously impaired even to the extent of endangering life. The intrepid balloonists Crocé-Spinelli, Sivel, and Tissandier in 1875 continued to ascend until two of them actually died, although means for their immediate descent were at hand. Experience after mine accidents also indicates that those who, at first sight, appear normal, may act quite irrationally and may simulate the condition of alcoholism. Clinically, restlessness, such as seen after hæmorrhage, is common and all stages from being " slightly off " mentally to delirium and coma are seen. In severe anoxæmia the effect of oxygen want is especially felt by the respiratory centre which rapidly becomes exhausted. Periodic breathing of the Cheyne-Stokes type often heralds the end which is brought about by the central failure.

In the more chronic forms of anoxæmia the mentality shows evidence of fatigue, and the individual may become very irritable and almost a neurasthenic. Clinically, the local effects of such anæmia are fairly common.

Local Anoxæmia.—Here again the onset may be sudden as when there is blockage of an artery from an embolus. Briefly, the symptoms of such a blockage must depend on the organs actually affected and on whether or not a collateral circulation can be established. The acute pain which may be felt is probably caused by stretching of the artery wall which we now know from experimental puncture of arteries to be extremely painful. The rate at which collateral circulation is established is often very great and it may be reasonably efficient. Thus, for example, in embolus of the axillary artery, the circumflex artery may become the main artery of supply to the arm. In areas where such collateral circulation does not exist, such as the cerebrum, the damage is in the nature of things permanent unless, as a result of organization of the embolus, the lumen again becomes patent. Similar effects may result from temporary pressure on an artery, and it is extraordinary how symptoms will persist, such as muscle weakness or, still more, nerve weakness from pressure in the brain, even when the anoxæmia has been of comparatively short duration. Spasm of blood-vessels may in the same way bring about local anoxæmia which may or may not cause serious damage to the tissues. Spasm of the retinal vessels as is sometimes seen after quinine treatment may produce permanent blindness, while in Raynaud's disease the tissues of the fingers and toes may even-

tually become gangrenous. Some consider that the slowly deleterious effects on the brain of epileptic attacks are of similar nature and the symptoms of an epileptic seizure can readily be explained as indicative of arteriospasm, although many factors may be concerned in producing such spasm.

Local anoxæmia may, however, be brought about as a protective mechanism to conserve heat. The blue hands and blue ears so noticeable on a cold day are produced in this way. Here the arterial constriction prevents the blood from reaching the skin and being cooled, while the blood in the capillaries loses its oxygen and becomes very venous in colour. In this respect it must be remembered that the ordinary pink colour of the white races is due to the presence of arterial blood in the skin capillaries.

Should the anoxæmia be the result of venous obstruction, the effect on the capillaries is very striking. The permeability of the vessel wall is markedly increased and fluid passes from the blood into the tissues, giving the clinical condition of œdema. It has been shown quite clearly by Bolton and others that if the venous return from a part is obstructed, the œdema is not produced necessarily during the period of the obstruction but may increase appreciably for a time after the obstruction has been removed. As a therapeutic measure in ulcers of the leg it has been claimed that local applications of oxygen, such as placing the limb in an atmosphere of the gas, bring about improvement. Where the circulation is normally slow, as in the feet, we find œdema particularly liable to occur, and where there has been obstruction to the veins, the œdema is accompanied by distension of the peripheral veins. The fact that œdema is not a marked feature of arterial obstruction is explained by the diminished capillary-pressure and flow which occur at the same time. Should the obstruction be temporary, however, it may be expected that the stage of pallor will be succeeded by a state of swelling, as in Raynaud's disease.

OXYGEN THERAPY

Few methods of treatment so obviously desirable have given such unsatisfactory results in the hands of the unskilled. Failure has generally been due to faulty methods in the administration of oxygen or in an attempt to secure improvement where none could be expected, often indeed when it has been too late. It would be well, then, to consider the conditions under which oxygen therapy may or may not be of value. We have seen

that if the blood is exposed to a gas mixture, as it is in the alveoli, containing 13 per cent of oxygen, it is practically saturated, that is, it takes up the maximum amount of oxygen it is capable of acquiring. Even if the blood is only 90 per cent saturated, which would occur with 9 per cent oxygen in the alveoli, the patient is fairly comfortable, but it has been shown that below this figure he may show signs of breathlessness and mental symptoms indicative of oxygen want (anoxæmia). If then the patient suffers from a condition which seriously interferes with the replacement of alveolar air so that the oxygen in the alveoli is appreciably reduced, the administration of oxygen will obviously be of value. On page 215 it was shown that obstruction in the respiratory passages, as in bronchial asthma, and the rapid shallow breathing of pneumonia and mitral disease, are particularly effective in preventing ventilation of the alveoli. There is no doubt that in such cases oxygen therapy is of great value and that the oxygen circulating in the blood is appreciably increased has been shown by actual investigation, chiefly by Meakins.

If, however, the general alveolar air is approximately normal, no advantage can be gained by increasing the oxygen percentage in the air breathed since the hæmoglobin is already saturated, if it is actually exposed to the air. But, as we have seen, a certain amount of hæmoglobin may not be exposed if certain of the alveoli or bronchioles are blocked and the venous blood gets through to the arteries. The saturation of the mixed blood will then be low. Oxygen therapy in such cases must depend on the amount of oxygen which the increased percentage causes to be taken up, not by the hæmoglobin, but by the plasma. The greater the percentage in the alveoli, the more will be taken up by the plasma, according to the Henry-Dalton Law.

The essential principle of oxygen therapy is therefore that the oxygen percentage in the alveoli must be increased to a maximum, and all methods of administration which do not effect an approximation to this are useless. It used to be thought from experiments on small animals that breathing a high percentage of oxygen would cause pneumonia, but now there is ample evidence that even on a prolonged administration of oxygen this is not so.[1] One point in relation to pneumonia may also be of importance: the pneumococcus is particularly sensitive

[1] This statement is true of oxygen the pressure of which does not exceed ten atmospheres. When, as in a compressed-gas chamber, the pressure of oxygen exceeds this, pneumonia may follow.

to oxygen, which inhibits its growth. Some have thought that the hæmoglobin may be able to take up oxygen from pathological accumulations of fluid in the alveoli if that fluid is saturated with oxygen. But when one considers the slight solubility of oxygen in such fluids it is difficult to see how this can be brought about. Direct solution in the plasma of unaffected alveoli is more possible. After all, the hæmoglobin gives off its oxygen to the tissues by way of the plasma, and the more that fluid holds in solution itself the more will it give to the tissues.

Methods of administering oxygen are various and for general purposes perhaps the original method is the best: the taking of oxygen into the air passages by means of a tube. Let it be said at once that the so-called funnel method is of no value; it does not really enrich the inspired air appreciably, and most of the oxygen, being heavier than air, is spilt from the funnel. The administration of oxygen through a nasal catheter, one nostril being blocked, is a method very generally applicable and is efficient, but unfortunately wasteful. The waste, however, can be materially reduced if an attendant is made to pinch the tube on each expiration. The more an attempt is made to economize the oxygen automatically, the more apparatus is required, and it must be remembered that pneumonia patients—and they are the class usually requiring oxygen—have a sensation of want of air, so that anything which adds to this is not well tolerated. The apparatus of Haldane which has a close-fitting face mask has economy as its aim. There is no doubt that it is efficient, but authoritative opinion is divided regarding its comfort. For hospital use it is possible, but it is doubtful to what extent the patient's friends could be persuaded to allow this procedure in private practice. However, if oxygen is given it must be given freely; according to Meakins, the best method is to pass the oxygen through a tube of 1 cm. diameter and to bubble it through a fluid at such a rate that the bubbles cannot be counted.

The use of special oxygen chambers or bed tents is ideal theoretically, but here again there is difficulty in attending to the wants of the patient whose dry mouth and lips add considerably to his discomfort and constantly require attention. Unless then the chamber is sufficiently large for attendants to get inside the value of such chambers is limited. Bed tents are also notoriously apt to leak and waste oxygen.

There is now ample evidence that oxygen properly given is of great value.

It is further essential not to delay oxygen administration until anoxæmia is extreme. Lack of oxygen favours the growth of most organisms, especially the pneumococcus, it weakens the heart, and the excessive breathing tends to exhaust the respiratory centre. Reference has already been made to the vicious circle which must be broken. So it is seen that if oxygen treatment is not a routine it should always, where the prognosis is bad, be given early and before there is cyanosis; then it must be continued until there is definite evidence that anoxæmia has disappeared.

Recently Yandell Henderson has pointed out the value of the recumbent position in reducing the arterio-venous oxygen difference since it increases the circulatory rate out of proportion to the demand for oxygen. The necessity of reducing muscular activity to a minimum is evident.

CARBON DIOXIDE THERAPY

Largely owing to the pioneer work of Yandell Henderson, carbon dioxide is now often given in conditions in which oxygen used to be administered.[1] It is given primarily to stimulate respiration and the vaso-motor centre when there is no impediment to the access of the atmospheric air to the alveoli. As we have noted, the atmosphere contains practically sufficient oxygen to saturate the blood. Reasons for carbon dioxide administration have already been given—in relation to surgical shock and anæsthesia—but there is good reason to believe that carbon dioxide has a generally stimulating effect on the nervous system, and when this is appreciated it may become much more extensively used. It has been shown by the writer, for example, that the circulatory response of cats to posture fails if the carbon dioxide of the blood is reduced, while in similar circumstances the rigidity of a decerebrate animal disappears but returns if carbon dioxide is administered.

THE RESPIRATORY FUNCTION OF THE BLOOD

The Carriage of Oxygen.—The carriage of oxygen from the lungs to the tissues and the removal of carbon dioxide in the opposite direction are essential to life. Thus, for its vital functions, the body depends to a large extent on the blood, which not only has a respiratory function but also carries nourish-

[1] The use of 7% carbon dioxide and 93% oxygen is now the routine treatment of carbon monoxide poisoning in America (Drinker).

ment and water to the tissues. So long as there is actual fluid in the blood-vessels this last function may be carried out. When we deal, however, with the carriage of oxygen and carbon dioxide we find that the mechanism responsible not infrequently becomes deranged. Although the carriage of oxygen is largely affected by the presence of carbon dioxide and *vice versâ*, it is well in the first instance to consider them separately.

While it is true that any watery fluid can carry a certain amount of oxygen in simple solution, it would be quite impossible for the large amounts of oxygen required by the body to be carried in this way. It can be demonstrated experimentally that if the blood of a frog is replaced by saline solution, and the animal kept in an atmosphere of oxygen, it may continue to live. As, however, the air contains only 21 per cent of oxygen it would be impossible for the animal to live except in a special chamber. For the purpose of carrying gas, therefore, a special chemical substance, hæmoglobin, is utilized in the blood. As a result the blood is capable of carrying forty times the amount of oxygen it would otherwise do. The hæmoglobin enters into chemical combination with the oxygen, and carries it to the tissues. Here the action is reversed, *i.e.*, dissociation occurs and the oxygen is set free. The reversible reaction may be represented thus :

$$Hb + O_2 \rightleftarrows HbO_2$$

If blood is exposed to pure oxygen or even to atmospheric air containing only 21 per cent of oxygen and allowed to take up its full complement, this amounts to 18·5 c.c. per 100 c.c. of blood. This measurement may be made either by exposing the fully oxygenated blood to a vacuum or by the addition of potassium ferricyanide when the oxygen is liberated. The outside air has 21 per cent. Alveolar air has an oxygen content of 13 per cent. This difference is due to the fact that blood is constantly taking up oxygen from the alveoli, and at each respiration only a part of the alveolar air is replaced. If blood is exposed to a mixture of oxygen and nitrogen containing this concentration of oxygen at atmospheric pressure, 100 c.c. still take up 17·3 c.c. Should the mixture contain carbon dioxide (which tends to reduce the amount held) to an extent approximating that which normally exists in the alveoli, it is found that as much as 13·5 c.c. are taken up until the oxygen falls to 9 per cent. Thus we see that the capacity of hæmoglobin to take up oxygen is not only very great, but in atmospheres

containing widely different percentages of oxygen it will take up over 90 per cent of the amount of which it is capable. The importance of this is obvious in relation to oxygen therapy, and it is of enormous advantage to the animal.

Now when we study the giving up of oxygen we have to consider the percentage of oxygen in the tissue fluids and, from the point of view of taking up or giving up this gas, it matters not whether it is in a mixture with other gases or dissolved in fluids. In the tissues the percentage of oxygen is less than 5, and commonly less than 1 per cent, depending on the activity of the tissues and their oxygen requirement. At these percentages, however, the power of the hæmoglobin to hold oxygen is very small. Indeed, if 100 c.c. of blood are exposed to a mixture containing 1 per cent oxygen and carbon dioxide even to the extent to which it is in arterial blood, it will take up only about 2 c.c. Thus in the body, if the blood has been loaded to the extent of 17·3 c.c. per 100, when it arrives at the tissues the additional oxygen is given off, if need be and time permits. In severe exercise the oxygen in the tissues may fall to zero and then the whole of the 17·3 c.c. carried by each 100 c.c. of blood may be set free, but at rest, as the tissue fluids contain about 5 per cent of oxygen, the blood in the veins holds still some 13 c.c. and only 4 c.c. of oxygen are yielded.

These percentages may be expressed graphically in the dissociation curve of blood. Here the rapid falling-off in the amount of oxygen taken up by hæmoglobin, if exposed to percentages under 7 per cent, is clearly seen and the almost negligible quantities which are held are under 1 per cent, which gives the curve a characteristic " s " shape.

This taking in and giving up of oxygen is further facilitated by other factors. Acids such as lactic acid and carbon dioxide noticeably reduce the amount of oxygen held by the blood at low pressures of oxygen, although they do not interfere to any extent with the amount taken at the higher pressures. Similarly, salts and temperature make a marked difference, not only in the rate at which the exchange takes place, but also in the degree of dissociation of the oxyhæmoglobin. It is to be noted that in exercise both heat and carbon dioxide are produced in the tissues which thereby directly facilitate their own oxygen supply when this is desired, quite apart from that brought about by the action of the carbon dioxide on the respiratory and circulatory systems.

What has been said above refers to normal life at pressures

approximately that of sea-level (760 mm. barometric pressure). If we consider life at high altitudes the matter is a little more difficult. Although possibly this circumstance does not come into the purview of many physicians, it has of recent years been a matter of general interest. As we ascend, the barometric pressure decreases approximately 25 mm. for each 900 feet. At 10,000 feet, then, the barometric pressure, instead of being 760 mm., is only about 490 mm. The relative percentages of the gases in the air remain the same, but a corresponding amount of oxygen occupies a very much larger space. To use an analogy, suppose we scatter a mixed dust of red and blue particles, the amount we should be able to collect would depend on the degree of scattering, although the relative percentages of each variety of particle may remain the same. Thus we see how 13 per cent of oxygen at 10,000 feet, so far as the amount of oxygen is concerned in a given volume, is equal to only 7 per cent at sea-level. It is customary to express these percentages in terms of partial pressure. Thus at an atmospheric pressure of 760 mm. the 13 per cent of oxygen which occurs in the alveoli will have a partial pressure of 100, but at 10,000 feet, where the barometric pressure is 490 mm., the partial pressure is but 63·7. The amount of oxygen taken in depends not only on its solubility in blood but on its partial pressure. Thus we see that at 10,000 feet, where there is much less oxygen, the blood will take up very much less oxygen than it does at sea-level. We need but refer to the dissociation curve to see what a difference the partial pressure would make on the amount of oxygen taken up.

The body attempts to compensate for this deficient supply of oxygen by accelerating the circulation and this it does with considerable success. It cannot, however (although the normal amount of oxygen is transported per minute), make up for the fact that the oxygen is loaded at an insufficient tension to which the respiratory centre is specially sensitive. This has been already considered. We have also seen that the amount of carbon dioxide appreciably affects the amount of oxygen which the blood can take up, while the amount of carbon dioxide carried by the blood is likewise affected by its oxygen content.

The Carriage of Carbon Dioxide by the Blood.—Just as the blood is specially adapted for the carriage of oxygen, so also is it adapted for the carriage of carbonic acid, for, just as in the case of oxygen, the body requires so much to be transported that it would be impossible to depend solely on the solution of the gas in the blood.

Further, the blood would become acid in reaction and this is incompatible with life. The actual method by which carbonic acid is carried has been a matter of considerable controversy in the past, but most authorities agree that carbon dioxide from the tissues to the lungs is carried in combination with sodium as sodium bicarbonate ($NaHCO_3$) and a small amount in solution. The sodium bicarbonate is faintly alkaline and the carbonic acid, H_2CO_3 (*i.e.*, $H_2O + CO_2$), is, of course, acid. A balance, therefore, is effected, so that there is no disturbance of the neutrality of the blood provided the amount of carbon dioxide in solution is not in excess. The hydrogen ion concentration of the blood, therefore, may be considered to depend on the ratio $\frac{H_2CO_3}{NaHCO_3}$. Hence there must be a reserve of sodium in the blood for the purpose of uniting with the carbon dioxide, and this alkali we understand as the "alkali reserve" of the blood. Now hæmoglobin itself is an acid, but oxyhæmoglobin is a stronger acid, and as such these substances compete with the carbonic acid for the available alkali. We have seen, however, that the oxyhæmoglobin formed in the lungs is reduced in the tissues to hæmoglobin, and as these substances are not of an equal acidity, it is evident that the competition with the carbonic acid is not a constant one. It is therefore possible for a certain amount of the alkali to alternate, as it were, between the oxyhæmoglobin and the carbon dioxide. In the tissues then, where the oxyhæmoglobin is diminished, the carbon dioxide is able to combine with the sodium to form sodium bicarbonate, while in the lungs the oxyhæmoglobin becomes attached to the alkali and carbon dioxide is given off. Or, it may be said that carbon dioxide is given off, and the oxyhæmoglobin becomes attached to the then available alkali. We have already seen that the less carbonic acid there is in the blood the more oxygen it can contain, and conversely.

The alkaline phosphates can also be made use of to provide sodium, as is seen in relation to the "Neutrality of the Blood," while the proteins of the plasma also supply a small amount of alkali.

We have now given a somewhat general idea of how this carbon dioxide is carried, but unfortunately the actual mechanism is not quite so simple. The alkali in the plasma is largely sodium, but the alkali in the corpuscles is largely potassium and the alkalies do not pass through the walls of the corpuscles readily. The adjustment, therefore, between the corpuscles and plasma has to

be made by the transference of more readily diffusible ions, especially chlorine. In the first instance we may look upon the carbon dioxide (in solution) as acting upon the sodium chloride of the plasma to form bicarbonate and hydrochloric acid, according to the law of mass action :

$$NaCl + CO_2 + H_2O \rightleftharpoons NaHCO_3 + HCl.$$

The hydrochloric acid formed passes at once into the corpuscles to react with the available alkali—in this instance potassium—set free in the reduction of oxyhæmoglobin to hæmoglobin, the latter being a weaker acid. The reactions may be indicated thus, since we do not as yet know the formula of hæmoglobin :

$$K_2HbO_2 + HCl = KCl + O_2 + KHHb$$
$$\text{and } K_2HPO_4 + HCl = KCl + KH_2PO_4.$$

The increased acidity of the acid phosphate is here counterbalanced by the decreased acidity of the hæmoglobin.

From these facts it is evident that the plasma of venous blood contains less chlorides than that of arterial blood, while the corpuscle contains more. Also the sodium which carries the carbon dioxide to the lungs passes back to the tissues as sodium chloride. A small amount of carbon dioxide itself may enter the corpuscle and, acting like the hydrochloric acid, may bring about a similar reaction. It is evident that the carbon dioxide facilitates the liberation of the oxygen. This we know to be the case from what has been stated in relation to oxygen transport. When the blood reaches the lungs it is exposed to conditions where the percentage of carbon dioxide is appreciably lower and that of oxygen higher than in the tissues. These gases are therefore exchanged and, to permit this, the processes described above are reversed.

Although this section is not strictly included in the title of the volume, it is included for completeness, as so much of what it contains is essential for a full knowledge of the subject.

CHAPTER XXV

THE PROTECTIVE RESPIRATORY REFLEXES

THESE reflexes are of the utmost possible importance to the clinician, although of less interest to the physiologist. They are essentially designed for the protection of the lung and are the natural means by which the respiratory tract is cleansed. Dust is continually being inspired and is deposited on the ciliated epithelium of the respiratory tract; by means of the ciliary movement it is brought up to the pharynx, where by a simple movement it is turned over into the œsophagus and swallowed. In inflammatory conditions, however, the mucous membrane may be unduly sensitive and there is then increased secretion in an attempt to wash out the irritant. This secretion itself may further act as a foreign body and irritate the mucous membrane. That secretions and reflexes are protective is commonly recognized, but what is often forgotten is that they are essentially reflexes and as such are liable, like all other reflexes, to exaggeration.

In **sneezing,** the sensory terminals in the upper respiratory tract are stimulated, and by a complicated mechanism with which we are all familiar, air is suddenly released from the lungs through the nose. The reflex concerns the clinician when it is exaggerated, as it is in chronic nasal conditions, which may or may not be associated with active pathological lesions. In many instances there is simple exaggeration of the reflex with possibly severe " running " of the nose and temporary congestion of the mucous membrane. Although the nasal condition may be important and the starting-point of the abnormal state, too much attention must not be paid to this. Some individuals sneeze every morning on getting up, but that this is really an exaggerated simple reflex or a habit is seen by the fact that the sneezing becomes worse during periods of hard work, when all reflexes tend to become exaggerated, and may disappear entirely during holidays. When the sneezing is accompanied by secretion it may be of considerable discomfort to the patient, but it is evident from what has been said above that local treatment is useless if the general state of the health is not improved. Cocaine sprays

or the application of other anæsthetics such as menthol have a deserved reputation in benefiting the condition as they paralyse the sensory terminations. The danger of the former, however, is well known in relation the formation of the cocaine habit.

Cough is a more serious matter and the mechanism of its production requires no description. Any part of the respiratory tract is sensitive although the relative sensitivity of different parts may vary. This is seen from the fact that instruments passed down the tract tend to cause coughing, but so long as the instrument is not being moved the irritation appears to be unappreciable. Thus a tracheotomy tube or even a bronchoscope causes little or no irritation when once it is in position. The pleura also is sensitive, a fact to be remembered in tapping a pleural effusion. If the lung is touched with the point of the needle, the latter must be withdrawn, as cough is likely to cause tearing of the lung against the point of the instrument. In the past it has been customary to describe any irritation of the vagus as causing cough. A stomach cough and even a uterine cough have been described. That these may not exist is not dogmatically denied, but we do know that many of the so-called stomach coughs have subsequently been seen to be really due to pulmonary tuberculosis and that severe stimulation of the vagus in the stomach, such as occurs in operations on that organ under local anæsthesia of the abdominal wall only, does not cause coughing; neither does gastric irritation sufficient to cause vomiting. What appears to be most likely is that those coughs which cannot be explained on a physical basis, *e.g.*, irritated throat or pulmonary bronchitic condition, are habit coughs or exaggerated reflexes and the result of an irritant condition at some previous date. This explains why coughs set up in the first instance by smoking often persist for some time, although the patient ceases to smoke. Physiologically this would be expected from a knowledge of reflexes, and there can be little doubt that this is the explanation of the fact that no fewer than twelve preparations in the pharmacopœia, including the much used Tinct. Camph. Co. and Dover's Powder, designed for the alleviation of cough, contain opium or a derivative which merely acts on the reflex centre. In this light the desirability of stimulating expectorants or of the haphazard doling out of Mist. Expect. Stim. in dispensary work is very doubtful, even though they do give relief in loosening the phlegm. After all, there is a vicious circle, secretion causing cough and cough causing secretion; the longer the cough persists the more

difficult it is to abolish the reflex or reduce it to its normal sensitivity and the more likely is chronic bronchitis to develop. In other words, the reflex nature of the cough must not be lost sight of in an attempt at temporary alleviation. In such cases the mechanical act of coughing, by increasing the pulmonary resistance and thereby overloading and so causing failure of the right ventricle, not to speak of the actual damage to lung tissue, is the real danger to the patient. As yet little attention has been paid to this point in relation to the so-called " winter " cough so common in our islands. It is of first importance to stop the cough even if the sedatives necessary do not add to the comfort of the patient. A winter in sunny climates is often sufficient to prevent a patient from becoming a chronic invalid.

There is little doubt that a considerable psychological element is often added to chronic bronchitis, the bronchitis being a convenient excuse for gaining sympathy or avoiding disagreeable work. The author has known of striking instances of successful treatment by psychotherapy.

Many cases of *asthma* are simply exaggerated reflex phenomena (see " Hypersensitivity ").

Another protective reflex which concerns the clinician is abdominal rigidity—the classical sign of the acute abdomen. The abdominal muscles become rigid in an attempt to protect and prevent movement of underlying viscera and the descent of the diaphragm is decreased. The importance of this reflex lies in its being an aid to diagnosis, and it is obvious that respiration may be affected.

The character of the cough depends on the circumstances in which it is produced. If pain is caused by the cough as in conditions of inflammation of the pleura, *e.g.*, simple pleurisy or pneumonia, the cough is short and suppressed. On the other hand, a loud barking cough often indicates the desire of the patient to attract attention, as in hysteria. The cough of the common cold which may extend to bronchitis with a frequent prolonged paroxysmal—and it may be wheezing—cough is unfortunately familiar to most of us. All varieties of this cough occur.

The husky cough is produced by inflammation of the larynx, while the rapid cough succeeded by a long continued inspiratory stridor or whoop is characteristic of whooping cough. There seems little doubt that there is a largely nervous habit element in this cough after acute symptoms have passed off. This is

suggested by the violent procedures often adopted for its cure. In some parts of Germany a severe whipping is administered to the child as a routine. Possibly the sympathetic stimulation thus caused prevents the spasm of the glottis which produces the whoop.

The most striking cough is that found in conditions which press on the trachea, aneurysm or tumour. This cough, reminiscent of the cry of a gander, once heard is seldom forgotten.

In the later stages of pressure on the recurrent laryngeal nerve, the paralysed left vocal cord fails to approximate to its fellow. The cough thus loses its quality of phonation, and comes to resemble that of the cow.

Sputum may be due to over-secretion by the bronchial mucous glands, to suppuration of the bronchial tree, to expulsion of an alveolar exudate, to suppuration and destruction of the lung tissue, or to rupture of an empyema or other collection of pus into the lung.

The sputum due to the first-named cause is mucoid, the mucin being a product of the activity of the mucous glands. In acute bronchitis the bronchi are at first congested, so that the sputum is scanty and a sensation of tightness in the chest is experienced. Later in the disease the glands secrete more freely and the sputum becomes muco-purulent. The secretion of the bronchi is increased by expectorants most of which act reflexly from the stomach, *e.g.*, ipecacuanha. Certain drugs, *e.g.*, creosote and the iodides, are excreted in small amounts in the bronchial mucus. For this reason creosote is given as a pulmonary antiseptic, but its action is much more potent when the fumes are inhaled. Potassium iodide tends, by increasing the amount of water present, to soften or loosen the sputum. Pilocarpine acts directly on the glandular nerve endings, and the increased secretion of mucus renders the drug dangerous in certain cases when used as a diaphoretic. In plastic or "fibrinous" bronchitis, casts of a portion of the bronchial tree are coughed up following a bout of severe dyspnœa; the cause of their production is not fully understood, but they are formed of coagulated mucin. Casts of the small bronchi, known as Curschmann's spirals, are present in the sputum evacuated after an attack of true asthma. They consist of a central thread with a spirally wound covering and eosinophile leucocytes are entangled in the structure. The mode of their production is as follows. During the attack of asthma mucus is secreted, and in this connection it is interesting to note that the vagus is the secretory as well

as the motor nerve of the bronchi. According to Hurst the mucin is retained at first, and coagulated by the enzyme *mucinase* which is known to be present in the mucosa. When after the paroxysm the plug of mucus is expelled, the ciliary action gives it a spiral motion and in this way the twisted covering is acquired. The Charcot-Leyden crystals also present in asthmatic sputum are probably composed of tyrosine, for they are blackened by the enzyme tyrosinase which is readily obtained from mealworms. The crystals are possibly derived from the leucocytes.

The foul sputum from bronchiectatic cavities is coughed up most abundantly on waking, and getting out of bed. Although sputum from any cause is usually more abundant in the morning, from diminution of the excitability of the cough reflex during sleep, in bronchiectasis another factor is present. The cavities fill up during the night. The subject on waking alters his position and some of the contents of the cavities spills over into healthy bronchi, and coughing is excited. The same mechanism is made use of therapeutically in postural emptying of bronchiectatic cavities, and here the emptying is more complete than in undirected coughing, because the force of gravity is allowed to act for a sufficient length of time.

The sputum in lobar pneumonia is tenacious because the alveolar exudate is rich in fibrin. After the crisis the exudate is liquefied, probably by enyzmes, some is coughed up but some is absorbed. In broncho-pneumonia where there is no such abundance of fibrin, the sputum is looser than in the lobar variety, hence the term "catarrhal" as opposed to "croupous" pneumonia.

When there is destruction of the lung substance, as in ulcerative tuberculosis, abscess or gangrene, elastic fibres appear in the muco-purulent sputum. In tuberculosis, tubercle bacilli will, naturally, be frequently found. The disgusting odour in gangrene is due to the presence of anærobic organisms. The colour of a sputum is sometimes characteristic. Blood mixed with the sputum of a patient who has "brought up blood" is valuable evidence that the bleeding was from the lungs. Anchovy sauce sputum is observed when an amœbic abscess of the liver has ruptured into the lung, but has also been observed in the case of an abscess due to primary cancer of the lung. The rusty colour in lobar pneumonia is due to altered blood to which cause also the tints of "currant jelly" and "prune juice" sputa found occasionally in cases of new growth of the lung are attributed. In

anthracosis the sputum is black, from particles of coal. Many of the particles are contained in special "dust cells," whose presence in the sputum is believed to be due to the stimulating action which coal dust exerts on them. In silicosis the particles of silica are also absorbed by the dust cells, but the cells are not thereby stimulated, and remain *in situ*. Silica predisposes to infection with the tubercle bacillus, whereas carbon particles have no such effect and the retention of the silica in bulk must greatly add to the danger of tuberculosis developing.

In cases of chronic heart failure the sputum contains "heart failure" cells in which particles of hæmosiderin are embedded. The hæmosiderin comes from the red blood corpuscles extravasated from congested blood-vessels.

In cases of superacute pulmonary œdema large amounts of frothy albuminous sputum may be coughed up or well up. The sputum represents a transudation from the pulmonary capillaries which during the attack are engorged. The cause of the engorgement is usually relative failure of the left ventricle in cases of chronic myocardial degeneration, but other causes occasionally operate, such as too rapid paracentesis of a large pleural effusion. To the common cardiac form of acute pulmonary œdema Albutt gave the picturesque term "ventricular defeat." This author regarded "cardiac asthma," the paroxysmal nocturnal dyspnœa so frequent in cases of hypertensive heart disease, as resulting from a less intense degree of ventricular defeat than is present in acute pulmonary œdema. In the treatment of acute pulmonary œdema, atropine as well as morphine should be given, for atropine diminishes the amount of bronchial secretion and dilates the bronchioles, and so allows a free passage for the escape of fluid and prevents additional obstruction of an already encumbered airway.

Protective Pain.—Pain in the chest of pulmonary origin is characteristically accentuated by the respiratory movements. The lung surface is not sensitive in the ordinary sense, but the prick of a needle in tapping a pleurisy with effusion may cause coughing—a point of some importance as it is necessary to withdraw the needle to avoid scratching of the lung surface.

The lining of the chest, on the other hand, is sensitive, and this accounts for the intense pain of pleurisy.

Briscoe has suggested that pain of muscular origin is very common, and he considers it to be due to man's assumption of the

erect posture. This involves abnormal work by some of the thoracic muscles. Within limits they act without complaint, but with greater stimuli they are driven into persistent and excessive tonus. Their protest takes the form of pain and distress which can be relieved by removing the source of the stimulus or by relieving the stress on the muscles mechanically. He has elaborated certain principles of treatment along these lines which will well repay study in the original, as they are valuable not only in immediate treatment, but also in after-treatment of pathological states in which the thoracic movements, especially those of the diaphragm, have become impaired.

Hiccup is a spasmodic inspiration taken through a narrowed glottis, and due to a sudden contraction of the diaphragm. It is usually reflex in origin, the arc passing through the medulla oblongata. Thus it may be excited in normal persons by tickling, particularly in the neighbourhood of the chin. Clinically, it is met with chiefly in irritation of the stomach, as in acute alcoholism and post-operative states. Irritation of the diaphragm as in peritonitis and diaphragmatic pleurisy is a potent cause, and in peritonitis hiccup is a grave omen. Irritation of the phrenic nerves by mediastinal tumour or caseous mediastinal glands or of the phrenic roots by hypertrophic cervical pachymeningitis is a rare but interesting cause. Even then the action must be a reflex one, for the spasm of the glottis implies that the nerve impulses must traverse the medulla oblongata. The hiccuping crises of tabes dorsalis are probably due to irritation of the posterior nerve roots or of the afferent vagus fibres. The mode of production of the serious uræmic hiccup is not well understood. Epidemic hiccup is believed to be related to encephalitis lethargica ; the medulla oblongata is believed to be affected by an inflammatory process. Hiccup may also occur in other intracranial diseases, notably chronic degenerative conditions affecting the bulb. Hiccup is not infrequent in hysteria.

Social hiccup (from excessive laughter, etc.) often yields to a simple respiratory discipline such as that involved in drinking out of the wrong side of a basin. Carminatives are also of value. Severe and protracted forms greatly exhaust the patient. They can sometimes be relieved by firm traction on the tongue, presumably because of the reflex stimulation of normal respiration which this procedure causes. Carbon dioxide, 5 per cent in oxygen, may be inhaled for a few minutes ; and also acts by stimulating normal respiration. Sedative treatment, *e.g.*, the administration

of bromides or of morphia, acts by lowering the excitability of the medulla oblongata. Chloroform inhalation is sometimes necessary.

Breath Sounds.—This subject is already familiar to clinicians, and only the barest essentials of the subject will be given for the benefit of non-clinical readers. When we listen with the stethoscope over the trachea, we hear pure *bronchial* breathing which may be imitated by holding the tongue in the position for the pronunciation of the guttural " ch " of the German word " Ach " or the Scotch word " loch," and breathing loudly by the mouth. Over the chest, however, the sound is obscured or modified by the sound of the air passing to and from the alveoli of the lung which intervenes between the bronchi and the chest wall. This gives the breath sounds their *vesicular* character. During inspiration there is a continuous rushing sound which passes almost imperceptibly into expiration, during which the sounds become less and less distinct. During quiet breathing, expiration is usually inaudible.

In some parts of the chest, *e.g.*, the roots of the lungs at the third dorsal vertebra and over the apex of the right lung above the clavicle and spine of the scapula, probably because of the proximity of the bronchi in these regions, a mixed type of broncho-vesicular breathing may be heard, with a harsh, somewhat blowing, expiration.

In some persons the respirations are irregular or jerky. This has been thought to be due to irregular opening of the bronchi, but it is more probably due to changes in the negative pressure in the chest produced by the heart beat (Hebert).

Weakness or absence of the breath sounds results from interference with conduction of the sound, and occurs in such conditions as thickness of the chest wall, bronchial obstruction, pulmonary fibrosis and collapse, pleural effusion and pneumothorax. In pleural effusion it is the collapse of the subjacent alveoli and bronchi, rather than the fluid, which is responsible, for fluid is a good conductor of sound and in certain cases of effusion, *e.g.*, empyema in childhood, the breath sounds may be deceptively bronchial. Certain types of collapse may, however, cause bronchial breathing, a fact which illustrates the complexity of the acoustics of the chest.

Bronchial breathing is characterized by a distinct pause between inspiration and expiration and by prolongation of the expiratory sound. It is heard over consolidated alveoli as in

pneumonia and also over cavities which are in communication with the bronchi. In consolidation, the breath sounds are high-pitched or " tubular," probably because they are conducted from the smaller tubes by the solid alveoli, whereas over a cavity bronchial breathing is low-pitched or cavernous, the sound being directly conducted from a larger tube. An additional possibility in the case of tubular breathing is selective conduction of the higher pitched tones. Amphoric breathing (Latin *amphora*, a flask), is a variant of cavernous breathing audible over a large cavity or pneumothorax with free communication with a bronchus. This type of abnormal breath sound can be imitated by blowing over the mouth of a bottle. A faint musical tone, superimposed on the low-pitched fundamental tone, gives amphoric breathing its characteristic quality. Post-tussive suction is a sudden short hiss due to inrush of air into a cavity just now emptied by coughing.

Adventitious Sounds.—Wheezing sounds or rhonchi are due to narrowing of the bronchi by swelling of the mucous membrane or by tough mucus. They are sonorous when produced in the coarser tubes, sibilant when arising in the finer tubes. Rhonchi are collectively known as dry sounds in contrast to râles (crepitations of certain authors) or moist sounds. Râles are called moist sounds because moisture is an essential factor in their production, whereas rhonchi depend on partial more or less dry obstruction. Thus coarse and medium râles are due to the bursting of bubbles of air through liquid in the larger and smaller bronchi respectively or in cavities. They are thus heard in bronchitis, tuberculosis, etc. Fine râles or crepitations, which resemble the sounds heard when the hair is rubbed between the fingers, are due to sudden separation of the walls of " sticky " alveoli at the end of inspiration, and thus occur in the early stage of pneumonia when the lung is congested. The congestion of the lung in early heart failure may produce a similar condition.

Râles may be subdivided into resonant and toneless varieties. Resonant râles have a higher pitch than the toneless ones, being produced in solid lung (as in broncho-pneumonia), or else in a cavity which is able to resonate to the sound. When the lung is diffusely as opposed to patchily solid, râles are absent, as in fully developed lobar pneumonia. In this condition râles are heard only at the onset (the fine crepitus indux) and during resolution (the coarser crepitus redux). Metallic râles are an extreme degree of the resonant variety and may be heard over a large cavity or

pneumothorax. Metallic tinkling, sometimes synchronous with the heart beat, may be audible over a pneumothorax, particularly when some fluid is present as well as air.

Pleural friction is a familiar example of an " extra-pulmonary " adventitious sound. For a discussion of adventitious sounds in detail and also vocal resonance and percussion, special works should be consulted.

CHAPTER XXVI

PHYSIOLOGICAL PRINCIPLES IN FEEDING

THE body is primarily designed for the production of work. Like any other machine it must therefore be supplied with fuel, and material for wear and tear. There are certain body processes which require the intake of special ingredients, such as vitamins and salts. At the same time the food has to be in a form suitable for the engine, *i.e.*, it must be suited to the absorptive and digestive mechanisms of the human being, allowing for the conditions under which he lives.

ENERGY SUPPLY AND TISSUE REPAIR

The intake of fuel is mainly in the form of carbohydrates and fats, that of the material for repairs, of proteins. The actual amount of fuel required, as in any engine, depends on the amount of work to be done ; repair is a more constant item, although, the more work, the more wear and tear, and the more protein usage (Cathcart). There are certain vital processes and mechanisms which must be kept going. Even the maintenance of the life of the tissues necessitates the expenditure of energy. A certain amount of protein is also necessary under all conditions. This is the irreducible protein minimum, and as proteins themselves vary in constitution there will be also a minimum of the special proteins which are required as special spare parts. Actually, proteins are such complex substances that, when all that is required for repair has been utilized, the protein molecule has its nitrogen removed and can be utilized as a source of energy. In the body energy is transformed into a variety of forms, such as muscle movement, secretion, and nerve energy, while incidentally a large amount is converted into heat, most of which is useless and is dissipated. Actually only about a fifth of the energy value of the food appears as external work, *i.e.*, muscle work, but even then the body is more efficient than an ordinary steam-engine in which a larger amount of energy is dissipated as heat.

All foods have a certain energy value depending on their chemical constitution. This is expressed in terms of large calories.

one calorie being the amount of heat required to raise the temperature of 1 kgm. of water 1° C.

The determination of the calorific value of foods is carried out by burning the substance (in oxygen) in a small steel vessel known as a bomb calorimeter. The vessel is surrounded by a known volume of water which is again enclosed in a non-conductor. Any rise of temperature brought about by the combustion raises the temperature of the water and from the rise thus brought about the calorific value may be calculated. For the main classes of food they are found to be approximately as follows, the values being given as the energy value of 1 gramme of food substance :

Carbohydrate, 4·1 calories ; fats, 9·3 calories ; proteins, 5·6 calories, but 4·1 in the body.

The energy value of foods burnt in the animal body may be investigated by a somewhat similar experiment in which an animal or man is placed in a chamber where the heat produced can be measured. This kind of experiment gives similar results for carbohydrates and fats, but as protein is incompletely oxidized in the body, the full value (5·6 calories) for the latter is not obtained.

From calculations made in such experiments it is found that a man doing moderate muscular work expends energy to the value of 3,000 to 3,500 calories daily. He must then be supplied with that amount of energy. If he lies in bed with only the essential functions of the body to maintain he will use about 1,700 calories. In the past this conveyed very little to average minds, but rationing during the Great War made us more appreciative of food values. When it is remembered that the Army ration is one of 4,500 calories, it will at once be realized that the average person consumes a diet which is certainly not deficient. The values of average dietaries are of considerable interest for comparative purposes, and where an attempt is being made to reduce or increase the energy intake. They are given at the end of the chapter.

The amount of energy expended at rest is remarkably constant in the same person from day to day, although it may vary over longer periods depending on the conditions of life. This is known as the **basal metabolic rate, or basal metabolism.** For comparative purposes it is expressed in terms of the calories expended per square foot of body surface. Of recent years the subject has become one of considerable clinical importance, for in many diseased conditions it may be of value as an aid to diagnosis and

treatment. Special methods by which the heat value can be calculated indirectly are now in extensive use. A fuller consideration of the subject is given in relation to metabolic rate.

Much interest has centred in the protein constituent of the diet. It is the most expensive part of a diet, and the condition of high blood pressure in adults appears to be associated with it. It is possible to exist on about one-third of the amount of protein usually taken. Compared with carbohydrates and fats, protein requires much more work to be done on the part of certain organs, especially the liver and kidney, and it seems possible that these may be overtaxed.

We have seen that there is an irreducible protein minimum, which depends on the source of the protein and which is less for meat protein than for that derived from vegetables. This is due to the different amount and nature of the amino-acids of which they are composed. Certain amino-acids, such as tryptophane, are essential to life, and from what we know of the chemical constitution of some of the internal secretions (thyroid and adrenal), it appears likely that these amino-acids are necessary for their formation. Special ones are required for the young growing animal, but this does not seem to be so essential in adults who have acquired the facility of forming some of the special amino-acids from their food. For young persons, therefore, no attempt should be made to limit the source of protein. Those which contain most of the amino-acids necessary for the formation of new tissue and blood are of the greatest value. Meat, milk, and eggs head the list, as being the most generally useful, or as having, as we may say, the greatest *biological value.*

Protein has a special property in that it stimulates metabolism. It has been noted that people on a reduced protein diet feel cold, and that the inhabitants of cold climates are almost invariably protein eaters. It must not, however, be forgotten that with meat there is always some associated fat which has a high calorific value. Moreover, the fat "burns in the fire of the carbohydrates," and the proteins fan the flame. If a man is fed almost exclusively on moderate amounts of protein and vegetables (which have but little carbohydrate content) his appetite will be satisfied, but the heat value of his diet may be insufficient for his requirements. One pound of lean meat contains only 1,000 calories, and this is more than can be agreeably taken daily by the average man. Further, even at rest, his metabolism will be

stimulated by the protein. He will therefore use up his own stores of energy and become thin. This is the basis of many forms of treatment for obesity.

If very large quantities of protein are consumed the object of the treatment will be defeated, for the heat value of protein (in the body) is equal to that of carbohydrate. If the amino-acids which result from protein digestion are not required, they are de-aminized and used as fuel. It is notorious that certain individuals become fat on a comparatively low diet. It can only be assumed that such people can carry out work, *if* they work adequately at all, with a minimum expenditure of energy. There is evidence that in such persons protein has a less stimulating action than in others.

We are still in difficulty regarding the amount of protein the diet should contain. On the one hand, we have (as pointed out by Leathes) evidence that an infant, even allowing for its growth, takes ten times that which might be regarded as its normal protein requirement. On the other hand, it is generally considered beneficial to reduce the protein intake in cases of high blood pressure. This effect may be the result of lessened strain on organs such as the kidney or diminution of intake of toxic substances which directly or indirectly cause vaso-constriction, or it may arise from the additional supply of depressor substances from the vegetable diet which usually replaces meat, but other considerations also require to be taken into account (see page 132). Those who take insufficient protein appear to be less capable of withstanding infection and are generally less robust. Halliburton suggested that so-called stamina or reserve force may be dependent on protein and, more recently, J. W. Macleod has drawn attention to the decided inhibitory action which certain amino-acids may have on the growth of bacteria. While this may be so, it is certain that those recovering from illness or building up new tissue require additional protein, as evidenced by the fact that their nitrogen excretion is reduced. Here may be repeated the time-honoured warning against beef and chicken tea which have gained such a reputation in the popular mind. In such decoctions the protein is coagulated in the boiling and falls to the bottom, and the tea, although no doubt deliciously tasty, is about as valuable as the water in which an egg is boiled so far as nourishment is concerned ! It is, however, a valuable stimulant of appetite and of digestive secretion and may be a convenient vehicle by which to convey nourishment when the appetite is flagging.

For men doing very hard muscular work, fat, as emphasized by Starling, is an essential part of the diet just as it is for those who live in the Arctic Regions and have enormous heat loss. When the energy expended is large the necessary intake cannot readily be obtained in carbohydrates, as these in excess become distasteful. Fat with its high calorific value of 9·3 is a concentrated form in which energy may be taken, and if it is not supplied the desire for fat may become a real craving.

At the same time, although we have said that carbohydrate is essentially fuel and may be much reduced, it cannot be entirely replaced by fat. Just as fat is not readily inflammable in the ordinary sense unless it is associated with other combustible material, so also in the body fat requires a more readily oxidizable substance to be burnt with it. The formula of a carbohydrate, *e.g.*, $C_6H_{12}O_6$, indicates that it contains sufficient oxygen to oxidize all its hydrogen to water, and that oxygen is needed only for the carbon. Fatty acids or fats, *e.g.*, palmitic acid, $C_{16}H_{32}O_2$, or tripalmitin, $C_{51}H_{98}O_6$, require oxygen not only for their carbon, but also for the hydrogen before the fat is wholly converted into carbon dioxide and water. Hence, in the burning of carbohydrates, the volume of carbon dioxide produced is equal to that of the oxygen taken in. The **respiratory quotient** (R.Q.), *i.e.*, the ratio

$$\frac{\text{volume of carbon dioxide given out}}{\text{volume of oxygen absorbed}} \text{ is } 1{\cdot}0,$$

whereas in the case of fat the value is 0·7. Here more oxygen is got rid of, not as carbon dioxide, but as water. It is evident that the R.Q. will be an index of the amount of carbohydrate being burnt as compared with fat. On a mixed diet the R.Q. is 0·8 to 0·9, whereas in diabetes (where there is reduction of carbohydrate metabolism) the R.Q. is lowered. On the other hand, in exercise, when a greater proportion of carbohydrate is used, the normal person has a slightly raised R.Q.

The Vitamin Content of Food.—The vitamins are the essential accessory factors of the diet, and so important has this subject now become that its discussion is allotted to a subsequent chapter.

The Suitability of the Food for the Alimentary Canal.—Many of the ailments of everyday life are the result of failure to recognize the importance of this factor. Food must not only be of a certain chemical constitution but it must be appetizing and have a considerable indigestible bulk. The more physiologists study

the subject, the more it is realized that food taken without relish takes longer to be digested. The nervous influences in alimentary secretion (see " Digestion ") are very great and, as the result of the stress of our civilization, too often ignored.

Further, the physical state of the food is of enormous importance. From what we know of the mechanism of ptyalin secretion we believe that carbohydrates should be taken reasonably dry in order that they may be mixed thoroughly with saliva and in order that the ptyalin digestion may be adequately continued in the stomach. Thus the taking of fluid carbohydrates should be condemned, although the practice is common. Such food often contains little or no indigestible material. In this respect specially refined cereals, such as those which constitute milk puddings, are particularly poor.

If the food has insufficient bulk the difficulty of the gut in driving it on may be compared with that of trying to climb a thin steel wire. This would be extremely difficult, for a proper grip cannot be obtained, whereas if the wire were replaced by a thick rope the matter would be easy. The beneficial effects of vegetables and fruits depend largely on the fact that the cellulose they contain remains undigested. Under modern conditions the problem of the supply of such articles of diet at a reasonable cost in winter is no easy one. These substances are also of great value, because of their vitamin content. Many of the benefits of porridge made with coarse oatmeal lie in the large amount of indigestible material associated with its high protein, salt, and carbohydrate content. Its general value is enhanced by the milk taken at the same time. Refined carbohydrates should then be taken in association with as much cellulose as possible. If milk puddings must be taken they should be accompanied with fruit. Coarse bread should be preferred to the finer varieties. Cooking has the effect of allowing digestive enzymes to penetrate better. The diet of the ordinary person is usually in excess of his requirements, and the taking of food in its natural state, though it may be wasteful, has much to commend it (provided it is not too irritant to pass the pylorus), for the undigested parts add much to its bulk. This matter is discussed further in relation to the movements of the intestine.

The physical state of the food also plays a considerable part in the production of dental decay. If a tooth is disused by removal of the opposing one, it too tends to degenerate. In like manner if we take food for which the teeth as a whole are not required, a

similar result will follow. This is further aggravated by the fact that the more bland starchy foods which do not require chewing tend not to stimulate the salivary gland. Sims Wallace has emphasized the large part which the saliva plays in the cleansing of the mouth and the prevention of fermentable food deposits around the teeth.

The Relationship of Nutrition to Sunlight.—It is a familiar fact that people, especially children, are in better health if they live to a large extent in the open air. Particularly has this been impressed upon us by the recent results of the investigations into rickets, which, it has been pointed out by McCarrison, are more common in the poorer classes in this country, but in the better classes in India. The subject is dealt with in more detail in the chapter on "Vitamins," but here it may be stated that it has now been conclusively shown that if a person is exposed to light the vitamin content of his diet need not be so high. Some of the older authors used to consider it possible for the body actually to receive energy from the sun. This may approximate to the truth after all, and certainly in many pathological conditions, *e.g.*, rickets and tuberculosis, sunlight has an undoubtedly beneficial effect. The general experience of the War and of native races suggests that sunlight plays an important part in the production of resistance against bacterial invasion.

Water and Salts.—The water or fluid intake per day should be at least 100 ounces to provide a satisfactory allowance for all the organs. Note here that fruit and vegetables contain over 90 per cent of water. Much constipation is due to an inadequate fluid supply, and various urinary deposits similarly result from the formation of a too concentrated urine. The water supply of the body is considered more fully later.

The salts of the diet are usually left to look after themselves, since the ordinary foods contain an abundance of those necessary. Pathological conditions teach us that the salt supply cannot be altogether neglected. Goitre has now been shown to be the result of iodine deficiency (see "Thyroid"). This salt occurs in many of the common articles of diet, such as onions, carrots, and eggs. The composition of hæmoglobin and the excretion of bile indicate that iron is an essential part of the diet. Phosphates are concerned in the maintenance of body neutrality. They appear also to play an important part as stimulants of intestinal movements. It should also be noted that though iodine and iron are supplied in

sufficient quantity, they may not be absorbed. This may be the result of intestinal conditions, and it is only when the latter are treated that the apparent deficiency is made up. In certain circumstances some salts, such as those of calcium, are more important during growth than others.

The absolute necessity of sodium, potassium, and calcium is seen in relation to the heart-beat, and to the contraction of smooth muscle. Neither will contract or relax normally if not adequately supplied with these ions. For the intestine a trace of magnesium also appears to be beneficial. No definite deficiencies in these salts have as yet been described, except for calcium. It was shown by MacCallum that there is low blood calcium in tetany, and the later work of Vines showed that this was true of parathyroid deficiency in which tetany may be an outstanding symptom. The work of Vines in this respect has not yet been reconciled with that of Noël Paton, who has given evidence that the tetany of parathyroid deficiency is the result of a deficient guanidine metabolism, but from the recent work of Collip it would seem that the reconciliation of the two views is not far distant.

The desirability of varying the sodium chloride content is dealt with in relation to the water content of the body.

The Feeding of Infants.—In the young, body weight and growth are almost inseparable and it is customary to consider the weight as an indication of whether or not a child is thriving. Unfortunately it is imagined that the growth depends entirely on what the child can be persuaded to consume, and many better-class children are often overfed with patent foods. In the poorer classes one meets with underfed babies and, more commonly, badly fed babies. Barley-water and all sorts of uneconomical preparations are used intentionally as substitutes for milk, and some mothers have apparently no conception of what a child can digest. Only recently the writer when in a shop inquired the cause of the severe distress of a baby in an adjacent room. The explanation was that the grandmother was endeavouring to "shove some treacle pudding into it" as it wasn't thriving. Seeing that the child was but a few months old the necessity for baby welfare clinics is obvious.

A normal child when born weighs from six to eleven pounds, and in the first week a few ounces are lost, no doubt because some of the stored energy is utilized in activity, and as lactose is not fully digested. Thereafter there is a gain in weight from 3 to 6 ounces per week, and this is continuous, except during the

time of teething, when there may be an interruption. During the first nine months the ideal food for the infant is its mother's milk, provided the mother's diet is adequate in regard to growth factors (see " Vitamins," below). The importance of ante-natal care, as well as post-natal, in this respect is now realized. It is a significant fact that all wild animals bear their young in spring and early summer, when both additional heat and vitamins are most readily available. The best substitute for human milk is cow's milk, provided the cows are properly fed, and here it may be mentioned that cabbages, kale, and turnips are a convenient source of vitamins for animals fed indoors in winter.

The milk should also be from cows which have passed the test of tuberculosis, but, to the disgrace of our modern civilization be it said, this is declared to be economically impossible at present. The provision of special dairies for the production of nursery milk is very necessary in all cities. Sterilization certainly is a safeguard against tubercle, but even pasteurization destroys the growth factors in the milk and these therefore have to be otherwise supplied.

Artificial foods are of value in proportion as they approximate to the natural milk, but nothing is to be gained by the excessive feeding of an infant. Fat babies do not necessarily become any better adults, and not infrequently the attempt to make them so results in serious upset of the alimentary tract. The following gives a sufficient energy intake for any child :

Six feeds a day, each consisting of 20 minutes at the breast or 3 to 7 ounces of milk from a bottle according to age, is *ample* for any child in the first nine months. As the chemical constitution of cow's milk differs from that of human milk, to the former must be added a half to a third of water to dilute the fat, and 1 teaspoonful of sugar (Demerara sugar is a convenient laxative) to make up the sugar content. Some physicians further add 2 grains of sodium citrate to each feed to prevent the formation of large milk clots.

THE FOOD AND CALORIFIC CONSUMPTION OF THREE NORMAL PERSONS

By R. D. Lawrence, M.A., M.D., Chemical Pathologist, King's College Hospital

The study of dietetics is a science of its own and has little to do with the control of our eating. Our eating is mostly an

instinct, perhaps partly an art, controlled by our appetites and our purses. Not even the dietetic expert chooses and eats his food in terms of calories. But the relation between the two is close and interesting, and, in the study and control of certain diseases such as diabetes and obesity, of great importance.

To give an idea of the exact relation of calories to the food eaten by the normal promptings of appetite, the average diet for the day of three men is recorded below in detail. Although only one day is recorded, other days were observed, and it is felt that the day's diet is fairly representative. No restraint was put upon the amount of food eaten. They helped themselves or asked for second helpings if desired but the food was weighed. The food values used are taken from the Food Tables of Harrison and Lawrence, and although it is somewhat difficult to compute the exact composition of mince pies and treacle cake, the calorific values and weights are as accurate as is ever practicable.

The main object being to show in practical detail the relation between the food eaten and its calorific value and content in carbohydrate, protein, and fat, no special attempt was made to study a perfectly average eater. Indeed, one large eater and one light were purposely chosen to provide a contrast. It is well known that the calorific requirements of the young male adult, leading mostly a sedentary student's life, as these three were doing, is usually from 30 to 40 calories per kilogram of body weight, and it will be seen that the heavy and light eaters fall respectively above and below this average, while the third is normal. All three are English and a few details concerning weight, obesity, etc., are given. It will be seen that the lightest eater is the only one who is at all obese, but it is not clear that this relation of input to output has always been the same.

Case A, aged 25 ; height, 5 ft. 11 in. ; weight, 11 st. 4 lb. (71·6 kgm.). Average weight for height is 10 st. 13 lb., so that he is slightly above weight ; habits not active except that he usually bicycles about 10 miles a day ; noticeably a *big eater*.

Food	Weight in Ounces	Food Content in Grams		
		C.	*P.*	*F.*
Breakfast				
Porridge . . .	10½	35	7	7
Sugar	1	30	0	0

Food	Weight in Ounces	Food Content in Grams		
		C.	*P.*	*F.*
Kipper	$1\frac{1}{2}$	0	8	3
Butter	1	0	0	25
Toast	$2\frac{1}{4}$	45	4	0
Marmalade	$1\frac{1}{8}$	27	0	0
Milk	3	5	4	4
		142	23	39
Lunch				
Roll, bread	1	15	3	0
Sausage	$1\frac{1}{2}$	1	5	12
Potato	4	27	3	0
2 Apples	10	32	1	1
		75	12	13
Tea				
2 Biscuits	1	20	4	0
Milk	2	3	2	2
		23	6	2
Dinner				
Soup, thick	$3\frac{1}{2}$	6	3	2
Steak	7	0	52	26
Pudding	$2\frac{1}{2}$	28	3	3
Onions	$8\frac{1}{4}$	11	2	3
Potato	$7\frac{1}{2}$	50	5	0
Bread	1	15	3	3
Stewed Fruit	4	15	2	0
Custard	$2\frac{1}{2}$	17	4	4
Sugar	$\frac{1}{2}$	15	0	0
		157	74	41
Supper				
Treacle Cake	6	120	3	10
Day's Total		517	118	105
Calories		2,068	472	945

Total Calories = 3,485.
Weight = 71·6 kgm.
= 48·7 calories per kgm. of body weight.

Case B, aged 35 ; height, 5 ft. 2½ in. ; weight, 9 st. 10 lb. (61·6 kgm.). Average weight for height is 8 st. 8 lb., so that he is above the average weight and is noticeably obese ; active and quick in his movements, but takes no exercise, not even walking ; noticeably a *small eater ;* has a distaste for fat and butter ; probably partly restricts his food to avoid obesity.

Food	Weight in Ounces	Food Content in Grams		
		C.	*P.*	*F.*
Breakfast				
Bacon, lean	½	0	5	5
Potato	1	6	1	0
Toast	¾	15	3	0
Marmalade	1	25	0	0
		46	9	5
Lunch				
2 Crumpets	2	30	6	0
Butter, 2 pats	½	0	0	12
Mince Pie	—	20	4	5
Jam Tartlet	—	25	4	0
		75	14	17
Tea				
2 Rock Cakes	1½	22	4	4
Dinner				
Soup, thick	3¼	6	3	2
Steak	3	0	22	11
Pudding	1½	17	2	2
Onions	4¼	6	1	2
Stewed Fruit	7½	28	3	0
		57	31	17
Supper				
2 Biscuits	1	20	4	2
Total for Day		220	62	45
Calories		880	248	405

Total Calories = 1,533.
Weight = 61·6 kgm.
= 24·8 calories per kgm. of body weight.

If we calculate his calorific usage on the average weight, which is more correct in some ways, as his " extra " fat is not metabolically active tissue, then we get the figure of 29 cals. per kgm. of body weight.

Case C, aged 24; height, 5 ft. 11 in.; weight, 9 st. 4 lb. (59 kgm.). Average weight for height is 10 st. 13 lb., so that he is considerably under weight and is quite thin; he is active and plays games occasionally, but not daily; eats slightly less than the average student.

Food	Weight in Ounces	Food Content in Grams		
		C.	*P.*	*F.*
Breakfast				
Porridge	5	16	3	3
Milk	5	7	5	5
Sugar	$\frac{1}{2}$	15	0	0
Bacon	$\frac{1}{2}$	0	3	8
Potato, fried	$2\frac{3}{4}$	20	2	5
Toast	1	20	4	0
Butter	$\frac{1}{4}$	0	0	6
Marmalade	$\frac{3}{4}$	19	0	0
		97	17	27
Lunch				
1 Sausage	—	1	5	12
Potato	6	40	4	0
Brussels Sprouts	4	4	2	0
1 slice Jam Roll	—	25	1	0
		70	12	12
Tea				
1 Banbury Cake	—	20	4	0
Milk	$\frac{1}{2}$	1	0	0
		21	4	0
Dinner				
Soup, thick	$5\frac{1}{4}$	8	4	3
Steak	3	0	22	11
Pudding	1	12	1	1
Potato	3	20	2	0
Onions	2	3	0	1
Stewed Fruit	4	15	2	0
Custard	$1\frac{1}{2}$	10	3	3
Milk	$3\frac{1}{2}$	5	3	3
		73	37	22
Total for Day		261	70	61
Calories		1,044	280	549

Total Calories = 1,873.
Weight = 59 kgm.
= 31·7 calories per kgm. of body weight.

CHAPTER XXVII

VITAMINS

VITAMINS are essential accessory constituents of the diet, but nearer than that we cannot get, for their chemical nature is unknown. Further, the amounts of these substances which we require are infinitesimally small and out of all proportion to their caloric value. We know, however, that they are essential to normal life and growth, and although in the past their supply has offered little difficulty, with the increasing congregation in towns this supply will be a more important problem. And there can be little doubt that many of the old adages regarding the eating of fruit and vegetables depend for their truth on the fact that these articles contain vitamins and at the same time stimulate the movements of the intestinal tract in virtue of their indigestible bulk.

We know of four classes of vitamins which non-committally are called " A," " B," " C," " D," and " E." " A," " D," and " E " are fat soluble, the other two water soluble.

Vitamin " A " and the Anti-rachitic Food Factor (Vitamin " D ").—These vitamins are of peculiar importance in this country and a great deal of controversy has raged around them, especially in their relation to rickets, but it is now clear that vitamin " A," which is essential for growth, is not identical with the anti-rachitic vitamin as was first thought. Vitamin " A " is, for example, destroyed by irradiation, while " D " is formed in certain substances by such treatment. For practical purposes, however, the anti-rachitic vitamin " D " is so like vitamin " A " in its distribution and properties that they may be considered together. Two distinct views had been put forward regarding the ætiology of rickets. One, the Glasgow School, headed by Noël Paton and Findlay, stressed the importance of light and general hygiene, while the Cambridge and Sheffield Schools, headed by Hopkins and Mellanby, laid chief importance on diet, and so resuscitated some earlier theories. Happily, the views of each are now blended and an honourable peace has been reached. The link was the discovery by Huldschidsky that ultra-violet

light would cure rickets, and would cause vitamin "D" to be produced in certain foodstuffs.

Source.—These vitamins are synthesized by all living chlorophyll-containing plants. If the plant has no chlorophyll, *e.g.*, a mushroom or a seedling grown in the dark, it has no vitamin. From this source the vitamins are obtained by animals directly or indirectly. As we have seen, they are soluble in fat and are contained in animal fat provided the animal has itself taken them. Thus milk may contain much vitamin "A" if the cow is on grass, but the content will be reduced or may be entirely absent in winter while the cow is fed on artificial food. The same is true of butter. Fishes whose fat contains much vitamin, *e.g.*, cod-liver oil, obtain it from the green algæ or the chlorophyll-containing organisms of the "plankton." Vegetable fats, on the other hand, which are made from seeds, curiously enough contain no vitamin "A" with the exception of palm-oil, which unfortunately is most unpalatable. It is evident, then, that the vitamin will be deficient in the cheaper margarines made from vegetable oils which, however, contain small quantities of "D." Normally we take our vitamins "A" and "D" in green vegetables, butter, milk, animal fats, and egg yolk. But it is evident that the poorer classes may find these articles difficult to procure, and their diets are often lacking in this respect.

Unfortunately, too, vitamin "A" can be destroyed by heat in the presence of oxygen, but complete destruction does not occur unless the heat is prolonged and in many instances unless actual steps are taken to destroy the vitamin. Butter may be raised to 130° C. without losing much of its vitamin "A," provided it is not aerated, and in the ordinary cooking of vegetables a fair proportion of their vitamin "A" appears to be retained. Milk, on the other hand, is particularly liable to lose its vitamin even in pasteurization, and if sterilization is necessary additional vitamin must be added. The drying of milk, however, by the roller process does not appear to be so destructive and, similarly, tinned meat which is not heated for any prolonged period retains a large proportion of vitamin in its fat.

There is now evidence that the vitamin "A" content of butter is related to its pigment carotin. Boiled unpeeled carrots are more effective than butter, and it is suggested that the pigment or something adsorbed to it is responsible for the vitamin action. Crystalline carotin is also very active.

Evidence of Vitamin "A" Deficiency.—This deficiency is best seen in puppies and in children, whose failure to grow soon becomes evident. Xerophthalmia and night blindness occur.

Deficiency in "A" leads to a weakening of the capability of the organism to withstand bacterial invasion, and herein the long-known advantage of giving cod-liver oil in chronic infections finds its scientific basis. Its action as an anti-infective agent, which is very limited, is chiefly due to the influence it exerts in maintaining the structural integrity of mucous membranes; it cannot be regarded as a general anti-infective agent (L. J. Harris).

Deficiency in "D" leads to rickets, but in minor degrees of deficiency there may be merely softening of the bones, as in knock-knee, without other sign of rickets. There is also marked malformation of the teeth, and there is an increasing weight of evidence that liability to dental decay is largely increased in this deficiency.

The softness of the bones is obviously a result of deficient calcification, and it is evident that if the calcium of the diet is reduced no amount of vitamin will make up for this deficiency. The bones of rachitic animals have the power to calcify if calcium is available (see "Growth"). Butter alone, which does not contain the calcium of the milk, is not nearly so good an anti-rachitic as cod-liver oil; and if the best effects are to be got from butter therapy calcium should be added to the diet.

Although we speak of diminished absorption of calcium, usually the result of vitamin "D" deficiency, as the cause of rickets, we must also take into account phosphate radicles. Probably what matters is the amount of calcium phosphate available in the blood. The normal serum Ca is 10 mgm. per 100 c.c., the inorganic P, 5 mgm. In infantile rickets of ordinary severity the calcium concentration is normal, but the phosphorus is diminished. In severe cases the Ca value also falls, and tetany is apt to develop if the figure is below 7 mgm. In cœliac disease, rickets not infrequently results, probably because there is defective fat absorption and therefore defective absorption of fat-soluble vitamin "D." Rickets in this disease becomes manifest during the remissions when growth recommences, for rickets is essentially a disease of growing bone.

Infantile and cœliac rickets are essentially a "low phosphate rickets." In renal infantilism bone changes resembling, but perhaps not identical with those of rickets, are present. Renal rickets is essentially a "low calcium rickets." As a result of chronic nephritis, retention of inorganic phosphate in the blood

occurs. The blood calcium is correspondingly diminished, and the osteoid tissue at the epiphyseal ends of the growing bony shafts fails to calcify.

The attention of the practitioner should not be exclusively engrossed by the changes in the skeleton in rickets, for other systems also suffer, and the child is liable to diarrhœa and bronchitis, and also to the more dramatic condition known as spasmophilia or tetany. Rickets is not associated with anæmia, except in certain rare cases in which striking changes in the blood picture occur under the name of anæmia pseudo-leukæmia of von Jaksch. Rickets is thus in contrast with scurvy in which anæmia is usually present. The old term " scurvy-rickets " is no longer acceptable, for most of the cases were infantile scurvy. It is true that deficiency of vitamin " C " and " D " can occur together, but scurvy develops after six months deficiency of " C," whereas rickets requires a somewhat longer period for its full clinical efflorescence.

There is now good evidence that various factors influence the activity of vitamin " D."

Sunlight.—By exposing animals and substances to ultra-violet light it has also been quite conclusively proved that the light can cause the production of vitamin " D " in the animal, possibly in the ergosterol. Many of the conditions previously included under the heading of general hygiene undoubtedly depend on the benefits of light. This explains the fact that while in this country rickets is a disease of the poorer classes, in India it is a disease of the richer classes whose children, particularly the girls, are kept much indoors. In the same way it can be shown that the milk of a cow kept in sunlight is richer in this vitamin than that of one kept in a dark byre.

The function of vitamin " D " is apparently to correct any improper balance between the calcium and phosphorus uptake, and the greater the disproportion of these two elements the more important the vitamin, but even if these substances are present in proper amounts the vitamin is necessary. The vitamin apparently increases the amount of calcium retained in the body or possibly absorbed from the bowel.

Exercise.—It is difficult to separate this factor from the effect of light, but evidence points to its being important ; after all, this is what would be expected, seeing that exercise of any part is a stimulus to greater power of function. It is to be expected, then, that greater work on the part of the muscle will stimulate more rigidity in the bones.

Carbohydrates.—That rickets is particularly marked in children whose diets contain an excess of carbohydrates has long been recognized by clinicians, and there is now evidence that carbohydrates inhibit the anti-rachitic vitamin. How this occurs is not yet certain, and meantime it can be best understood by the assumption that the carbohydrates contain a specific antagonistic substance. Mellanby has found that certain cereals are more potent than others in this respect and that oatmeal is particularly so. Dwellers north of the Tweed need not be alarmed, as, normally, additional vitamin "D" is taken in the milk at the same time as porridge. Inhibition can be counteracted by increasing the vitamin content of the food.

Reference has been already made to one type of "calcium rickets." In the adult, softening of bone associated with hypocalcæmia occurs in women during pregnancy and constitutes the disease known as osteomalacia. "Like rickets, osteomalacia is a disease bred of darkness and dietary deficiencies" (Peters and Van Slyke). The added strain of pregnancy causes the disease to appear in women whose dietary is deficient in calcium and vitamin "D," and who suffer from lack of sunlight. The fœtus withdraws calcium from the mother, in order to calcify his developing bones. Osteomalacia does not develop apart from pregnancy, as the normal adult calcium needs are slight. The disease is common in China, but although it is rare in England, dental caries commonly occurs here during pregnancy for an analogous reason.

Vitamin "A" and "D" Therapy.—The natural products, cod-liver oil and whole milk from grass-fed cows, still remain the best sources of these vitamins, but recently the Medical Research Council has prepared a crystalline product (calciferol) having anti-rachitic properties. The results of vitamin therapy have been most brilliant and do much to confirm the hitherto much criticized vitamin theory of the origin of rickets. The therapy carried out by Chick, Hume, and others in Vienna, has convinced some of the most hardened sceptics, and when combined with light supplied either from the sun, from a mercury vapour lamp, or an arc, there can be no doubt about its efficiency in the treatment of rickets. A common disease in children is fat dyspepsia, which is characterized by pale crumbly or soapy stools, and in which a reduction of the fat intake is indicated. It must not then be forgotten in the treatment of this condition that there is a point

below which the fat content of the food cannot be reduced without detriment to the patient unless it is replaced by other vitamin-containing substances.

The efficiency of light therapy does much to consolidate our knowledge of the subject. Here again is the too often ignored lesson to be learned that although scientific controversy is stimulating in that it builds up a pile of facts on each side, nothing is to be gained by one side attempting to ignore the results of the other. The true solution is found from all the facts.

Of peculiar interest for the future is the fact that all animals must have light or something which is produced by light, and if they cannot obtain this directly from the sun they must obtain it indirectly through the agency of plants.

Vitamins " B " and " C."—To the average practitioner these vitamins appear of less serious moment, as the classical diseases which result from their deficiency, beri-beri and scurvy, are comparatively rare. There is, however, evidence that many of the indefinite malaises and dyspepsias of adult life may be in part due to their deficiency. Five vitamins of the " B " complex have been described.

Vitamin " B_1 " is contained in seeds, such as the grain of cereals, in yeast, egg yolk, and in lesser quantity in meat. It can, therefore, be stored in the dry state in wholemeal flour and unpolished rice. The vitamin appears to be quite close to the surface and the more the grain is milled or the rice polished the more vitamin is lost. It also can withstand ordinary cooking, as in the making of wholemeal bread or biscuits.

Commonly this vitamin is referred to as the anti-neuritic vitamin, since its absence brings about conditions in which polyneuritis is the characteristic feature, as in beri-beri. This was one of the first diseases shown to be due to dietetic deficiency. Clinically, it manifests itself as a neuritis, with weakness, disturbance of sensation, sometimes with pain, wasting, and paralysis. In some patients there is œdema. Actually, severe beri-beri is very rare, even in those individuals who habitually take only white flour. It is to be presumed that they take sufficient vitamin " B " in other ways.

Vitamin " B " is absent from white flour and practically from white bread as the yeast is destroyed.

Vitamin " B_2 " has the same distribution as " B_1," but it is thermostable and is not present in alcoholic extract of yeast like " B_1." Several observers have attempted to show that deficiency

of this vitamin results in pellagra, a disease of hot countries [1] characterized by great intestinal disturbance, diarrhœa, and degeneration of the bowel wall. The evidence is not, however, conclusive. In rats there is an inflammation of the skin with loss of fur.

The other vitamins, B_3, B_4, and the γ factor, which have different resistances to chemical procedures which destroy them, are also present in yeast and are necessary for normal growth and nutrition.

Vitamin "C."—This vitamin, like the vitamin "A," is present in green plants, but it is not fat soluble and is present in fruits. In times past scurvy, caused by its deficiency, was the scourge of ships and prisons, but experience in the Navy at some stations where fresh fruit was available led to the use of lemon-juice as a prophylactic. A mistaken idea, however, that lime-juice being more acid would be more powerful in this respect, led to the adoption of the latter as a regular ration. We now know that the juice of fresh oranges, lemons, swede turnips, and cabbages contain more of this vitamin than other substances, although it is present to a lesser degree in all green plants. Unfortunately it is the least stable vitamin and is extremely easily destroyed by heat. It is specially liable to be destroyed in stews and forms of cooking taking over three-quarters of an hour. Only a trace remains in vegetables after cooking. It is evident that the best way to obtain this vitamin is to eat fresh fruit, oranges and lemons for preference ; a small amount is contained in meat and milk. It is especially interesting to note that in the cooking of acid fruits the vitamin is not lost, and the same refers to the manufacture of tinned acid fruits. But the cooking of vegetables in alkaline solutions is very destructive.

Deficiency of this vitamin brings about the typical scurvy which is seen in the swelling of the gums and loosening of the teeth, with a tendency to hæmorrhage and fracturing of bones.

Special stress has been laid on the signs of the deficiency in adults, but it must not be forgotten that the absence of "B" and "C" interferes with normal growth and the vitamin content of milk is of special importance for the young. The attempts to render milk approximately sterile reduces the vitamin content and may entirely destroy vitamin "C." Pasteurization is even

[1] Pellagra sometimes occurs in England without bowel degeneration, but with characteristic rash, sore mouth and postero-lateral cord degeneration.

worse than boiling for a short period. On the other hand, the giving of extra vitamins when the food already contains a normal quantity can serve no useful purpose. When vitamins must be given this may be done conveniently—" B " by yeast extract, " C " by orange and lemon juice.

Vitamin " E."—This vitamin has been shown to be necessary for normal fertility in rats, but whether or not it may affect human fertility is not known. The vitamin is present in the embryos of wheat and other seeds, in green leaves, and to a small extent in animal tissues. It is present in vegetable oils, but is absent in cod-liver oil, and little is contained in milk. In its absence there is degeneration of the testes, and in the female there is faulty development of the embryo. An interesting observation is that of Verzar, who has found that the injection of this vitamin into the peritoneum has the same effect on the genitals of rats as the injection of extract of the anterior lobe of the pituitary, and it is suggested that the vitamin is necessary for pituitary function.

Vitamins and Human Diets.—A recent report of the Medical Research Council makes the following important observation : " So far as Western civilization is concerned, it is true that the rareness of the occurrence of frank deficiency diseases such as scurvy, xerophthalmia and beri-beri indicates that an absolute deficiency scarcely ever exists in the individual diet. On the other hand, it is now becoming generally recognized that much subnormal health and development and even incidence of disease are associated with a partial deficiency of one or more of these accessory substances. The influence of such partial deficiencies, even when relatively slight, may be extremely serious when they occur in early life, and if we may judge from the results of experiment on animals an adequate supply of these indispensable dietary components later in life may fail to make good the damage caused by a deficiency in youth. There is also danger that the effects of such a partial or latent deficiency may persist as a chronic deficiency throughout life." The report also emphasizes the importance of considering vitamins where patients have for one reason or another to be put on special diets and in special circumstances such as severe work, pregnancy, and lactation.

CHAPTER XXVIII

SWALLOWING. DIGESTION IN THE STOMACH

SWALLOWING

In swallowing, three distinct mechanisms are involved. First the food is pushed by the musculature of the mouth into the pharynx. Here it sets up a reflex by which the complicated movement of the pharyngeal muscles is brought about while the superior sphincter of the œsophagus is opened. As has been pointed out by Negus, the upper end of the œsophagus is normally closed by the sphincter assisted by the rotation of the cartilages of Santorini. This prevents the entrance of air during inspiration. The first two movements result from the action of striated voluntary muscle, while the third, by which the food is carried down the œsophagus to the stomach, depends on the involuntary muscle of the gullet.[1] Clinically we may see all three phases upset. Upset in the first phase is fortunately rare, but may be seen in bulbar paralysis, which also affects the second stage. Simple interference with the latter, however, is best seen after nose operations when cocaine from the nasal packing has anæsthetized the mucous membrane of the pharynx. The food is forced into the pharynx, but the reflex mechanisms of the latter and the opening of the œsophagus do not take place and nothing further happens. Besides being intensely disagreeable and alarming to the uninitiated, in young children it might clearly be very serious.

Dysphagia is infrequently caused by pathological conditions obstructing the œsophagus, but may be caused by cancer, by pressure from without, *e.g.*, of an aneurysm, or occur in any condition where there is an inflammatory lesion in the vicinity of the food passages, *e.g.*, larynx, pericardium, or œsophagus itself. *Total* obstruction of the gullet is nearly always due to cancer. The proper sequence of events in the act of swallowing can be shown experimentally to depend on the nervous and not on the muscular connections. This is also seen clinically in

[1] The muscle of the upper part of the œsophagus is actually striated, although not under the control of the will. This is probably to give greater speed of action.

certain nervous diseases, such as thrombosis of the posterior inferior cerebellar artery, in which condition the lack of co-ordination in the muscles of swallowing may be the most frightening symptom. This artery supplies, not only the cerebellum, but also the lateral aspect of the medulla and the dysphagia is probably due to disturbance of the latter, rather than the former, as palatal paralysis is present. The reflex found in animals by which stimulation of the pharynx brings about a relaxation of the cardiac sphincter has not been observed by X-rays in man, but on the other hand this method could scarcely be expected to show it unless special steps were taken.

Achalasia of the sphincter is its failure to open when the normal peristaltic wave reaches it. A simple form may be seen after eating very dry food, say sandwiches without any fluid. The food is swallowed, but, from lack of lubrication, passes down the œsophagus so slowly that by the time the lower end is reached the cardiac sphincter has closed again, and tension set up in the œsophagus may be extremely painful. This explanation necessitates the existence of the reflex, but it may be that the size of the bolus in the absence of lubrication is the sole cause. The pain may be relieved by a normal peristaltic wave, but a strong wave, if it is held up by a foreign body, causes intense pain because of the stretching of the wall over the foreign body (Poulton).

Hurst has put forward strong evidence that there is no actual spasm of the sphincter. The latter, indeed, does not exist as an anatomical entity. He considers that a true achalasia is always the result of disease of the nervous control or of reflex stimulation.

DIGESTION

In its complete physiological sense digestion refers to all the processes by which food is prepared for absorption. These processes begin at the mouth and are continued to the ileo-cæcal valve. The actual chemical processes of digestion and metabolism are discussed elsewhere separately. While, unfortunately, we know little of the physiological mechanisms regulating the secretion of the digestive juices of the small intestine, other than that of the pancreas and bile, we are fortunate in having, at least so far as we know, few clinical conditions in which these mechanisms are upset. Digestion, as we meet it clinically, refers to gastric digestion and the term indigestion refers to discomfort in the region of the stomach. The factors upon which complete gastric function depends are very complex, not only in themselves,

but also as they are influenced by the condition of the bowel further down, especially by stasis. The stomach serves as a container, while it also continues, for a time, carbohydrate digestion, and initiates protein digestion. It is also of importance in sterilizing and warming the food. Further, to carry out its functions adequately it must pass on its contents at a reasonable speed.

Mastication.—The preliminary process of grinding is undoubtedly of first importance, for food inefficiently broken up tends to be held up at the pylorus. Further, in chewing, the flavour of the food is appreciated, without which the secretion of digestive enzymes is reduced, while the presence of food in the mouth facilitates the digestion of carbohydrate by the saliva.

Salivary Digestion.—This depends for its efficiency on (1) the admixture of the substances to be digested, *i.e.*, the starches, with the saliva; (2) the amount of salivary diastase or ptyalin secreted; and (3) the time allowed for its action.

The first factor concerned is, as indicated above, satisfactory mastication. The amount of saliva secreted varies in the first instance with the relish with which the food is anticipated and taken, and here, as in the secretion of gastric juice, psychical impressions play a most important part. It can be shown that these impressions form what we know as a conditioned reflex with an afferent path from a sensory organ such as the eye or nose, and an efferent path to the effector organs, the salivary glands. Once this reflex is established in association with definite conditions, it continues in the presence of these conditions, whether the original sensory organs are stimulated or not. For example, a dog always fed to the accompaniment of a certain note of the piano will secrete saliva reflexly when this note is struck even if food is not actually presented.

Salivary digestion is under the control of two sets of nerves, the sympathetic and the parasympathetic, *e.g.*, chorda tympani. The latter is responsible for making the saliva more fluid and the former for making it thicker and more mucous. In the past several dogmatic assertions were made regarding the nature of these secretions, but animal experiment on this point has given such varied results that further work is now necessary. It is, however, known that the secretion produced varies appreciably with the nature of the stimulus. Thus dry food causes greater secretion than moist food, and it is held by some that the more carbohydrate there is in food, the more ptyalin is secreted.

The effect of the higher centres on salivary secretion is a matter

of everyday experience. It is inhibited by emotion, such as fear. The old trial by ordeal in which the suspect had to eat a quantity of dry flour depended for its efficiency on this physiological fact. In the same way the thirst of public speakers can be accounted for. Of great clinical importance is the extreme thirst after atropine administration, which causes paralysis of the nerve ends of the parasympathetic. Disturbances of salivary secretion, bilateral and unilateral, are met with in disease of the nervous system affecting the salivary innervation.

It used to be taught that ptyalin was active only in alkaline solution, but it has now been shown that it is even more active in neutral and faintly acid solution. The drinking of acid wines is not, then, of such disadvantage as was imagined. The fact that ptyalin digestion can continue in faintly acid solution must be of great value in the continuance of salivary digestion in the stomach.

We shall see later that the movement and distribution of the food in the stomach are so arranged that the entering food passes into the centre of the food already there, and that until it passes into the pyloric end of the organ there is little mixing of the contents provided they are not too liquid. This procedure prevents the food from coming immediately into contact with the hydrochloric acid secreted by the gastric mucous membrane, and the inhibition of the ptyalin is thus delayed.

That the digestion of starch actually does continue in the stomach in man may readily be seen when the evacuation of the stomach is delayed experimentally or as a result of severe exertion; it is then found that a considerable amount of starch has been digested (Campbell, Pembrey, and others).

Some articles of diet, especially badly made pastries or potatoes cooked in fat, although easily masticated are not easily digested because the fat protects the starch granules from the enzyme.

Protein Digestion in the Stomach.[1]—The efficiency of protein digestion depends on the admixture of the protein with the digestive juice and the adequate activity of the latter.

The admixture of the protein with the gastric juice depends in the first instance on the fineness of the protein particles or on the ease with which they can be separated. This again depends on the physical nature of the protein and the efficiency

[1] Here the subject is discussed from the point of view of gastric indigestion. Actually protein digestion is perfect after total gastrectomy in man and in achlorhydria.

of mastication. On the physical nature of protein depends the reputation of the special digestibility of white meat, such as chicken and fish, which are not only easily masticated, but the digestive juice can penetrate more readily between their fibres than between those of red meat. In the same way white meats have less fat than red, a point of importance, as fat not only prevents the access of the pepsin and hydrochloric acid to the protein, but actually tends to inhibit the secretion of gastric juice and cause delay in emptying. Certain fishes, such as mackerel and salmon, have for similar reasons a reputation for indigestibility. These matters are worthy of serious consideration only in individuals whose digestion for some reason or other has become impaired.

The amount of gastric juice secreted depends on two factors: the relish with which the food is taken, and the nature of the food itself.

The original observation of Pavlov on dogs indicated the importance of the anticipation of food or *psychic secretion*, but from recent work, especially that of Carlson on a patient with an œsophageal obstruction and a gastric fistula, it does not appear that this psychic secretion is so important in man as was first thought. No doubt people vary in this respect and may further vary according to their actual state of hunger or otherwise at the time of the experiment. We also have seen above that it is common experience that the psychic secretion does influence salivation in man. The passage of a secretion such as saliva which is usually alkaline into the stomach will, we know, stimulate the gastric secretion of HCl, and in this way the higher centres have indirectly an influence on gastric secretion.

The actual *satisfying of the appetite*, both in man and animals, has been shown to be particularly important even though the food does not reach the stomach. A reflex is set up by the stimulation of the olfactory and gustatory nerves, and obviously varies with the palatability of the food. We know (from the work of Hornburg, who in 1904 investigated the case of a boy with gastric fistula) that it is not the mechanical act of chewing which is responsible for the increased secretion. The chewing of an indifferent substance such as indiarubber did not cause secretion, while tasty articles of diet, as was also shown in the case of Carlson's, caused marked secretion. In Carlson's patient, for example, the more he liked certain articles of diet, the greater was the rate of secretion of gastric juice.

This is a conditioned reflex and depends on the previous associations of some particular taste and smell. The subject has been further dealt with on page 43, where this type of reflex is discussed more fully.

The importance of studying the likes and dislikes of a patient cannot be over-estimated, especially in patients recovering from illness in whom the digestive secretions are often reduced. This aspect is of importance in the training of the young.

The giving of highly flavoured foods to children is pernicious, as it tends to cause the more staple articles of diet to appear uninteresting and tasteless and subsequently difficult to digest. It is, however, interesting to note that many of the dislikes of children are brought about by monotony, especially of a carbohydrate diet, and we know that a dietary over-balanced in this respect has disadvantages. From the point of view of vitamins it may be said that dislikes are seldom formed for the more natural foods, although this does occasionally occur.

The chemical nature of the food plays a considerable part in causing the secretion of gastric juice, and is responsible for secretion being continued after food has been taken. Several articles of diet have a directly stimulating effect on gastric secretion. The best known are the extractives of meat. Indeed, this is practically the only value of substances such as beef tea and bovril which have little or no food value, unless special measures are taken in making them. It has also been shown that drinking water has a markedly stimulating effect on secretion. Drinking at meals is disadvantageous from the point of view of salivary digestion as water is a diluent, but clearly it is beneficial as far as gastric secretion is concerned. The best time to drink is immediately before a meal, when the water has time not only to stimulate secretion but at the same time to wash out the stomach.

Of special interest is the effect of the *products of digestion,* particularly peptone and dextrin. It was found by Edkins that if such substances are boiled with cells from the pyloric end of the stomach and the decoction neutralized, filtered, and injected into a vein, gastric secretion is stimulated. We may take it, therefore, that normally when such substances come in contact with the pyloric end of the stomach, a substance, to which the name of "gastrin" has been given, is produced which, when absorbed, causes the stomach to secrete. More recently it has been demonstrated by several workers that histamine (a putrefactive derivative of protein) has a similar effect, and in the light

of this the existence of gastrin appears to require further investigation. It is to the increased secretion which results from the absorption of the putrefactive substances that the practice of hanging certain game, such as grouse, to improve its digestibility owes its value. The tissues also become more friable.

Some substances, on the other hand, have little or no effect, or may even inhibit the secretion of gastric juice. In this latter respect fats are especially powerful, a point of considerable therapeutic importance, as we shall see below. This fact also suggests that in the ordinary eating of meat the fat normally counteracts excessive stimulation by the extractives and products of the protein metabolism. White of egg, bread, and starch are among the substances which have no effect on gastric secretion.

If the foregoing indicates anything, it shows how well mankind has established his habits in accordance with his physiological mechanisms. The fact that members of a household usually take their meals together, besides being a convenience, tends to make the repast more light-hearted and to discourage pessimism and anxieties. In this way and by the general appurtenances of the table everything is done to encourage the psychical effects and the relish with which food is taken. People who take their food alone, which usually means also hurriedly, or while working, are notoriously apt to be subjects of gastric disorder.

Tasty *hors d'œuvres* and soup act as stimulants for the digestion of the more solid protein courses to follow. Sweets as carbohydrates are added later and at a time when conditions are most suitable for the continuance of salivary digestion in the stomach. Fruit subsequently cleanses the teeth. The addition of potato to the protein has no good basis, but on the other hand the addition of cream or butter to carbohydrates will by reducing acid secretion assist salivary digestion.

The beneficial effects of alcohol at mealtime can be attributed to the fact that it tends to lessen the sense of fatigue and increase the sense of well-being, with the result that the food is taken with more relish, while at the same time it causes a secretion of gastric juice. This latter has recently been confirmed by Maclean. Some assert that the main action of bitters, which have a considerable reputation as stimulants of digestion, is through the alcohol in which they are commonly taken. Recent accurate work by different workers on the gastric contents of man has certainly failed to show that gastric secretion is increased by bitters, but it appears uncertain that the absorption necessary for the action

of bitters had taken place, a point insisted upon by the older exponents of Materia Medica. Although the modern sciences of physiology and pharmacology are as yet uncertain of the method of their action, there is so much clinical evidence of their therapeutic value in gastric conditions that they cannot be ignored, and their action may yet be satisfactorily explained.

The influence of the palatability of the food indicates the importance of cooking which Macleod aptly refers to as the only digestive process over which we have direct control. In this respect we prefer the many-course dinner to a large amount of one dish, but this is really a matter of habit, as a dish which may be appetizing to one person may be revolting to another, *e.g.*, oysters. There are many accustomed to so-called plain fare, which often means indifferently cooked fare also, who appear to thrive on it. Of these it must simply be said that it is well that they have not often tasted of better things.

Control of the Acidity of the Gastric Contents.—The acidity of the gastric contents has for many years been appreciated, and its clinical investigation has frequently been of value in diagnosis. The factors which may influence it are therefore worthy of attention. We have seen that the gastric secretion is initiated reflexly, and is continued as a result of a chemical process. As secreted it contains about 0·4 to 0·5 per cent of hydrochloric acid. After admixture with the food and partial neutralisation, the percentage falls to about 0·2, which gives almost the optimum of H-ion concentration for the action of pepsin. As the neutralizing elements are used up the acid in the stomach tends to rise. A maximum is reached about one and a half hours after a meal, and thereafter falls, until in the resting period the total acidity is only about 0·03 per cent. This has now been shown to be due to the neutralization of the acid, caused by regurgitation of the alkaline contents of the duodenum through the pylorus. There is, in other words, a normal mechanism (until comparatively recently unrecognized) by which the amount of free acid in the stomach is not normally allowed to exceed 0·2 per cent. This contribution to physiological knowledge, founded on the work of Boldyreff, we owe mostly to clinicians, especially to Bolton, who has investigated the subject chemically and, with Salmond, by means of X-rays. Their results do appear to explain the clinical findings but are not universally accepted. Maclean considers that when the acidity of the gastric juice reaches 0·2 per cent the secretion is automatically shut off. The administration

of other acids causes the secretion of HCl to cease. The continued rise of the chloride content he ascribes to the secretion of chloride. It seems not impossible that both mechanisms occur, neutralization and cessation, and certainly Bolton's views best explain hyperchlorhydria.

He is supported by the results of operations, although curiously enough it was not with this in view that the operations were originally carried out.

It seems quite likely that the opening of the pylorus for the purpose of regurgitation may be under chemical control. The early findings of Pavlov, later elaborated by Cannon, to the effect that the pylorus was controlled by conditions of alkali or acid on each side of it, and which Cannon considered to indicate the normal mechanism of evacuation of the stomach, may really refer to the normal mechanism of regurgitation. With the recognition of pyloric regurgitation as a normal mechanism appears the explanation of the common "bilious attack." It seems that some quality of the food, commonly excessive fat or sugar, which may cause a late hypersecretion,[1] causes an exaggeration of the regurgitant mechanism instead of the normal evacuation. As a result, bile is brought into the stomach and gives its character to the typical bilious vomit. This explanation is supported by the fact that there is usually retention, even an increase, of gastric contents, and a disagreeable sensation relieved by vomiting. The bilious back-flow may continue to some extent for several hours.

In investigating gastric contents the two methods commonly in use are those of Ewald and of Rehfus. In the former a test meal is given consisting of a pint of tea and a small piece of toast at breakfast time, and after an hour the stomach contents are siphoned off with a stomach tube. In the latter method the patient swallows an Einhorn tube through which samples may be drawn off by syringe every quarter of an hour. This tube is of rubber and of small bore, so that it can be swallowed and retained in position for long periods with little discomfort. The meal contains a pint of oatmeal porridge made from two tablespoonfuls of fine oatmeal and strained through muslin to facilitate aspiration.

In carrying out a scientific investigation of gastric contents the Rehfus method certainly gives the most complete information,

[1] In the case of fat we know that late hypersecretion and retention do occur, although, in the first hour, secretion is reduced (Roberts).

but to be really complete an estimation of the chlorides, which is commonly omitted, is as important as investigation of the hydrochloric acid in virtue of the now recognized possibility of duodenal regurgitation. Otherwise it is impossible to differentiate between cessation of secretion and neutralization, which will be indicated by no decrease in the level of the chloride content, although the hydrochloric acid content may diminish. As time, however, is often of importance such investigation cannot always be made and clinical laboratory workers claim to obtain a large amount of information from estimations of the hydrochloric acid and free acidity only. An excessive amount of free hydrochloric acid *after an hour* used to be considered an indication of hypersecretion, but we now know that it is more likely to be due to pyloric obstruction from organic change or functional spasm. By the Rehfus method this is made still clearer by the failure of the hydrochloric acid concentration to fall. A true hypersecretion shows itself in a large increase not only in hydrochloric acid, but also in the chloride. Recent work has shown that this condition is really quite rare.

If the stomach be emptied before the Ewald meal to avoid errors of dilution and, incidentally, to obtain evidence of undue retention, a considerable amount of information can be obtained. Its comparative simplicity has much to commend it, while its value is enhanced if the chlorides also are estimated.

Movements of the Stomach.—A knowledge of gastric movements is becoming more and more essential for an understanding of gastric symptomatology, for, with the exception of the coarser sensations of heat and cold, all sensations are associated with contraction or tension of the gastric musculature. It has also been suggested that pain is caused by anæmia. (See also "Gastric Pain," page 256.)

The movements of the stomach have been studied by X-ray and also by introducing into the organ balloons connected by means of tubes to recording tambours.

Functionally the stomach is divided into two parts, in a way reminiscent of the actual anatomical division of the stomach in ruminants. The proximal end is composed anatomically of the fundus and half the body and this forms the gastric reservoir where the food is stored under a small amount of pressure. The stomach wall simply adapts itself to its contents whatever the amount and exerts a postural tonus similar to that of the bladder. At the cardiac opening the sphincter and its immediate neighbour-

hood are normally kept contracted, but, as we have seen, are relaxed reflexly on stimulation of the pharynx by food. On relaxation, not only is food allowed to pass the sphincter, but by relaxation in its neighbourhood, room is made for more food, which then, by virtue of the anatomical position of the cardiac opening, passes into the centre of the food mass in the stomach. This has been substantiated by much recent work since it was first recorded by Grützner. In this way, provided the food is not too fluid, salivary digestion continues in the stomach for some time, in fact, until the ptyalin is completely inhibited by the penetration of the HCl. It is well to remember, too, that ptyalin is most active in neutral or in very faintly acid solution, and not only in alkaline solution, as used to be imagined.

The distal half of the stomach one may call the gastric churn; in it the food is churned up with the pepsin and hydrochloric acid and rendered sufficiently fluid to pass through the pylorus. Anatomically the two halves of the stomach are divided at the middle of the body (incisura angularis), a region of considerable functional importance, as the work of Cannon and others has amply demonstrated. From this point the peristaltic waves sweep towards the pylorus and churn up the food. From experiments on animals Cannon rather emphasized the fact that the waves begin at the incisura, but there can be no doubt that in man some waves are seen in the fundus. These waves carry the food forward slowly, but as they travel faster than the food itself they override it and in so doing churn up the contents; hence the food is gradually driven towards the pylorus. The existence of these waves can readily be demonstrated by means of X-ray observation and, when the abdomen is thin, they may be seen through the abdominal wall in cases of obstruction of the pylorus in which they are exaggerated. Generally the pyloric sphincter opens when the peristaltic waves reach it and corresponding waves in the duodenum below the cap carry on the food, but in many circumstances the sphincter, according to its irritability to sympathetic activity or to the nature of the food, does not open; instead, it holds up the food in the stomach. There is now no doubt that alkaline and neutral fluids leave the stomach without undue delay. Cannon has pointed out that different foods are retained for varying times in the stomach; for example, carbohydrates, if taken alone, are retained scarcely at all, while fat and protein are retained for long periods. To what extent

this knowledge should influence our dietetic habits it is difficult to decide, but it is an excellent argument in favour of the simple French breakfast. On the other hand, in view of the fact that special arrangements have been made for the digestion of carbohydrates during retention in the gastric reservoir, there seems to be every provision for a mixed diet.

When the food in the stomach becomes largely digested and its acidity over 0·2 per cent, reverse peristalsis and regurgitation of the duodenal contents take place to prevent, according to Bolton as we have seen, excessive acidity. That reverse peristalsis may occur lower down in the bowel in some circumstances is certain.

For diagnostic purposes, however, the time of emptying of the stomach is of great importance. Food begins to leave the stomach at once, provided it is mainly of a carbohydrate nature, like the ordinary barium meal, by which such an investigation has been made. Discharge continues for some time, but at the end of three hours the stomach should be empty and degrees of retention can be estimated by finding the time taken for complete emptying.

Evidence of delay is best obtained by observation with X-rays of the time of evacuation of an opaque meal. The presence of charcoal in the stomach when a charcoal biscuit has been given the night before a test meal is not necessarily an indication of much retention. It may merely indicate very sticky mucus due to gastritis. Similarly, the presence of a large amount of fluid in the stomach during resting periods (seen when a stomach tube is passed), its large size, and the presence of splashing, all indicate retention.

The Position and Type of the Stomach.—The older physicians used to pride themselves on the accuracy with which they could determine the position of the lower border of the stomach, while the anatomists from a study of the cadaver were prepared to indicate the position of the full and empty stomach. X-rays have sadly shaken the confidence of both and have indicated that the position of the stomach is subject to great and rapid variation in the same person, especially as the result of mental states. It has been shown, for example, that extreme fear may cause the stomach to lose its tone (Langdon Brown, Wingate Todd), while it has long been known that gastroptosis and dilatation are commonly associated with general exhaustion, although, as we shall see later, these states are not necessarily accompanied by symptoms. Hurst describes an instance of a first-class rugby footballer who

had a symptomless gastroptosis which was discovered accidentally. Certain persons seem to have a long low slowly emptying stomach, others a short high and rapidly emptying stomach.

Whether these differences are inherited or acquired is a very interesting question to which no satisfactory answer has yet been given. It is usually considered that the differences are essentially constitutional, but in view of the great changes which we know may occur from changes in autonomic or hormonal balances it is best not to be dogmatic.

CHAPTER XXIX

DIGESTION. INTERMEDIATE METABOLISM

CARBOHYDRATE METABOLISM

CARBOHYDRATES exist naturally in many forms. The commonest are starch (vegetable and animal), cane sugar, fruit sugar, and milk sugar. Chemically, they are substances which contain carbon together with hydrogen and oxygen in the same proportion as in water. They contain sufficient oxygen to oxidize the hydrogen to water, and it is necessary to supply oxygen only for the combustion of the carbon to carbon dioxide. When carbohydrates only are being consumed, therefore, the amount of carbon dioxide given off will be the same as that of the oxygen retained. Hence in carbohydrate combustion the respiratory quotient $\frac{CO_2}{O_2}$ is unity.

Carbohydrates are classified according to the number of their carbon atoms. Thus glucose, $C_6H_{12}O_6$, is a mono-saccharide, while $C_{12}H_{22}O_{11}$, lactose and cane sugar, are disaccharides, and $(C_6H_{10}O_5)_n$, starch, is a polysaccharide. The chemical differences of these substances need not be entered into here. It is, however, occasionally necessary to differentiate between lactose and glucose clinically, as, for example, in the investigation of the nature of the glycosuria in pregnancy. They are both reducing sugars, but may be differentiated by their power of reduction, the differences in their osazones, by the polarimeter, or by fermentation.

All sugars before being absorbed normally are converted into monosaccharides and eventually probably all into glucose, which is often referred to as the current carbohydrate coin of the body. It is true that if a disaccharide is ingested in excess, some, since it is soluble, will find its way into the blood, but if this occurs it is treated as a foreign substance and excreted in the urine.

Carbohydrate metabolism begins when starch is hydrolyzed through the catalytic action of the ptyalin of the saliva into the disaccharide maltose, and is continued by the maltase of the intestine. Digestion by ptyalin, as we have seen, begins in the

mouth, but is continued in the stomach, although the hydrochloric acid of the latter finally inhibits it.

Uncooked starch is surrounded by an envelope (fortunately seldom complete) of a cellulose nature, and unless this is broken down in cooking, the starch cannot be fully digested by the saliva. Hence the well-known indigestibility of badly cooked cereals. It is, however, of interest that most of the natural unprepared cereals themselves contain diastase which assist their digestion. Again, since the starch is often treated with fat, there is a further difficulty in digestion, giving rise no doubt to the bad reputation of roasted potatoes and pastries in causing indigestion. Not only does the fat prevent the action of the saliva on the starch, but masses of such food are liable to be formed and these are difficult to force through the pylorus. The indigestibility of new bread most likely depends on this ; the remedy is good mastication. The carbohydrate undigested by the ptyalin is completely digested, or at least should be, by the amylase of the pancreatic juice which attacks the starch, together with the maltase and lactase of the succus entericus which attack the maltose and lactose respectively, converting them into monosaccharides. There is a little maltase in the pancreatic juice also. Cane sugar is converted into fructose and glucose by the enzyme invertase. In adults the power of digesting lactose or sugar of milk is small. Milk, then, is mainly of value to adults by virtue of its protein and fat, although bacterial action may possibly assist later in the breakdown of the lactose. In the infant, on the other hand, lactase is abundant, but the amylase of pancreatic juice is absent in the first six months of life. Starch should not, therefore, be given at this period. There can be little doubt, in view of the large amount of carbohydrate eaten, that a quantity of it is never digested or absorbed, but is really wasted in the fæces.

The importance of bacterial fermentation of undigested carbohydrate as a cause of one type of dyspepsia has been emphasized by the work of Hurst.

On being absorbed carbohydrates are either used as fuel or stored. The storage may be as glycogen in the liver or other tissues, especially muscle, in which form it is readily available for use, or in a more permanent and less bulky form as fat. These stores can be readily drawn upon, especially the glycogen, which can be converted to glucose with extreme rapidity through the agency of the enzyme glycogenase.

The liver appears to be specially concerned in the conversion

of monosaccharides such as lævulose. This is produced normally from cane sugar by the action of the invertase of the intestinal juice. Should the liver be diseased, the power of converting lævulose is reduced. If a quantity of lævulose (say 50 grammes) is administered, this reduced power is indicated by an abnormal rise in the blood-sugar. The **lævulose test** is a delicate one for the estimation of liver efficiency.

Finally, the carbohydrate is burnt to carbon dioxide and water in all active tissues, lactic acid being an intermediate product. The actual combustion of the carbohydrates need not take place during the contraction of the muscle, which may occur in the absence of oxygen. The great advantage of this arrangement is obvious. In conditions of severe stress it may not be possible to supply the tissues with oxygen at a rate sufficient for their requirements. This formation of an oxygen debt has already been alluded to.

FAT METABOLISM

Fats are not digested appreciably until they reach the duodenum, where they come into contact with the pancreatic juice and bile, by the action of which they are broken down into fatty acids and glycerin. The bile really acts as an adjuvant to the lipase or fat-splitting enzyme of the pancreatic juice. It also brings about the secretion of pancreatic juice by causing the absorption of secretin from the duodenal mucosa. Bile is not only alkaline, but its salts have the property of reducing surface tension and so rendering possible the formation of a very fine fat emulsion. The advantage of this emulsion is that it causes an enormous surface of fat to be exposed to the action of the lipase. The fatty acids formed are themselves soluble in bile, while their soaps, the products of interaction of the alkali, are, like the glycerin, soluble in water. The insoluble fat, then, is in this way converted into products which are readily soluble and absorbed. It is possibly true that in some animals and in some conditions fat is thus broken down before absorption, but Mellanby has shown that in the cat, for example, fat may be dissolved and absorbed in bile. The bile salts, it will be remembered, are re-utilized as cholagogues and in the bile itself keep cholesterol in solution during its passage down the liver ducts. If for any reason, possibly as a result of the products of bacterial action, the bile can no longer keep the cholesterol in solution, it is precipitated with the formation of gall-stones.

When absorbed the fat is rebuilt in the intestinal wall into a fat suitable for the animal. Fatty acids may be removed or added to give the characteristic of human fat. Under experimental conditions the fats of other animals may be stored as such, but this only takes place when the fatty acid reserves of the animal have been exhausted. The neutral fat built up passes, not into the portal system like the carbohydrates and amino-acids, but into the lacteals of the intestinal villi and thence into the thoracic duct, thus entering the venous system near the beginning of the superior vena cava. Why the fat thus short-circuits the liver is an interesting speculation.

Fat is then utilized as fuel and burnt, forming carbon dioxide and water, or is stored in the fat depôts, especially in the omentum and subcutaneous tissues. The details of the oxidation of fats cannot be entered into here, and the reader is referred to larger works. Of clinical interest, however, is the fact indicated by the formula of a fatty acid, $C_{18}H_{36}O_2$ (stearic acid), that, unlike carbohydrates, fat does not contain sufficient oxygen to oxidize all its hydrogen to water ; this no doubt contributes to its value as an economical method of storing energy from the point of view of space. Its calorific value is 9·3, compared with 4·1 for carbohydrate. During the combustion of fat, therefore, oxygen is necessary for the burning not only of the carbon but also of the hydrogen. The oxygen which goes to the latter and forms water is excreted as such and does not appear in the examination of the expired air. Hence the oxygen absorbed is in excess of that excreted as carbon dioxide, giving a low respiratory quotient (see page 262), such as occurs in diabetes in which an excessive amount of fat is utilized. Further clinical aspects are dealt with under diabetes, in which condition the faulty combustion of fats is of the most serious consequence.

Fatty Stools.—The fæces in health contain digested fat (fatty acids and their soaps) to a variable extent, up to 30 per cent of the dried weight. Only a small proportion of undigested or neutral fat is present. Where there is a deficiency of pancreatic juice with its contained lipase, as from obstruction of the pancreatic duct, the percentage of undigested fat is greatly increased. The stools are foul and greasy and the excess of fat may float on the top. Undigested muscle fibres are also present in excess, and indicate defective protein digestion.

It was to the greasy stools of pancreatic diarrhœa that the term *steatorrhœa* was originally applied, but the term has been extended

to include other conditions characterized by bulky fatty stools. Among these we may mention cœliac disease of childhood, a condition which closely resembles tropical sprue. In cœliac disease there is for some as yet unknown reason a failure of fat absorption. The wall of the gut is thin and atrophied. While some failure of fat absorption occurs in cases of disease of the mesenteric glands with obstruction of the lacteals, this seems unlikely to be the explanation of most cases of cœliac disease. Growth and development are interfered with, and, should the patient survive, result in infantilism—formerly erroneously called pancreatic. Part at least of the disturbance of growth is due to deficient absorption of the fat soluble vitamin " A." There is also deficiency of vitamin " D " absorption as shown by the development of rickets. Usually the rickets shows itself in the remissions, when growth is resumed. Tetany may occur as a complication. Idiopathic steatorrhœa has been described in adults by Hunter and others, quite apart from tropical climates. Sprue and similar types of steatorrhœa are frequently accompanied by anæmia, often pernicious in type. In cœliac disease and the analogous condition in adults, the excess of fæcal fat is " split." In the rare *congenital* steatorrhœa the bulk of the fat is undigested, the stools in infancy resembling butter.

Excess of fat in the stools is found in the fat dyspepsias of childhood, and in jaundice. In the latter, absence of bile salts from the intestine hinders the absorption of fat which is, however, digested.

METABOLISM OF PROTEIN

Exogenous Protein Metabolism.—Proteins are nitrogen-containing substances and are essential constituents of all living tissues. Their supply is necessary to make up for wear and tear and for the growth of new tissues, although they may, if not required for this purpose, be utilized as fuel. The proteins vary greatly in chemical constitution, but they are all built up of amino-acids which are themselves complex. As the diet of man contains proteins derived from a large variety of sources, a mechanism exists by which these are converted into the proteins of man. This is accomplished by the breaking down of the foreign proteins in the process of digestion and the subsequent absorption and building up of the amino-acids required. The amino-acids which are not required are otherwise utilized.

The digestion of protein is begun in the stomach by the action

of pepsin and hydrochloric acid. The latter is secreted by the so-called oxyntic cells of the fundus, while the former is produced by the chief or peptic cells of the glands of the body and the cells of the pyloric glands. In the stomach, digestion does not appear to go beyond the peptone stage by way of the metaprotein and proteose stages. Acid digestion is brought to an end at the pylorus, where the food passes into the alkaline zone of the intestine. Digestion is then continued by the alkali and trypsin of the pancreatic juice which hydrolyzes the protein more completely into polypeptides and amino-acids, in which form they are absorbed.[1] A similar digestion is continued by the erepsin of the succus entericus. In all such actions we believe that the enzyme, the chemical constitution of which is not known, simply acts as a catalyst, hastening a reaction which would be brought about much more slowly by the action of the hydrogen and hydroxyl ions alone.

On absorption the amino-acids are utilized according to the requirements of the body, but, as was indicated on page 260, some amino-acids are more necessary for the organism, especially when young, than others. Such amino-acids as are required for the building up of tissue protein are used for this purpose and the remainder are broken down to be utilized as the source of energy and fuel. This de-amination of the amino-acids takes place chiefly in the liver. By this process the amino-group is split off, while the remainder of the amino-acid becomes available as fuel like any ordinary fatty acid. The relationship of an amino-acid to a fatty acid may be seen by the formulæ, from which it is evident that the former is simply a fatty acid in which one or more hydrogen atoms have been replaced by an amino group NH_2, *e.g.*, CH_3CH_2COOH, propionic acid—a fatty acid, and $CH_3CH.NH_2.COOH$, alanine—an amino-acid.

The fate of the amino-groups is to form urea which is the most abundant nitrogenous waste product excreted. The exact stages by which urea, CON_2H_4 is derived from amino-acids are uncertain. The old view was that ammonium carbonate and carbamate were the intermediate substances, but the work of Werner has suggested that cyanic acid HOCN is the immediate precursor of urea. It is well known that ingested ammonia increases the urea output, but this does not decide the question, as ammonia doubles the yield of urea from cyanic acid *in vitro*. The blood in the portal

[1] A study of anaphylaxis (*q.v.*) shows that some foreign protein may be absorbed unchanged.

vein contains more ammonia than the arterial blood, because of the production of ammonia in the intestine, quite apart from the ingestion of ammonium salts. There is no evidence that ammonia is liberated in quantity into the blood during tissue metabolism.

Ammonia is used as an alkali reserve for the neutralization of acids such as the abnormal acids produced in diabetes or chronic retention of carbon dioxide. In such conditions the ammonium salts in the urine are much increased, and the urea is correspondingly reduced. In over-breathing the oppposite occurs. There is evidence that the ammonia utilized for the neutralization of such acids does not come directly from the proteins. It may be specially formed, possibly by the kidneys for purposes of neutralization. It can, however, be formed only from amino bodies, and at the expense of the urea, whatever the details of its actual origin.

In uræmia the breath has often an ammoniacal smell. This is, in part at least, due to the fact that the urea of freshly secreted saliva is transformed into ammonia by bacteria in the mouth. In uræmia both the urea in the saliva and the oral bacterial flora are excessive, so that more ammonia is produced in the saliva than in the healthy individual.

From a clinical point of view proteins, especially those of meat, have a somewhat evil reputation in relation to the production of high blood pressure, and in the treatment of the condition the exclusion of meat from the diet is of recognized value. Why this is so is by no means clear. It may be that the meat contains pressor substances, and the existence of pressor amines is well established. It may be, on the other hand, that the vegetable diet commonly substituted contains valuable depressor substances such as choline. There is good evidence that even the depressor substances like histamine (produced as decomposition products from the amino-acids, *e.g.*, from histidine) may by dilating capillaries or rendering them abnormally permeable bring about a compensatory arterial constriction to maintain blood pressure. That such constriction may eventually become excessive or lead to arterial hypertrophy seems to be a possible way by which the arterial pressure may become persistently high.

Endogenous Protein Metabolism.—This term is applied to the utilization of the protein of the body tissues which goes on from the wear and tear of structures. This may occur to a large extent under special conditions when other energy sources are deficient, but normally there is always a certain amount of tissue breakdown. Exogenous metabolism depends on diet, while endogenous

metabolism is dependent on the general state of the body, and is much more constant. Cathcart has emphasized that this metabolism increases in severe exercise from wear and tear.

Both kinds of metabolism give rise to urea, and sulphur compounds derived from the sulphur-containing amino-acid cystine. These products are excreted in the urine. In the case of cystine derived from the diet, it passes by way of the portal vein to the liver, where it is oxidized in part to inorganic sulphates. That liberated from tissue breakdown does not pass through the liver to any extent. It therefore escapes complete oxidation, and appears in the urine as neutral sulphur.

Another characteristic product of endogenous metabolism is creatinine. This has been shown by Folin to be excreted in very constant amounts independently of the diet. So constant indeed is its concentration in the blood and urine that its estimation in these fluids has been taken as an index of kidney efficiency, although now other tests are more convenient.

Purine Metabolism.—This variety of protein metabolism, which concerns the breakdown of nucleo-proteins, is of special interest in relation to gout, in which deposits of uric acid occur in certain areas and will be more fully discussed in a later chapter.

CHAPTER XXX

GASTRIC PAIN. COMMON GASTRIC AILMENTS. VOMITING

In few branches of medicine is there such confusion as in regard to diseases of the stomach, for each author has his own classification. To realize the truth of this statement one has only to pick up half a dozen textbooks, and attempt to get from them a clear conception of what is commonly called indigestion or dyspepsia. It is far from the intention of a physiologist to attempt to rectify what is certainly a difficult position, yet there can be no doubt that in such classifications much of the confusion is due to failure to appreciate the gradual transition from one so-called disease into another.

Gastric pain or discomfort is the most common symptom, less commonly there is perforation or hæmatemesis.

The Causes of Pain in the Alimentary Canal.—From the evidence of operation under local anæsthesia it is shown that the stomach is insensitive to ordinary stimuli which cause pain, the organ may be cut or cauterized without pain being felt; only stretching causes pain. Experimentally it has been shown that in the chloralosed cat only stretching of the gut causes the pupil to dilate (McDowall). The dilatation may be taken as indicative of sensory impulses reaching the central nervous system.

In view of the fact that pain in a hollow viscus is commonly found in conditions in which peristalsis is exaggerated, it was suggested that the pain was due to an excessive stimulation of the nerve endings in muscle when it goes into spasm (Mackenzie). Since then there has been much discussion on the way in which the stimulus is set up, but from the work of Hurst and, later, of Poulton and Payne, it is clear that stretching of the wall is the appropriate stimulus to the nerve endings. It must, however, be agreed that it is physiologically inconceivable that electrical stimulation of the nerve trunks leading from the abdominal viscera, *e.g.*, the splanchnic, does not produce sensations, but this experiment has not been done. Why the cutting or cauteriza-

tion of the ends of the small nerves in a viscus is not an adequate stimulus has not yet been worked out.

Poulton has shown that when pain originating in a certain region is present it is actually relieved by the successful passage of a peristaltic wave in that region, presumably because the muscle fibres take up the strain and relieve the nerve endings of the tension. This can be shown on voluntary muscle. If the arm is passively bent horizontally backwards the strain on the pectoral muscles causes pain, but if the pectorals are now contracted the pain is relieved.

It should be noted, however, that Poulton believes that peristalsis may in certain circumstances cause stretching. For example, if the pyloric canal is attempting to force on a foreign body some degree of stretch must take place over the foreign body and between it and the contraction wave. The more powerful the contraction the greater the pain.

In labour also the pain is probably produced by the fœtus being forced down and stretching the cervix and other tissues, for once the fœtus is expelled there is no pain, although the uterus may be felt to be firmly contracted. The pain produced during the passage of a gall stone is similarly produced.

When an ulcer is present we may imagine that the surrounding inflamed area is particularly sensitive to being stretched. In acute dysentery, which is frequently associated with ulcer, the peristaltic waves produce intense tenesmus, which is of an excruciating nature, which those who have experienced it are not likely to forget. The presence of persistent colicky pains in one region has long been used as a diagnostic sign of dysenteric ulcer. The expulsion of a little mucus and blood only, however, suggests that the severity of the contraction may be sufficient to cause pain, and so does the pain which is caused by a palpable spastic colon. It may be, of course, that severe contraction causes a stretching of the mesentery.

No one appears to have pointed out that it is quite unphysiological to have prolonged pain caused by peristalsis, for the pain, if severe enough, causes sympathetic stimulation and paralyses the gut. This may in part account for the intermissions of colic. Nor does anyone appear to have studied extensively the effect of adrenaline or ephedrine in alimentary pain although atropine is used to alleviate spasm of the colon by paralysing the parasympathetic.

Poulton's view has received most remarkable support from the

work of Mathews. The latter has shown that while sensory impulses pass up the sensory nerves from the muscle spindles of striped muscles when they are stretched, the impulses cease to do so if the muscle is made to contract. If, however, the stimulus is very great impulses may pass up. This state may correspond to intense muscular spasm.

Gastric Pain may then be caused by conditions which bring about stretching of the viscus or its attachments. These are: (1) resistance to the passage of the contents, whether solid, fluid or gaseous, (2) distension, and (3) possibly spasm. It seems probable that ulceration and congestion make the nerve endings abnormally sensitive.

According to Bolton, who has analyzed 1,000 cases, pyloric pain occurs characteristically late in the digestive process, while pain from the fundus is usually earlier. The former occurs usually somewhere between the transpyloric line and the umbilicus, and the latter between the same line and the ensiform cartilage. Moynihan had previously drawn attention to the relation of the pain of ulcer to the time of taking food. Gastric pain is associated with rigidity of the left rectus muscle, and duodenal pain with rigidity of the right.

Resistance to the Passage of Food.—This may be merely functional, as the result of abnormal contraction of the pyloric region, or of congenital hypertrophy; but in order of frequency it is produced by swelling and œdema in the region of an ulcer, cicatricial contraction after ulcer, and by carcinoma (Hurst and Stewart). We may look upon the pylorus as not allowing articles to leave the stomach until of a reasonably fluid consistency. Operation has shown that certain articles may be retained for twenty-four hours, and Bolton considers that the pylorus may develop an abnormal irritability. Here we find the explanation of indigestion caused by the gulping of food, since the coarse particles cause the pylorus to contract. Further, it will not allow excessive hydrochloric acid to reach the duodenum, and will not pass on food to the small intestine under conditions of emotional emergency, or when there is inflammation lower down. This latter is in the nature of a protective reflex.

Hurst, to whom we owe much regarding the sensibility of the alimentary canal, distinguishes between an actual spasm of the pyloric sphincter and achalasia or failure of the pylorus to open normally. The pain, he considers, is probably due to tension produced by contraction of the pyloric antrum, which attempts

to force its contents through the closed pylorus, but it may be due to stretching of the pylorus as a result of contraction of the fundus.

In the protective reflex spasm or in achalasia of the pylorus we have the physiological explanation of the dyspepsia secondary to inflammatory conditions such as chronic appendicitis. Such pain is not affected by food (Moynihan). Some surgeons are of opinion that spasm is produced from non-inflammatory states, such as kinking when the cæcum has a long mesentery (Tennant) or even the accumulation of gas. Walton and Bolton deny that dyspepsia is so produced except by acute appendicitis. That such spasm excites pain is rather unexpected for any condition severe enough to provoke it might be expected at the same time to reduce the stomach movements which are in part responsible for the pain. It seems, therefore, that the spasm somehow of itself produces the pain. In the dyspepsia resulting from emotional states such as worry and anxiety, or in excessive mental work, we have no doubt a relic of the fact that animals under such emotional stress do not partake of food, the alimentary canal being brought to a standstill by contraction of all the sphincters and relaxation of the bowel wall. (See "Sympathetic-parasympathetic Balance.") An analogous condition is produced in acute disease which brings into operation the same mechanisms which were intended for natural emergencies such as occur in fighting. We have a similar adaptation of the natural mechanism of exercise to the requirement of disease in the essential supplies of oxygen and elimination of carbon dioxide from the body and there is a similar output of fuel from the storage areas into the active circulation. In all such conditions associated with undue contraction of the pylorus, whether of the sphincter or the antrum, there is a tendency to increased acidity of the stomach contents or hyperchlorhydria. The pyloric contraction is intensified by the hyperchlorhydria itself. The primary condition may be determined by means of the fractional test meal. A primary spasm or achalasia will show increased hydrochloric acid, and a lack of neutralization, there being no increase in the total chlorides. A true hypersecretion, on the other hand, is characterized by a rapid rise in the acid and total chlorides. The amount of acid will depend on how much neutralization has taken place, while there is also a rise of alveolar carbon dioxide (*q.v.*). Hyperchlorhydria is then not a necessary accompaniment of hypersecretion and *vice versa*. Hyperchlorhydria, acidity, acid dyspepsia due to pyloric spasm and subse-

quent lack of neutralization are the most common forms of functional disorders of this kind, and are, as we shall see, often associated with ulcer.

A true hypersecretion may be brought about. Here we must remember the normal mechanisms by which secretion occurs. If the reflexes generally are exaggerated it is to be expected that reflex secretion of gastric juice will be similarly affected. In such cases if the food, say as a result of faulty mastication, is detained in the stomach, its retention may, depending on its nature, bring about excessive secretion. In the same way substances which will produce gastrin or histamine are inclined to cause excessive response. In this relation Lim has clearly shown that histamine is a powerful gastric stimulant, easily produced from decomposing proteins. It is seen from such experiments and from the examination of "normal" men, or at least men without any stomach complaints, that a great increase in gastric hydrochloric acid may occur without any discomfort. It may indeed be said that to consider the symptom as due to hyperchlorhydria *per se* is like considering sputum to be the cause of a chest complaint.

The increased resistance may be the result of stasis in the bowel lower down. Whether this stasis is of such a degree as to impede the emptying of the stomach in all cases is very doubtful, but it is certain that much indigestion is cured by simple attention to the bowels. No doubt the effect of the absorption of toxic substances on the gastric secretion and tone plays a part, while it is common experience that constipation causes lack of appetite, insufficient salivary secretion, a nasty taste in the mouth, and a foul breath, although indigestion may not actually supervene.

Distension.—In this condition the organ is stretched but has not lost its power of tonic contraction. It may occur secondarily to obstruction, but may be brought about by continued over-eating, although there is ample evidence that the stomach, like any other organ, will adapt itself to considerable overwork. The accumulation of air or other gases in the stomach is a frequent source of such indigestion. This is discussed later under "Flatulence."

By far the most importance source of gastric pain is that of ulcer in which there appears to be increasing evidence that localized stretching of the wall of the gut is concerned.

Gastric and Duodenal Ulcer.—The recognition of these conditions has of recent years become more and more clear, thanks to

patient clinical observation combined with observations made at operations and post-mortem. Their characteristic feature is pain in the region of the epigastrium.

As first pointed out by Moynihan, the site of the ulcer may be indicated by the time of the onset of the pain. If the ulcer is gastric the pain comes on within an hour of taking food, and later disappears. If the ulcer is a duodenal one the pain is worst when the stomach is almost empty, two or three hours after food, and then persists until more food is taken. In gastric ulcer vomiting relieves the pain, and hæmatemesis may occur, or the existence of bleeding may be shown by the presence of blood in the stools. The clinical history is often sufficient to make the diagnosis clear.

The Cause of Pain in Gastric Ulcer.—This question is by no means easy to answer. Acids tend generally to accentuate pain, and Palmer has advocated most strongly that the acid is directly responsible for the production of the pain. This is shown by the fact that the administration of acid to patients causes pain, while alkali relieves the pain. It is doubtful, however, whether or not the acid acts directly on the ulcer, since it accentuates the pain if it is administered to patients with appendicitis or cholecystitis (Hardy). This has been confirmed by Christensen, who points out that some normal persons do get pain when dilute hydrochloric acid is poured into the stomach. Some, however, do not, and it is well known that hyperchlorhydria alone does not cause pain, and it is sometimes found that after an ulcer has been cured the acidity is greater than it was at the commencement of treatment when associated gastritis had reduced gastric secretion somewhat. Hurst also points out that the administration of acid does not always cause pain, while Carlson and Ginsberg have noted pain when the gastric contents are less acid than normal or even alkaline. Hurst further has noted that the presence of a moderate amount of food in the stomach is more effective in producing pain than acid alone, and considers that this supports his view that the pain is due to muscular contraction driving the contents against the wall of the organ. On the other hand, Reynolds and McClure have seen the complete cessation of gastric movement in the presence of pain. This fact supports the view of Poulton, put forward in relation to gastric pain generally, that the pain is caused by tension not necessarily caused by contraction of the stomach.

Poulton has given evidence that the pain of ulcer is due to an

increase in the diastolic pressure in the organ. It is relieved by normal contraction. In the absence of evidence to the contrary, we must assume that a rise of diastolic pressure is brought about by contractions not in the immediate vicinity of the ulcer, and possibly in the intestine or possibly by a kink. The nerves in the region of the ulcer are presumably also more than normally sensitive.

We may then conclude that acid is not necessarily the cause of pain in ulcer, but may be so because it brings about increased movements not necessarily in the vicinity of the ulcer. The movements cause the pain by raising the diastolic pressure in the sensitive region of the ulcer or by causing traction in adjacent parts.

Hurst suggests that the pain may arise in still another way, namely, as a result of contractions of the active pyloric canal attempting to drive its contents through the sphincter, which has failed to open normally. The failure of the sphincter to open may be the result of an ulcer in its vicinity. According to Hurst, therefore, the pain arises in the same way as pain experienced when there is failure of the cardio-œsophageal sphincter to open (achalasia). This contraction may be seen by X-rays. Some clinicians are agreed that cases of merely irritable pylorus occur and may produce symptoms in this way.

Duodenal Ulcer.—What has been said in relation to gastric ulcer probably applies to duodenal ulcer. It has been shown (Miller) by investigations controlled by X-rays that the cap of the duodenum is contracted instead of being relaxed,[1] and that manual filling of the cap by pressure on the gastric contents causes the musculature to relax and relieves the pain. The idea that the pain in duodenal ulcer was brought about by excessive contraction causing traction on the pyloric region was also put forward by Alexis Thomson.

It is interesting to remark in the above connection that authorities are agreed that pain simulating duodenal ulcer may occur in patients in whom it is not possible definitely to diagnose an ulcer by the usual deformity of the duodenal bulb or the presence of occult blood in the fæces. Hurst suggests that such patients have a pre-ulcerative duodenitis which if left untreated will develop ulcer.

Gastric Tenderness which is elicited on palpation is not to be confused with gastric pain. Often distinct pain is felt by a patient

[1] Normally the duodenal cap is relaxed.

over the region of an ulcer but the viscus itself is quite insensitive. This practically proves that the tenderness is due to an inflammation of the overlying parietal peritoneum, the visceral peritoneum, as we have said, being insensitive.

The Relation of Acid to Ulcer.—The relationship of ulcer to the hydrochloric acid of the stomach is of considerable importance in the progress and treatment of ulcer, gastric or duodenal. The amount of free hydrochloric acid in the gastric juice varies greatly in such cases. It may be normal or even less, though it is usually more. From what has been stated in the previous chapter the hydrochloric acid content will depend on the amount of neutralization which has taken place. We do know, experimentally in dogs, that free hydrochloric acid in the stomach delays the healing of the ulcer.

The methods adopted by some surgeons for the cure of these gastric conditions are of great interest in this connection. Gastro-enterostomy, in which the jejunum is attached to the stomach, was at first fashionable. Later this was combined with local treatment of the ulcer, by cauterization or excision, as in Balfour's operation. More recently Moynihan recommends partial gastrectomy as the best operation. Jejunostomy is sometimes performed, so that the patient can be fed directly into the small intestine, and various other methods have been tried. Experienced surgeons are not yet in complete accord regarding the best operation and the number available indicates that agreement has not yet been reached. When the physiologist considers the variety of conditions concerned he does not expect to find a universal surgical panacea. From a study of the operations referred to above, it is evident that each in turn brings about a separation of the ulcer from hydrochloric acid, and naturally gastrectomy is the most efficient, as by it most of the ulcer-bearing area and, no doubt, a large number of the acid-producing cells are both extirpated. Although a cell of the gastric mucous membrane at first sight "is born, lives, and dies in an acid medium," it does not really do so. The superficial cells of the mucous membrane can withstand dilute acid (the various influences which prevent the gastric mucous membrane from being digested are incompletely understood), but the tissues at the base of the ulcer and the deep part of the mucous membrane where the cells are dividing are normally in an alkaline medium.

That the benefits of successful gastro-enterostomy for gastric ulcer (for there have been successful cases) depend on neutraliza-

tion of the hydrochloric acid is shown by the fact that the hydrochloric acid in the stomach is reduced and the symptoms may disappear, although the food may continue to pass not through the new opening but through the pylorus as the muscular arrangement of the stomach tends to make it do. Unsuccessful cases of gastro-enterostomy, however, do not show this neutralization. Let it be clearly understood, however, that where there is organic pyloric obstruction, surgical measures which prevent the retention of food in the stomach have a very real value ; they may be of advantage even in functional spasm, for there is great difficulty in getting patients to carry out medical treatment for the necessarily long time when they have to pursue some avocation. It must also be remembered that mere section of the stomach wall would tend to cause cessation of the spasm of the musculature and give relief, while, as we shall see, it will temporarily break the vicious circle.

Surgery has proved without doubt the association of ulcer with hydrochloric acid in the stomach. The fact that the acidity is often subnormal does not affect the conclusion which both clinical and experimental evidence shows, that it facilitates the formation and delays the healing of ulcers. The actual agent responsible for the formation of the ulcer is a matter for the pathologist. More and more evidence is being brought forward to indicate that it is the result of local septic infection such as we may get in any other part of the body. This may originate in injury or transference of septic emboli from elsewhere, *e.g.*, the teeth (Stewart). Local conditions from faulty dietetic habits and increased sympathetic action (see " Sympathetic-parasympathetic Balance "), bring about an interference with the normal control of the musculature, while excessive hydrochloric acid undoubtedly predisposes to ulcer and prevents the healing which normally occurs ; otherwise most of us would be victims.

Surgery indicates that the hydrochloric acid in the stomach is responsible for delay in the healing of the ulcer, but we have seen that normally the acid is neutralized by regurgitation of the duodenal contents. It is evident, then, that undue closure of the pylorus must indirectly prevent this neutralization. We have, then, in gastric ulcer a vicious circle : an ulcer acted upon by hydrochloric acid causes spasm of the pylorus, this spasm prevents normal neutralization so that an excessive amount of acid is allowed to accumulate and possibly extend the ulceration. On physiological principles we must break this circle either by

reducing the amount of acid secreted or by neutralizing it or by preventing the pyloric spasm.

The essence of **medical treatment** is the provision of the necessary protein of the diet in a form which will not stimulate acid secretion and in which it will pass easily through the pylorus. Meat extractives and highly flavoured dishes should be therefore forbidden. Fatty foods which tend to inhibit gastric secretion are to be preferred and with this in view a teaspoonful of olive-oil or cream may be given before meals. It is important, however, to realize that this inhibition is confined to the early stage of digestion, for Roberts has shown that a hyperchlorhydria may ensue later. If then fat is administered the late administration of alkali is essential. White of egg, milk, and bread will supply the majority of the proteins required by the individual, while atropine may also be administered in view of its action in reducing secretion. Hourly feeds provide any acid with something else than the stomach wall to act on. At the same time alkalies must be given to neutralize acid. It is true that alkalies in small amount, especially if given before food, tend to cause an increased secretion of gastric juice, and this crude fact has been used by surgeons as an argument against the rationale of the alkaline treatment. Such criticism may be justified of the sodium bicarbonate treatment of thirty years ago. Elementary chemistry teaches us, however, that the best neutralizing effect is to be expected from the alkaline salts of the divalent metal, magnesium, which, further, do not have the same stimulating effect as sodium salts. Magnesium is to be preferred, as it has a mild laxative effect which is an advantage, while bismuth tends towards constipation. The work of Crohn and Bennett shows that alkalies should be given some time (one-half to two hours) after food, to exert their neutralizing effect to the best advantage.

In the light of what has been said the rationale of the stock remedies of the last generation for gastric pain becomes evident. Milk and soda as a complete dietary were commonly advised. Later on bismuth and soda became more fashionable, the bismuth being supposed to coat the ulcer. The routine treatment of gastric ulcer where there was no actual bleeding was, frequently, two ounces of milk and water two-hourly. The fact that the administration was every two hours materially assisted in the reduction of the acid content. This, no doubt, as the physicians used to say, prevented too great an accumulation of milk clots in the stomach. By confining the patient to bed his caloric require-

ments were reduced to a minimum. These treatments were directed towards neutralization of the hydrochloric acid, and while quite effective for new cases (where such neutrality was quite sufficient to bring about a cure), they lost their reputation when applied to the treatment of severe chronic cases.

Spasm of the pyloric canal is reduced by the administration of atropine, which also reduces secretion. That the whole benefit of this drug is not wholly due to diminished secretion is seen by the fact that although the free acid is reduced, the chlorides continue to rise slowly, since the acid as secreted is neutralized by duodenal regurgitation. The atropine or belladonna is often given in a little olive-oil or cream before a meal. All these features of treatment were incorporated in the elaborate dietary of Sippy, which is scarcely possible except where there is adequate supervision. Less elaborate methods, such as those of Bolton, Hurst, and Maclean, are quite adequate.

Recent insurance statistics of cases of ulcer in medical men, who presumably carry out this treatment efficiently, indicate an advantage in favour of medical treatment. This is founded on the foregoing physiological principles and accompanied, no doubt (and this is essential), by rectification of the primary cause of the condition, which is usually dietetic, using the term in a general sense.

Of recent years rest in bed has been most strenuously advocated in treatment, indeed, some investigators claim that this treatment alone, without any dietetic restriction, will cure ulcer. Almost all are agreed that where an ulcer is present, a month or six weeks in bed is essential in medical treatment, and if no ulcer is found it is of great benefit to rest before and after meals. Whether the benefit depends on posture or on the relief of fatigue, or on some other factor, is an interesting problem.

SOME GENERAL ÆTIOLOGICAL CONSIDERATIONS

From what has been said above it is evident that a primary factor in the causation of ulcers of the upper alimentary canal is the presence of excess hydrochloric acid in the stomach, and it may be profitable to consider how the excess may be brought about. There are two obvious possibilities, namely, that there is a hyper-secretion and that there is insufficient regurgitation through the pylorus. Hurst points out that while 80 per cent of the population have stomachs capable of tolerating great dietetic abuse some

10 per cent have constitutionally a tendency to hyperchlorhydria and therefore to ulcer, while 10 per cent have a similar tendency to hyposecretion and liability to anæmia or carcinoma. It is not, however, to be assumed that all cases of carcinoma have achlorhydria, for some may supervene on ulcer. Bolton, on the other hand, while agreeing that hypersecretion may occur, emphasizes the importance of inadequate regurgitation from the duodenum.

It is probable that both factors are concerned in production of the hyperchlorhydria.

It has been emphasized by Keith that many of our greatest writers have recorded their stomach complaints, *e.g.*, Carlyle, Darwin, Huxley, Spencer. Indeed he suggests that in this sense the stomach, which is an organ designed for the large intake of energy necessary to exercise, is antagonistic to the brain. An illustration will indicate how readily the gastric mechanisms become upset and how closely allied are physiology and pathology.

Consider an individual leading a somewhat exacting sedentary life. His meals are hurried and probably badly masticated, so that food not suitable to pass through the pylorus is taken into the stomach. At meal times he is often tired, may think of all kinds of things other than his food and may even read serious literature; it is evident that he loses all the advantages of psychical and of appetite secretion. His food therefore takes longer to digest and becomes a local irritant. He may consume foods which are difficult to digest and may take an excess of tea or coffee. The latter, especially if boiled, is particularly harmful to some persons because the fats it contains bring about a late hyperchlorhydria. Alcohol, especially whisky, gin, or cocktails, on an empty stomach is especially injurious in those otherwise liable, so may spices, condiments, tobacco and drugs taken for other reasons. Often infective material from the mouth is swallowed. There is evidence that during intense mental work the sympathetic nervous system is active (see also "Sympathetic-parasympathetic Balance"), and causes pyloric constriction, delaying the emptying of the stomach, exactly as we know severe exercise does. The first stage in the onset of dyspepsia is probably, then, simple pyloric spasm, probably associated with and aggravating a hypersecretion which most of us may experience from time to time, as a result of temporary indiscretions of the nature indicated above. Associated with pyloric spasm are the failure of the normal regurgitation of the duodenal contents and the

accumulation of hydrochloric acid which is increased further by the action of the putrefactive products and substances taken with the diet. This we know clinically as the stage of hyperchlorhydria, during which there is great liability to ulcer should the stomach wall become damaged from the action of bacteria or possibly mechanical injury.

Why some persons are subject to gastric ulcer and why others to duodenal ulcer is a matter of some interest. Hurst points out that duodenal ulcer is liable to occur in those with short, high, rapidly emptying stomachs and practically in no others, while those who have the low, slowly emptying stomachs are more liable to suffer from gastric ulcer. The occurrence of these two types is well recognized by radiologists (Barclay).

It is easy then to imagine that when undigested food is habitually retained in the stomach, gastric ulcer is liable to occur, but when it is driven into the duodenum by a highly active stomach, duodenal ulcer is more liable to be produced. The recognized importance in treatment of a physically smooth diet emphasizes the mechanical factor in the causation and healing of ulcers, and it may be agreed with Hurst that excessive roughage in the diet may be a disadvantage at the upper end of the alimentary canal. If the epithelium of the stomach is to be " treated rough," it must, like the epithelium of the hands, gradually become adapted to such ill usage.

Or there may be retention of the stomach contents, which causes dilatation and gastric atony, with possibly actual degeneration of the acid-producing cells from chronic gastritis and the production of hypochlorhydria, which by reducing digestion aggravates the condition. As would be expected at this stage, since the muscle has failed, the symptoms are not acute. Indeed, there may be a sense of fullness rather than of pain. The exact stage when dilatation sets in appears to depend on the general state of the patient, and it will be remembered that gastric pain is notoriously depressing. This subject is discussed more fully under " Atony."

Variations of this course may obviously occur. During the hyperchlorhydria the stomach or duodenum may receive an injury and ulceration may follow. The hyperchlorhydria may extend the ulcer and perforation may occur. Or, again, the scarred tissue of healed ulcers may lead to stenosis which will bring about dilatation.

Whether all cases of dilatation and increased acidity are brought

about in the way indicated above is not quite certain, but such a sequence of events is common and it must be emphasized that no amount of drug treatment can compensate for faulty dietetic habits. After all, the pathological conditions are but the result of disturbed physiology.

How common is indigestion of one kind or another is indicated by the vast number of proprietary preparations which are now available in any apothecary's shop. By far the majority of these preparations are alkalies made up with flavouring agents. It is still more disconcerting to remark the number of young men who take alcohol, especially on an empty stomach, and to note how many of them resort to some alkaline treatment to neutralize the acid which the alcohol produces.

A study of gastric function in relation to symptom production would be most valuable. Much can be done by the general practitioner in correlating faulty dietetic habits with symptoms. These are the result of a disturbed physiology and no matter what treatment is adopted none can be of real value if the patient lapses into his old habits. Here surgical measures have a moral advantage, since the thought of subsequent operation acts as a corrective. The physician should seek the primary cause of the condition, and this is true clinical research. More detailed examination by X-rays, at surgical operation, and post-mortem examination, brought into relation with symptomatology, would also be of the greatest value. Much more light is needed on the various stomach-aches to which we creatures of civilized diet and habits are heir. This, however, must be insisted upon: most gastric complaints are as preventable as they are common, and in view of the incapacity they produce, instruction on their prevention is essential in the interests of the public health of the future.

Achlorhydria or Hypochlorhydria.—Of recent years an increasing amount of importance has been attached to hypochlorhydria as it has become evident its occurrence may bear a causal relation to disease, the more so as pointed out by Hurst, as exacerbations of the condition may occur as a result of temporary gastritis. Hypochlorhydria may follow a hyperchlorhydria produced by gastritis or may be the result of treatment. It seems very likely that in the allergies, *e.g.*, asthma and skin irritations, that the protein sensitization is in part due to faulty protein digestion. It has been shown also that the hydrochloric acid of the stomach is concerned intimately with the later absorption of iron and is

largely if not wholly responsible for the condition of achlorhydric anæmia of women which is curable by treatment with iron and attention to the gastritis present.

Of still greater importance is the relationship of achlorhydria to pernicious anæmia, for it has been shown that the dried stomach wall of the pig or human gastric juice, especially if incubated with meat, is just as efficacious as liver extract. (See p. 189.)

The absence of hydrochloric acid in the stomach will also permit of the passage of bacteria, etc., into the lower reaches of the alimentary canal and predispose to intestinal infection. Achlorhydria is often found in cases of chronic diarrhœa which is then frequently mitigated by the administration of dilute hydrochloric acid. What the exact relation of the achlorhydria to diarrhœa is in these " gastrogenous " cases is not yet clear, but is certainly an intimate one.

The exact relationship of achlorhydria to carcinoma has not yet been discovered, but its frequent occurrence in this condition makes it hardly likely that it is coincidental.

Where the gastric juice is foul, dark coloured from altered blood, and the total acidity, mainly lactic and butyric, relatively high carcinoma is suggested. Other evidence of stagnation, such as charcoal in the test meal, supports this diagnosis.

Atony or Dilatation.—These are not primary states, indeed, they are common in persons of the asthenic type wholly free from symptoms, but who have long as distinct from short stomachs. A few patients have a sense of fullness as well as pain, which is produced by stretching of the wall itself or of the mesentery. They are often suspected of having a gastric ulcer and are given a milk diet which is badly digested and merely aggravates the condition. (See also p. 312.)

Barclay points out that for some obscure reason, possibly less fear of X-rays, the more attractive meal or possible changed habits of dress or diet, the atonic stomach is becoming distinctly less common.

The importance of the mental state cannot be over-estimated. Barclay has observed by X-rays that a nauseating smell may cause definite loss of tone of the stomach wall. Langdon Brown also gives a good instance in which the atony was clearly associated with the mental effects of air raids. The X-ray investigations of Wingate Todd have also shown that the tone of the stomach may vary very much from time to time according to mental circumstances even in normal persons. Any circumstances which cause

the individual to lose heart, feel beaten or " down and out " appear to bring about a loss of gastric tone. Once dilatation is begun and the muscle loses tone, there is a tendency for the emptying of the stomach to be less and less complete. Fermentation is superadded, and by producing increased distension aggravates the condition.

FLATULENCE

Although not usually a symptom of serious disease, flatulence is an extremely common source of discomfort. The sensation produced is one of distension which may not be sufficient to be considered pain. Sometimes, however, the pain is very great and appears to pass through to the back. Commonly a colicky pain is produced from increased local tension caused by the bowel attempting to drive on its gaseous contents, and in this connection Hurst offers a very reasonable explanation of the relief of gastric flatulence by bicarbonate of soda. He considers that the additional gas produced by the action of the gastric acid on the bicarbonate succeeds in stimulating the stomach wall to expel its contents. Gas in the alimentary canal arises from two causes, namely, the swallowing of air and the fermentation of food.

The swallowing of air is now considered to be much the commonest cause of flatulence and may become very marked in neurotic women although it may in part be the result of an attempt to dispel some discomfort in the epigastrium. In such cases the air is swallowed with small quantities of saliva but similar swallowing may accompany the taking of food or drink at an excessive speed. It is interesting to note that soups have a reputation for producing flatulence, while hot water has a reputation for relieving it. The latter must, however, be carefully sipped. The gas when eructated or withdrawn by a tube is found to be air. The air swallowing may, however, be an attempt to relieve the discomfort of ulcer or cholecystitis. It is important, then, to note that the sensation of fullness may be due to neurasthenic causes and may not be due to gas, and even if gas is present a more important pathological state may at the same time be present also. The sensation may be general or local, depending on the distribution of the gas. When local it is particularly liable to be appreciated in the regions of the left epigastrium and of the cæcum. In the former region the pain may be mistaken by the patient for cardiac pain. It may give

rise to palpitation and other cardiac symptoms from pressure upwards. In the latter it may give rise to spasm of the pylorus, especially if the pylorus is irritable, and produce a condition which is liable to be mistaken for duodenal ulcer ; but the diagnosis is made from the fact that a manual emptying of the cæcum almost at once relieves the pyloric pain. There is little doubt that gaseous distension of the cæcum and ascending colon accounts for the very common failure of pathologists to find any sign of chronic disease of the appendix when this organ has been cited as the offending structure by an enthusiastic surgeon.

Gaseous distension in the intestine may be due to fermentation of various substances, usually carbohydrate, which leads to the formation of carbon dioxide ; but methane and hydrogen are also found. The latter is inflammable and has been known, to the great alarm of the patient, to catch fire if belched during the lighting of a pipe or cigarette.

The formation of gas from the foodstuffs may occur in the stomach in conditions of gross accumulation in that organ where there is pyloric obstruction, but this is rare. More often the gas is produced in the cæcum and large intestine as a result of the fermentation of foodstuffs which have escaped digestion. The escape may depend solely on the quantity of food taken. The amount of bread and potatoes consumed by some people is enormous and the limitation of these is sufficient to bring about complete relief.

This escape may also be the result of the indigestibility of the food itself or fault in the digestive process. Notably among articles of diet liable to produce fermentation are carbohydrates in excessive quantity or treated with fat in the cooking, so that the starch granules are so coated that salivary digestion in the stomach becomes impossible. The coarser vegetables and fruits have also a considerable reputation for causing flatulence, presumably because they act as protecting media for fermentable material. With some persons preserved foods or fruits in almost any form cause acute flatulence, but the cause of this is inexplicable unless it is that they are liable to contain certain bacterial spores which eventually lead to the production of gas.

The digestive processes may be at fault in several ways. The digestive juices may be deficient. Hurst and Knott have drawn particular attention to the importance of the hydrochloric acid in the stomach in facilitating the complete digestion of carbohydrates. We must also presume that a deficiency of the pan-

creatic juice and of the succus entericus would also lead to faulty digestion, but a study of the stools in relation to pancreatic digestion apart from its interest in gross pancreatic disease does not appear to have been undertaken.

In many patients, no doubt, the juice may be sufficient to deal with certain foods in limited quantities, but not with others, *e.g.*, starch protected by fat as in fried potatoes.

The reduction of the digestive juices may be purely temporary. As Hurst has emphasized, it may result from gastritis produced from the irritation of insufficiently masticated coarse food or abuse of condiments and alcohol. It seems reasonable to believe that " end of term " flatulence, so common in those leading sedentary lives, may be due to the effect of general fatigue of the digestive secretions. Such patients benefit from a holiday and treatment designed to stimulate the secretion of the digestive juices.

Flatulence may, however, occur where there is hyperchlorhydria and rapid emptying of the stomach, although which is responsible is a little difficult to decide. It may be that the acid passes through the pylorus in sufficient quantity to destroy (J. Mellanby) or upset the production of secretin, which is the normal stimulant, produced in the duodenum, of pancreatic secretion. This is suggested by the fact that flatulence is a common symptom of inflammation of the gall bladder, but it is probable that in cases of cholecystitis there is also considerable chronic inflammation of enzyme-producing regions of the small intestine.

It may be that excessive activity of the alimentary canal may cause the food to be transferred too rapidly to the large intestine. The accurate diagnosis requires radiological examination. A barium meal may reveal that the food reaches the cæcum in less than two hours instead of the usual four. Alkalies, a fatty diet, and belladonna or atropine to slow down the activity of the parasympathetic, often work wonders in such patients. A well-known professor of medicine has stated that he owes his fortune to alkalies and atropine judiciously administered. Why hyperchlorhydria and excessively active intestine should so often occur even in the absence of symptoms is an interesting question. Hurst suggests that certain persons have a constitutional liability to hyperchlorhydria in response to chronic irritation (see " Hyperchlorhydria ") but whether excessively rapid emptying frequently goes with it does not appear to have been investigated. This

is an important point as it might throw light on the possibility that both states are due to excessive vagal activity and hence the value of the atropine, the great vagal paralysant. The value of the drug is well known in pyloric spasm, but its action may be because it reduces the secretion of hydrochloric acid in the stomach, which would tend to keep up the spasm, for we know that constriction of the pylorus is brought about by the sympathetic rather than the vagus, and therapeutic doses of atropine do not, so far as we know, materially affect the sympathetic.

VOMITING

During the act of vomiting the œsophagus, cardiac sphincter and fundus of the stomach are relaxed, while the pyloric portion is contracted. The diaphragm descends and the glottis is then firmly closed. The abdominal muscles contract and raise the intra-abdominal pressure. The contents of the stomach are thus expelled into the œsophagus and through the mouth. The œsophagus is emptied at a later stage by contraction of the various expiratory muscles including the abdominals, the diaphragm having by this time relaxed ; as the glottis remains closed the thoracic pressure is raised and the œsophagus compressed. It is thus seen that the closure of the glottis not only prevents vomited material from entering the bronchi but also assists by preventing expulsion of air from the lungs. The nose is to some extent protected by raising of the palate, but in many instances some particles enter it.

If in an animal the stomach is replaced by a rubber bag connected to the œsophagus, vomiting of the contents can be induced by suitable procedures, so it appears that the essential force is supplied by the abdominal muscles. Normally the stomach cannot, however, be regarded as being entirely passive, for the contraction of the pyloric end brings the contents nearer the cardia and the loss of tone by the fundus allows the organ to be forcibly compressed. If vomiting occurs repeatedly the pyloric sphincter relaxes from time to time and bile enters the stomach.

Vomiting is preceded by a profuse secretion of saliva due to reflex stimulation of the salivary glands. The feeling of nausea which usually precedes the act is probably due to impulses arising in the gullet (Poulton) but the region of the brain in which they rise to consciousness is unknown.

The reflex centre for vomiting is in the medulla. It is closely

related to the vagus nucleus and can be excited directly, from the cerebrum and reflexly : (1) Impulses may reach it from the cerebrum as in emotional and hysterical vomiting ; a few people are able to vomit at will. (2) The centre may be excited reflexly, especially from the stomach itself, *viâ* the vagi and from the fauces by way of the glossopharyngeal nerves. Disgusting odours may cause vomiting and although previously acquired psychological associations play a part, the rich connections of the olfactory pathways with the brain-stem facilitate the reaction. Stimulation of the vestibular apparatus will cause vomiting as in Menière's disease and sea-sickness. It is stated that when certain animals are rotated symptoms resembling sea-sickness are produced, but can be prevented by section of the eighth nerve. On the other hand it has been suggested that sea-sickness is due to longitudinal intermittent stretching of the œsophagus, stimulating the nerve-endings responsible for nausea. There is no doubt that psychological factors predispose. Painful stimulation of various afferent nerve-endings, as in renal and biliary colic, is a potent cause of vomiting. (3) The centre may be excited directly. This occurs in cases of increased intracranial pressure as in cerebral tumour. Here the vomiting may be classed alongside of the cardiac slowing which occurs from asphyxia of the vagus centres.

In the majority of cases vomiting is reflex in origin, usually from irritation of the stomach, and its occurrence in the specific fevers suggests the occurrence of gastric irritation in such conditions.

When the irritation is the result of pyloric obstruction the expulsion of the gastric contents may be so characteristically forceful that the diagnosis in infants of congenital pyloric hypertrophy is strongly probable on this symptom alone.

Action of Emetic Drugs.—With the exception of apomorphine, which acts on the centre, these drugs act reflexly. The fact that they still cause vomiting when injected into an animal in which the stomach is replaced by a rubber bag does not detract from the truth of this statement, for other nerve-endings are then involved. Narcotic poisons may depress the activity of the medulla and so prevent the action of emetics. As Hamill and Murrell state, where an emetic is indicated the use of a stomach tube is almost always preferable, but in an emergency in poisoning a dose of mustard and water may be more readily available.

In the gastric crises of tabes vomiting may accompany pain, but the two symptoms are produced differently for although the

pain may be relieved by section of the posterior nerve roots the vomiting may persist.

Vomiting in Obstruction of the Intestine.—In obstruction of the small intestine the material expelled gradually becomes fæculent. True fæces are, however, vomited only in cases of gastro-colic fistula and in hysteria. The contents of the stomach, duodenum and jejunum and ileum are vomited in turn. Antiperistalsis has been assumed to be responsible for the backward passage of contents, or forward peristalsis with a retrograde central current. The former is certainly not a true explanation and the latter is an inadequate one. The intestinal contents, much increased by abnormal exudation from the walls, passively flow towards the stomach and are then vomited. The foul odour is due to rapid multiplication of indole- and skatole-producing organisms.

Chronic duodenal ileus is due to visceroptosis and is a cause of "bilious attacks." The dropping of the intestine drags on the mesentery and superior mesenteric vessels. The vessels are thus caused to exert pressure on the duodenum where they cross it and dilatation of the viscus above the obstruction ensues. Violent peristasis of the distended duodenum is visible on the X-ray screen after administration of an opaque meal.

Effects of Vomiting.—The vasomotor and cardio-regulatory centres which lie close to the vomiting centre are apt to be adversely affected, especially if vomiting is prolonged or severe, and pallor, faintness and even collapse may ensue.

In continued vomiting alkalosis may ensue. This is partly due to loss of hydrochloric acid and partly to loss of salt. Loss of salt tends to lower the osmotic pressure of the blood plasma, provided the fluid which is expelled is more concentrated than the normal saline basis of the plasma, and the kidney in its efforts to preserve the osmotic pressure retains alkali for this purpose, and may excrete an acid urine although alkalæmia is present.

The loss of fluid makes the blood more viscous than normally, so that it circulates with greater difficulty. This aggravates any degree of collapse which may have occurred. The tissues also become seriously dehydrated. In the later stages of intestinal obstruction the non-protein nitrogenous constituents (urea, creatinine, etc.) of the plasma are increased. This is due partly to renal failure, a sequel of defective circulation, partly to other causes, such as tissue disintegration. Many surgeons believe that the accumulation of certain toxic nitrogenous constituents plays an important *rôle* in determining a fatal issue.

In many cases toxæmia is responsible for certain of the more serious manifestations, as in strangulation of the gut, and we must be careful not to attribute too readily to simple chemical and physical derangements what are really toxic effects. In strangulation, according to Whipple, a poisonous proteose is liberated from the wall of the gut into the blood-stream, as well as into the lumen of the gut. Emigration of bacteria through the strangulated wall also occurs. That the results of loss of salt and water are of themselves sufficiently serious is seen in cholera. In this condition loss occurs from both vomiting and diarrhœa and gratifying results have been obtained from treatment by intravenous injections of hypertonic saline, as in Rogers' method.

Acute Dilatation of the Stomach.—This disaster is usually a sequel of abdominal operations, particularly on the gall-bladder or kidney, but may arise apart from these in specific fevers, etc.

At post-mortem examination the duodenum is nearly always dilated as well as the stomach, the dilatation reaching the point where the root of the mesentery crosses it. The stomach is enormous.

Clinically the patient vomits repeatedly, bringing up enormous quantities of fluid which soon becomes bilious but not fæculent and it is thus evident that duodenal contents are vomited as well as gastric. Severe collapse sets in. According to the older view, the primary cause of the condition is obstruction of the duodenum by the superior mesenteric vessels dragged on by the intestinal coils. The observations of Mathieu and Roux make it probable, however, that the kinking is secondary to the great distension of the stomach which presses down the mesentery and intestine which now drag on the vessels. The duodenal obstruction in any case aggravates the gastric distension by causing regurgitation of the bile and pancreatic juice, and by preventing onward passage of the gastric contents.

The explanation of the primary dilatation of the stomach is that it is due to aerophagy. The patient, on recovering consciousness, feels his mouth dry and swallows air and saliva. The presence of a tight abdominal bandage aggravates his nervousness and he gulps down more air. Bennett, who supports the French authors, draws a lurid picture of the vicious circle of influences in which the administration of bicarbonate of soda plays a part.

Some authors are of the opinion, however, that loss of tone on the part of the gastric musculature is an important accessory factor.

It is generally agreed that gastric lavage is an indispensable method of treatment, the tube being left continuously in position. This removes gas and liquid from the stomach. Further, the " many-tail " bandage should be slackened and postural treatment, such as raising the foot of the bed, etc., adopted. In this way the traction on the superior mesenteric artery is diminished and the duodenal distension mitigated. Preventive treatment is important and consists in avoidance of the conditions already mentioned as favouring the onset and in giving the patient frequent mouth washes and occasional drinks (Bennett).

X-RAY APPEARANCES IN THE BARIUM-FILLED STOMACH

The shadow of the meal in the stomach is surmounted by a translucency due to a bubble of air which becomes enlarged in aerophagy. Peristaltic waves can be observed on the screen, and their state at any one instant is also shown on a film exposed at that time. Interruption of peristalsis at the site of a filling defect is suggestive of a carcinoma which has infiltrated the gastric musculature, but sharply local interference with the movement may be due to spasm. The fundus of the stomach slowly contracts down on the contents, as these decrease in quantity from intermittent escape into the duodenum.

Entry of the semi-fluid gastric contents into the duodenum occurs soon after ingestion of the meal and from moment to moment the duodenal cap is visible above and to the right of the pylorus. The presence of a duodenal ulcer causes irregularity due partly to the entry of barium into the ulcer, partly to the local spasm which the ulcer excites in the duodenal musculature. Irregularity of the duodenal cap from spasm also occurs as a reflex phenomenon in cholecystitis and appendicitis. Irregularity is usually accompanied by tenderness.

The stomach is usually empty within four hours. Unduly rapid emptying occurs when the tone and peristalsis of the gastric walls are increased. This condition is often associated with hyperchlorhydria, and Hurst speaks of it as the " hypersthenic gastric diathesis." In a number of these cases duodenal ulcer is present, probably because the " hypersthenic diathesis " predisposes its subjects to duodenal ulceration. Rapid emptying occurs also in the case of leather-bottle stomach in which infiltration of the pylorus with carcinomatous cells renders the sphincter incompetent and the meal shoots through into the duodenum, although no peristalsis is visible in the stomach.

If the stomach contains barium after six hours, abnormal delay is present. This may be due to atonic dilatation, with feeble peristalsis. The extreme degrees of this condition are probably much rarer than was formerly supposed. Gross delay in emptying results from pyloric obstruction, which may be due to œdema round or scarring of an ulcer, especially on the duodenal side of the pylorus, to a carcinoma or, on rare occasions, to the pressure of an adherent gall-bladder. The stomach wall reacts to cicatricial pyloric stenosis in one of two ways. In one of these the muscle gives up the struggle and the organ becomes grossly dilated, in the other the peristalsis is increased (being often clinically visible) and although the meal tends to accumulate in a bowl-shaped area and may, in part at least, be retained many hours, the stomach is not dilated. Minor degrees of pyloric obstruction may be due to spasm (achalasia of Hurst), in certain cases of duodenal ulcer, cholecystitis or appendicitis.

Local spasm of the gastric wall, often accompanied by tenderness, occurs not only from gastric ulcer, but also in cases of appendicitis and of cholecystitis, when it is assumed to be reflex in origin. Sometimes spasm of a band of the circular muscle is so marked that an hour-glass appearance results. This can be differentiated from organic hour-glass stomach, due to cicatrization of an ulcer many years old, by the fact that the degree of stricture is apt to vary from moment to moment. Further, spasm can be relaxed by massage or by the hypodermic injection of atropine. When the stomach is both atonic and ptosed an " orthostatic " hour-glass may be seen. The explanation of this condition is that the first taken portion of barium drags down the lower part of the stomach. The middle region is thus made tense and narrow and the last taken portions of the meal are held up near the fundus. As might be expected, the stricture disappears when the patient lies down.

Too much stress should not be laid on undue length and minor degrees of atony of the stomach, as these are not incompatible with perfect health.

Barium in the crater of gastric ulcer may be visible in profile, as a projection, usually from the lesser curve, known as a " niche." There is frequently spasm in the opposite greater curvature, forming a " notch." Barium may be retained in the crater as " fleck residue " after the main mass of the meal has left the stomach. Filling defects are seen at the site of a carcinoma.

Duodenal ileus is referred to under " Vomiting."

CHAPTER XXXI

INTESTINAL MOVEMENT AND PAIN

PHYSIOLOGISTS recognize three kinds of intestinal movement: peristalsis—by which the food is moved along; segmentation—by which it is broken up and absorption facilitated; and pendular movements. The clinician is interested chiefly in peristalsis, as deficiency in this respect (constipation), together with the common cold, are probably the most common complaints among modern peoples. We have seen that intestinal stasis may interfere unduly with the emptying of the stomach, but what is just as important is the toxic absorption which may also result. Normally, the small intestine is the region from which the products of normal digestion are absorbed, but if the contents stay there too long then putrefactive products are formed and absorbed to the great disadvantage of the sufferer. Such intestinal stasis is, however, usually secondary to failure of the large intestine to move on its contents.

So far as the small intestine is concerned, excessive peristalsis most commonly interests the clinician. Such peristalsis may be brought about as the result of irritation of the mucous membrane lining the gut. This sets up excessive muscular action, just as we have seen that an ulcer may produce excessive contraction in the stomach. The irritant may be the result of the ingestion of food substances, *e.g.*, green gooseberries, or it may be bacterial, as in typhoid fever. In each instance the excessive peristalsis and subsequent diarrhœa are Nature's method of expelling the irritant. Advantage is taken of this in the treatment of early or suspected ptomaine poisoning in which a brisk purgative (castor-oil is the favourite) often averts more serious symptoms. It should be noted that unripe fruit which causes irritation of the bowel also causes diarrhœa in virtue of its indigestible bulk, which causes distension and stimulation of the bowel. That muscular movement may be so stimulated is well known and it may be due to fluid, gas or food. The effect of distension may be seen in a piece of rabbit's intestine kept warm in saline and oxygenated. The bowel is quiescent, but, on introducing a distending object

into its lumen, movement commences and drives on the obstruction. It will be seen, too, that the wave of contraction is preceded by a wave of dilatation, which is as essential a part of the peristaltic movement as the constriction. If the object is a little too large for the lumen, if there is insufficient lubrication, or if a kink is made in the gut, special efforts are made to drive on the object. A succession of waves commences a few inches from the obstruction and apparently gathers in intensity as it reaches the object. There is a rest period and then a further succession of waves. A similar state occurs pathologically when there is obstruction in the intestine, *e.g.*, a carcinoma ; local hypertrophy of muscle immediately behind the obstruction takes place owing to the excessive amount of work, and this condition is looked for by the surgeon when trying to find the obstructed point.

In some instances, especially spasm of the large intestine, the pain appears to be due to a slow wave rather than to a succession of waves. The slow waves are commonly regarded as of the nature of a spasm or tetanus, although they cannot be imitated outside the body except by chemical stimulation of smooth muscle, *e.g.*, by barium or calcium. Spasm of the colon is quite frequent. Such spasm is almost always confined to the large intestine, the pain is intense and may simulate various other conditions. Colic spasms are quite frequent as the result of the excessive use of purgatives or in colitis, and in such cases, if the patient is thin, the colon in the iliac fossa can often be felt to contract under the hand and feels like a sausage. Not infrequently this is mistaken for a tumour or a fæcal accumulation. The actual way in which the pain may be caused is discussed in relation to gastric pain. Atropine is almost a specific in such cases, just as we noted in pyloric spasm, and morphia is commonly necessary for immediate relief. Treatment of such conditions consists in giving the individual a diet with little or no indigestible material until the irritation has passed off, a treatment which throws considerable light on the physiological principles which apply to intestinal stasis and constipation.

Intestinal stasis must always be considered physiological in so far as it is impossible to avoid it in a large number of people unless special steps are taken ; it is largely the result of the assumption of the erect posture in man and in many the necessary adaptations are deficient.

Intestinal stasis is the result of inefficiency of the large intestine

in passing on its contents. In man the large intestine acts only as an organ for the absorption of water and for the excretion of certain salts, such as sulphates and phosphates, and the salts of calcium, magnesium, and iron.

The evidence is conflicting regarding the action of magnesium sulphate. Most pharmacologists hold that it acts by causing water to be retained in or drawn into the bowel, which becomes distended and stimulated. This certainly does occur experimentally. Hurst and others have produced evidence that this is not so in all patients, and that it acts after absorption. This seems unlikely, since magnesium sulphate is an anæsthetic. Whether this action is responsible for the constipation which follows the use of Epsom salts is an interesting question. Research on a considerable number of patients is necessary, as in some undoubtedly evacuation is caused long before the sulphate has time to get to the rectum. In some persons no doubt the gastro-colic reflex is very active.

It seems possible that phosphates have a special relation to intestinal movements. We know that the oral administration of phosphates has a greater laxative effect than would be expected, and when di-sodium hydrogen phosphate (Na_2HPO_4) is injected intravenously the stimulating effect on the intestines is very striking. This beneficial effect may be demonstrated on pieces of isolated intestine.

There is no doubt that undue concentration of the bowel contents often results from an inadequate intake of water. This should preferably be taken before meals so as to interfere as little as possible with digestion. As the bowel contents are normally fluid at the exit from the small intestine it is obvious that the more fluid they are at this point the more fluid they will still be when they reach the pelvic colon. The beneficial effect of a large tumblerful of water before breakfast is well known and at watering-places patients can be persuaded to take as much as twenty ounces, although they would never think of doing so at home. The fact that it is taken before breakfast is of great importance : at this time the small intestine is empty and the water passes through it so rapidly that there is little time for absorption. Such a quantity of fluid could not produce the same benefit if taken with a meal, as it is delayed at all stages, although absorption of the food is actually somewhat facilitated by the taking of reasonable amounts. The fluidity of the bowel contents may, however, be improved by adding to the diet a

substance which is fluid and not absorbed. Such a substance is liquid paraffin. The paraffin simply acts as a diluent and lubricant. There is, however, evidence that it may lead to an impairment of absorption, so that it should not be used in ill-nourished persons. This, however, is denied by Hurst.

It has been suggested and much preached that as the result of the erect posture certain parts of the bowel are liable to kink or to constriction by peritoneal bands. It has been claimed that these bands are the unfortunate results of our heredity. The fashion for considering these kinks as important has, however, now definitely "gone out," and surgical procedures such as anastomosis between the ileum and pelvic colon are considered positively harmful.

What has been said above regarding the fluidity of the bowel contents is of great physiological importance, but so also is the nature of the food, as was briefly stated on page 262. It is obvious that it is much more difficult for the bowel to propel a soft pultaceous mass than one containing reasonably resistant particles of cellulose. The average diet contains too little indigestible material or roughage. In our modern diet the majority of the carbohydrates have had their cellulose removed or reduced to powder, as in the white flour which in some form or other forms so large a part of our dietary. Additional cellulose is necessary and is best taken as fruit and vegetables. From this point of view faulty mastication of, say, meat adds to the solid contents of the large intestine and people with defective teeth, if they do not suffer from indigestion due to pyloric spasm, often suffer from looseness of the bowels. Insufficient mastication would of course be a most unphysiological treatment to recommend as it upsets gastric function and would be a most wasteful procedure. The influence of the diet in spasm of the colon has been referred to above and indicates clearly the effect of roughage in stimulating the bowel.

In any consideration of the cause of constipation or diarrhœa each individual case must be considered, for the whole intestinal tract is influenced by the general state of the body and habits. Diarrhœa may be a manifestation of general irritability and excessive secretion by the mucous membrane. Of such a nature is colitis, where local treatment is of little avail without general measures. Similarly, constipation may be due to general lack of secretion and body tone as in the aged, the anæmic, the melancholic, or in the febrile states. The condition may be further

accentuated by particular substances, as, for example, calcium of milk or hard water, which reduce the normal secretion. Notoriously, too, sedentary habits are liable to cause constipation from lowering of the general tone and especially that of the abdominal muscles. The latter if permitted to grow slack allow the viscera to be displaced, and render the work of the intestinal muscle more difficult.

Undoubtedly, too, the physiological calls of Nature are often neglected. Evacuation of the bowel should take place after breakfast, a time which for most of us, unfortunately, is for other reasons a most occupied time of the day. When the stomach is filled two reflexes operate: the gastro-ileal, by which the lower end of the ileum becomes active and passes on its contents through the ileo-cæcal valve to the large intestine, and the gastro-colic by which the colon passes on its contents into the rectum. The latter causes the "call to stool." It is probable also that these reflexes are in part "conditioned." Neglect to evacuate the rectum when loaded tends to cause atony of that part of the bowel which becomes insensitive. There is good evidence that if the call is neglected, solid matter passes by reverse peristalsis back up the descending colon. Although no X-ray evidence is available it is suggested by the fact that a foreign body inserted into the rectum may pass up as far as the splenic flexure. The possibility of reverse peristalsis and the withdrawal of water still further emphasizes the importance of regular habits in relation to the evacuation of the bowel. Regular habits in this respect are therefore essential.

Another aspect of constipation which has received little or no attention is the effect of mental stress. After a painful injury constipation is the rule, and must be considered the normal physiological sequel to stimulation of the sympathetic which we know inhibits gastric and intestinal movements. It is probable, however, that much less degrees of mental stress are important also. Thus many persons are much less constipated when on holiday than when at work even although the diet is similar. Constipation indeed may for this reason be considered a complaint due to civilization.

The sympathetic may be concerned in constipation in still another way. Among the products of bacteria in the small intestine is histamine (E. Mellany), and should it be in excess as a result of stasis it may become absorbed and bring about the secretion of adrenaline, the great sympathetic stimulant. Thus

is produced a vicious circle, the breaking of which may be responsible for the beneficial effect of an occasional purgative in bringing about an increased action of the bowel which may continue much beyond the actual effect of the purgative. It is along the above lines that the detrimental effects of chronic constipation may be explained.

As has been said, stasis has been claimed to be the result of the erect posture and the possible results of the stasis can be best appreciated if we glance at the functions of the large intestine in lower animals where the indication of its real function will be seen. This was well described by Barclay-Smith in 1902 and has subsequently received much attention. In herbivorous animals the colon and particularly the cæcum are well developed and serve as organs wherein the cellulose is broken down by bacteria, for cellulose is not normally attacked by the digestive enzymes. To facilitate the entrance of the food into the large cæcum there is reverse peristalsis in that which corresponds in man to the ascending colon. This anti-peristalsis persists here as a relic in man. At the same time, too, it is necessary that the ileo-cæcal valve should be efficient to prevent the food being driven back into the small intestine, while to deal with any bacterial leak we have developed the well-known lymphoid nodules or Peyer's Patches at the lower end of the ileum. With the assumption of the erect posture the work of the muscle of the ascending colon becomes appreciably increased and it may break down, with the result that whether or not the ileo-cæcal valve becomes incompetent, or retains its efficiency, mere stasis in the cæcal region will result in food remaining too long in the ileum. As the result of bacterial decomposition taking place in this region, the toxic products are absorbed and the effects of these have been emphasized, particularly by Metchnikoff and subsequent writers. It is well known that the former conceived an idea of counteracting the bacteria of decomposition by the addition to the diet of other bacteria which would antagonize them. Obviously, this method is much less physiological than those which promote the activity of the intestine. A great deal, however, of what has been written regarding intestinal stasis is really true, although exaggerated claims have been made in relation to its being the cause of specific diseases. There is not the slightest doubt that in this condition there is general depression, lessened mental and bodily vitality, and reduced power of withstanding infection. There have been some marvellous

sequels to short-circuit operations in some cases, but these successes have been so completely outweighed by the failures that resort to surgery is not justifiable. Anyone who has seen the beneficial effects of colon treatment supplemented by exercises, such as that elaborated by Chalmers Watson and many others for a variety of chronic conditions, cannot but be impressed by its efficiency in the many conditions to which no actual disease label can be attached, quite apart from definite pathological states.

So important are the movements of the intestines clinically that one must be able to estimate their efficiency. In the first instance it must be said that daily evacuation of the bowels is an indication which cannot be relied on. The patient may give a history that this does occur, but the amount excreted may be insufficient or should perhaps have been got rid of some days before. Further, when fæces become packed and dry in the pelvic colon they tend to set up irritation which may even bring about diarrhœa which, alternating with the constipation, will mask the constipation, from the point of view of the patient, although the passage of hard lumps during this so-called diarrhœa indicates the real condition to the clinician. The consistency of the motion is then an important indication, as it depends on the time of retention in the colon.

The most satisfactory method of investigation is by X-rays, as introduced by Cannon, in which the times taken by a bismuth meal to reach different parts of the intestinal tract are noted. The method generally, of course, can be applied only to those parts of the intestinal tract which have a fixed position. It cannot therefore be applied to the small intestine, but it is suitable to use in the large intestine where it is most necessary. A bismuth meal is seen to appear in the ileo-cæcal region four hours after the meal has been taken, preferably in the morning. The hepatic flexure is reached in six to seven hours, the splenic flexure in ten hours, and the pelvic colon in twelve hours. By this means, also, local points of constriction may be observed and any special abnormality in the position of the colon noted.

Often, however, X-ray apparatus is not available, and then a purely clinical examination has to be relied upon. Charcoal biscuits may be given and the time taken for the charcoal to be evacuated noted. Palpation of the pelvic colon per rectum should reveal an empty colon after the bowel has been evacuated and colon lavage or an enema should give little or no result. There

should be no undue dullness or fullness in the cæcal region. These signs, together with inspection of the stools, indicate whether or not the activity of the large intestine is reasonably normal.

A great deal of information can also be acquired from investigation of the bacterial flora of the gut obtained, preferably, after a wash-out. Little attention as yet has been paid to this aspect of physiology, very largely no doubt because few physiologists have a good training in bacteriology. It is, however, impossible to admit that the bacteria can play a considerable part in the economy of the lower animals, such as the herbivora and even as low down as the molluscs, and yet ignore their presence in man. We have, indeed, special lymphoid tissue scattered along the intestinal wall, particularly at the lower end of the ileum, which is apparently intended to deal with any bacteria which may escape from their usual habitat in the large intestine. If the intestinal bacteria are in excess they get into the lymphatics and, as the evidence collected by Kidd shows, are excreted by the kidney, which must be looked upon as a normal channel of excretion, although it is admittedly difficult to see how the bacteria pass through living membranes unless they cause partial lesions. It may be that they cause lesions too small to be significant. It is only when such a comparatively harmless bacterium as *bacillus coli* is excessive that it has any pathological significance in the intestine or in the urine. According to Chalmers Watson the normal stool from an intestine not unduly stagnant and loaded with bacteria should be odourless.

We are familiar with the fact that typical pathological bacteria find their way to the kidney from the intestine, such as *bacillus typhosus*, and that nephritis is a common complication of scarlet fever. These facts suggest that the kidney may be also a normal channel of excretion. There is, indeed, some evidence which suggests that chronic nephritis may in many cases be produced in this way by an excessive excretion, necessitated by chronic intestinal stasis and infection.

INTESTINAL SENSATION

What has been said in relation to gastric sensation applies to the intestine. The viscera themselves are insensitive to all ordinary sensation except pain which is produced only by stretching the intestinal wall.

The pain is commonly associated with contraction, but the

experiments of Poulton suggest that the contraction causes the pain by bringing about stretching of the wall over the bowel contents. It is admittedly a little difficult to accept fully Poulton's view that the pain is essentially due to the stretching and not to the contraction, for the bowel contents may be negligible as in spasm of the colon in which the bowel may be felt to contract. Further, as we have already noted in relation to gastric pain, it has been shown that severe contraction may cause nervous impulses to pass up the sensory nerves although gentle contraction may bring about a cessation of those set up by stretching a muscle. On the other hand, in cholera the getting rid of fluid affords relief, and although there may be colic in this disease it is not always present in spite of the intensity of the diarrhœa. When the bowel is inflamed the pain, however produced, is undoubtedly greater as in acute poisoning by irritants, while if the mucous membrane is damaged there may be intense pain or tenesmus as in dysentery. Presumably the nerves are more sensitive when irritated or inflamed. This probably explains Rovsing's sign—the fact that an inflamed appendix will cause pain if distended when the hand is drawn down over the ascending colon.

The pain of colic is characterized by its intermittent nature, and this and the fact that it is relieved by pressure serve to differentiate it from inflammatory pain. Intermittency is a characteristic of peristalsis, which is best brought about by stretching and direct irritation.

Pain due to excessive peristalsis is very difficult to localize unless the parietal peritoneum or the mesentery is involved. It is this which probably accounts for the indefinite localization in the early stage of an appendicitis (Morley), when the appendix is probably attempting to get rid of a foreign body (Alexis Thomson). Later when the parietal peritoneum is involved the pain becomes localized over the region of the appendix wherever it chances to be lying—usually in the right iliac fossa—and local tenderness, previously absent, is now present. If for some reason or other, *e.g.*, adhesions, the parietal peritoneum does not become involved and the tension in the appendix is no longer kept up because the organ has necrosed, the pain may subside. Its disappearance may suggest recovery when in reality the patient is developing an abscess or other complication. Local (but very careful) palpation, the pulse rate, a leucocyte count, and possibly the temperature, are then of the utmost value in diagnosis.

Pain is also produced by traction on the mesentery, and no doubt this may occur in many abdominal conditions. It is not possible to discuss at length the various ways in which the pain is produced in hernia, intussusception, perforation, and spastic colon, but in general it may be said that the principles exemplified in this section and in that on gastric pain apply.

Embolism of one of the mesenteric arteries also causes severe pain, the nature of which is not quite certain, but experiments of Lewis on striped muscle in which the circulation has been arrested suggest that the accumulation of metabolites sets up a tension in the muscle fibres and causes a stimulation of the nerve endings.

Intestinal pain is often relieved by carminatives such as ginger, which tend to disperse "wind." Atropine paralyses the vagus and is specially valuable in spastic colon. The colic of lead poisoning is relieved at once by intravenous calcium, which apparently takes the place of the calcium fixed by the lead.

In what has been written above it has been almost presumed that constipation is necessarily a harmful complaint, but it must be remembered that the evidence for this is by no means conclusive. Hurst goes so far as to suggest that the symptoms often said to be produced by constipation are really those of the abnormal use of purgatives which are liable to hasten unduly the absorption of incompletely digested protein. Instances are on record of apparently normal people whose bowels act not oftener than once a week; an example of action only once in three weeks is known to the author. Also some persons suffer from considerable malaise or may develop an attack of asthma when the bowel contents are hastened by purgatives.

We should then keep an open mind on this subject and ask ourselves how far we are the victims of the vendors of patent medicines in regard to our instruction on this subject, and if undue purgation is not as harmful as constipation.

CHARACTERISTICS OF ABDOMINAL PAIN

The old "case-taking" sheets made before we knew much about symptom production recognized the following varieties of gastric discomfort: feeling of load or distension, nausea, heart-burn and pain.

The sensation of load is probably purely mechanical and related to stretching of the mesentery or abdominal wall. Nausea

suggests gastric irritation which may later cause vomiting, but it may be produced by stimulation of other sense organs such as those of taste, smell or of the labyrinth. The burning sensation of heart-burn is probably œsophageal and its relief by water or alkalies and eructations indicates that it is due to acidity. Hurst has pointed out that HCl is not the chief agent, probably irritating organic substances are concerned. So far as we know, only the lower end of the œsophagus is capable of appreciating such pain. The pain may, however, be referred to other regions such as that of the duodenum.

Pain itself may be of many degrees. Excessive general distension may amount to pain as in severe flatulence. The pain may be definitely cutting in nature, or it may be a dull local ache, but when primarily dependent on peristaltic contractions it is intermittent.

X-RAY APPEARANCES IN THE COLON

Barium meals are valuable in showing the time taken for the colon to evacuate itself, and thus differentiate colonic stasis from dyschezia. They further differentiate spastic from atonic forms of constipation, and also reveal such conditions as dilatation of the colon, including Hirschsprung's disease. In the latter condition the haustræ are frequently absent, whereas in dilatation due to other causes, they persist. Dilatation of the colon, diverticulosis and obstruction by cancer are as a rule more easily revealed by examination after a radio-opaque enema has been administered than by the ordinary opaque meal, as better filling of the colon is secured.

The cause of Hirschsprung's disease is not definitely known, but a theory favoured to-day is that the underlying disturbance is an achalasia or failure of relaxation of the pelvi-rectal sphincter. The sympathetic nerves are inhibitory to the general musculature of the gut, and motor to the sphincters and division of the pre-sacral nerves appears of all treatments to afford the best prospect of relief.

CHAPTER XXXII

BILE. JAUNDICE

THE FORMATION AND EXCRETION OF BILE

THE comparatively crude fact that bile is composed of pigments formed from the destruction of effete red blood corpuscles and of cholesterol dissolved in a solution of bile salts has long been known, but of recent years a flood of new light has been thrown on the subject by clinical workers, especially by McNee and van den Bergh. Many of our older conceptions of bile formation and of jaundice require revision, especially the location and method of the formation of **bile pigments.**

It is now reasonably established that bilirubin is produced by the breakdown of the red blood corpuscles by the cells of the reticulo-endothelial system which are found in the spleen, the bone marrow, and the venous capillaries of the liver, where they are known as the von Kupffer cells. The best evidence that bile is not necessarily formed in the liver is that there is more in the splenic vein than in the splenic artery (van den Bergh), that the destruction of the liver in cases of poisoning (Dixon Mann and Clegg) bears no relation to the amount of jaundice, and in acholuric jaundice the removal of the spleen brings about recovery. This is supported by the finding of increased bile pigment in the blood in conditions of hæmorrhagic effusions and extravasations, while the colouring of a bruise has always been suspected as a process closely akin to the formation of bile.

The bilirubin when formed passes to the liver and is apparently modified in some way by the ordinary glandular cells. This modification is made evident by the van den Bergh test (which is a modification of Ehrlich's diazo reaction), in which sodium nitrite and a specially prepared solution of sulphanilic acid in hydrochloric acid are added to a sample of the blood serum and compared with the reaction given by a solution of bile. The appearance of a violet colour is known as the immediate direct reaction, but the appearance of the colour only after alcohol has been added is known as the indirect reaction, which is given by

unmodified bile pigment. Unmodified bile also gives a *delayed* direct action, in which a reddish colour, deepening to violet, starts to appear in a quarter of an hour. By this test it is quite possible to determine bile pigment in the blood both qualitatively and quantitatively by comparing with known standards. It is considered that not until the blood concentration of modified bilirubin has reached four units does bile appear in the urine. [The arbitrary unit is one part of bile in 200,000 (Andrews).] The renal threshold for unmodified bilirubin is appreciably higher. A convenient method of estimating the amount of bilirubin in the blood serum is by comparison with a standard solution of potassium bichromate. The colorimeter is used for this estimation, the reading obtained being known as the *icterus index*.

This conception of bile formation certainly affords an explanation for many of the known forms of jaundice and allied phenomena. The well-known discoloration in bruising has now been shown to be due to the formation of a true bile pigment, and it has been shown that there is an increased quantity of unmodified bilirubin to be found in the blood when blood extravasations are being absorbed. The occurrence of slight jaundice under such conditions has often been noted. It has really been from a study of varieties of jaundice that our modern conception of the physiology of bile pigment formation has been drawn. This emphasizes the necessity for scientific physiology to keep in close touch with what appears to be purely medical research. Such correlation has proved necessary in the past in relation to work on the thyroid, pituitary, and pancreas. The debt of physiology to the clinical observer becomes increasingly obvious.

Jaundice may arise according to this conception in three different ways :—

1. **Hæmolytic Jaundice.**—There may be increased blood destruction to an extent which the polygonal cells of the liver cannot deal with, as the pigment is being so rapidly produced. In this category will come those forms of jaundice which used to be called hæmatogenous, of which the anæmias, especially pernicious anæmia, and cases of absorption of hæmorrhagic effusions, are examples. Such forms are now more accurately known as hæmolytic jaundice. As the bile pigment forms in excess and has not been modified by the liver, the blood serum will give an indirect van den Bergh reaction.

2. **Toxic or Infective Jaundice.**—Here the bile pigment may be normally produced but, as the result of the impairment of the liver, it may not be drained off sufficiently rapidly. The unmodified pigment will accumulate in the blood and give a marked indirect van den Bergh reaction. The impairment may occur to any degree, and thus the test may be of little value in distinguishing between this type and the hæmolytic variety, although where the liver is diseased the reaction is more marked. It will be obvious, too, that should the impairment not be severe, or be local, some of the pigment may become modified, but, owing to the state of the liver and its passages, it may not be adequately excreted and on being reabsorbed will cause a direct reaction. Ordinary catarrhal jaundice appears to be of this combined variety. There may be an intense indirect[1] reaction from liver impairment, probably hepatitis, especially at first. Later on, possibly from obstruction by coagulated inflammatory products or cholangitis, there is reabsorption of fully formed pigment and a direct reaction is obtained as well as an indirect one. This supports other evidence, *e.g.*, lævulose and leucocyte tests (*q.v.*), which indicates that catarrhal jaundice has a very definite hepatic origin.

Hurst distinguishes between hepatitis and true catarrhal jaundice. The latter he believes to result from the production of a plug of mucus which blocks the ampulla of Vater.

In order to distinguish the indirect van den Bergh reaction due to hæmolytic anæmia and toxic liver states, it is necessary to do a series of blood counts and reticulocyte counts. In the hæmolytic anæmias there will not only be anæmia, but an increased number of reticulocytes day after day, without any rise in the blood count, while in toxic liver conditions there may be no anæmia, and if there is anæmia there will not be any increased reticulocyte percentage. The recognition of this principle is of great importance. When this is combined with the van den Bergh and icterus index we are a long way on in the differential diagnosis of hæmolytic anæmias from liver diseases.

3. **Obstructive Jaundice.**—Here the bile pigment is normal in quantity and quality, but cannot escape from the liver, and reabsorption occurs from the bile capillaries. Such a condition will occur in simple obstructive cases, due, for example, to gallstones impacted in the common duct, cancer of the head of

[1] A delayed direct reaction is also obtained, and, in some cases, a biphasic reaction, *i.e.*, a red colour appears immediately, deepening slowly to violet.

the pancreas, or new growths otherwise pressing on the bile duct ; the van den Bergh reaction will be direct, for the bile passes through the liver in the normal way.

In diagnosis the van den Bergh reaction must obviously be interpreted with due regard to the state of the patient and the duration of the complaint.

Of special interest is the fact that the reaction has brought to light instances in which the patient, in virtue of a high amount of unmodified bilirubin in the blood, may be assumed to have what may be called a *latent jaundice*, which will become evident if the liver becomes further impaired, *e.g.*, in salvarsan treatment. The fact that glucose (Harrison) has been found of value in preventing jaundice after salvarsan suggests that the glucose may play a part in the normal modification of bilirubin in the liver, just as does the alcohol if added to the unmodified bilirubin *in vitro*. The close relationship of glucose to alcohol chemically appears to favour this possibility. On the other hand, the explanation may be that liver cells are less liable to necrosis by salvarsan and other poisons when full of glycogen than when empty.

Quite apart from the jaundice, the retention of bile will tend to bring about the characteristic pale and fatty stool of steatorrhœa, since we know that the bile salts play an important part in facilitating the digestion and absorption of fats, by stimulating the secretion of, and by co-operation with, the pancreatic juice. The colour of the stools is, then, of importance, as is also the content of fat in arriving at a conclusion regarding the cause of jaundice.

The **bile salts** have another important function in keeping in solution cholesterol which is derived from the breakdown of red blood corpuscles and nervous tissue. Normally this solution is complete, but in certain circumstances, such as excessive production of cholesterol, or as a result of the addition of bacterial products, the cholesterol may become precipitated and give rise to gallstones.

Of considerable clinical importance, also, is the fact first noted by Meltzer that magnesium sulphate applied to the duodenum in the region of the ampulla of Vater causes the relaxation of the sphincter of Oddi, contraction of the gall bladder and expulsion of bile, while use has been made of this by Lyon in investigating the biliary tract by means of the Einhorn tube passed into the duodenum (see also page 287). It is considered that

three distinct fractions of bile can be obtained : one, a golden-brown, is derived from the bile duct ; the second, from the gall bladder, is darker and more viscid ; while the third, from the liver, is thin and watery. The bile should be examined for bacteria, leucocytes, epithelial cells, cholesterol crystals, lipoid material, pigment granules, and excess of mucus (Hurst).

The Excretion of Bile.—The activity of the gall bladder can now be studied by X-rays, since a substance, tetraiodophenolphthalein, opaque to the rays, is excreted in the bile. By its use it may be shown whether or not the liver is excreting normally and whether or not the gall bladder and duct are patent and acting normally. The gall bladder concentrates the bile, so that the shadow increases in density, as shown by successive plates, if this function is retained. Absence of the shadow indicates obstruction of the cystic duct, provided the liver—and otherwise cholecystography should not be carried out—is functioning properly. Gallstones show up as clear areas, but if pigmented or calcified may give positive shadows. The use of the method has shown that the taking of fatty substances causes a contraction of the gall bladder, an observation of some importance ; we know that bile assists in the digestion of fats. The gall bladder contracts very well if cream and yolk of egg are taken or adrenaline injected.

Cholagogues.—The best stimulant of the secretion of bile is bile itself, since, as shown by Schiff, the bile salts are reabsorbed from the intestine. There is then a circulation of the bile salts. The bile salts are derived from protein and cholesterol-like substance. The effect of excessive purgation and loss of bile salts offer an interesting speculation in relation to the formation of gallstones.

CHAPTER XXXIII

THE METABOLIC RATE

THIS term is used to indicate the rate at which oxidation processes are taking place in the body. This rate varies enormously with the activities of the individual, mental and physical, especially the latter.

Basal metabolism, or the basal metabolic rate (B.M.R.), has of recent years been brought into prominence. It represents the heat expended by the body at rest and in circumstances under which it is doing a minimum of work, all functions being reduced accordingly. There must also be a state of mental quietude, often difficult to obtain in nervous patients who only attain mental rest when they are accustomed to the necessary procedures.

The heat is expressed in large calories, one such calorie being the amount of heat required to raise the temperature of 1 kgm. of water 1° C. For full details of the method of determining the B.M.R., reference must be made to practical works, but the principles may be indicated here. Ideally, the amount of heat produced by the patient ought to be measured by placing him in a calorimeter or chamber in which the heat he produces can be measured directly. Such expensive apparatus is, however, not generally available, and use must be made of indirect methods by which the oxygen used is determined and the heat produced calculated.

In Benedict's method the patient breathes to and from a spirometer containing pure oxygen, his expired carbon dioxide being absorbed by soda. The amount of oxygen used is then measured directly.

Another method in use in this country is that of collecting the patient's expired air for ten minutes in a Douglas bag. The latter is an air-tight bag of about 50 litres capacity, and used with a valved mouthpiece. From an analysis of the inspired air and expired air the amount of oxygen used during the period can be calculated, and from the amount of nitrogen in the urine, the oxygen used in consuming the protein. The remainder is used

in the oxidation of carbohydrates and fats, the relative proportions of which are indicated by the respiratory quotient. The caloric value of a litre of oxygen used to consume these foods being known, we can calculate the number of calories produced.

Having already found the amount of oxygen used in a given time, we can determine the total number of calories expended in that time.

Apart from some experience of gas analysis which is not difficult to obtain, no special technical experience is required and much calculation can be avoided by the use of tables. Douglas's method has the advantage that it can be used in the study of work under different conditions. The Benedict apparatus is less portable but gives more rapid results.

It is obvious that a man with a low metabolic rate is one who requires less energy supply for his essential functions, and he will, therefore, have more to spare for other work. If the excess is not used in such work there will be a tendency to grow fat; those with a high metabolic rate tend to become thin. As would be expected, febrile conditions raise the basal metabolism provided the reserves of the body have not been exhausted by long illness. Various attempts have been made to use this as an aid in the diagnosis of obscure conditions, *e.g.*, tuberculosis, whether the patient is febrile or not, and so on. It is clear, however, that in such conditions the basal metabolism will depend on the actual state of the individual patient. Obviously, too, the taking of a large protein meal will increase the B.M.R. in view of the specific dynamic action of protein, and for purposes of comparison the desirability of making observations before breakfast is obvious.

A little difficulty exists in finding a really accurate method of expressing the results for purposes of comparison. We have said that for an average adult the basal metabolism is about 1,700 calories per day. The energy output is commonly expressed in terms of body surface, the surface being calculated from the height and weight, but others prefer to express the result as a percentage increase or decrease on the normal, the normal being considered 40 calories per hour per square metre of surface. It will, however, be realized that the surface of a very large individual may not depend on an increase of active tissue but on fat. It is generally admitted that there is a ± 15 per cent experimental error.

Benedict has constructed elaborate tables which give the

standard metabolic rates for a variety of people of different size, age, weight, and sex. The last is necessary, as men have a slightly higher rate than women.

The nervous system has also a marked influence on metabolism. We are all familiar with the highly-strung neurasthenic who is thin although he may take large supplies of food. In such a man the reflexes are exaggerated and the increase in tone uses up more energy, while the man himself expends more energy in maintaining the essential functions. Such individuals have not infrequently a decided liking for proteins and highly flavoured articles of diet and may have even a disgust of fats. This dietetic selection will further contribute to their thinness, as has been indicated above. The opposite effect is evident in the imperturbable happy and rotund individual who seldom gets flurried. Such a mental state, added to excellent digestion, the two acting beneficially on each other, forms a good physiological basis for the truth of the old adage : " Laugh and grow fat."

The metabolic rate while at a sedentary occupation is about 2,000, while at an active physical occupation it may be 4,000 or 5,000. At very severe work, cycling or wood-cutting, over 8,000 has been recorded.

THE METABOLIC RATE AND THE THYROID GLAND

We now know that the metabolic rate is controlled by the secretions of the thyroid gland, which if diseased may have a profound effect on metabolism. The thyroid elaborates a " catalyst " which hastens the fundamental reactions of metabolism, and thereby confers on man and the higher animals a greater range of activity than would otherwise be possible. The truth of this is seen in observing the limitations placed on those suffering from a deficiency or excess of its secretion. The thyroid is also largely responsible for growth (*q.v.*).

In **Myxœdema**—or Thyroid Deficiency—there is evidence of slowed metabolism. All the bodily functions are slowed, and in consequence heart rate and body temperature are low. The mental responses are sluggish. The failure to burn fuel results in the deposition of fat. The skin becomes dry and the hair thin if not lost. The characteristic sign, however, from which the condition receives its name is the myxœdematous or mucoid degeneration of the subcutaneous tissue which is differentiated from true œdema by the fact that it does not pit on pressure unless

complicated by renal disease. The etiology of myxœdema is unknown.

Hyperthyroidism.—Of more serious consequence is hyperthyroidism in which there is excessive action of the thyroid gland. Hyperthyroidism exists clinically in many different degrees. It is characterized by all the signs of excessive metabolism, and excessive sympathetic activity. The heart rate is extremely rapid, the nervous system responds extremely rapidly to stimuli, the skin sweats, the pupils are dilated, and the patient in general appears to be in a very nervous and excited state. In the severer variety there is exophthalmos or protrusion of the eyeballs. Myocardial degeneration is specially liable to occur in patients over the age of forty, probably because at that time of life the myocardium is prone to degenerate. The nervous manifestations are more intense in young subjects, for in them this system is not yet fully stabilized. There is no doubt that there is an excessive or abnormal action of the thyroid. This is well seen in the clinical results achieved by surgery or X-rays which bring about almost certainly practical disappearance of the state which otherwise would lead to the death of the patient, as a rule, from cardiac failure. Anyone, too, who has seen the records, such as those of Rowden—over 300 unpublished—of cases treated by X-rays, some of which have actually become myxœdematous as a result, cannot but be impressed by the relationship between the thyroid and the pathological states. When marked, the exophthalmos, however, does not disappear although the patient has otherwise recovered. Incidentally such records show the efficacy of X-ray treatment *properly carried out.* The disadvantage is that X-rays cause considerable fibrosis around the gland and render subsequent operation extremely difficult.

Whether the thyroid is the primary seat of the disease is another matter, and many attempts have been made to associate it with disease elsewhere in the sympathetic or endocrine system. The failure to obtain evidence of increased thyroid secretion in the condition may be due to the fact that the secretion is itself abnormal. Evidence has accumulated which indicates an antagonism between the suprarenal cortex and the thyroid. Further than this it is not desirable to go, except as an interesting speculation. The withdrawal of the normal antagonists would be expected to result in over-action of the thyroid. It is now abundantly proved that small doses

of iodine may be of considerable temporary benefit in hyperthyroidism. There is diminution in the basal metabolism and heart rate, together with a marked increase in body weight and a striking improvement in the general condition of the patient (Fraser). How this improvement is brought about it is difficult to see, but it may be noted that the thyroid undergoes histological involutional changes after administration of iodine in exophthalmic goitre. That some profound disturbance of the sympathetic headquarters in the hypothalamic region underlies some of the cases of exophthalmic goitre has been suggested. Lesions in this neighbourhood at least cause some of the symptoms also found in hyperthyroidism.

Apart from iodine treatment and surgery, all medical measures which tend to rest the patient physically and mentally are of great value. Not infrequently rest in bed is insisted upon prior to operation. The rate of the heart becomes noticeably reduced by such treatment. This is important, for the cardiac state adds greatly to the danger of operation. The activity side of the sympathetic-parasympathetic system is reduced by the rest, and also that of the endocrine balances which are described in a later chapter. The cardiac condition found in hyperthyroidism has been dealt with in relation to the rate of the heart.

The nature of the substance elaborated by the thyroid gland and passed into the blood-stream for long escaped elucidation, largely because of the difficulty in determining small quantities of iodine which was shown by Bauman as long ago as 1895 to be contained in the thyroid.

The active principle of the gland, to which the name thyroxine is given, has now been isolated and synthesized by Harrington, and has been shown to be an iodized amino-acid. Its chemical constitution indicates that it is derived from two molecules of tyrosine, which is an amino-acid derived from the digestion of protein. It is interesting to note that this amino-acid had already been shown by Hopkins to be important in relation to the growth of young animals.

Here, too, we may remind ourselves that the most advanced nations of the world are the greatest protein eaters, and we have noted the greater sphere of activity which a wide range of metabolic rate confers.

THE THYROID AND SIMPLE GOITRE

The thyroid, lying around the upper rings of the trachea, and

extending upwards and downwards on each side, and covering with its lateral lobes a part of the thyroid cartilage, is largely responsible for the rounded contour of the neck. Changes in its size may be readily noted, and this special feature considerably affected the old ideas concerning its functions. It was thought, even by Wharton, to play a part in the mellowing of the voice, and in beautifying the neck of woman, in whom it is the more prominent.

Old paintings suggest that goitre or simple enlargement of the thyroid was much more common than at present. The term " goitre " is given to an enlargement of the thyroid not associated with any symptoms except those due to pressure on neighbouring structures, such as the trachea. There is an accumulation of colloid in the vesicles of the gland which become distended.

The accumulation of abnormal colloid in the vesicles of the gland is now looked upon as a secondary change analogous to the occurrence of colloidal degeneration in other conditions, although in some instances it may be due to retention. The colloidal degeneration is preceded by a proliferation of the glandular elements.

Simple goitre has been shown, largely as a result of the work of Marine, to be brought about by *iodine deficiency.*

Normally we obtain our iodine from articles of diet, such as fish, milk, eggs, certain cereals and vegetables, and we require such small quantities that we need not worry about them, although this does not appear to be so in certain districts of America where the iodine in the soil is low.

In districts in which goitre is endemic amongst human beings or domestic animals, such as sheep, the administration of iodine has been of enormous benefit. In some instances potassium iodide has been administered to school children on a large scale with most satisfactory results, while in Michigan iodine, administered for convenience in conjunction with rock salt, has made sheep rearing possible.

For some time there was difficulty in reconciling with the above the striking evidence of McCarrison as to the infectivity of goitre as a water-borne disease. This had been corroborated in many quarters. It has now been realized, however, that iodine, like iron, must be not only supplied, but absorbed, and many factors may interfere with its absorption and utilization. These factors have been worked out experimentally, especially by McCarrison, and the results support clinical experience. The absorption may

be interfered with by certain intestinal bacteria, and iodine deficiency so produced is common apparently in this country and more so in India where the conditions for the spread of water-borne disease are more favourable. It has been shown that such cases benefit not only by treatment with intestinal antiseptics, such as thymol, but also with iodine and preferably with both. The benefits which accrue from the administration of antiseptics indicate the bacterial factor associated with the disease, even in sporadic cases in this country, although why the condition remains sporadic is difficult to understand.

Excessive calcium in the diet brings about a similar interference, and this is considered to account for the endemic goitre associated with Derbyshire. The excessive calcium, according to McCarrison, increases the viscosity of the normal colloid of the gland and favours its accumulation, while an additional supply of iodine counteracts this effect, although unfortunately an abnormal amount of colloid may still be maintained in the gland, as the normal storehouse for iodine is in the thyroid, as is shown by the effect of thyroid feeding.

Certain fats also, especially butter and the unsaturated oleic acid, have been shown to cause goitre in animals, but the ways in which this must be brought about are very numerous, and it is by no means clear how they act, although it seems most probable that they combine with the iodine and somehow prevent its utilization.

CHAPTER XXXIV

BLOOD-SUGAR AND PANCREATIC EFFICIENCY

THE modern treatment of diabetes by insulin and its control by estimation of the blood-sugar makes this determination of great clinical interest, and it is a good example of the influence of pure physiology on clinical medicine.

The level of the **normal blood-sugar** varies from 0·08 to 0·17 per cent, and depends chiefly on the amount of carbohydrate being absorbed. One must suppose that this concentration is necessary for the satisfactory working of the vital organs just as a certain concentration of carbon dioxide is necessary. If the blood-sugar in a starved rabbit is reduced by insulin injection below 0·04 per cent, the animal goes into convulsions and dies. This was taken advantage of in the original standardization of insulin, the strength of which is estimated by its effect on a rabbit of given weight and under given conditions, but now a standard agreed upon by a League of Nations' committee is accepted. Recovery from the convulsions may be brought about by the injection of glucose. Interesting cases have been described of patients with adenomas of the pancreatic islet tissue who exhibit symptoms of hypoglycæmia and learn to keep the condition in abeyance by eating sweets. Hypoglycæmia may also occur as a result of gross liver lesions and in this connection it may be pointed out that Mann and M'Gath found that dogs whose livers had been extirpated died rapidly from hypoglycæmia, unless given frequent feeds of carbohydrate. Nadler and Wolfer have described a case of liver neoplasm, not composed of islet tissue, in which severe hypoglycæmia was present. This, however, was thought by Tuttle to be due to over-production [1] of insulin by the tumour. Rabinovitch has also described hypoglycæmic symptoms in adrenal lesions and Cammidge has long maintained that mild degrees of hypoglycæmia are a not infrequent cause of general debility. Hypoglycæmia also occurs in the rare von Gierke's hepatomegaly, in which the enlarged liver contains an

[1] Tuttle believes that all the cells of the body produce a certain amount of insulin for their internal metabolism.

excess of glycogen. Warner has shown that in von Gierke's disease injection of adrenaline fails to evoke the usual rise in blood sugar. The accumulation of glycogen in the liver in this condition is attributed to absence of the enzyme *glycogenase*, which normally converts glycogen into glucose. Any excess of sugar in the blood above 0·17 per cent is excreted by the kidney. This percentage is often referred to as the " renal threshold " for sugar. This is also called the " leak point " of the kidney, and is of important clinical significance. It is not until the blood-sugar has exceeded the renal threshold that sugar may be detected in the urine, by such common tests as that of Benedict. The finding of sugar by such a test is therefore clear evidence of abnormality. As soon as the blood-sugar rises above 0·2 per cent there is a marked decrease in the power of the kidney to retain sugar (Hamburger), and a much greater proportion of the excess appears in the urine. It is evident that, should the threshold be reduced, although the blood-sugar is not excessive, there will be glycosuria of the type known as *renal glycosuria*, which occasionally occurs as a harmless anomaly. The mere presence of sugar in the urine does not necessarily indicate hyperglycæmia, *i.e.*, excessive sugar in the blood, and should steps be taken to reduce the blood-sugar further by injection of insulin, disastrous results may obviously ensue. Actually the stores of sugar or glycogen would first be used up, for it is more difficult to produce convulsions in a well-fed animal than in one which has been starved. Impairment of the kidney by disease, such as nephritis, on the other hand, raises the renal threshold. In many diabetics, particularly in older subjects, a rise of the threshold is frequent, and although the urine may be free from sugar, the blood-sugar level is high.

A rise of blood-sugar will occur: (1) if an excessive amount of sugar is absorbed from the alimentary canal ; (2) if the sugar is insufficiently used ; and (3) if sugar is liberated from the liver in excess.

Here perhaps it should be said that the term sugar is held to mean the copper-reducing monosaccharides, but chiefly glucose.

Should the hyperglycæmia and consequent glycosuria be due to excessive sugar ingestion this will at once be indicated by the diet, but it is evident that if there is any deficiency in the sugar utilizing powers of the patient, less sugar than normal will cause the glycosuria. This has been applied to the diagnosis of diabetes. Normal adults should be able to assimilate one or two hundred

grammes of glucose without any sugar appearing in the urine, and some individuals can ingest as much as 500 grammes. So many factors, however, such as absorption from the gut and the habit of the individual, may influence the result that this test, according to Macleod, cannot be relied upon. The assimilation power, as it is called, has for many years been of considerable value in the dietetic treatment of the diabetes ; indeed, it was the basis of treatment prior to the discovery of insulin, and is still used for milder cases of the condition. The patient's diet is regulated so that the carbohydrate intake is just short of that which causes glycosuria, and he can as a rule be taught to make simple urine tests for his own guidance. The danger of cutting off carbohydrate suddenly will be dealt with below.

The clinical test now commonly used for ascertaining the power of the body to deal with carbohydrate is the determination of the *blood-sugar curve* or *Sugar Tolerance Test.* In the test 50 to 100 grammes of glucose are given in water by the mouth and samples of blood are taken for the estimation of the blood-sugar each half hour for three hours. The maximum value is normally reached in one hour and at the end of this time the blood-sugar begins to fall and returns to normal or even below by the end of the second hour. The highest level should not exceed 0·15 per cent, and certainly a reading of over 0·17 per cent is pathological. The fall in the blood-sugar is apparently due to the secretion of insulin by the pancreas, which can deal with the sugar as rapidly as it is absorbed, since the further ingestion of glucose has no effect. In diabetes this rapid fall does not take place, a high blood-sugar being maintained for some hours. In certain individuals a " lag curve " is found. There is a delay in the storage of sugar, so that the curve overshoots the renal threshold, but soon returns to normal. Such a condition frequently, but not always, represents the earliest stage of true diabetes. In any case it calls for dietetic restriction in the matter of carbohydrates.

Hyperglycæmia or increased blood-sugar will also result from inability to use sugar, although the intake may be normal. This condition is seen pathologically in *diabetes mellitus*, and can be produced experimentally by stimulation of the splanchnic nerves, injection of adrenaline, and stimulation of the floor of the fourth ventricle, or of the pituitary region.

The body uses sugar in three ways : it burns it as fuel, it builds it up into glycogen or animal starch in the liver and muscles as a store of energy for immediate use, and it transforms it into fat, in

which form the energy store occupies less space, although it is less easily available.

The work of Banting and Best (1922) and those who followed in their wake has clearly demonstrated that the Islets of Langerhans in the pancreas are largely responsible for the proper utilization of sugar in the body, thus confirming the many pathological observations which demonstrated pancreatic disease in diabetes. It was shown in 1889 by von Mering and Minkowsky that removal of the pancreas brought about in dogs a condition similar to diabetes in man, and it was subsequently found that such a condition was not brought about by mere ligature of the pancreatic duct, although this procedure caused the secreting alveoli to degenerate.

The experiments of Banting and his collaborator Best, founded as they were on the earlier and purely scientific investigations, make a great modern romance and are an excellent example of how investigations—vivisection, in fact—made in the first instance purely for the sake of knowledge may be of enormous value to mankind.

Modern diagnosis of diabetes and treatment with insulin rest upon an accurate determination of the blood-sugar. An increase of blood-sugar and glycosuria may also result from a variety of states, even when there is no actual disease of the pancreas. Normally the blood-sugar rises during severe exercise, and after a long boat race it is common to find sugar in the urine of the oarsmen. This is no doubt the result of the mobilization of the liver glycogen in excess of what has been needed by the muscles.

How this takes place and how increased requirement of muscular tissue brings about the discharge from the storage areas is by no means clear, although we know that both nervous and hormone stimulation may bring about excessive discharge from the liver and cause hyperglycæmia with glycosuria. Any stimulation of the sympathetic nervous system calculated to cause an outpouring of adrenaline from the suprarenal brings this about, and some of the methods referred to above for producing glycosuria experimentally are of this nature. In the same way, any emotion calculated to bring into action the emergency mechanisms has a similar result, and the advantage in such circumstances of throwing into the circulation additional supplies of immediately utilizable fuel is obvious. It is considered by some that mental anxiety and strain may bring about a similar sequence of events. This is somewhat conjectural, and during war-time diabetes was not

unduly common, but in this instance the effect of the anxiety may have been counteracted by dietetic reductions. It is also quite certain that this in no wise accounts for all cases of diabetes, as many most phlegmatic persons are victims of the disease.

The secretion of insulin appears to be controlled by an area in the hypothalamic region sensitive to the concentration of the sugar in the blood (Beattie), and from which impulses pass down by the vagus (Clark and others) to the pancreas. Stimulation of this nerve in suitable circumstances lowers blood-sugar. Hoet and his co-workers have claimed that if sugar is injected, glycogen is not stored if the vagi are cut, but this has not been confirmed (Clark). The normal stimulus to the secretion of insulin appears to be the blood-sugar, since if after 100 grammes of glucose have been given and the blood-sugar has returned to normal, a further quantity is given, the blood-sugar does not rise nearly so high, if at all.

The parasympathetic control of the secretion of insulin suggests that circumstances in which the sympathetic is stimulated may have the opposite effect.

Such sympathetic stimulation is seen in exophthalmic goitre, in carbon dioxide retention such as may occur in cardiac disease or interference with the respiratory tract, in tumour or injury to the brain, especially if there is interference with the region of the pituitary or the floor of the fourth ventricle. It may also be noted during pregnancy and in a variety of temporary conditions such as epileptic convulsions, the paroxysms of malaria, the collapse of cholera, or injury to the liver, all of which are of interest not only to the clinician but in the more purely academic study of carbohydrate metabolism.

It has also been found that when the body temperature is raised diabetics require more insulin than usual to keep their blood-sugar at the normal level. In all these states we may consider that the high blood-sugar is the result of increased sympathetic activity which occurs in such circumstances and the consequent discharge of the liver glycogen. If the blood-sugar rises high enough to allow of escape from the kidney, glycosuria also occurs.

The glycosuria of pregnancy may depend on increased sympathetic activity and partly on increased pituitary secretion which Dixon claimed to occur. Pituitary extract has been definitely shown to antagonize insulin.

Diabetes Mellitus

It has long been known that disease of the pancreas is associated with the clinical condition of *diabetes mellitus* and that this condition can be simulated experimentally by extirpation of the pancreas from an animal. The essential feature of the condition is faulty utilization of carbohydrates, which we now know results from the inefficiency of the secretion of the Islets of Langerhans. Carbohydrates are absorbed from the intestine into the blood, but as they cannot be utilized[1] the blood-sugar rises above the renal threshold and the excess of sugar passes out by the urine and is wasted. The excretion of sugar at the same time necessitates a considerable loss of water, and polyuria results with a urine of high specific gravity. From the lack of carbohydrate fuel we have excessive appetite, and as a result of the polyuria, excessive thirst. There is often a feeling of considerable weakness. When the symptoms are clear the diagnosis is confirmed by the finding of sugar in the urine, but absolute confirmation is obtained by determination of the blood-sugar and an indication of degree by the blood-sugar curve (see page 349). There is a considerably diminished resistance to infection, and most cases of diabetes succumb eventually to intercurrent disease. Often some minor symptom of this nature, such as boils, carbuncles, or pruritus, is the actual complaint of the patient. Peripheral neuritis with absence of reflexes, and various other nervous and eye phenomena are common complications. How these changes are brought about is not yet understood, but it seems likely that nervous tissue is particularly sensitive to inadequate metabolism and we know that lack of oxygen rapidly abolishes nervous function.

The most serious result of deficient carbohydrate metabolism is that the fats are insufficiently burnt, for, as we have seen, "the fats burn in the fire of the carbohydrates." Normally the fats are oxidized for the most part, as shown by Dakin, by the process of *beta*-oxidation to CO_2 and water. In this process the carbon atoms are oxidized two at a time and the fatty acid reduced to a lower member of the fatty acid series, a process made possible by the fact that all the natural fats contain an even number of carbon atoms.

[1] By "utilized" is meant both "stored" and "catabolized." The relative failure of carbohydrate catabolism is shown by the low respiratory quotient found in diabetes, the failure of storage by the low liver glycogen. Indeed, the liver cells in the diabetic actually form glucose from amino-acids.

The chemical reaction taking place may be indicated thus. Caproic is taken as an example of a long chain fatty acid which becomes oxidized at the *beta* position. Thus caproic

$$\overset{\beta \quad \alpha}{CH_3 . CH_2 . CH_2 . CH_2 . CH_2 . COOH} + 3O_2$$

becomes butyric acid $CH_3 . CH_2 . CH_2 . COOH + 2CO_2 + 2H_2O$. The breakdown of the latter may be shown to occur in stages, but normally all the reactions occur together.

$CH_3 . CH_2 . CH_2 . COOH$ (butyric).
$+ O = CH_3 . CHOH . CH_2 . COOH$ (β-hydroxybutyric).
$+ O = CH_3 . CO . CH_2 . COOH$ (aceto-acetic or diacetic) $+ H_2O$.
$+ 4O = CH_3 . COOH$ (acetic) $+ 2CO_2 + H_2O$.
$+ 4O = 2CO_2 + 2H_2O$.

In passing through the stage of butyric acid, that is the four carbon atom stage, oxidation appears to be difficult, and if, from deficient carbohydrate metabolism, combustion is not sufficiently complete, instead of the intermediate butyric acid being oxidized rapidly through to CO_2 and water, the intermediate products as the result of the slow reaction are found in such quantities that they may actually be excreted as such in the urine. These are β-hydroxybutyric and aceto-acetic acids, from which latter acetone is formed by losing CO_2:—thus $CH_3 . CO . CH_2 . COOH - CO_2 = CH_3 . CO . CH_3$. The formation of these two acids tends to deplete the alkali reserve of the blood and its carbon dioxide combining power and leads to a so-called acidosis or, what is more usual because of the keto bodies, to a ketosis. Proteins may also contribute to their production. In addition, these substances are in themselves poisonous, and may account for some of the symptoms of the condition. There is, for example, excessive stimulation of the respiratory centre as the result of their existence, and the carbon dioxide in the alveolar air becomes appreciably reduced, a point often of value in confirming a diagnosis. If the state remains untreated, the accumulation of these abnormal substances finally overcomes the organism, and coma and death follow.

Diabetic coma is accompanied by severe dehydration, because the water lost by evaporation in the expired air is excessive on account of the air-hunger and also because of antecedent diuresis.

TREATMENT.—Knowledge of the physiological processes at fault at once indicates the treatment. In all modern treatment, in

the severer cases at least, the administration of insulin overshadows all others. Insulin was so named by Sharpey-Schafer somewhat prophetically, for at the time the name was given, it was not absolutely proven that the Islets of Langerhans contained the hormone responsible for efficient carbohydrate metabolism, although the evidence pointed in that direction.

Starting from the work of Banting and Best, who showed by the use of extracts of fœtal pancreas in which the power to produce trypsin is not developed, and of glands of which the duct had been tied (to cause degeneration of the trypsin-producing cells of the gland), that trypsin destroys the insulin produced by the islets, Collip made use of the fact that the enzyme is inactive in alcoholic solution. He prepared active alcoholic extracts of the gland with which dogs rendered diabetic by removal of the pancreas were successfully treated. It should be said that previous work, such as that of Zuelzer, had been attempted along these lines, but then apparently overdoses were given, as the blood-sugar level could not then be used as a control, and as the positive evidence, such as that of Banting, that the hormone was contained in the islets and was destroyed by trypsin, was not available, the experiments were abandoned. Commercial insulin is made by improvements on the alcoholic extraction method. By its use many patients have been rescued from coma which must otherwise have been fatal. Insulin is, therefore, a drug which should be in the possession of every practitioner, as a diabetic patient may often go into coma with dramatic suddenness. The insulin simply takes the place of the deficient internal secretion of the pancreas and renders adequate carbohydrate metabolism possible. The treatment is relatively new, but it is doubtful if its continued administration allows the pancreatic islets to regenerate in most cases. The older methods of treatment calculated to rest the pancreas and to allow it to recover must therefore be continued.

Rest to the pancreas is accomplished by reduction of carbohydrate intake. Here it may be mentioned that it has long been a well-known clinical observation that diabetes not infrequently occurs in those who have been habitual overeaters. Allen has shown that the giving of large quantities of carbohydrate to dogs, rendered slightly diabetic by partial depancreatization, causes them to develop more severe diabetes. From this fact the value of keeping a mild diabetic on a low carbohydrate diet is evident, and many so treated never develop severe diabetes.

Diabetes of any severity is usually treated to-day by putting the patient on a diet which contains a fixed ration of carbohydrate 75–100 grm. daily, with or without standardization of the fat and protein. It appears from our own experience as well as from the work of Lawrence, that the amount of protein and fat may be safely left to the tastes of the average patient. If the patient cannot metabolize this amount of carbohydrate, or if he is a child, he needs insulin. Further, if he loses too much weight, the diet must be increased and more insulin given if necessary. The insulin is injected twice daily half an hour before meals. Should a septic or other infection develop, the sugar tolerance falls and the insulin dosage may need increase. The treatment should as far as possible be controlled, not only by urine testing and the body weight, but also by blood-sugar estimations. High carbohydrate diets have been favoured recently, but the time is too early to pass judgment as yet on their advisability. At the same time general attention must be paid to the alimentary canal, which, as Cammidge has shown in a large number of cases, may have contributed to the production of a pancreatic condition of a chronic inflammatory nature. Details of treatment must be studied from textbooks on therapeutics, but sufficient has been said to indicate the general physiological principles involved.

A word of warning is, however, necessary regarding the cutting off of carbohydrates suddenly, especially in fat diabetics. On starvation, the store of glycogen is, of course, first used up, but if the individual has a store of fat, this is now used ; its utilization may result in the flooding of the system with keto-acids, and coma may ensue. The carbohydrates, then, must not be taken away too quickly. Such an occurrence is not so apt to happen when the individual is thin, and there is little or no fat storage.

Once coma has developed little but insulin is of any avail, but accessory measures of treatment directed against the collapse and dehydration which accompany diabetic coma must not be neglected. The onset of coma, however, is reasonably preventable. Diacetic acid in the urine (aceto-acetic), which gives a red colour with ferric chloride, is always a danger sign, and, when present, alkalies should be given and the carbohydrates not unduly reduced.

It must be realized, however, that the giving of insulin is not free from risk, as dire results may occur from overdosage. The patient may indeed pass from the coma of diabetes to the coma of hypoglycæmia without regaining consciousness.

It is therefore desirable to give glucose or carbohydrate by the mouth or, if the patient is in coma, intravenously, at the same time as the insulin. If the patient is conscious the onset of hypoglycæmia is marked by nervous symptoms such as excitability, perspiration, and tremor, often accompanied by hunger, flushing, or pallor. In an emergency adrenaline may be injected to mobilize the liver glycogen or pituitary extract to antagonize the insulin, but if the glycogen stores are depleted adrenaline is dangerous. One effect of an injection of insulin is to call forth a secretion of adrenaline which is in a sense compensatory. In cases of diabetes with cardiovascular degeneration the rise in blood pressure and cardiac stimulation due to this secretion are not entirely without danger, and in these insulin should be used with caution.

The Blood-Sugar in Pregnancy.—In pregnancy glycosuria is common, quite apart from lactosuria, which is apparently due to absorption of lactose from the breasts. This we may consider to be related to the pituitary body. It has been shown by Herring that the pituitary body increases in pregnancy, while Dixon and Marshall have brought forward evidence of an increased secretion of pituitrin, and we have since learnt that the pituitary is responsible for the changes in the breasts in pseudo-pregnancy (*see* Menstruation).

About 20 per cent of pregnant women have glycosuria about the fifth month. There is also a marked fall of sugar tolerance. Alimentary glycosuria is much more readily produced than in the normal ; indeed, this is occasionally used as a test for pregnancy, although the investigation of the blood-sugar curve would now be looked upon as a more accurate means of diagnosis.

Watson has shown that this functional diabetes may produce an actual ketosis from faulty oxidation of fats. As pointed out by this author there is not necessarily a high blood-sugar or glycosuria in pregnancy, since the carbohydrate not used by the mother is used by the child ; indeed, in this way more sugar is made available for the child. An actual diminution of blood-sugar is indeed possible if the utilization by the child is excessive. This still further aggravates the ketosis which is relieved by the administration of glucose.

CHAPTER XXXV

DISORDERS OF METABOLISM

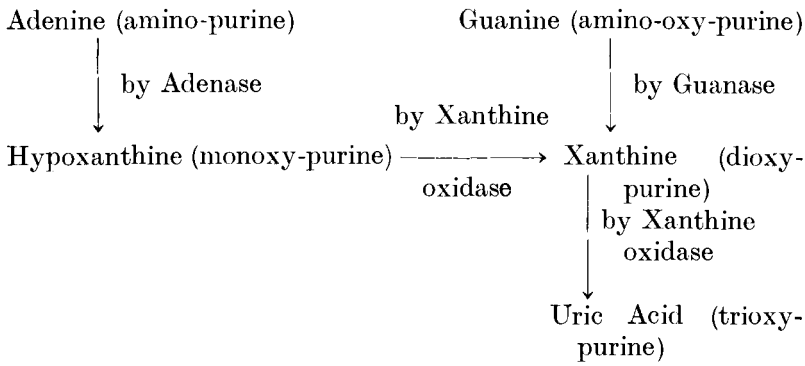
DIABETES mellitus has already been considered in the last chapter, and is probably caused by a disturbance of the islets of Langerhans of the pancreas, although the recent work of Himsworth and others suggests that another as yet undetermined accessory factor may be concerned. In this chapter will be discussed certain other disorders of metabolism of which some are inborn, such as cystinuria, and in others, such as gout, a strong inherited predisposition occasionally operates.

Gout.—In 1797 Wollaston showed that the tophi of gout contained uric acid. Actually they are composed of sodium bi-urate. A. B. Garrod in 1847 demonstrated, by means of his thread test, the presence of uric acid in gouty blood, or, in the light of modern chemical knowledge, the presence of an excess of uric acid, for normal blood contains 1–3 milligrammes per 100 c.c. in the form of sodium bi-urate. Although it is believed that excess of uric acid in the blood is an essential feature of gout, some other factor must also be at work, for in leukæmia and in chronic nephritis the blood uric acid level is high without gout being present. Modern work has been specially directed to discover what this cryptic influence may be, and, as will be seen in the sequel, has brought out many interesting facts but has failed to give a complete and universally accepted explanation. Before gout is considered, normal purine metabolism will be briefly discussed.

The uric acid of blood is the end product of the catabolism of purine bases. The urinary uric acid comes from the blood and about 0·75 gramme is excreted daily on a mixed diet. Of this amount about one-third is endogenous, that is to say, results from the wear and tear of nucleo-proteins of the tissue-cells, part at least representing the destruction of the nuclei of the developing red-blood corpuscles. The remainder is exogenous and is formed by the catabolism of the purine derivatives of nucleo-protein ingested in food after the tissue needs have been satisfied. The exogenous fraction is more variable than the endogenous and is

increased when substances rich in nucleo-protein are taken, such as kidneys, liver, sweetbread and tomatoes. Although nucleic acid is the main constituent of the chromatin of cell nuclei, nucleo-protein also occurs in cytoplasm. The endogenous output of uric acid is increased in pneumonia and leukæmia. The nuclear metabolism of the excessive numbers of leucocytes is not the sole source of the high blood uric acid values found in these conditions, for Martin and Dennis found that when in leukæmia the numbers of the leucocytes were diminished by X-ray treatment, there was little effect on the uric acid, and in pneumonia a high uric acid value may be present in the absence of leucocytosis. It would appear that tissue autolysis in these conditions plays an important part as a source of purines. The body has some power of synthesis of purine bases, when purified foods free from these are given, from amino-acids such as histidine and arginine.

The purine bases which are constituents of nucleic acids and therefore of nucleo-proteins are adenine or amino-purine, and guanine or amino-oxy-purine. During catabolism these are converted by deaminizing and oxidizing enzymes, in the liver and elsewhere, through a series of intermediate compounds into uric acid which is trioxy-purine. These changes are indicated in the following scheme :—



Xanthine and hypoxanthine are also present in small amounts in muscle, which as meat constitutes an important part of the dietary, and are, after they have been absorbed, converted into uric acid. Hence, in the treatment of gout, not only should the amount of foods rich in nucleo-protein be restricted, but also some moderation in the taking of meat should be advised. The methyl-purines, caffeine of tea and coffee and theobromine of cocoa, are not appreciably converted into uric acid in the body.

The Nature of Gout.—We must clearly bear in mind that arthritis, although the most obvious, is not the only part of the disease. Cardio-vascular and renal changes are important sequels, and in this connection it may be recalled that the contracted granular kidney used to be called the "gouty" kidney, for although it often occurs apart from gout, yet it is very frequent in gouty subjects.

Dietetic indiscretions in the matter of nucleo-proteins, by increasing the amount of uric acid formed, undoubtedly increase the frequency of articular attacks in the gouty subject, in whom there is an undue lag in the excretion of uric acid, whether exogenous or endogenous. Rich wines and beer are also adverse influences. The decreasing frequency of the disease in modern times is probably to be related to the temperate habits with regard to both food and drink now prevalent.

Gout is in no way due to increase in the endogenous production of purines, the output of which approximates to the lower values found in health. An important factor is the difficulty with which the kidney in the gouty subject excretes uric acid. This difficulty is in turn due not so much to a primary renal defect, but rather to some abnormality in the state in which the uric acid circulates. Minkowski believed that in health the acid is loosely combined with protein and van Noorden put forward the suggestion that in gout the protein is deficient or abnormal and that renal excretion of uric acid was rendered correspondingly difficult. In chronic nephritis high blood uric acid values are often found, and deposits in the tissues may occur. The deposition is, however, gradual, not sudden as in gout, so that local symptoms are not produced.

Immediately before an attack of articular gout the excretion of uric acid is low, but once the attack is established, is higher than it was before. The general opinion, however, is that, although the blood uric acid level is high in gout, violent fluctuations such as would determine acute arthritis are not a common finding. This has led German workers to suppose that the attack is a manifestation of allergy, and good results have been claimed from the intravenous administration of calcium chloride.

The basis of the acute attack of articular gout is the sudden deposition of crystals of sodium bi-urate in the hyaline cartilage and synovial fluid. There is also a general systemic disturbance as shown by mild pyrexia and leucocytosis. Repeated attacks result in chronic gouty arthritis and tophi accumulate at the affected joints, but are deposited in the pinna at an even earlier

date. The bones at a chronic gouty joint often show considerable translucency to X-rays at the site of the uratic deposits, and the appearance produced on the film is spoken of as "pot-holing of the articular surface."

According to Gudzent sodium bi-urate circulates in a soluble but unstable lactam form which is very apt, by a small intramolecular rearrangement to change into a less soluble, more stable lactim variety, so that precipitation readily occurs. In leukæmia, although the concentration of uric acid in the blood is increased, renal excretion is rapid, and no given portion of the uric acid content lingers long enough in the body for deposition to occur. The rapidity of deposition which is such an essential feature of the gouty paroxysm depends probably on the properties of a supersaturated solution such as would be produced when the change from lactam to lactim form took place. A slight disturbance of a supersaturated solution is well known to be able to cause rapid and quantitative precipitation. Gudzent's theory, although it does not offer a complete explanation of gouty deposition, is worthy of careful consideration.

Various explanations of why gout has a predilection for certain joints, particularly the metatarso-phalangeal joint of the great toe—"podagra," and the region of the wrist—"cheiragra," have been submitted. These include local trauma from the boot in the case of the big toe and in the case of hand and toe the lower temperature of the distal joints.

In most mammals part of the uric acid is converted into allantoine by the enzyme uricase in the liver. There is no evidence that this enzyme exists in man, but, nevertheless, there is considerable evidence that the human body, particularly in gout, can, by some as yet unknown means, destroy some of its uric acid.

Although gout is to-day in England a rare disease, the possibility of its being the cause of any obscure case of arthritis should always be borne in mind and the ears examined for tophi and, if necessary, the blood uric acid estimated. Although a raised blood uric acid level is not pathognominic of gout, yet a repeatedly low level is strong evidence against the presence of that disease. "When in doubt, think of gout" is still a useful clinical injunction. In cases of lead poisoning, typical gout is not infrequent, and a diagnosis of gout should always raise the question of plumbism.

Sometimes during acute gout serious gastro-intestinal, cerebral or cardiac symptoms arise while the local inflammation of the

joint subsides. Such an event used to be known as retrocedent or metastatic gout, the older writers supposing that the local attack retroceded and the disease " flew to " the stomach, heart or brain. It seems probable, in view of the frequency of renal and cardio-vascular disease in gout, that the gastro-intestinal and cerebral symptoms are due to uræmia, and that the degenerated myocardium is also liable to fail under the strain of the general systemic disturbance which accompanies an acute attack.

The mode of action of colchicum in relieving acute gout is unknown. Cincophen, also known as quinophan and atophan, is of value, especially as a preventive measure, in virtue of its action in promoting excretion of uric acid by the kidney. Cincophen has occasionally caused a dangerous hepatic necrosis, and for this reason is best administered, well diluted, on three consecutive days only of the week, glucose being taken during this time, for it is believed that glycogen-laden liver cells are less liable to necrosis than are starved ones.

Avoidance of purine-rich foods, champagne and heavy wines is a rational therapeutic measure. Alkalies are of value in keeping the uric acid in solution. Aperients and liberal amounts of fluid are useful adjuncts to treatment, but their administration should not be excessive.

Cystinuria is an " inborn error of metabolism " in which the body is unable to deal with the sulphur-containing products of protein metabolism in the normal fashion. The condition is often inherited. The chief clinical importance of cystinuria is the deposition in the urinary tract of cystine stones the cut surface of which when exposed to the air develops a greenish colour. The stones may also have a characteristic soapy feel. They are opaque to X-rays.

In health the urine contains sulphur in the form of, (1) inorganic sulphates ; (2) ethereal sulphates ; and (3) " neutral sulphur." The " neutral sulphur " is contained in, among other compounds (taurine, thiocyanates, etc.), the amino-acid cystine, which is dithio-aminopropionic acid, having the formula

$$\begin{array}{l} S - CH_2CH.(NH_2)\ COOH \\ | \\ S - CH_2CH\ (NH_2)\ COOH. \end{array}$$

The details of sulphur metabolism are dealt with under " Metabolism " and " Urine," but may be conveniently summarized here. (1) The inorganic sulphate is largely a product of exogenous

protein metabolism, and therefore represents the oxidized end-result of the body's intake of sulphur over and above the immediate tissue needs. A small fraction must necessarily be endogenous. (2) The ethereal sulphates, such as indoxyl-potassium sulphate or "indican" and phenyl-potassium sulphate, result from the detoxifying action of the liver on the indole and phenol produced in the intestine by bacterial decomposition of tyrosine and tryptophane respectively, and are increased at the expense of the inorganic sulphate when bacterial action is excessive as in intestinal obstruction. (3) The neutral sulphur results mainly from endogenous metabolism ; a part—the thiocyanate fraction—represents the detoxification of cyanide radicles.

In cystinuria, the excretion of ethereal sulphate is approximately the same as in the ordinary healthy subject, the increase of cystine being at the expense of the inorganic sulphate. Even on a sulphur-free diet, however, the quantity of cystine excreted is greater than the normal (Alsberg and Folin), so that part of the excess is endogenous. Robson found that when a diet poor in sulphur was given to a case of cystinuria a steady condition of excretion was obtained. When to the purified diet was added an excess of cystine, this was almost entirely converted into inorganic sulphate, but when instead of free cystine a cystine-rich protein was given, the output of cystine was greatly increased. In Loewy and Neuberg's case, however, ingested cystine was excreted unchanged. Usually, only a part of ingested cystine is so excreted, and whatever may be the explanation of the different findings in different cases it is evident that the power of the body to oxidize cystine is not as a rule completely abolished in cystinuria. Normally, cystine liberated during protein digestion is absorbed as such. The observations of Robson suggest that when sulphur-containing proteins are taken by the cystinuric, the sulphur is absorbed in the form of a compound more complex than the amino-acid cystine, perhaps a peptide which, escaping oxidation in the liver, is hydrolyzed by tissue enzymes, only to be excreted by the kidney. Otherwise, since the patient could oxidize ingested cystine, her inability to oxidize the cystine derived from protein in the diet cannot be explained.

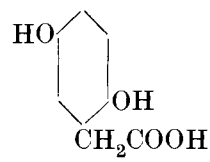
Cystine in cystinuria may be the sole abnormal urinary constituent or may be accompanied by other amino-acids, viz., tyrosine and leucine. In a third group of cases the diamines putrescine and cadaverine are present. In acute necrosis (acute yellow atrophy) of the liver, cystine accompanies the other amino-acids

such as leucine and tyrosine which pass into the urine in excess, having escaped deamination in the liver. Part of the excess of amino-acid in this condition may also come from the breakdown of protein liberated by the dying liver cells.

Melanuria.—Whereas very dark urines are encountered in various conditions such as very deep jaundice, hæmoglobinuria and hæmatoporphorynuria, etc., true black urine is due to the presence of melanin. If the urine is diluted the colour alters to reddish if the derivatives of blood pigment are present, but the effect of dilution in true melanuria is merely to dilute, not alter the colour. The black colour usually appears only on standing ; in freshly passed urine a colourless melanogen is present. The change depends on oxidation under the influence of light, and can be artificially brought about by the addition of nitric acid. Melanin is a sulphur-containing pigment and its presence in the urine is almost pathognomonic of melanotic sarcoma.

Ochronosis signifies blackening of the fibrous tissues and cartilages, and is clinically visible in the superficial structures such as the conjunctiva, ears and knuckles. It occurs after the prolonged absorption of carbolic acid, as in the treatment of chronic suppuration, and in the condition known as alkaptonuria. Carbolic acid gives rise to a certain amount of hydroquinone (catechol), which in turn is easily oxidized to dark-coloured substances, especially in urine which has stood.

Alkaptonuria is an inborn error of metabolism—" Chemical malformation " of Garrod. Like cystinuria, it tends to be inherited. The urine, which darkens on standing to a dark green and which therefore stains the linen, contains homogentisic acid. This substance is dioxyyphenyl acetic acid,



Its chief clinical importance is that it reduces Fehling's solution, and so may be mistaken for sugar, and this, together with the pigmentation, may lead to an erroneous diagnosis of " bronze diabetes " being made. Alkaptonuria is harmless, nor is the liver enlarged as in bronze diabetes, and if a drop of ferric chloride is added to the newly passed urine a deep blue colour is transiently seen. The pigmentation is readily distinguished from that of

Addison's disease, not only by its distribution, but also by the low blood pressure which obtains in the latter condition.

If tyrosine or phenylalanine is administered to the alkaptonuric subject, the output of homogentisic acid is proportionately increased. It is thus evident that the presence of homogentisic acid is due to an inability of the body to oxidize these substances fully, and the ratio of the amount of homogentisic acid to that of the total urinary nitrogen suggests that the tyrosine and phenylalanine set free during protein metabolism are also converted into homogentisic acid.

The amount of homogentisic acid which the alkaptonuric daily excretes is usually 3–5 grammes, but Mathews states that cases have occurred in which the daily total was 16 grammes. It seems to us that the latter figure must imply a remarkably high intake of protein, or else some of the homogentisic acid was derived from sources other than the ordinary amounts of tyrosine and phenylalanine available in the body.

Much work has been done and various theories advanced as to the essential metabolic defect in alkaptonuria. It is uncertain whether homogentisic acid is a normal intermediate stage in the oxidation of tyrosine and phenylalanine, alkaptonuria being due to arrest of oxidation at this stage, or whether, as Dakin suggests, some previous stage cannot be carried out properly and an abnormal end-product, homogentisic acid, results.

Hæmochromatosis.—This rare condition is limited almost entirely to males. It is characterized clinically by the very slow development of a brown or slaty pigmentation of the skin chiefly in the exposed parts of the body, by cirrhotic enlargement of the liver and spleen and by a strong tendency to the later development of severe diabetes; when diabetes is present it is called bronze diabetes. The hepatic cirrhosis may give rise to ascites.

The structural basis of the disease is a slow pigmentary destruction and fibrosis of certain tissues, particularly of the liver, spleen, pancreas and lymph-glands. Some degree of pigmentation is present in most of the tissues of the body. The pigment, of which the liver contains a large share, is hæmosiderin, *i.e.*, an iron-containing pigment which gives the Prussian-blue reaction. Hæmofuscin is also present, and contains less iron than does hæmosiderin.

In health the body contains about 4 grammes of iron. The amount taken in the diet is roughly 10–20 mg. daily. The iron is used chiefly in the formation of hæmoglobin by the developing

red-blood corpuscles in the bone marrow. The iron compounds liberated during the destruction of worn-out red cells are stored in the liver and spleen for a time, so that if the body is deprived of iron this reserve can tide it over for a period. The iron which leaves the body is excreted chiefly by the large intestine.

The essential defect in hæmochromatosis is unknown. Muir and Dunn showed that in this condition the body might contain 40 grammes of iron. If it is assumed that the iron ingested in the food is 20 milligrammes daily, or about 7 grammes a year, and this is probably a generous estimate, the tissues in hæmochromatosis must contain iron equivalent to the total intake of six or seven years. It is evident, therefore, that there is considerable retention of iron. There is no evidence of hæmolysis or anhæmopoiesis, such as cause the hæmosiderosis of pernicious anæmia, and Muir and Dunn explained the accumulation of iron-pigment in terms of a pathological affinity of the tissue-cells for iron. Certain authors have claimed that the cirrhosis of the liver is the primary thing, the changes in iron-metabolism, secondary. There is, however, but little support for this view, and the late development of diabetes suggests rather that the cell-destruction and fibrosis, as Sprunt suggested, are in part at least secondary to pigmentation, for when the liver is saturated with hæmosiderin, deposition in the pancreas is automatically increased. The diabetes, although severe, and, if untreated, fatal, can be controlled by insulin.

The evidence therefore suggests that hæmochromatosis is the result of some metabolic error which causes the accumulation of iron in the body cells. Cell destruction and interstitial fibrosis follow, with the development of cirrhosis of the liver and, in a majority of cases, diabetes. Such dire sequels do not follow hæmosiderosis from other causes, such as pernicious anæmia, for the length of time is insufficient. The nature of the metabolic error is unknown. While it has been claimed that there is a difficulty in the anabolism of iron into hæmoglobin, the absence of anæmia makes this view unlikely to be true. There may be an increased affinity of the tissue cells for iron or even an inability to excrete this substance in proper amounts. In any case, there is no proof that all the iron in the tissues in hæmochromatosis is derived from hæmoglobin ; some of it represents iron derived directly from the food.

CHAPTER XXXVI

BODY WEIGHT

QUESTIONS regarding body weight have to be answered daily by the practising physician. As a rule they fall into two categories: anxious parents who consider their children are too thin, or are not growing rapidly enough; and middle-aged people who find themselves becoming too stout.

Body weight is indicative of the balance between energy intake and output. A brief consideration will here suffice to indicate the innumerable factors upon which it depends. There are great differences in various individuals, all of which we must consider as physiological and which depend on the stature. A man of five feet will be fat if he weighs 11 stones, but a man of the same weight whose height is six feet will be thin. Stature depends largely on heredity, but how far this can be influenced by conditions of life and the internal secretions is a subject regarding which we have only a very general and vague conception (see later).

In the chapter on "Growth" we shall see that there is every reason to believe that diet before the age of twenty-five may play a large part directly, or indirectly through the ductless glands, in determining stature. On the other hand, children reared in apparently similar conditions may vary appreciably.

Apart from stature there is little evidence that heredity plays much part in the determination of body weight.

Energy, Intake and Output.—It must be realized that energy intake is not synonymous with what goes in by the mouth, but is that part of the actual intake which is absorbed and utilized. A baby which is fed each time it cries may consume enormous quantities of milk, yet it will not grow fat. Probably, indeed, it will not thrive at all. Actually a large proportion of the milk is found undigested in the stools—the so-called lienteric diarrhœa. The presence of this excess of material in the alimentary canal brings about irritation and pain, causing the child to cry and creating a vicious circle. In adults, too, the presence of undigested material in the stools will indicate

faulty absorption. Excess of fat, for example, indicates that the fat portion of the diet is not being utilized and is usually a sign of pancreatic disease and deficient secretion of lipase. It is commonly associated with other evidence of pancreatic deficiency.

Not infrequently the actual intake is deficient, as in starvation, in which case the individual utilizes first the carbohydrate stores of glycogen, then his fat, and later his protein. Starvation may occasionally be due to an inability to procure food. More often it is a matter of difficulty or pain on swallowing, as is seen in œsophageal stricture, where, if gastrostomy is not performed, the patient starves to death, or in a case of gastric ulcer where the pain caused by the food may bring about fear to eat. More commonly still the lack of intake is from lack of appetite which influences the intake and largely, as we have seen, the process of digestion. **Appetite** is closely allied to **hunger,** but the two are not absolutely identical. Appetite is almost a mental state and may occur in a person who is not necessarily feeling the pangs of hunger. Hunger is a sensation appreciated as the result of increased pressure in the empty stomach, probably caused by contractions of one part, the other part being relaxed ; the sensation is somewhat similar to that of gastric ulcer, except that the pain of the latter is usually felt more in the lower half of the stomach. Our knowledge of hunger we owe largely to the work of Carlson and his collaborators, especially Luckhart, who have subjected themselves to starvation. Hunger has been shown to be associated with rhythmical contractions of the fundus and, moreover, the pains are in proportion to the contractions, but, as Poulton has pointed out, when the contraction involves the whole stomach and the pressure in the stomach is at its highest, the tension is taken off the nerve endings, and the pain passes off temporarily. These are superimposed upon the normal variations of tone of the fundus. The gastric pressure may be recorded by passing a small balloon into the stomach and connecting it by means of a small tube to a tambour carrying a writing lever.

Hunger depends greatly on habit. Some people can easily miss a meal, while others would be brought to the verge of collapse as the result of an overwhelming feeling of weakness. Most likely this is a psychical result of the sensations and due to ignorance of the fact that the body has adequate stores of energy, since the eating of anything, even that which supplies no energy, will ameliorate the sensations. An Englishman visiting France

feels positively starved by mid-day, but after a few days he becomes accustomed to a light French breakfast. Similar changes in hunger sensation can be noted in changing from a mid-day dinner to a light lunch and evening dinner. It would seem not improbable that hunger contractions are set up by a mechanism like conditioned reflexes. We know, for example, that if a bell is rung half an hour before a dog is fed, the dog will eventually salivate regularly at the end of the half hour, even when no food is produced. Stomach contractions occur when the stomach is empty and when the habitual time for filling arrives. The hunger movements have been shown to begin before the stomach is absolutely empty, and their onset depends possibly on the habitual amount of filling, for a man accustomed to large meals feels hungry just as rapidly as one who eats little, and this fact bears no relation to their energy output. If the hunger pain is not " treated," after a few days it weakens and there may be an actual disgust of food. " Hunger striking " is therefore not so difficult once the first few days are past and the enthusiasm lasts. Carlson and others remark indeed on the great sense of well-being and vigour which succeeds such a fast.

The above is of considerable clinical importance, since it indicates that the incentive to eat is largely habit. Over-eating and under-eating tend to be continued to the detriment of the individuals concerned, and it is only by inflicting considerable hardship during the preliminary few days that the habits can be altered. We see, too, the great disadvantage of taking snacks and eating sweets between meals : they mitigate the sensations of hunger and reduce the appetite, and the habit of reduced appetite is readily established. Under-eating is common in neurasthenic women, who tend to become thin and suffer from neuritis, which appears to be commonly associated with deficient fat in the body ; the extent to which such individuals benefit from temporary hydro-life and the incentive to eat is notorious.

The intake of an individual may be adequate, digestion and absorption efficient, but the absorbed food not properly utilized. This is well seen in diabetes, where the carbohydrate is absorbed but is not sufficiently rapidly burnt or stored, so that it accumulates in the blood and escapes in the urine. This is, however, but an example of the influence of the internal secretions on metabolism, which is dealt with later.

In a large number of people excess of energy intake is a habit which is almost a disease. Such persons have apparently so

stretched their gastric walls that they do not feel replete until they have consumed an amazing amount of food. They apply to the physician for advice and are disgruntled when they are told the truth.

In the treatment of obesity or excessive storage of energy there are three possible methods : diminution in intake, increase in output of external work, and increase of the internal work or basal metabolism. The first and second are to be advised, but they may be extremely difficult to attain ; the third requires a minimum of effort on the part of the patient. It must be realized that no advantage is gained if the hunger brought about by increased work is satisfied by increased intake. All the factors must be considered. Further, the real meaning of reduction of intake is seldom appreciated by the layman. Only too often, if sugar and potatoes are cut off by the physician, an additional supply of bread is taken. Only recently there came to the personal notice of the writer the case of a lady of 15 stones who had been forbidden carbohydrates and had a list of articles of diet to be excluded. She consumed, however, over half a bottle of port wine a day because she felt the lack of food so much.

In relation to exercise, too, it is well known that some stout people walk a great deal. This will be dealt with when the effect of exercise is considered. Here it is sufficient to say that an adaptation occurs to habitual exercise of moderate degree so that less fuel is used. Therefore the exercise recommended for weight reduction should be for preference one to which the patient is not accustomed unless the exercise is unusually severe. Lack of physical exercise is a very common cause of obesity, and a vicious circle is established : the lack of exercise causes obesity, and obesity makes the patient disinclined to take exercise and liable to fatigue even if it is moderate. Fatty heart often ensues with all the signs and symptoms of cardiac insufficiency. If the diet is only slightly reduced, so that it is just not uncomfortable, then there will be no noticeable loss of weight for a long time and the *régime* will have to be persisted in for many months. Much of the so-called inherited tendency to obesity is acquired, being due to appetite and sloth, though the victims stoutly deny such suggestions. It must also be recognized that overeating may be a thing of the past, and the patient's energy intake may at present almost balance output. Energy stored as fat will not disappear until it is actually required for use. In practice the best method is to get the patient to demonstrate to himself or herself

the effect of diet on body weight, and to set a standard of loss to be attempted every week.

While there cannot be the slightest doubt that the occurrence of fat in the body is the result of intake of carbon by the mouth, it must be admitted that the metabolism of some persons is set at a higher level than that of others or is more liable to influence by chemical and nervous stimuli. For example, some persons are more stimulated by mental influences, excitements, and worries, and in some the stimulating effect of protein on metabolism is greater than in others. In others the ductless glands reduce metabolism abnormally.

Increase in basal metabolism (see p. 340) offers the laziest way of getting thin. It may be brought about by excessive protein eating, which at the same time gives satisfaction in the amount consumed. Care must be taken that the meat is really lean. As a temporary measure thyroid administration may be undertaken, and so long as the pulse is under 100 per minute, this treatment may be considered safe. In general there is much to be said against it (see page 342), and in any event it is so dangerous that it cannot be put in the hands of the patient without proper supervision. The dose should be in terms of Thyroideum B.P. 1932. A small proportion of stout people suffer from want of balance of the internal secretions, but even in these hormone therapy is secondary to dietetic measures and increased energy output.

The Relationship of the Ductless Glands.—From what has been said above in relation to the pancreas and the thyroid gland, it is evident that these two glands may play a considerable part in the regulation of body weight. The pancreas is essential for the storage of glycogen, while the thyroid gland regulates the speed with which the fuel is utilized. When the thyroid gland is excessively active the patient becomes thin, while when the gland is underactive, as in myxœdema, the patient becomes fat. A simple overaction of the pancreas with increase in weight has recently been described. The patient discovered that unless she took large quantities of sugar she felt very unwell with symptoms of low blood sugar. A simple tumour of the islets of Langerhans was discovered in the pancreas (Cushing). On the other hand, the untreated diabetic patient becomes thin from failure to store sugar and convert it into fat.

Evidence is now available that the pancreas and thyroid may also affect body weight by a direct effect on each other. The sugar tolerance of the myxœdematous patient is high while that

of one suffering from hyperthyroidism is low. These facts suggest that the thyroid affects the activity of the pancreas, while the action of the latter on the thyroid is suggested by the increased metabolism in diabetes (Benedict).

A final confirmation of the antagonism between the thyroid and pancreas is shown by facts that thyroidectomized rabbits are hypersensitive to insulin (Burn), and the effect of thyroid feeding is counteracted by insulin (Harrison).

It is convenient therefore, so far as body weight is concerned, to consider the thyroid and pancreas in the opposite sides of a balance, and anything which affects the balance must affect body weight.

The posterior lobe of the pituitary body weighs in against the pancreas and for the thyroid. In 1923 Burn showed that pituitrin counteracts insulin, and this is supported by later work, that needling of the pituitary body or administration of pituitrin causes glycosuria and decreased sugar tolerance.

On the other hand, old Italian workers have shown that animals whose pituitary bodies have been partly removed or injected with chromic acid have an increased sugar tolerance and tend to become obese. Similarly, in tumours in the region of the pituitary body extreme adiposity is often a characteristic feature (hypopituitarism). The "fat boy" of Dickens was possibly such an instance. Cushing has pointed out that tumours in the region of the stalk of the pituitary are specially liable to bring this about, no doubt because they prevent absorption of the pituitary secretion. The basal metabolism of such patients is also low, indicating that the thyroid is depressed. The inter-relation of thyroid and pituitary is shown also in the increased size of the pituitary, which occurs after experimental thyroidectomy.

There seems little doubt that the increase in weight which occurs commonly after the menopause or ovariotomy is also related to the endocrine balance. The mechanism of the relationship has not yet been worked out, but it seems likely that there is a reduced pituitary function, for there is evidence that the anterior lobe of the pituitary is intimately related to sexual activity.

The opposite occurs in pregnancy in which the patient may become very thin, although this is not a constant feature, as there is also a considerable increase in appetite and energy intake. It is possible also that the cortex of the suprarenal gland plays a

part, since there is evidence that this organ antagonizes the thyroid, while it is well known that the suprarenal cortex increases in pregnancy. It appears possible then that the suprarenal by inhibiting the thyroid may cut down the metabolism of the mother. The basal metabolism of a pregnant woman is not increased until the pregnancy is well advanced, but since the fœtus is certainly growing in the early months we may presume a reduction in the metabolism of the mother apart from the fœtus.

The medulla of the suprarenal gland comes in also, but against the pancreas and on the side of the thyroid, for adrenaline mobilizes the glycogen and increases metabolism. Since adrenaline is secreted in excitement we may consider that this is one of the reasons why excitable people are frequently thin.

We have seen then that the pituitary gland, the thyroid, and suprarenal medulla act in a similar direction, and it is of interest to realize that these three glands adapt the body to its physical requirements. The pituitary gland adapts the body to its physical requirement and requirements for the continuance of the species. These are probably the most important functions of the body. Given certain physical adaptations the next most important mechanism in the body is that by which metabolism is controlled and adapted to varying needs. The thyroid brings about adaptation, a sustained requirement, while the suprarenal medulla adapts the body to its more immediate requirements. These considerations have a general biological interest and emphasize what ought to be a keynote of body function, the enormous adaptability of the body for the performance of physical exercise.

Water Content.—The body weight increases when œdema is present. The increase in weight fore-runs the actual demonstrable œdema. In practice, a decrease in weight is an indication of the efficacy of treatment in chronic parenchymatous nephritis. How far salt and water retention should be treated in cases of obesity is a matter of dispute. Certain authorities limit the salt intake, but it is difficult to believe that in, for example, the case of a woman who weighs twenty stones such treatment is likely to be of value, or even to be safe. In such a case post-mortem examination shows extensive fat deposits, and dehydrative treatment can only be justified in the milder cases.

CHAPTER XXXVII

GROWTH

THE clinical phenomenon of growth depends on the power of the cells which make up the body tissues to multiply. Each variety of cell has its own conditions of growth, but each is integrated to form the normal body structure. In the growth of the body as a whole many factors are concerned. The most important is undoubtedly that of diet.

Diet.—The essential principle of diet in relation to growth is that there must be supplied not only fuel for energy and substances necessary to make good the normal wear and tear of the body as in the adult, but sufficient for the building up of new cells. Some tissues, such as bone, may require an increased intake of certain substances (calcium and phosphorus), apparently in excess of what is necessary for adult life. The possibility of the interference of such substances with metabolism has received considerable attention in the past few years, but until we know accurately the exact mechanisms of their metabolism and the exact rôle which they play in the growth of the tissues, we can do nothing but guess how pathological conditions are produced. Fortunately Nature generally provides such salts in abundance when they are necessary. A child whose diet is deficient obviously cannot be expected to grow, and the general ignorance concerning such matters is truly appalling. It is no uncommon thing for a parent to imagine that rice or barley water may be substituted for milk, although, if the child has been overfed with milk, such reduction of its diet may be of advantage provided it is not continued too long. It is also difficult to eradicate the habit of giving lime water with a view to increasing the calcium intake, although in reality less calcium is contained in this fluid than in milk.

In general the body weight may be taken as an indication of growth, but this cannot be said without reservation. If, for example, a child is fed on excess of carbohydrates, so common in patent foods, a large amount of energy is supplied, the excess of which may be stored as fat. But the child will not grow if the

food has not an adequate biological value (see page 260), that is, unless it supplies the factors, other than energy, necessary for growth. In the latter respect milk and meat take first place, no doubt because of the number of amino-acids they contain which are suitable for the building up of human proteins. In the adult we have seen that the biological value of the diet is not so important, as adults appear to have the power of synthesizing certain of the essential amino-acids which a child cannot do.

Should the metabolism of the infant be excessive because it has to counteract some infection, such as syphilis, tuberculosis, or various intoxications, this will, of course, tend to interfere with growth, as energy is used up.

The above presumes that the child possesses no abnormality which prevents the intake of food. Mechanical difficulties in sucking or pain caused, say, by stomatitis are common causes of diminished intake. The mere giving of food, also, in abundance is of no value if the powers of absorption from the intestine are deficient. Various forms of enteritis interfere with absorption, and no factor is more potent in the production of such conditions than a faulty diet, especially, according to Hutchison, excessive fat.

The more general principles of diet are considered in a separate chapter.

Vitamins.—The diet must also contain an adequate supply of the accessory food factors, especially vitamins A, B, and D, and, indeed, it was failure of young animals to grow on a diet deficient in these substances which led to their discovery. No method of reducing this factor is more efficient than complete sterilization of the food in an attempt to protect the child. For purposes of convenience vitamins are discussed in a separate chapter, in which the importance of *light* is also pointed out.

Certain of the endocrine organs also play an important part in growth and have to be considered in this connection.

Thyroid Gland.—Forty years ago it was noted by Kocher in Switzerland that patients from whom the complete thyroid had been removed bore many resemblances to *cretinism* which was so common in that country and he noticed further that in this latter condition it was very difficult to palpate the thyroid. The relationship of the gland to such conditions was clearly shown by Schiff in 1884, but it is only in comparatively recent times that the rôle of the thyroid in relation to growth has been clearly understood. The thyroid we now know is responsible for the elaboration of a

substance which is a stimulant of general metabolism. In the adult this serves to give a greater range of metabolism and consequently a greater sphere of activity. The disadvantages of limitation in this respect are seen clearly in myxœdema and exophthalmic goitre. In the child the hormone produced is responsible not only for the general metabolism, but also for the general growth of tissue, or, put differently, for the speed of metabolic and proliferative changes in the individual cells. This fact was first shown by Gudersnatsch, who found that the speed with which tadpoles metamorphose was greatly increased by the administration of thyroid extracts.

Clinically, the effect of deficiency of thyroid on growth is seen in the condition of cretinism in which the child remains infantile with all its functions retarded. Similarly all organs whose functions are dependent on the metabolic rate are affected (see page 343). The growth of the skeleton is slow and ossification is delayed, while the cold dry skin covers a myxœdematous subcutaneous tissue, giving the child a short thickset appearance and bloated countenance. According to John Thompson these features are seldom marked at birth, with the exception of a swollen protruding tongue, a fact which suggests that, prior to birth, the thyroid of the mother supplies the necessary hormone. The fact, however, that since the introduction into general use of thyroid extract in myxœdema there has been a diminution in cretinism, even in those areas where it used to be very common and in which myxœdema is still common, gives weight to the statement that the mother of a cretin must also to some small extent suffer from hypothyroidism. More commonly the mental dullness which results from impairment of cerebral growth first attracts attention and this, together with the stunted figure and the delayed closure of the fontanelles, is sufficient for the diagnosis which is confirmed by the marvellous effects of thyroid administration. The conversion of a potentially idiot dwarf into a useful member of society by the administration of the extract is one of the triumphs of modern science and is a striking example of how the surgeon and physician and pathologist have contributed to physiological science and how the co-operation of all has been of benefit to mankind.

The Pituitary Body.—The anterior lobe of the pituitary body exercises a special function in relation to the **growth of bone.** It was first noted by Marie that over-activity of the gland in a young person before the epiphyses have joined leads to a general over-

growth of the skeleton and to the production of gigantism. In adults, however, when the long bones have attained their maximum length, similar activity results in *acromegaly* in which only certain areas are affected. The hands and feet enlarge greatly in size and become characteristically spade-like, while the growth of the bones of the face effects a profound transformation in the countenance of the individual, which is characterized by heavy plainness. Final confirmation of the condition is obtained by an X-ray photograph of the skull which reveals that the sella turcica has become enlarged to accommodate the gland. At the same time general metabolic changes occur at first from stimulation and later destruction of the posterior part of the gland which is more intimately related to metabolism, especially that of carbohydrates.

It has been found that the injection of extract of the anterior lobe of the pituitary causes gigantism in animals.

Underactivity of the gland results in infantilism, but there is considerable variation in the clinical conditions found. In the so-called Fröhlich's syndrome or dystrophia adiposo-genitalis, there is overgrowth of the genitals and deposition of fat, while in the Lorain type there is an absence of the secondary sexual characteristics, but the lack of growth of the skeleton is the only other abnormality. The best known type is that of Brissaud, which is typified in the fat boy of Dickens, fat, chubby and sleepy. The Brissaud type is probably an early stage of the Fröhlich syndrome. The mental backwardness is associated with a low metabolic rate.

The variations which occur are no doubt the result of different parts of the organ being affected at different stages in disease of the organ.

The Parathyroid.—The work of Macallum, of Vines, and of Collip has eventually led to conclusive proof, after much dissension, that the parathyroid elaborates a hormone which has the power of increasing the blood calcium. Macallum had shown a lowering in the blood calcium in tetany. Tetany is a symptom of parathyroid deficiency, and Collip produced a reliable parathyroid extract. It has now been shown that in parathyroid tumours there is a high blood calcium and a corresponding loss of the calcium in the bones which may become soft and show the condition known as generalized osteitis fibrosa. The blood phosphorus is low and the daily excretion of calcium in the urine may be three times the normal 0·3 gramme (Hunter). Calcified stones may

even be deposited in the urinary tract. Great pain in the bones occurs. Exploration of the neck should always be undertaken and the parathyroid tumour sought for and removed.

Calcium is necessary for a large number of body processes, contraction of cardiac and smooth muscle, and blood coagulation, but apparently great variation in blood calcium may occur without these processes being seriously affected.

Thompson in this laboratory has now found that an acid extract of the parathyroid contains an additional hormone which retards the growth of animals. It has already been noted that patients with parathyroid tumours stop growing. There is also considerable subsidiary evidence that this is true. This discovery opens up a completely new field of investigation, since it suggests that such an extract may be of value in the treatment of neoplasms. Already most promising results have been obtained, but clearly the treatment is fraught with difficulty owing to complicating factors and the fact that an ideal standardized preparation has not been found.

Racial and other hereditary characteristics undoubtedly play a considerable part in the determination of stature and no doubt obey the ordinary laws of inborn characteristics. How far these characteristics are determined by hereditary variation in endocrine activity is extremely difficult to say, but the fact is that poor hygienic conditions and faulty diet, such as occur among the dwellers in slum areas, lead undoubtedly to impairment of mental and bodily growth. It is possible that they may bring about their effects by affecting the endocrine system, and indeed recent evidence suggests that vitamin deficiency, so common in such conditions, may affect growth in this way. More than this it is most dangerous to postulate.

Whether the above are all the factors on which growth depends we do not know. Clinically we unfortunately still find cases of so-called primary wasting or marasmus which have no obvious cause and which only too frequently have a fatal end. These cases are becoming fewer because they are dealt with at an earlier stage than heretofore and toxic and like conditions are treated. Many children who would otherwise become marasmic become quite normal when placed in physiological surroundings on a physiological diet. Many diseases affecting chiefly the bones are as yet not understood, such as achondroplasia and Paget's disease. Why, however, the bones of some regions are in certain conditions affected more than others is unexplained. Thus in chronic

pulmonary conditions, clubbing of the fingers is sometimes observed, due to definite enlargement of the terminal phalanges, and, more rarely, there is thickening of the ends of the long bones. The face escapes. On the other hand, in that rare condition, known as leontiasis ossea, the skull bones are the seat of a peculiar overgrowth ; some of these cases are really examples of Paget's disease, others result from a " creeping " periostitis.

The **chemistry of ossification** has of recent years received a considerable amount of attention from Robison and his co-workers. Ossification finds a justifiable mention in any treatise on growth, because it in a sense " crystallizes " skeletal growth and also without it growth would be distorted. From the sequel it will be seen that the osteoid tissue first formed is later calcified, and further that this process is reversible. There is good reason to believe that the blood is a supersaturated solution of calcium salts. An enzyme has now been discovered (phosphatase) in ossifying tissue which will convert the soluble calcium salts of phosphoric esters of the blood into insoluble calcium phosphate. The distribution of this enzyme strongly supports this view of its activity. It is, for example, found in all very young ossifying bones but not in cartilage, such as the larynx in the first half of life, which does not ossify. A faulty distribution of the enzyme may therefore lead to abnormal calcification. Rachitic bones, on the other hand, have a deficiency of calcium and a normal supply of phosphatase, and if immersed in a calcium phosphate solution will even cause calcium to be deposited. Kay has shown that in conditions in which rarefaction and absorption of bone are occurring, such as osteitis fibrosa and Paget's disease, there is a liberation into the blood of phosphatase in great excess, up to twenty times the normal value. Some increase in the blood phosphatase also occurs in healing fractures, when it is due to the great activity of the multiplying osteoblasts. In active rickets the blood phosphatase is also increased, and Jean Smith has shown that a figure of double the normal value is highly suggestive of vitamin " D " deficiency. She has further shown that during the treatment of rickets, the blood phosphatase returns to normal long before the X-ray signs disappear.

Robison and his colleagues have recently demonstrated a second calcifying mechanism in ossifying tissue in the form of the highly specialized ground substance which is secreted by the osteoblasts. This mechanism is distinct from phosphatase, but its essential nature is unknown.

Dwarfs and Giants.—Dwarfism is an extreme defect of stature, and although it may result from factors which produce infantilism, the two terms are not synonymous. Among the diseases which cause dwarfism without infantilism are certain conditions in which the skeleton suffers, such as severe rickets, severe spinal caries and achondroplasia. The second of these is exemplified in the "hunchback" of literature, the last comprises the various mentally quaint dwarfs such as the rather villainous Mr. Quilp of "The Old Curiosity Shop," and also miniature public entertainers. If we define infantilism as the "retention, in varying degrees, of the characteristics of childhood—sexual, bodily, and mental" (Tidy), it will be seen that the achondroplasics and hunchbacks are not truly infantile even in their bodily characteristics. Achondroplasics are in their sexual development often precocious and virile; there is for some unknown reason a defect in the formation of cartilage-bone particularly in the limbs and basis cranii, hence the short limbs but normal trunk, the short skull base but normal vault. Many are born dead, but those which survive the first year are usually strong and healthy.

Gigantism signifies excessive stature. The relationship of heredity to stature has already been discussed. Quite apart from hereditary influences which produce tall families, giants, *i.e.*, individuals over $6\frac{3}{4}$ feet in height, crop up from time to time. Many giants, perhaps 40 per cent of the total, are examples of hyperpituitarism which has occurred before the epiphyses of the bones have joined with the shafts—in other words, before general skeletal growth has ceased. In this connection it is interesting to note that in the rat, in which the epiphyses never join, the repeated injection of anterior lobe extract causes gigantism, rather than acromegaly. Many of the so-called "normal" giants, however, show acromegalic tendencies, are of poor mental and bodily strength, and die during the first half of life. The mental rather than the physical weakness of giants is recorded in various legends such as that of the Cyclops in the Odyssey. Excessive growth of the skeleton may be associated with the obesity which follows castration.

Infantilism, as already stated, may be bodily, sexual or mental, frequently a combination of all three. From what has already been said, it will be gathered that infantilism may result from (1) endocrine disorders, (2) chronic infections such as syphilis and malaria in childhood, (3) the anoxæmia due to congenital heart disease, (4) general underfeeding, (5) failure of fat and vitamin

"A" absorption in cœliac disease—intestinal infantilism—and disturbance of calcium metabolism in renal infantilism; in both these conditions, cœliac disease and renal infantilism, particularly the latter, other factors not yet clearly understood probably also affect growth and development, (6) early and prolonged administration of alcohol—"a nip of gin to keep the baby quiet"—rare nowadays, (7) failure of cerebral development, as in Mongolian and microcephalic idiocy.

The endocrine deficiencies which can cause infantilism are: (1) thyroid—in cretinism; (2) pituitary—a simple defect of the anterior lobe results in the Lorain type in which the patient is infantile physically and sexually but not fat; defect of the posterior lobe or adjacent hypothalamus of the brain, perhaps associated with some degree of anterior lobe deficiency, results in the Brissaud and Fröhlich types. Various types of pituitary disturbance result from the supra-pituitary tumours which develop from embryonic remnants of Rathke's pouch. Diabetes insipidus may also occur; (3) disturbances of the sexual glands; (4) polyglandular syndromes.

Progeria is a rare condition in which premature senility with fibrosis of the arteries and kidneys, etc., culminates in death before the age of puberty. The cause is unknown. Progeria thus presents a remarkable contrast with the Lorain type of infantilism.

Local Growth.—The mechanism of the control of local growth is not only one of the most interesting problems of physiology, but one of the utmost clinical importance, as pathologically local overgrowth of tissue not infrequently takes place. Such an overgrowth may be confined to certain tissues and remain circumscribed, such as skin epithelium in the simple wart, while on the other hand a certain tissue may invade other tissue; we have again an example in skin epithelium producing an epithelioma, a form of cancer. Unfortunately we are quite in the dark regarding the reasons why a tissue should break its boundaries, except that in many instances irritation, and in some instances a specific virus, is to a large extent responsible for local overgrowth. Within recent years, however, it has been found possible to grow various tissues outside the body in suitable media and under sterile conditions after the manner utilized for the culture of organisms in bacteriology. For adequate growth the cells have to be supplied with suitable nourishment, but what is of still more interest is the fact that the speed and nature of their multiplication may be influenced by other tissue cells and their extracts. Normally each

tissue adheres to a certain boundary concordant with normal function, although how this balance is maintained we do not yet know. This problem is a very important one in the study of neoplasms in which an excessive proliferation of certain cells occurs, with, in the case of malignancy, the power of invading other tissues. A great advance in this field of work is hoped for in the near future as a result of the discovery of specific substances which bring about abnormal proliferation and invasion.

Such tissues grown *in vitro* are greatly stimulated by the addition of embryonic extract, and it is suggested that growing tissues produce a hormone which stimulates growth. Carrell finds that, similarly, senile tissues have an inhibitory effect. These facts, especially the latter, must be of considerable importance in the cancer problem, but unfortunately the inhibitory action has not been adequately confirmed.

Normally the great stimulant to local growth of tissue is use. The efficiency of every organ in the body is increased by use, and where it is necessary to obtain increased efficiency, an actual tissue hypertrophy may be brought about. Thus, there is an increase of muscle tissue for heavy muscular work or an increase in kidney tissue with excessive drinking. How the work stimulates the increase is unknown, but it appears that whenever an amount of work is such that there is no reserve in the tissue, an increase results so as to create a reserve and make it possible for certain areas to rest intermittently (see page 466). How far this principle can be carried is uncertain, but it does play a part. We are familiar with the thickening of the skin of the hand which occurs in manual labour, and indeed if this is begun at an early age the size of the hands is often increased. Many observers have endeavoured to apply the principles to disease. Arbuthnot Lane, for example, has emphasized the relationship between occupation and arthritis deformans in which there is an overgrowth of the bony structure of joints and in which, for example, the knee of the miner or the hands of the pianist are commonly affected. Or, again, according to the same principle, it is possible that excessive utilization of the vaso-motor system from excessive physical or mental work or various intoxications may lead to an arterial overgrowth which, like all other overgrowths, is abnormally liable to degeneration. The utilization factor is often extremely difficult to evaluate and determine, as other factors are undoubtedly concerned. Otherwise everyone having the same occupation and living under similar conditions should be similarly affected,

although it must be added that circumstances of life of different people often appear more similar than they really are. In these, like so many other conditions, physiological, pathological, and clinical investigation must go hand in hand, and such active co-operation must always be more fruitful in that it gives a more complete view than when each independently waits on the advance of the other.

CHAPTER XXXVIII

THE URINE

MICTURITION

NORMALLY a desire to empty the bladder arises when the pressure of the urine in the bladder reaches about 15 cm. of water. The sensation arises from pressure on the nerve endings in the bladder wall, and no doubt this is accentuated by the sound of running water and especially by the presence of urine in the urethra. This latter fact is of some practical importance, as young males may have difficulty in commencing micturition in a public urinal. Voluntary expression by expiration with the glottis closed of a few drops of urine may be sufficient to cause commencement of the normal act. At the commencement of evacuation the bladder contracts and the intravesical pressure may reach 30 cm., but if the desire is ignored the organ relaxes, the pressure falls, and the sensation of fullness temporarily abates.

The desire to micturate is affected not only by the amount of urine in the bladder but by the state of the bladder wall. The commonest cause of frequency of micturition is irritation, which may result from infection (commonly *B. coli*), ulceration, tumour, or more usually from undue acidity or the presence of crystals. Various other conditions arising in the kidneys, urethra, or rectum may also be responsible, the stimulation of the bladder then being reflex.

When voluntary control of the bladder is lost the actual effect on the bladder varies according to the site of the lesion responsible.

If the reflex arcs responsible for the control are affected the urine simply dribbles away. This is specially liable to occur in injuries if the 1st and 2nd lumbar roots are affected, since from these roots arise the sympathetic fibres which relax the bladder and close the sphincter. The parasympathetic fibres, the nervi erigentes, which arise from the 2nd and 3rd sacral roots have the opposite action. This latter fact is the basis of the treatment of the nocturnal incontinence of children with atropine, which paralyses the parasympathetic which is liable to be unduly

predominant during sleep, when small quantities of urine may set up afferent impulses from the bladder. Various other factors contribute to this form of incontinence.

When the spinal cord is damaged and there is interference with the normal control of sphincters, there is a retention of urine. This may also occur when, for any reason short of gross permanent obstruction, the bladder is not emptied. As soon, however, as the pressure of the urine rises sufficiently, overflow occurs. This is not to be confused with true incontinence. The retention of the urine favours bacterial growth, and the pressure causes malnutrition of the bladder wall. The use of the catheter is therefore essential.

In lesions of the spinal cord the greatest possible care has to be taken of such patients to prevent infection of the bladder, which is so liable to occur and to lead to acute and fatal infection of the kidney. In acute injuries high up in the spinal cord if care is taken in the early stages reflex micturition may become established, and may occur as the result of sensory stimulation. The onset of such reflex micturition should be specially looked for from time to time with the catheter in position, since its establishment greatly reduces the liability to infection consequent on the use of a catheter.

A variety of other disturbances in micturition may occur in nervous diseases, the best known being " preabilitate micturition," in which the desire is followed almost immediately by an uncontrollable reflex emptying. This may occur in pyramidal disease. In tabes, the desire may be absent, and the bladder is then distended, dribbling occurring at intervals until the patient attends to the function voluntarily. In a large number of tabetics a fatal issue is determined by ascending infection of the urinary tract.

Painful Micturition.—The site of the pain which is associated with the act of micturition depends on the part of the urinary tract which is affected.

Irritation of the uretdra is experienced in this region and may be referred particularly to the point of the penis in the male. When due to an acid urine passing over an inflamed region and less so during the passage of crystals, the pain is somewhat scalding in nature. It may be experienced by a normal person if the urine is rendered markedly acid, *e.g.*, by taking acid phosphate and a large dose of hexamine which, in an acid urine, is converted into the highly irritating formaldehyde. The occurrence of this

variety of pain must be anticipated when hexamine is being used in the treatment of infections of the urinary tract higher up when an acid urine produced by acid phosphate or a ketogenic (fatty) diet is of great advantage in inhibiting the growth of infecting organisms.

Pain from irritation of the bladder occurs at the end of micturition when the inflamed walls of the neck of the bladder come together. It may occur as the result of cystitis due to micro-organisms, or may be caused by a simple crystaluria. The pain may be very severe and there may be set up at the same time a very painful spasm of the muscles of the bladder and of the upper end of the urethra. A surprising number of people living a sedentary student life have occasional attacks of strangury due to simple phosphaturia, a curious constitutional condition of excretion of alkaline phosphates which become excessive in circumstances of mental overwork and worry.

The pain set up by obstruction of the urinary tract higher than the bladder has been dealt with in relation to Referred Pain (p. 36).

Some interesting physiological points occur in relation to the treatment of infections of the urinary tract. The common infection by *B. Coli* is usually treated in the first instance by making the urine alkaline by the ingestion of sodium bicarbonate and potassium citrate, but if resistant organisms (whether *B. coli* or pyogenic cocci) are present, an acid urine is most inhibitory against their growth. Apart from the use of acid sodium phosphate the introduction of the ketogenic diet has been a distinct advance. This consists of giving a diet which is as fatty as possible.

It is usual also to give large quantities of water or barley water to drink to flush the urinary tract. The fact that such excessive drinking may lead to extreme weakness and liability to superinfection from a washing out of the body salts has been generally overlooked in this connection, although it is recognized in relation to excessive sweating. A salt solution containing 0·9 per cent sodium chloride, 0·042 per cent potassium chloride, and 0·024 per cent calcium chloride is the physiological diluent of the urine.

THE URINE

The importance of the examination of the urine in almost every case of disease has been impressed upon generations of medical students. While physiology continues to emphasize its value in

diagnosis, one must bear in mind the fact too often overlooked, even in scientific circles, that the kidney is only part of the general excretory system, and that the large intestine and skin may be quite as important.

For many years the pure physiology of the urinary system has been dominated by arguments for, and against, the various theories of urine production. To clinical observers there is another aspect which is more important, namely, the effect which deficient kidney excretion may have on the body, and the prospects of treatment and recovery.

A few anatomical details of the structure of the **kidney** should be kept in mind. The starting-point of urine formation is the glomeruli—bunches of capillaries invaginated into the capsules of Bowman which are really the dilated beginnings of urinary tubules. The glomeruli are limited to the region of the cortex. Each capsule becomes continuous with a uriniferous tubule. These tubules in different parts exhibit varying features, in one part being straight and lined with a flat epithelium, in another being convoluted and lined by cells suggestive of active function. Briefly stated, the position regarding kidney secretion is as follows: It is admitted that the fluid part of the urine is for the most part excreted by the glomeruli, probably by a process very analogous to filtration. But the difficulty is in regard to the solids. There are two main divisions of opinion in this matter, one that the urine with the solids in very dilute solution is filtered off by the glomeruli and that the urine is subsequently concentrated during its passage down the tubules; and secondly, that water is the chief excretion of the glomeruli and that the solids are added to the urine in its passage down the tubules. That both processes in the modern forms of these views require the assistance of some vital action on the part of the tubule is generally admitted, as it can be demonstrated that oxygen is required in proportion to the activity. There is, perhaps, a weight of opinion in favour of the reabsorption theory championed by Cushny, largely because many pathological findings can be explained by it. There are, however, many facts which it does not explain. To one who studies the evidence impartially it does not seem impossible that the truth may lie between the two opposing views, for each is not exclusive of the other, as at first sight might appear. We know, for example, that in disease of the kidney certain substances normally excreted are retained. But the retention of different substances, such as urea

and creatinine, has no constant relationship either to each other or to the extent to which they are concentrated in the urine as compared with the blood. These facts indicate that different parts of the kidney mechanism have different and selective functions in the excretion of solids. This view is supported by the observation that certain of the urinary contents are influenced by the injection of various hormones, while others are unaffected.

The functions of the kidney are : to excrete water ; to excrete unrequired salts and products of metabolism, especially protein metabolism ; to assist in maintaining (by varying the excretion of phosphate and ammonia) the neutrality of the blood ; and to eliminate toxic substances and bacteria. Examination of the urine, then, will give a considerable amount of general information regarding the body as well as local information regarding the kidney.

Quantity and Specific Gravity of the Urine.—Normally an adult leading an average life in à cool climate should pass about 50 ounces daily or 1·5 litres, but as shown in more detail, in relation to the water content of the body, the actual amount depends entirely on how much water is lost in other ways, *e.g.*, by the skin, by the lungs, and by the intestine. Here it should be said that it is often impossible to take the word of a patient in relation to polyuria, as not uncommonly frequency of micturition is confused with polyuria. Attempts have been made to use the quantity of the urine excreted in a given time after a given intake of water as an index of kidney efficiency, but this is found most unsatisfactory because of individual variation. Those who habitually consume large quantities of fluid may, by this test, appear to have very efficient kidneys, although a large part may be out of action.

Excretion is increased if the body requires to get rid of any soluble substance. Sulphates, for instance, have a diuretic action, as has sugar in diabetes, presumably because their presence in the glomerular filtrate prevents reabsorption of water for physical reasons. In the polyuria of chronic nephritis, on the other hand, the urea which is in excess in the blood has a direct stimulating action on the kidney cells. The excessive excretion of urine is not then necessarily due to the usually accompanying high blood pressure, as has been suggested, although no doubt this assists. Normally, more urine is excreted by day than by night, but as the total amount of solid does not vary so much, night urine is appreciably more concentrated than day urine. The normal specific gravity varies from 1·015 to 1·025. In chronic nephritis, because of the increased urea in the blood, the diminution of

night volume is not seen and the specific gravity remains below normal throughout. A high specific gravity of the day urine suggests the presence of sugar.

The association between the facility with which solids can be excreted and the amount of urine passed is also seen in diabetes insipidus, where the polyuria may be the only symptom. There is no excess of sugar. The injection of pituitary extract acts as a charm in causing the amount secreted to return to normal. The experiments of Starling and Verney have suggested that the posterior lobe of the pituitary controls the facility with which the kidney can excrete chlorides. In diabetes insipidus this appears to be reduced, and, as we shall see in the case of difficulty in excreting urea, more water has to be got rid of in order to obtain the same *total daily* excretion of chlorides which would otherwise increase progressively in the blood. Until we are clear about the exact mechanism of urine secretion it is difficult to go further than this, but that the pituitary body has a definite action in this respect is seen clinically in the case of certain tumours of or injury to the gland. The polyuria of chronic interstitial nephritis is brought about in a similar way by local conditions which interfere with the urea excretion; the retained urea acts as a diuretic. Polyuria is also commonly found after fevers and during the absorption of exudations in waxy kidney. In hydronephrosis the polyuria is temporary and is associated with the disappearance of the swelling in the loin. Almost any nervous disease, organic or functional, may also lead to polyuria, especially those associated with sympathetic stimulation and skin constriction.

A **reduction** in the amount of urine secreted will be brought about by diminished intake of fluid, or, if there is excessive loss by the bowels or skin. This is dealt with more fully in Chapter XXXIX. Anuria may result from local obstructive conditions, such as blockage of the ureter, and is a very serious condition. It may, however, be due to increased tension in the kidney from acute inflammatory causes, for the capsule of the kidney is inelastic, like the pericardium, and any increased tension must result in compression. Various attempts have been made to relieve such tension by stripping the capsule. This operation cannot be expected to do good where there is no increased pressure, as in the more chronic conditions. There is evidence which suggests that any improvement which results may also, in part, be due to reduction of the channel of infection which apparently may be by way of the lymphatics and the capsule.

Similarly, there is anuria if the kidney is destroyed by poisons, such as lead or phosphorus. Of considerable interest, too, is hysterical anuria, a condition which emphasizes the nervous control of the kidney, presumably of its blood vessels.

The Reaction of the Urine.—The reaction of the urine when passed is, in man, distinctly acid as the result of a preponderance of faintly acid salts, chiefly the acid phosphates. In this connection it is well for those not acquainted with the subject to read Chapter XLIII at this point, where the significance of the balance between the alkaline and acid phosphates is discussed. It will there be seen that whenever the body requires to neutralize acid an additional amount of acid phosphate is excreted, the alkali being available from the alkaline phosphates. On the other hand, if respiration has been stimulated by any means other than by carbon dioxide, an excessive amount of this gas is washed out of the lungs and acid phosphate is retained in the body to counteract the alkalæmia produced. That the two salts are readily interchangeable is seen by the formulæ and the following reaction:

$$Na_2HPO_4 + HCl = NaH_2PO_4 + NaCl$$

alkaline phosphate + acid = acid phosphate + neutral salt or, what is more usual physiologically:

$$Na_2HPO_4 + H_2CO_3 = NaH_2PO_4 + NaHCO_3$$

alkaline phosphate + carbonic acid = acid phosphate + sodium bicarbonate.

The alkaline salt acts as a store of alkali and the acid salt as a store of acid, which is of value in maintaining the neutrality of the blood. There is also a change in some of the other substances excreted, *e.g.*, ammonium salts and urea, but the reaction of the urine is not affected by these.

Use has been made of the determination of the reaction of the urine in the investigation of *acidosis*. The determination of the hydrogen ion concentration is now of recognized value. This may be done directly by the use of some of the newer indicators, or an estimation may be made of the amount of alkali which has to be added to render the urine neutral. It has been found by Van Slyke, the well-known authority on the subject, that when the urine excreted is neutral to phenolphthalein the carbon dioxide combining power of the blood is maximal. If this power is reduced the urine will be correspondingly acid.

The determination of the amount of sodium bicarbonate which has to be administered to an individual to change the reaction of

the urine is recommended by L. J. Henderson and Palmer. It is considered by many who have experience of it, to be the best method of ascertaining the presence and degree of acidosis. A series of colour standards which correspond to a given hydrogen ion concentration and the required indicator is easily procured. In a normal individual 5 grammes of bicarbonate of soda will suffice to lower appreciably the hydrogen ion concentration of the urine. This test of Sellard is, however, according to Maclean, of no value as an index of acidosis in nephritis, for the defective kidney fails to eliminate the alkali.

In the above tests the urine must be freshly voided, for if allowed to stand, the urea is easily broken down by bacterial fermentation. Toluene may be used as a preservative. Thymol is not so satisfactory as used to be thought.

Leathes has shown that in the forenoon the respiratory centre is more active than at other times, and an excessive amount of carbon dioxide is got rid of. Less acid is therefore excreted by the kidneys and the urine becomes alkaline. Forced breathing will also bring about a similar result. He suggests that changes in this alkaline tide might be utilized as an indication of the alkaline reserve of the blood.

The same will apply to cases where there is infection of the urinary tract or undue retention. An alkaline urine will usually result from a herbivorous diet, because of the carbonates which result from the breakdown of the organic acids present. This should be borne in mind, for phosphates may be precipitated, giving a milky appearance to the urine which may cause alarm.

On the other hand, an unduly acid urine may result from excessive meat eating, from certain fruits (prunes and cranberries) which contain benzoic acid, and even cereals which contain much protein—whole wheat or rice. In diseases where there is a great breakdown of protein, the acidity of the urine is increased. This is still further the case when abnormal acids are produced, *e.g.*, β-hydroxybutyric in diabetes. Excessive exercise will lead to the production of a urine of increased acidity because of the increased production of carbon dioxide and lactic acid.

THE CONSTITUENTS OF THE URINE

Of recent years a great deal of attention has been paid to the significance of the constituents of the urine in health and disease, as it is found that some of these may be an index not only of the *functional efficiency of the kidney* but also of a large variety of

conditions which may influence the neutrality of the body. It is convenient to consider several of the more important constituents, one by one.

Urea.—This is undoubtedly the most important urinary constituent. Indeed, there is evidence that urea is the normal stimulant of the kidney just as carbon dioxide is of the respiratory centre. Urea, as we have seen, results from the de-amination of the amino-acids derived from the breakdown of protein. The amount excreted must depend, obviously, to a large extent, on the amount of protein in the diet. In an individual on an average diet urea is found in the blood to the extent of 20 to 40 milligrams per 100 c.c. of blood or 0·02 per cent to 0·04 per cent, the upper limit being reached in older people, in whom it is not infrequent to find the higher figure exceeded. The daily excretion of urea in the urine amounts to 30–40 grammes. As emphasized by Maclean, this daily amount cannot be appreciably reduced, otherwise the individual would soon become saturated with urea. It seems that in some normal individuals, but especially those with chronic interstitial nephritis, a high concentration or " head " of urea is necessary before the daily output of urea can be got rid of. The blood urea is, therefore, not an index of the efficiency of the kidney except where there has been gross impairment. Animal experiments suggest that the organ may be destroyed to the extent of three-quarters before there is an actual accumulation of urea. This, however, may occur in more acute varieties of nephritis. According to Maclean, whatever the clinical condition of the patient, even when he is apparently improving, so far as his general condition and œdema are concerned, a rising blood urea indicates that a fatal termination is not far distant ; while, on the other hand, however severe the symptoms, a falling blood urea indicates a good recovery. Special warning is given regarding the value of blood urea estimations in cardiac and infected conditions in which the blood urea is apparently high simply because the blood does not pass through the kidneys sufficiently often. To be of value blood urea has, then, to be considered with other evidence of kidney efficiency.

The mere estimation of urea in urine is, unfortunately, not of the same value, for the percentage is so liable to be affected by a large number of conditions, such as those affecting body neutrality, diet, and the like. By the method of Maclean and de Wesselow, the patient, after emptying his bladder, is given a quantity of urea (15 grammes) in a small quantity of water (100 c.c.). Speci-

mens are taken, one and two hours afterwards, and if the kidney is efficient these should contain about 2 per cent of urea. Occasionally the test is interfered with by excessive diuresis (over 120 c.c. in the first hour), and hence the second specimen is more trustworthy than the first. A third specimen and restriction of the fluid intake prior to the test may be necessary. It has been found that the **urea concentrating power of the kidney** is reduced in nephritis long before the blood urea rises, as indicated above. The factor obtained, however, by dividing the concentration of the urea in the urine by that in the blood is also some indication of the urea-concentrating power of the kidney. This is normally about 90, but in severe nephritis may be reduced to below 10. This test obviously requires more time than that just mentioned.

Ammonia.—This is derived from the same source as the urea, namely, the de-amination of the unrequired amino-acids which result from protein digestion. Small quantities may be taken as such in the food or may be produced by bacterial action. Normally, as we have seen, the ammonia which is formed is converted into urea chiefly by the liver. The daily excretion is 0·6–0·7 gramme.

The ammonia plays an important part as a source of alkali in the body, as it is used to neutralize acid radicals which may be excreted as ammonium salts, the amount of urea being correspondingly reduced. There is evidence that in this neutralization the kidney plays an important part by breaking down the urea again and so forming ammonia. It has been found, for example, by Nash and Benedict that if the kidneys are removed there is diminution in the ammonia in the blood, and that normally the concentration of ammonia is greater in the renal vein than in the general blood stream which contains the merest traces of this substance. Although urine ammonia is increased by the injection of acid, this is not so with the ammonia in the blood, as might at first sight be expected. It has also been found by Maclean that in conditions of acidosis due to kidney disease, the increased ammonia excretion found in other forms of acidosis is not seen.

The ammonia-urea ratio (normally 1 to 50) is a usual method of following changes affecting body neutrality. Alternatively the ammonia nitrogen may be expressed as a percentage of the total nitrogen. This is normally about 5 per cent, but pathologically in acidosis may reach 20 per cent. Throughout the above remarks it is to be understood that what has been said refers to urine

freshly secreted, as on standing the urea is readily broken down by the micrococcus ureæ with the formation of ammonia.

Creatinine.—The constancy of the amount of creatinine (1 to 2 grammes per day) excreted normally is as striking as the variability of the urea content. As shown by Folin, variation in diet makes practically no difference in the amount. It is thus quite clearly a product of endogenous metabolism, and is found approximately in proportion to the total muscle in the body. The exact origin of this substance is not quite clear, but its excretion is definitely increased when tissue is being broken down, as in starvation or the involution[1] of the uterus. The constancy with which it is produced has caused its excretion to be used as a test of renal efficiency. It is generally accepted that a high blood creatinine (over 5 milligrams per 100 c.c. as compared with 1 to 2 milligrams) is of very grave significance in chronic nephritis. It is not until the kidney is much diseased that there is any appreciable creatinine retention.

Uric Acid.—This is derived from the nucleo-proteins of the diet, especially from tissues rich in nuclei, such as liver and sweetbread. A small amount is endogenous. It may appear as a "cayenne pepper" deposit in urine, but usually it is combined with alkalies to form urates which, when concentrated, fall out of solution and cause the typical brick-dust deposit on standing, especially in an acid urine.

Phosphates.—These, we have seen, play a special rôle in relation to the maintenance of body neutrality. The acid hydrogen phosphate, NaH_2PO_4, is chiefly responsible for the normal acid reaction of the urine, since normally the acid products in an average meat diet preponderate. If, on the other hand, a vegetable diet is taken, it is necessary to get rid of alkali excess, which is done by increasing the amount of alkaline phosphate excreted (Na_2HPO_4). The following reaction indicates how the alkali is available for the neutralization of acid, $Na_2HPO_4 + HCl = NaH_2PO_4 + NaCl$. The acid phosphate and the sodium chloride are excreted. The phosphates are commonly excreted as sodium, potassium, or calcium salts, but in a fermented urine the triple phosphates NH_4MgPO_4 (ammonia-magnesium phosphate) appear. The latter are commonly seen as crystals of the typical coffin-lid type and when they occur in freshly voided urine are considered to indicate the presence of infection in the urinary tract which facilitates ammoniacal fermentation. In a stale

[1] During involution of the uterus the urine also contains *creatine*.

urine, in which the ammoniacal fermentation has taken place outside the body, the presence of such crystals is of no significance.

Clinically, the passage of a milky urine is often found when the urine is alkaline and if phosphates excreted for reasons given above are excessive. This can easily be remedied by increasing the protein intake. Normally the phosphates are derived from the phosphorus-containing articles of the diet, such as the nucleo-proteins, lecithins, and the like. Phosphaturia may indicate excessive waste of nervous tissue, as in excessive mental work, wasting diseases and the like, and there seems to be little doubt that in some individuals such conditions bring about an increase in the phosphorus excreted. The actual variety of phosphate will depend, in the absence of disease affecting the excretion, on the variety of the diet and the amount of exercise taken, as the latter produces carbon dioxide and lactic acid and thereby brings about the excretion of the acid variety.

Occasionally alkaline phosphates are just kept in solution by the amount of carbon dioxide which is dissolved in the urine. On heating this is driven off and the phosphates are precipitated. This opalescence may be confused with that due to albumin and hence the necessity of faintly acidifying the urine (best with acetic acid) before so testing.

Oxalates.—These have a special significance in that some individuals appear to be unable to break up oxalates efficiently. Such substances occur in tomatoes, rhubarb, strawberries, cabbages, spinach, and asparagus. A little occurs in apples and grapes. Apparently all the oxalates of the urine do not come from the food, as a dog fed on meat and fat excretes oxalates (Mills). Experimental and chemical evidence suggests that oxaluria may be brought about by abnormal oxidation of uric acid. The urine on standing is described as having a "powdered wig deposit" on the top of the mucus or any other deposit present. If concentrated, it may give rise to disagreeable symptoms of irritation during micturition. So sensitive are some people that they may be affected by a single strawberry. Treatment is obviously directed to elimination of oxalates from the diet and the administration of diluents.

Excretion of Dyes.—Although, as yet, we are somewhat in the dark regarding the exact mechanism of the excretion of dyes, there seems to be little doubt from clinical evidence that the facility with which the kidney can excrete these substances is a measure of its efficiency as an organ of excretion. Dyes such as

indigo-carmine or methylene blue are often sufficient to give an indication of the relative amount of excretion by each kidney. The outpouring of the dye in spurts from the ureters may readily be observed by the use of the cystoscope, but for more accurate work catheterization of the ureter is desirable and the amount of dye excreted by each kidney should be estimated. The phenol-sulphonephthalein test of Rowntree and Gerraghty has received most attention in this connection. In carrying out the test the dye is injected into the buttock of the patient, and estimation of the amount passed after one hour and after two hours is then made by comparing the urine colorimetrically with a standard solution. It is considered that 70 per cent of the pigment should be excreted in the second hour. If only 50 per cent, recovery is to be expected under treatment, while below 20 per cent prognosis is bad, and if this low value persists death is not far distant.

Diastase.—Normally, the diastase used for the conversion of starch and glycogen into sugar is excreted by the kidney and in different individuals the daily excretion is very constant. The measurement of the concentration in urine is easy, a unit of diastase being the number of c.c. of 0·1 per cent starch solution which is digested by 1 c.c. of urine in half an hour. Normally, this is 6 to 30 units, but in renal disease it may be under 1. Fallacies are very common: for example, it might be considered that in diabetes the diastase would be appreciably reduced, but it has been pointed out by Cammidge, Forsyth, and Howard that the diastase in the blood is not appreciably dependent on the pancreatic diastase and its re-absorption, but is produced by the liver. They have shown that excision of the pancreas tends to cause the blood diastase to be increased, whereas destruction of the liver brings about reduction. Liver disease, as found by Harrison and Lawrence, also appreciably reduces the blood diastase which apparently is that elaborated by the liver for the conversion of glycogen into glucose. The estimation of the diastase excretion, although it may be of supplementary value, does not therefore necessarily give much information regarding the kidney. (See " Addendum," page 399.) The test is of value chiefly in the diagnosis of acute hæmorrhagic pancreatitis in which values of 100 to 200 units have been recorded.

PROTECTIVE SYNTHESIS

The Sulphates.—When certain toxic chemical substances are taken into the body, the body commonly excretes them in two

ways, as sulphates or glycuronates. These sulphates are to be distinguished from the sulphates which are derived from the sulpho-proteins ingested in the food or broken down in the body.

This combination of harmful substances with sulphuric acid takes place normally in relation to the products of bacterial action in the intestine. By such action, portions of the side chains of certain amino-acids produced normally from protein become broken off, the remainder being not only incapable of being oxidized in the body but also actually harmful. For example, from tyrosine is produced cresol and phenol, while from tryptophane is derived indoxyl. The toxic substances are absorbed from the alimentary canal but when they reach the liver they are coupled with sulphuric acid to form what we know as the ethereal sulphates. The amount of these in the urine is therefore a measure of the amount of bacterial decomposition in the alimentary canal. They are increased in constipation. One of the ethereal sulphates, indican, is of special interest, since it can be readily oxidized to indigo blue by hydrochloric acid and potassium chlorate, and thus detected. The blue colour is made more evident by shaking the urine to which the reagents have been added with chloroform which dissolves the indigo. Therapeutically, sulphates are administered as an antidote in phenol poisoning.

Glycuronates.—These are of special importance because when they appear in the urine they give the same reducing reactions as glucose because of their free CHO group which is easily oxidizable. The glycuronates are formed from glycuronic acid, which is an oxidation product of glucose, and are the form in which a large number of drugs administered medicinally are combined and excreted.

Hippuric Acid.—When benzoic acid is administered it is very rapidly compounded with the amino-acid glycine to form hippuric acid, so called because it occurs normally in the urine of the horse and other herbivorous animals. In this way harmful compounds of the benzene series are excreted by the kidney. The benzoates are administered therapeutically to render the urine acid where there is infection of the urinary tract. An acid urine is required to liberate formaldehyde from urotropine (hexamine or hexamethyltetramine) when it is administered.

PATHOLOGICAL SUBSTANCES IN URINE

Albuminuria.—According to Maclean the best test for albumin in the urine is the addition of a few drops of a saturated aqueous

solution of salicyl sulphonic acid unless the urine is exceptionally alkaline. Then a few drops of dilute acetic acid should be added as in the usual heat coagulation test. The cold nitric acid test is also excellent if properly done.

Albuminuria is not, however, necessarily a grave condition, and, apart from pus, spermatozoa and secretions from the urethra, albumin may be found, often in apparently normal adolescents especially after severe exercise. Such patients often present a somewhat unhealthy general appearance and have an unduly excitable circulatory system. No other signs of renal disease are present, but there may be calcium oxalate crystals in the urine. Such adolescent albuminuria may be considered harmless, and even the presence of casts in the urine does not indicate that the kidney is inefficient (Maclean). On the other hand, grave kidney disease may be present when there are no casts and no albuminuria.

To sum up, therefore, we may say that the presence or absence of albumin in the urine gives very little information regarding a kidney case. Its presence at least indicates that it is desirable to carry out tests for renal efficiency. These have been given above under " Urea " and " the Excretion of Dyes." Where, however, the albumin is accompanied by pus or blood the condition is more serious, and the presence of urethritis, pyelitis, or calculus must be considered.

Sugar.—The urine contains sugar, recognizable by Benedict's or Fehling's tests, whenever the blood sugar exceeds the renal threshold of 0·17 per cent. This may occur after a large meal of carbohydrate, especially of starch, and after severe exercise. After a boat race it has been found that the urine of men commonly contains sugar. In this instance the blood sugar has been increased by the sympathetic stimulation and possibly the secretion of adrenaline during the exercise. Both these cause a rapid mobilization of the liver glycogen and its conversion into glucose which passes into the blood-stream. Sugar is found in the urine for a like reason after the injection of adrenaline or thyroxine, and during asphyxia and anæsthesia. Similarly, it may be found in exophthalmic goitre.

The presence of sugar in the urine at once suggests the possibility of pancreatic disease, the blood sugar having risen because of the difficulty in burning carbohydrates (see Diabetes). After the injection of pituitrin, and in stimulation of the posterior lobe of the pituitary body in the early stages of acromegaly, glycosuria

is common, since pituitrin antagonizes the normal activity of the internal secretion of the pancreas.

Occasionally sugar appears in the urine, because the leak point of the kidney is abnormally low. The condition is harmless, and it is easily differentiated from diabetes mellitus, in which the height of the blood sugar is abnormally high.

Bile.—This need only be mentioned, as it has been dealt with in relation to jaundice. The presence of bile in the urine indicates that there is an abnormally high amount of bile in the blood.

Acetone and aceto-acetic (diacetic) acid should always be tested for when sugar is found in the urine, as they are of the greatest importance in assessing the degree of the faulty fat metabolism which results from the inability of the body to burn carbohydrates efficiently. When fat is being oxidized it passes through the stages of butyric acid, β-hydroxybutyric acid, aceto-acetic or diacetic acid, to carbon-dioxide and water. These stages are shown in relation to diabetes.

In diabetes the reaction stops or is delayed at the hydroxybutyric acid and aceto-acetic acid stage. These substances themselves may appear in the urine, but the aceto-acetic acid readily loses carbon dioxide to form acetone $CH_3 . CO . CH_3$, which gives the breath and the urine a characteristic apple-like odour.

Blood.—The presence of blood in the urine is usually of serious import. It may be present with (hæmaturia) or without (hæmoglobinuria) blood corpuscles, which are recognizable microscopically. Large quantities of blood give the urine a red colour, but the pigment, methæmoglobin produced by the action of the urine on the blood, causes the urine to have a characteristic smoky appearance. The fallacy of menstrual blood must be avoided by using a catheter.

When the blood is bright red and comes at the beginning of micturition it is probably of urethral or prostatic origin, but when it comes most freely at the end of micturition, especially if in clots, it is probably of vesical origin. Calculus and tumours and, in the East, bilharziasis are probably the commonest causes of hæmaturia, but it may occur in cystitis, varix, scurvy, and purpura.

The smokiness of urine caused by blood indicates that the blood has been long enough in the urinary tract to be intimately mixed and to become methæmoglobin. The other signs and symptoms usually point to disease of the kidney.

Addendum.—In summing up the importance of tests in relation to kidney disease attention should, as pointed out by Geoffrey Evans, be drawn to the fact that single tests are of little value. It is the progression or otherwise which really is important in determining the seriousness of the kidney disease in a given case.

CHAPTER XXXIX

ŒDEMA AND THE WATER CONTENT OF THE BODY

For absorption to occur through the gut wall, the substance to be absorbed must be in solution.[1] Water, the physiological solvent, is therefore an essential constituent of the diet. Food stuffs are better utilized if the fluid of the diet is not unduly reduced. This finds popular expression in the idea that drinking with meals causes stoutness. The truth is that insufficient fluid intake may cause thinness.

The amount of fluid required for absorption is usually in excess of that needed permanently in the body and must therefore be got rid of. This is done mainly by the kidneys, skin, lungs, and intestines. The body, however, is economical in its working and makes use of the fluid excretion for other purposes. Thus the urine contains many substances which the body must get rid of, the sweat is utilized to keep the body cool, and the fluidity of the bowel contents is essential for adequate removal of the undigested part of the food.

Now the water available for all these purposes is limited by the amount taken in, and the more that is used for one function the less is there available for others. Thus, if a great deal of water has been required for the production of sweat, less is available for the urine ; the urine then tends to be unduly concentrated and this explains the special liability to calculus in the residents of hot countries. Similarly, the obvious physiological treatment in cases of gravel or tendency to crystal precipitation in the urine is increased consumption of bland fluids. Intense diarrhœa also, or loss of fluid by the intestine seen typically in cholera, causes urine secretion to cease. Actually in this condition the blood is so deprived of water and becomes so concentrated that it is described as being tarry. It is doubtful if this fact is fully appreciated in ordinary cases of poisoning with severe diarrhœa. In such instances the consumption of enormous quantities of fluid is essential ; otherwise fluid will be taken from the blood. In

[1] This is not strictly true, as small quantities of apparently insoluble substances may be taken in.

cholera the hypertonic saline treatment of Rogers depends on the fact that not only is fluid injected intravenously, but its high salt content and osmotic pressure prevents its being removed so rapidly from the blood-vessels and the fluidity of the blood is maintained. Excessive loss of water in the urine is seen in conditions in which the kidney requires water in order to get rid of certain substances, *e.g.*, sugar, or when that organ is unduly stimulated, *e.g.*, by urea. In the former condition we have the well-known thirst of diabetes produced in a way strictly analogous to the thirst of excessive sweating.

The production of thirst is one of the protective mechanisms of the body, as is the production of appetite. Appetite, however, is largely a question of habit and cannot be taken as a trustworthy guide of the individual's needs. Thirst, on the other hand, is generally, but not always, a better guide.

Thirst is essentially the result of diminished secretion from the salivary glands, and the effect of the dryness on the nerve endings at the back of the tongue. That this latter fact is so, is seen by painting the tongue with cocaine which rapidly abolishes the thirst in an otherwise thirsty person. The salivary glands are very rapidly affected by the slightest reduction of the fluid content of the blood such as occurs from excessive loss by one channel or another and act as an indication of the fluid need of the body. Paralysis of the salivary glands, and the thirst produced thereby are well seen after the injection of atropine which affects the glands directly. They occur, for example, after operation where atropine has been administered (as a routine, by some anæsthetists to diminish the possibility of vagal inhibition during anæsthesia, especially the first stage, or where it has been given to reduce secretion in operations of the nose, mouth, or throat). Nothing except personal experience can give full appreciation of the thirst after atropine, which has the great disadvantage that the patient, if allowed to drink excessively, is unduly disturbed by the necessity of getting rid of the excessive fluid imbibed. This may have obvious disadvantages where quietness is essential from the point of view of the hæmorrhage of the operation, say in the nose. Treatment by painting the back of the tongue with cocaine is obviously indicated when the thirst is severe. The tissues and nerve endings at the back of the tongue may be dried by local applications. This occurs especially on the application of substances which normally withdraw water. Thus we have the thirst caused by the taking of salty foods, of alcohol, and of

sugar in the so-called mineral waters. In the latter case the addition of sugar is intended by enterprising manufacturers to cause further thirst. It is thirst of this nature which may cause a drift towards chronic alcoholism. In the latter condition the state is aggravated by diminution in salivary secretion.

Retention of excessive fluid in the body may be due to general or local causes. The fluid may infiltrate the tissues as in *œdema*, or collect in serous cavities as in ascites. The possibility that the plasma may become diluted through the loss of its protein is dealt with below under the treatment of nephritis.

There may be an upset of the mechanism by which fluid is retained in the blood-vessels. The elucidation of this mechanism we owe especially to the work of Starling, and is as follows: The capillary wall appears to be of the nature of a semi-permeable membrane, which will allow the passage of crystalloids (*e.g.*, salts and sugars) but not of colloids. Normally there is a balance of forces. On the one hand the capillary blood pressure tends to drive fluid out of the vessels, while on the other the osmotic pressure of the plasma proteins tends to prevent its leaving, for the osmotic pressure of the tissue fluids is less than that of the plasma. Œdema may result from an increased capillary pressure as would be brought about by a venous back pressure, from a lowering of the osmotic pressure of the blood by dilution (as in general water retention), or from an increased permeability of the capillaries which may permit the passage of proteins. In disease the last possibility appears to be specially important, for permeability may be altered by conditions such as anoxæmia, toxæmia, and some abnormal nervous states.

General retention is seen in *acute and subacute nephritis*. The fluid tends to accumulate in those parts of the body most dependent and where the subcutaneous tissue is loose and the circulation least efficient. Thus a man often notices his puffy face, especially round the eyes, in the morning after getting out of bed. This disappears during the day and in the evening the ankles are seen to be swollen and "a ridge is formed on the top of the boot." In severe cases the œdema of the face may not pass off and, of course, does not if the individual is kept in bed. Death may be brought about if the more important parts of the body, such as the pericardium and the lungs, become œdematous, the individual drowning as it were in his own fluid. The cause of nephritic œdema is obscure. In subacute nephritis the loss of albumin in the urine lowers the albumin content of the blood, the

albumin-globulin ratio being increased and the plasma has thus a diminished power of holding fluid from the tissues. An additional factor is salt retention by the diseased kidney, but the problem is by no means fully solved.

The characteristic of œdema is that the fluid may easily be pressed out of the part affected. The sign of "pitting on pressure" is of great diagnostic value, as it is not given by conditions such as myxœdema, or fat, which may appear similar.

It should be noted that in the "solid" œdema of lymphatic obstruction pitting on pressure may be absent or slight. This is due to the fact that the lymphatics are already full, and no additional fluid can be pressed into them.

In *cardiac failure*, the œdema remains more or less fixed in position and begins in the more dependent parts where the circulation is deficient, and the venous pressure high. In reality this œdema results from the local changes, viz., increased capillary permeability and tissue alteration at the site of the swelling. It has been shown by Bolton that this is not all due to a high venous pressure as such causing a high capillary pressure, but to an anoxæmia or want of oxygen causing increased permeability of the capillary walls from the resulting stasis, of which the high venous pressure is an index. It has, for example, been shown experimentally that if the vena cava is obstructed the œdema is not synchronous with the time of the obstruction, but there is delay in its onset, and in its recovery, as would be expected from definite tissue damage. It has been suggested that imperfect metabolism brings about a local increase of osmotic pressure, while increased H ion concentration causes the colloids to take up water.

The above state of affairs will occur whenever there is venous obstruction, and the blood is not allowed to return sufficiently rapidly from any part of the body. The return of the venous blood depends on a variety of factors; the heart, the veins themselves, the respiration, and the arterial pressure; enduring failure of the latter two is almost impossible as it is incompatible with life, but failure of the heart and veins is comparatively common.

Cardiac œdema, as has been said, is not confined to any special area but it is most marked in those parts of the body where there is most strain, below the level of the heart itself, as on the veins of the legs in the erect posture. Thus, œdema of the ankle is often an early sign of cardiac failure and is best elicited over the surface of the malleoli. Attention has already been drawn to the importance of venous pressure as an index of

cardiac efficiency. Not infrequently there may be a combination of factors as in chlorotic shop girls. Here there may be a mild degree of cardiac inefficiency owing to the increased work necessary on the part of the circulation, increased dilution of the blood, and local effect on the veins from excessive standing.

Œdema in cardiac cases is often very persistent and taxes all the therapeutic resources of the physician. The œdema may affect all tissues, and in the lungs predisposes to hypostatic pneumonia. This is a frequent cause of death in aged people who have been brought to bed from some other cause such as injury, for œdematous tissues have very little resistance to infection. It must be realized that cardiac œdema is often the result of myocardial failure without antecedent valvular disease and that œdema with slight breathlessness on exertion (often taken for granted by the individual as a consequence of his age) may be the only sign of the condition.

Simple *failure of the veins* occurs when limbs have been kept dependent for an unusual length of time, as after marching. The hands even in a normal soldier may become sufficiently œdematous to be appreciated subjectively. It is a well-known fact that shoes become tight after an abnormal amount of walking and especially standing, in which, as there is little muscle movement, the compression of the veins which facilitates the return of the blood is absent. It is recognized by bootmakers that even ordinarily the feet are larger at the end of the day, especially if the individual has been standing a great deal. It may be shown by standing in large cylinders of fluid that the lower limbs increase definitely in volume after twenty minutes in this position. In these instances an unaccustomed strain has been thrown on the veins and some of the valves may have given way. We now know that the veins do possess a definite vaso-motor mechanism under central control, but apparently, like all other mechanisms, it requires to be frequently used to act efficiently. As the individual becomes accustomed to a particular exercise or position, œdema is less readily brought about, provided, of course, that it is not allowed to persist in the first instance. Otherwise the subcutaneous tissue appears to enlarge, and, as in the case of the feet, the annular ligaments become stretched and permanent thickening of the ankles may result. A similar condition is also seen in horses, and treatment by tight bandaging is obvious.

A similar venous stasis and anoxæmia of the capillary blood-vessels results from any gross *venous obstruction*. In cirrhosis of the

liver the portal system is affected, and the œdema is indeed a most serious symptom. Here the portal capillaries become extremely permeable from the obstruction to the veins of the liver and fluid accumulates in the peritoneal cavity in enormous quantities.[1] Such a condition will be confined entirely to the portal area whatever position the body is in, and there is no œdema of the ankles until the abdominal pressure becomes very high and the inferior vena cava becomes pressed upon.

Any obstruction of veins or lymphatics brings about the same result, the symptoms depending on the actual veins obstructed. The œdema, especially if unilateral or localized, may be of considerable diagnostic value in obscure cases, *e.g.*, œdema of the conjunctiva and eyelid in thrombosis of the cavernous sinus, where it may be an early indication of the condition. Œdema of the right side of the face and of the right arm results from obstruction of the superior vena cava by the pressure of an aneurysm or mediastinal growth.

The permeability of the tissue capillaries directly or indirectly may be affected by *nervous* means, for we have evidence that the capillaries are under nervous control. In definite nervous lesions of the reflex arc, such as locomotor ataxia, œdema or even herpes may occur in common with the general trophic changes. In the same way from nervous changes as yet incompletely understood, we have angio-neurotic œdema, the œdema of neuritis or neuralgia, intermittent hydrarthrosis, and the blebs of herpes zoster. Our knowledge of the laws which govern permeability of the capillaries, or indeed of any tissue, is very scanty, but the evidence of Dale, Lewis, and their colleagues suggests that the nerves act by providing chemical substances at their terminations.

We do know, however, that *toxins* affect the capillary wall. Various wheals and swellings after the injection of toxins are produced in this way. The injection of histamine, nettle stings, bites of insects, certain articles of diet in sensitive individuals, all cause œdema. That of the chest wall in empyema may be looked upon as similarly produced. The transudation of lymph in *inflammation* no doubt also depends on similar mechanisms. Lewis has shown that in those individuals whose skin vessels and local mechanism for dilatation are unduly irritable the œdema which makes dermatographia possible is apparently due to the formation of a toxin in the region of the stroke of the writing

[1] In certain cases chronic peritonitis, simple or tubercular, is an additional cause of ascites in hepatic cirrhosis.

object. This he suggests may be one of the mechanisms which control local capillary dilatation and in such condition brings about the additional amount of blood which is necessary to deal with the toxin.

Finally, we know that the permeability of the capillaries is reduced in vitamin deficiency, as in scurvy and beri-beri, in which latter the wet or dropsical form has long been a definite entity. A similar state may be present in cachectic states.

In all conditions of œdema, other than those of mere dilution, we have changes, possibly only local, in the normal water content of the tissues from change in the capillaries. This view is perhaps somewhat arbitrary. It is held by some that the real change is one in the tissue due to devitalization and the formation of substances which attract the fluid from the blood-vessels. The actual result is the same whatever view may be held.

TREATMENT.—From the point of view of treatment, the primary cause is most important. Removal of the cause is, of course, most desirable, but not always possible, and local and general treatment has to be resorted to. Local treatment consists in removing the actual fluid accumulated, such as the tapping of ascites in liver cirrhosis. In this condition attempts have also been made to assist Nature, as in the Talma-Morrison operation, by making an anastomosis between the portal and systemic venous systems. These, however, have been only moderately successful, although instances occur in which there has been amelioration to a considerable degree and even disappearance of symptoms for several years. In this category also is the use of Southey's tubes, by which fluid is drained away from œdematous parts. Large quantities of fluid may often be thus removed, but it has to be remembered that œdematous tissue is particularly liable to infection. General treatment is more commonly used in cardiac and kidney cases. In the latter, the retention of the products of metabolism is even more important than the water retention, and therapy concerns itself in increasing the excreting activity of the skin and the intestine. This is more fully dealt with in relation to kidney cases on page 408.

In cardiac cases there are several physiological principles which are essential to proper treatment. The pumping action of the heart, which is at fault, needs first attention and cardiac tonics must be administered (page 203). If the œdema is severe the patient must be kept in bed to assist the venous return and in convalescent heart cases it is often surprising how difficult it is

to get the patient to understand this, for he feels comparatively well provided he does not do severe work. The longer, however, the œdema is allowed to persist the more difficult it is to get recovery, as the capillary wall apparently becomes more and more damaged from the anoxæmia which is itself aggravated by the œdema. On the other hand, œdema, if treated energetically and as soon as observed, clears up even in severe cases as if by magic. Anyone who has attempted to cure varicose ulcers will realize the lack of vitality of the tissues in which the venous return is impaired. The ulcer may heal while the patient lies in bed, but breaks down directly he gets up. This, like the œdema, is all a matter of the oxygen supply to the tissue, and the condition indicates the importance of keeping the feet up in œdema. In pregnancy also when the venous return from the legs may be interfered with by pressure, and œdema in the feet is seen to come and go according to the extent to which the feet are kept up. In cardiac œdema there is every indication that the administration of oxygen would be of value, and Leonard Hill and his co-workers have obtained considerable improvement from immersing the patient in an atmosphere of oxygen by means of a bed tent.

In the treatment of œdema the reduction of sodium chloride in the diet is well appreciated. It is of course necessary in the first instance to reduce the intake of fluid as far as possible, a point not infrequently forgotten, for the kidneys may be congested and every effort has to be made to reduce their work to a minimum. The blood plasma contains normally various salts[1] equivalent osmotically to a 0·9 per cent solution of sodium chloride, and if it is diluted, the excess of water is rapidly excreted by the kidney. Obviously, then, the amount of salt in the body governs to some extent the amount of water held. If the diet contains salt the saline absorbed is but slowly excreted and in disease particularly slowly, for there is usually difficulty in excreting chlorides. But if, on the other hand, salt is cut out of the diet as far as possible all the fluid taken in simply dilutes the blood and is excreted. Of course a certain amount of fluid has to be taken for purposes of the absorption of nourishment and excretion. Further, in excreting the fluid a certain amount of salt is lost and still more fluid will have to be excreted to maintain the normal concentration of the

[1] The actual percentage of NaCl is 0·58. Blood plasma thus contains roughly a decinormal solution of NaCl. The figure for whole blood is lower, 0·45 per cent, because of the lower NaCl content of the corpuscles.

blood. Actually this does not go on indefinitely as the kidney ceases to excrete sodium chloride when the salt in the diet is reduced. Excessive excretion, on the other hand, by the skin may actually take place to an extent which may lower the salt content of the body to a danger point. The procedure, however, of lowering the salt content of the diet is of obvious assistance in the elimination of excessive water from the body.

It is equally true to say, as pointed out by Maclean, that the amount of fluid in the body regulates the excretion of salt. When water is retained in the body it is retained as saline, and hence in any condition of an œdematous nature there is a retention of chlorides causing a fall in chlorides in the urine.

Recently more attention has been paid to the protein of the diet. It used to be considered that as the kidney was an important organ in the excretion of the products of tissue metabolism, it ought to be spared such work and protein should be reduced to a minimum. In chronic parenchymatous nephritis, however, it has been definitely proved that there is an excessive loss of the plasma protein ; this will lead to a fall in the osmotic pressure of the blood and to œdema, which will be increased by reduction of the protein in the diet, as emphasized by Epstein. Where there is excessive protein loss there should be no reduction of diet in this respect ; this is borne out by the observations of Maclean.

Important, too, is the elimination of water by the skin, and this can be brought about by keeping the surface of the body at a high temperature. Hot packs stimulate the skin generally, but hot air baths are best for the excretion of water, as the dry air can take up more water vapour. A bath of this kind can readily be improvised by hanging electric lamps inside a cage which is covered by blankets or preferably by a piece of asbestos sheeting. By using the modern gas-filled lamp fewer are required than if the older varieties are used. A patient under such treatment should receive frequent sponging or real baths. In hot air baths, salts may be deposited on the skin, and not only will they be irritating but they will interfere with further skin action. The dilatation of the skin vessels in cardiac cases is also of value in that it enlarges the capillary area, and, by reducing venous pressure, relieves the heart. Measures must be taken to keep the skin warm, not an easy matter, for the patients are often propped up to relieve breathlessness.

The extent to which sweating will occur under conditions of

high temperature does not appear to be limited by the salt content of the body, as in the cases of water loss by the kidney, as remarked above. Provided sufficient fluid is taken to maintain the fluidity of the blood, sweating may take place to an extent which is actually dangerous, because of the excessive loss of salts. A condition erroneously known as "water intoxication," and due to excessive drinking of water after great sweating is found among those who work in deep salt mines in America.

The use of drugs to stimulate sweating, such as pilocarpine or salicylates, is of advantage. The former, although possible in kidney cases, cannot be used in cardiac cases because of its depressant action on the heart by vagal stimulation.

In cardiac failure the circulation should also be stimulated, the common cardiac tonic, digitalis, being of value. As a diuretic urea is often efficient and has the advantage of being Nature's remedy. The caffeine series is also useful, but probably more irritating. The commonly used diuretin is theobromine-sodium-salicylate. Recently, the organic mercurial diuretics such as salyrgan have been found to be of the utmost value in the treatment of œdema. These substances are believed to act, not directly on the kidney, but by decreasing the affinity of the tissues for fluid. Their action is enhanced by ammonium chloride, perhaps because of the acidifying action of this salt (see later, Desiccation). They are of value chiefly in cardiac œdema, but the claim has been made that their use is legitimate in cases of chronic parenchymatous nephritis.

The intestines may also be utilized as a channel for getting rid of excess fluid. Any vegetable purgative may be used, and compound jalap powder has considerable reputation. Sodium sulphate (Glauber's salt) is most efficient and is a good diuretic. The purgative saline must be given in concentrated solution, in contrast to that given in dilute form purely to move on the intestinal contents. Brisk purgation is not a method which can be prolonged indefinitely.

The use of calcium chloride is now strongly recommended by Blum as an "interstitial diuretic." This worker brings forward evidence that it is the sodium rather than the chloride which is retained. It has long been known, however, that calcium reduces permeability and this property of calcium may be concerned.

From what has been written regarding the factors maintaining a balance between the amount of fluid in the blood and tissues,

it will be clear that to promote the flow of fluid from the tissues into the blood it is necessary to increase the osmotic pressure of the blood or to lower the capillary pressure. The former is accomplished by the brisk purgative, since fluid is withdrawn from the blood into the bowel. In the severe diarrhœa of children the blood may become very concentrated, and those who suffer from the polyuria of chronic nephritis tend to have somewhat dehydrated tissues.

A reduction of capillary pressure should on physiological grounds be brought about most effectively by venesection. The fall of arterial pressure is largely recovered from, but the venous fall is prolonged. This will not only relieve the heart but will also drain the tissues. As in chronic cases at least there is often an increased number of red corpuscles, blood can therefore all the more readily be spared by the patient.

Desiccation.—The importance of the desiccation which occurs when there is excessive loss of fluid from the body has already been referred to under "Vomiting," and occurs in such conditions as severe vomiting, severe diarrhœa and acidosis. The desiccation affects the blood and tissues. The blood becomes concentrated unduly and, therefore, scanty and more viscous, so that it circulates with difficulty. Less is known about the exact effects of tissue desiccation, but its importance cannot be over-stressed. It is usually secondary to loss of fluid from the blood. Loss of salt and water go together, and although more salt than water may be lost, the balance of water soon escapes from the blood because of osmotic forces. For this reason normal saline given rectally, subcutaneously or intraperitoneally, or, as in cholera, hypertonic saline (2 per cent strength) injected intravenously, is usually the fluid of choice to remedy the loss. When the patient is conscious, fluid should be given by the mouth whenever possible.

In most conditions in which acidosis (including ketosis) is present, anhydræmia results. The reason for the dehydration which accompanies acidosis is to be found in the response of the kidneys in excreting large amounts of water. This presumably represents an effort on the part of these organs to get rid of acid by diuresis. Water is also lost in moistening the excess of air which is respired as a result of stimulation of the respiratory centre. In diabetic coma the diuresis associated with glycosuria has prepared the way for desiccation.

Clinically, dehydration is revealed by the dry inelastic skin and

shrivelled appearance. The intra-ocular tension is low and in infants the fontanelle depressed. A condition resembling shock, with low blood pressure, is finally produced. From the practical point of view, in the treatment of gastro-enteritis, intestinal obstruction, etc., and also of diabetic coma, measures must be taken to make good the loss of fluid.

CHAPTER XL

THE TEMPERATURE OF THE BODY

MAMMALS are enabled to work under very variable climatic conditions because their body temperature is maintained at a constant level. For this purpose a special mechanism has been developed. The warm-blooded differ from the cold-blooded animals in that they are able to limit heat loss, while the latter, although they produce heat, are rapidly reduced to the temperature of their surroundings.

The normal temperature of the body is the result of a balance between heat production and heat loss, both of which are variable. The balance in man is adjusted at about 37° C. or 98·4° F., but if the patient is resting in bed the temperature may be a degree or more lower. This temperature is registered in the rectum; that in the mouth is about a degree lower, and that of the axilla lower still. The sublingual temperature, with the mouth closed, is probably the most trustworthy for general purposes. If the respiration is excessive, even in nasal respiration, an appreciable lowering of the temperature may be recorded owing to the entrance of cool air, a point to be noted in taking the temperature of breathless or hyperpnœic patients. There is also an appreciable diurnal variation, the temperature in the early evening or late afternoon being about one degree higher than it is in the early hours of the morning. There is so much general variation in different individuals that the clinical normal may be considered to vary between 96° and 99° F. The diurnal variation depends to some extent on the habits of the individual, and those who habitually work at night may experience the reverse of the above. It is considered that the sequence is due to intake of food and increased metabolism during the day, but sleep itself is no doubt a factor, for metabolism is noticeably reduced in sleep, and also the activity of the nerve centres. The diurnal variation is exaggerated in certain conditions, typically in tuberculosis or chronic *bacillus coli* infections; this is probably due to the general irritability which occurs. On the other hand, a swinging temperature

always suggests the presence of pus, and is specially common in pyæmia ; although the intermissions may be very great, they do not necessarily observe accurately diurnal variations, and are much more irregular. The cause of the intermissions has never been explained, but they probably depend on a variability of adrenaline secretion or other substance controlling the vessels of the skin. In septicæmia the temperature may run at steady high level, or show marked variations.

Heat production has already been discussed under the questions of feeding and growth, where it is seen that the heat produced in the metabolism of the essential organs is fairly constant in the same individual for long periods.

The heat which is associated with muscular work depends on the amount of work done. That excess heat is produced by muscular work is universal experience. Even in the resting individual, provided he is not asleep, skeletal muscles play a considerable part in the production of heat, which is associated with the tone of the muscles and the integrity of the reflex arc. If in an animal the nerve endings of the motor nerves are paralysed by curari and artificial respiration maintained, there is an appreciable diminution in heat production. Similarly, under anæsthesia or alcoholism, much less heat is produced ; we see therefore the necessity for keeping an anæsthetized person warm, the more so as it is now known that a fall of body temperature may add greatly to the risks of surgical shock. It has also long been known that alcoholics are especially liable to suffer from the effects of cold. The same applies to anyone suffering from any injury or disease of the nervous system in which muscle tone is reduced. In the severe shock after wounds in war-time it was found that the keeping of the patient warm was of primary importance.

This is to be explained by the fact that cold exhausts the suprarenals (Cramer, Crowden). It has been amply shown that these organs are concerned with the protection of the body against toxic products which produce shock, *e.g.*, histamine (Kellaway and Cowell).

In cold weather heat production is raised by increased muscular tone. It may be sufficient to bring about shivering, which is really a reflex mechanism or an effort of Nature to maintain body temperature under the control of the heat-regulating centre. The fact that greater activity is necessary to keep up the body temperature in cold atmospheres has probably been one of the

most important factors in the superiority of the races of the cooler climates.

The production of heat depends, for the most part, on the need of the individual to do muscular work. To maintain a balance, an automatic arrangement is necessary for the regulation of the heat loss. This is effected by means of the heat-regulating centre in the hypothalamic region, which, as we shall see later, is the region in which all the centres peculiar to the higher animal seem to be situated. The centre reacts to changes in the temperature of the blood and controls the amount of heat lost by the body. This can readily be shown experimentally by heating or cooling the blood passing to the brain and observing the reactions produced (Barbour).

Heat is lost for the most part through the lungs, by the skin, and by warming the food. In dogs, whose skin is not so active in this respect, as they have no sweat glands (except on the pads of the feet), the respiratory tract is the more important. It is a familiar fact that a dog lying in front of a hot fire will pant in order to make maximum use of the tract as a means of heat loss, which is brought about by the vaporization of the water and the heating of the expired air.

In man, however, the skin is much the more important, and it is the skin mechanisms which are varied by the activities of the regulating centre. The skin is for this purpose supplied with an enormous number of blood-vessels, and when they dilate, an increased amount of blood comes into comparatively close contact with the cool surface of the body and loses heat by conduction and radiation. To make up for this skin dilatation and to maintain the total size of the vascular bed reasonably constant, constriction of vessels elsewhere has to be brought about. Individuals, therefore, whose vascular reflexes are in poor condition, and whose internal blood-vessels do not correspondingly constrict, suffer under certain conditions from what may be described as relative hæmorrhage and fall of the aortic pressure. They notoriously suffer from faintness in hot weather or in church.

In addition to loss of heat by radiation and conduction there is loss of heat by the evaporation of the sweat, the secretion of which is stimulated. This mechanism is particularly useful in hot atmospheres in which conduction and radiation are reduced. The heat lost by evaporation of sweat, therefore, depends on the humidity of the atmosphere. Here we find the reason why the inhabitants of humid climates and districts tend to be less active

(*i.e.*, produce less heat to be got rid of) than those who live in dry areas, and it is a familiar fact that a hot and wet muggy day is very enervating. During the War, the effects of a hot humid climate were well seen in Mesopotamia, where cases of heat stroke from excessive heat retention were common. Sweating goes on normally in all of us, but it is only when it occurs at a greater rate than its rate of evaporation that we appreciate its existence. This is seen in the fact that more urine is passed normally on a cold day. Sweating, like the dilatation of the skin vessels, depends on the stimulation of the autonomic nervous system under the influence of the heat-regulating centre.

It is obvious that individuals differ considerably in their powers to lose heat. Tall thin men lose more heat by conduction and radiation than short stout men whose surface is not only smaller but whose heat loss is also diminished by subcutaneous fat. The latter then require greater activity on the part of the sweat glands and the greater discomfort of such people on a hot day is obvious.

The power to regulate temperature depends no doubt also on the speed with which individuals can produce heat and on the condition of the vascular reflexes. The latter deteriorate appreciably if not utilized. By proper training and a reasonable amount of exercise great benefit often takes place. It is well known that those who take little exercise are particularly liable to feel cold and also to suffer from disease. We are all familiar, too, with people who wear an enormous amount of clothing even in summer. On the other hand, the dress of modern woman would have made her grandmother shudder and would indeed have killed her had she attempted it without due acclimatization.

When the body surface is exposed to cold the blood-vessels of the skin close down and the skin becomes pale. If, however, in the closing down of the arterioles, some of the blood becomes entrapped in the capillaries, it loses its oxygen, and gives a blue appearance which is particularly well seen when the circulation is not good. The skin becomes rough from the production of the so-called goose-flesh, a survival no doubt of the mechanisms of lower animals whose hairs stand out to entangle greater amounts of air in cold weather. Sweating is in abeyance.

The amount of heat which can be lost or gained by exposure of a part to undue cold or heat is surprising and has been accurately and very fully investigated, especially by Stewart. By placing the hands or feet in cold water more heat can be lost

than is produced by the body at rest, and in this lies the truth of the well-recognized fact that wet feet or wet clothes bring about various infections, since a lowering of the body temperature reduces resistance. In these instances the lowering is brought about by excessive evaporation. Similarly, excessive movements of air by increasing evaporation and conduction by changing the air in the immediate contact of the body, increase the heat loss, and herein lies the danger of draught which depends on the speed of the inrush of air. A fully open window, for example, although it brings in just as much air, does not cause so much draught as a window a little open through which air enters at a much more rapid rate and which will cause much more cooling of the body if the individual be in the rapid current of air. The tendency to chill after a hot bath has been recently shown to be due to the lowering of body temperature as a result of paralysis of skin vessels which remain dilated in spite of excessive heat loss. Similarly, alcohol may, by leading to capillary dilatation of the skin, bring about excessive heat loss, although, as after a hot bath, the superficial dilatation of vessels may give a pleasant sensation of warmth. Such instances show the importance of the maintenance of body heat in keeping up resistance against infection. We have seen how the eating of protein by increasing the heat production is of value in this respect. At the same time it is clear that if the body, especially the mucous membranes, are in a physiological condition, considerable lowering of temperature can take place without infection occurring. Thus in war-time men were often exposed to cold which would almost certainly have had a very serious effect in civil life. Local injury or fatigue has a similar effect in localizing infection when the blood contains pathological organisms, *e.g.*, tubercle.

Cold, we have already noted (page 413), is also an important factor in the production of surgical shock. The effect of cold is exaggerated by oxygen want. The climbers of Mount Everest complained particularly of the cold. The effect of local stasis (see "Œdema") is seen in the tendency to frost-bite and cold feet produced by standing in cold weather.

After exposure to cold the body should be heated up as rapidly as possible and muscular exercise is usually possible. Thus, sportsmen may continue to expose themselves to conditions of heat loss, *e.g.*, from wet garments, provided they keep moving, and it is only when a halt is called that there is a danger of a chill.

Local heat is in the same way very effective in raising body

temperature, and there is evidence that the anti-bacterial power of the blood is increased when the body temperature is increased. The beneficial effects of a hot foot bath, poultices, and the like are thus explained, although from this point of view the exact situation of the poultice does not appear to matter.

Human beings rely to a great extent on *clothing* for the prevention of heat loss (this is dealt with further on). Ideally the skins of animals are to be preferred, and it will be noticed that such " apparel " entangles a maximum amount of air and is extremely light. These are the essentials of clothing and in the maintenance of warmth it is the retention of a layer of warm air near the body which is most important. At the same time, the clothes must be so constructed as to interfere as little as possible with evaporation, and here lies the disadvantage of rubber or oiled silk garments, although when it is very desirable to retain heat it is not usually necessary also to sweat.

The natural products, wool and hair, are the best materials to make clothes from, as they have the advantage of being better non-conductors than vegetable products or silk. The looser woven the material is the better, but here we must not confuse warmth with wear. Many of the more expensive materials for and methods of weaving give no advantages over cheaper varieties of clothing as regards warmth, although they wear better. From what has been said about the entanglement of air it is evident that two garments are much more efficient than one of double thickness, provided they are not too open at the free edges. Two cotton or silk garments are then very efficient articles of clothing, and but for this it is difficult to see how the modern woman would keep warm at all. In this respect it will be noted that the dress of woman, like Highland dress, is concentrated at the waist, and experience of the latter makes the wearer appreciate that the chilliness of the kilt is much more apparent than real. The wearing of cholera belts signifies the importance of keeping this particular region of the body warm, for the alimentary canal is a region especially liable to be infected as the result of cold. The production of diarrhœa or the return of symptoms after an attack of dysentery, which may follow a cold bath or sea-bathing, has long been recognized.

The subjective *sensation of temperature* is, however, quite a local matter and bears no relation to the temperature of the body. We appreciate heat and cold by groups of special nerve endings in the skin which we know as the hot and cold spots.

We may feel generally quite warm and have a normal temperature, yet one part of the body may be intensely cold. Of more importance, however, is the fact that substances which stimulate the skin give a feeling of warmth. Rough garments are considerably warmer than smooth garments for this reason. There can be no other explanation of the predilection some people have for coarse undergarments. It is even possible to feel warm although the body may be actually losing heat, and such a condition is produced by exposure after taking alcohol or a hot bath. The pleasant afterglow which is experienced is merely the result of the dilatation of the skin blood-vessels and the effect of the hot blood on the nerve endings. Actually it cannot be demonstrated that alcohol does anything but appreciably increase the heat loss and the use of alcohol as a protection against exposure probably depends on its excretion (page 490).

Fever.—A rise in body temperature above normal is probably one of the most reliable pieces of clinical evidence of the existence of a pathological condition. It results usually from the introduction into the body of living bacteria, but that bacterial toxins will suffice is seen in such a procedure as anti-typhoid or tuberculin inoculation.

The relationship of organismal invasion to fever is shown in malaria where the fever in the different types corresponds with the liberation of new crops of organisms into the blood-stream, as demonstrated by a blood examination. It has been suggested that the fever is brought about as the result of protein destruction. That there is excessive protein breakdown in the condition is undoubted. Whether this is primary or secondary to the fever is not at all clear. That it is secondary is suggested by the fact that protein destruction may be largely prevented by feeding with carbohydrates and that experimental high temperature increases protein metabolism. The advantage of a carbohydrate diet in fevers must be noted.

On the other hand, the fact that injection of foreign protein may produce fever as in anaphylaxis suggests that fever following an infection may be due to a similar breakdown in protein. In anaphylaxis, however, there is so much disturbance, especially of the vascular system, that one cannot lay stress on this point.

From first principles, fever may be due to increased heat production or diminished heat loss, but these two factors are really very interdependent, since a rise of body temperature, due to diminished heat loss or any other cause, must result

in an increased heat production consequent on increased metabolism. But that increased heat production alone is not sufficient to produce fever is evident from the fact that conditions where there is a much greater increase, such as exercise or exophthalmic goitre, do not bring about fever. Further, anaphylactic fever is said to be accompanied by diminished heat production.

That there is diminished heat loss in fever is undoubted, and there is general agreement that this is brought about by vascular changes and a reduced flow of blood to the skin. When the body deals with any toxic substance blood is drawn to the part. This is evident, if the lesion is near the surface, from the typical heat, redness, and swelling which, with pain, are the four classical signs of inflammation. An additional supply of blood is also necessary for the toxin-destroying and eliminating organs. In order to supply this blood, since the amount in the body is limited, there is, as in hæmorrhage, a diminished blood supply to the skin. It has been clearly shown by G. N. Stewart that a diminished flow through the hand occurs in fever. If the condition is of a mild degree, the individual may be described as merely "looking pale," but if more severe, he may, as a result of diminished flow to the nerve endings in the skin, feel a sense of cold or chilliness which is often experienced at the beginning of infection, such as influenza or pneumonia. At the onset of a malarial attack the patient is extremely pale, even blue, and there is actual shivering although even at this stage there is a rise of body temperature. A similar state of affairs is seen in the rigors of pyæmia. An interesting point has been drawn attention to by Cramer, namely, that the conditions which present themselves in the early stages of fever are closely akin to intense action of the sympathetic, such as would occur from adrenaline secretion, evidence of which he has brought forward.

Although the heat loss may be thus diminished heat continues to be produced, and if retained in excess, metabolism is stimulated, producing more heat. There comes a point, therefore, when the effect of the rise of temperature gains the upper hand and the skin mechanisms for loss of heat are brought into use. The skin becomes very hot and may at first be quite dry. The heat-regulating mechanisms are not really thrown out of use as has been imagined, for the body can be shown to react to changes in external temperature even during fever. It appears, however, to be set at a higher level and the reason for this seems clear.

There is set up an antagonism between the heat-regulating mechanism requiring blood to be sent to the skin and the causal agent which requires the blood internally. It is not until the temperature is appreciably above normal that the heat-regulating mechanism succeeds in getting the upper hand. Thus we see that in conditions in which there is an intense vaso-constriction with, say, shivering, there must follow an enormous rise of temperature to counteract this, as is well seen in the typical rigors of pyæmia and malaria. It seems also possible that the larger and more vascular the area affected the greater the liability to high temperatures. If little local reaction is set up there is, on the other hand, seldom much fever. Further, we see that where there is intense skin reaction, as in skin diseases, fever is usually absent. Where the condition, however, is not confined to the skin, as in the exanthemata, fever is common, although in some conditions, such as small-pox, the appearance of the rash is associated with a decline in the fever until there is an absorption of toxin from the pustules.

Further, a point indicating the vascular element is the fact that a cold bath given to a typhoid patient does not lower temperature so well at the beginning of the disease as it does at the end, when the typically large diurnal variations are seen. This would be expected, as there is so little blood in the skin to be cooled at the early stage.

The above hypothesis is a simplification of that of Barbour and his co-workers, to whom we owe much on this subject. He suggests that as a result of the infection there is a shift of the water to the tissues from the blood, which therefore becomes concentrated. In the reduction of blood volume, blood is no longer available for the skin vessels, and this brings about the sensation of coldness with further vaso-constriction in the skin with heat retention. Much weight has been placed on the increased concentration of the blood. Increase in the cell content of the blood would readily account for this, and we know there is often an enormous leucocytosis and increase in the red cells, but our knowledge of the normal variations in the plasma is as yet very scanty. It is difficult also to understand this claim to increased concentration, in view of the reduction of the chlorides, which are normally the most abundant salts in the blood. We could also presume that according to Barbour's hypothesis the drinking of large quantities of fluid would reduce the concentration. Conditions which bring about concentration of the blood,

such as hypertonic saline, certain purgatives, and concentrated sugar solution, do bring about fever and may do so probably by increasing the difficulty in sweating; but in fever the concentration, if it exists, may be due to loss of water through the skin. This is suggested by the fact that there is diminution in the secretion of urine. The appearance of salts from the evaporation of sweat on a dry skin suggests that the insensible perspiration in fever may be greater than normal. What exactly happens to the sodium chloride which leaves the blood has yet to be shown, and it has to be demonstrated that it takes water with it, but until we know this the water shift hypothesis appears very uncertain, nor does there appear to be any necessity for such an elaborate explanation when a simple vascular one is available.

The beneficial effects of a cold bath in high fever are then evident, as by the cooling of the skin less circulation is necessary to keep down the temperature and more blood is available to deal with the infection. That simple constriction of the skin vessels can bring about a rise of body temperature was pointed out by early observers in the days when bleeding was a common practice. It was also noted by Lauder Brunton. In pneumonia, also, it is well known that the crisis is associated with the onset of perspiration, while the patient is obviously less anxious and ill. At this time, too, the muscles, hitherto tense, and no doubt producing heat suggestive of protection against the cold of the skin, become quite flaccid.

Antipyretics lower temperature by reducing heat production, and some consider that quinine acts in this way. More commonly they increase the heat loss by local action, causing stimulation of the sweat glands, as with salicylates, or by acting through the heat-regulating mechanism. Phenacetin appears to act in this way, for its action is said to be abolished if the region of the heat centre is removed. How this occurs if the blood volume is appreciably reduced (as in the water shift theory of fever) is difficult to see. The patient would be liable to faint from a relative loss of blood. According to the purely vascular conception of fever put forward above, the heat-regulating centre need only be made more sensitive to the heat, a method of pharmacological action which is well known. It cannot be shown that all antipyretics dilute the blood, while how they can cause sweating, if the blood is concentrated, is difficult to understand.

Whether antipyretics are ever justifiable is very debatable, as

the fever may be but an indication of a physiological mechanism. Whatever theory is held, it is much more in keeping with physiology to apply cold to the skin, as baths or packs. In carrying out such procedures the danger of excessive lowering of resistance must be remembered. It is desirable to remove the patient from the bath when the temperature has fallen to 100° F., as a further fall may be anticipated. The importance of the administration of fluids in fever (even injections) cannot be over-estimated from a physiological point of view.

Low temperature is a rarer state than fever and is usually brought about by diminished heat production. This is well seen in myxœdema in which the basal metabolism may be very low. It may occur in any debilitated condition, so that the normal loss of heat may result in the lowering of temperature to a dangerous degree. In the aged, this is very marked and old people frequently die from infectious conditions, *e.g.*, pneumonia, without any increase in temperature. Excessive rest from compulsory confinement to bed, say from an injury, results in lowered heat production and practically all patients in hospital not suffering from an infective condition have a subnormal temperature. A subnormal temperature in the morning associated with a slightly raised temperature in the evening is considered to be indicative of tuberculosis. It is usually found that these individuals, as stressed by Philip, have a considerably increased irritability of tissues generally. Thus the pectoral muscles, if stroked sharply, are seen to contract and the stroke itself gives rise to undue skin reaction. We can look upon this increased irritability as bringing about the excessive diurnal variations. Such a state would, of course, be expected in any chronic infection provided it was not too severe, and tuberculosis is the most common.

Lowered temperature from excessive heat loss and apart from exposure to cold is less commonly seen. It occurs in alcoholism and in chronic moist skin conditions. Babies less than a week old are specially liable to lose excessive heat and hence the necessity of keeping the newly-born very warm. Children have a comparatively large body surface and therefore have to have a more intense metabolism. It is very doubtful, therefore, if attempts at " hardening " are really justifiable, and it is most desirable to prevent excessive heat loss provided this does not actually amount to coddling. Later, when the vaso-motor and heat-regulating mechanisms are fully developed, more liberties may be taken, apparently with even beneficial results, as in sanatoria.

CHAPTER XLI

THE SKIN

WERE it necessary to obtain evidence in support of the statement that a true physician is born, not made, it would be obtained in the different amounts of information which two doctors (apparently equally trained) can obtain from a glance at the face of a patient. For the general practitioner, the more rapidly the information can be obtained the better. A mere look at the face plays no inconsiderable part in his everyday diagnosis. The expression, the pupils, the teeth, have each a special significance, but that of the skin and subcutaneous tissue is more general.

The skin is designed as a protective covering; at the same time it has functions in relation to the regulation of body temperature and as an organ of excretion. It presents certain normal characteristics which, in virtue of these functions, vary noticeably in pathological states.

Colour.—The colour of the skin of the so-called white races is dependent on the blood which flows through it or, to be more accurate, on the amount of hæmoglobin in the corpuscles occupying the superficial blood-vessels. Let the blood be removed or the percentage of hæmoglobin much reduced and the skin becomes pale. Clinically, all degrees of pallor are seen. For in conditions of blood loss, the vaso-motor system conserves the existing blood for the more important organs by reducing that flowing to the skin. Skin pallor, then, may indicate hæmorrhage, and is an extremely valuable sign in cases of internal or concealed hæmorrhage. It may, for example, indicate the rupture of a vessel in the lung or alimentary canal, an unsuspected aneurysm, or a ruptured extra-uterine pregnancy. Taken together with the previous appearance of the patient, it may be of the utmost importance, for life may depend on immediate surgical measures. The pallor of vaso-motor disturbance commonly associated with fainting is of a similar nature, but in this instance the blood has accumulated in the splanchnic area. The pallor of death is, similarly, due to constriction of the skin vessels as the result of

the stimulation caused by the fall of arterial pressure. Subsequently, when the capillaries and arterioles lose their tone, they are filled with blood from the venous side, and a bluish appearance results.

Pallor of a more chronic nature may be due to frequent loss of blood, as in hæmorrhoids, from which large quantities of blood may be lost without the knowledge of the patient. More commonly such pallor is due to a reduction of the percentage of hæmoglobin in the blood, as in anæmia. The skin indeed is pale for the same reason that any hæmoglobinometer would give a low reading ; in a given area of skin, just as in a given quantity of blood, there is a reduced amount of hæmoglobin. The pallor seen in many illnesses is generally due to anæmia caused by bacterial invasion or toxins ; other conditions often lead to characteristic shades such as the yellow-green of the anæmias, or the dead waxy white of nephritis, which is exaggerated by any œdema.

The blood supply of the skin may be interfered with mechanically, as in embolism, arterial disease or spasm. Or the interference may be in the skin itself as in œdema, in which the pressure of the fluid in the subcutaneous tissues interferes with the skin circulation and produces its pearly pallor. Thus is produced " the large white body " of chronic tubular nephritis, and it must be remembered that such tissue is, because of its scanty blood supply, extremely liable to infection.

A heightening of the colour is caused by the correspondingly opposite processes and is due to an excessive amount of blood or hæmoglobin. The flushed skin seen in exercise and fever indicates the attempt of the body to get rid of heat.

Local Variations in Skin Colour.—The mottling of the skin known as " granny's tartan " and commonly produced by sitting in front of a fire, has been investigated by Lewis who has found that the capillaries in adjacent pale and dark areas are the same in number, the depth of the colour being due to a difference in size and tone of the vessels. From a study of the reactions of the vessels, Lewis suggests that the pale areas are those of maximum blood flow, while in the darker areas the circulation is further from the main supply and therefore is more liable to damage or to become more or less permanently dilated and cease to act to the usual capillary constrictors. Hemingway has observed that the capillaries in some regions are permanently open, while in other areas they are seen to open and to close at

intervals after the manner of the capillaries in the web of the frog described by Krogh. How far this is related to the alteration of the position of the hot and cold spots noted by Herring and Waterston, or to the spontaneous changes which occur in the electrical resistance of the skin (Hardcastle and McDowall) has not been determined.

A dominant influence in the colour of the skin is the size of the venules and, as age advances, the venules appreciably increase, especially in exposed regions. Once skin has been injured—*e.g.*, by ultra-violet light—it continues for a long period to flush more readily than normal skin. Thus is explained the fact that in blushing the reddening of the skin is confined to those areas which normally are exposed to light. As pointed out by Darwin, the flush is less confined in races which wear less clothing.

The vessels of certain areas have been found by Wetzel and Zotterman to have greater tone than others as indicated by the suction necessary to counteract the constrictor action of adrenaline in different regions. The force of contraction is much greater in the circumorbital and circumoral regions than elsewhere in the face. These regions are also remarkably free from dilated venules. It seems probable that the difference is related to the fact that these regions are the most active, and Lewis points out that they are least exposed to sunlight and are warmest in cold weather.

Distribution of Rashes.—It seems reasonable to assume that the distribution of rashes is dependent on the considerations mentioned above ; eruptions tending to show themselves first in those areas in which the vessels are permanently dilated or the contractile force least. In the face the malar region is most liable to be affected, hence the malar flush in tuberculosis or the distribution of *lupus erythematosis* or *acne rosacea*. In severe fevers, especially in children, and in emotion, or when atropine is injected, the flushing is largely confined to the cheeks while the circumoral and circumorbital regions escape. The circumoral pallor of scarlet fever has long been of diagnostic significance. Its absence in measles is probably related to the greater activity of these areas in this condition in which there is irritation of the upper respiratory passages.

In purpura, scurvy, and other hæmorrhagic diseases, there are often extensive hæmorrhages into the skin. It has been suggested that purpura is due to a diminution in the blood platelets, but since such a diminution may occur without the occurrence of purpura there must be some other factors concerned. Little is as yet

known regarding the exact method of production of such blocd effusions.

The quality of the blood may cause the skin to be highly coloured as in polycythæmia, where the number of red corpuscles is in excess of the normal. Should the blood contain abnormal coloured substances they will be evident in the skin, as bile in jaundice, melanin in Addison's disease, methæmoglobinæmia, and chronic poisoning with dyes or metals such as silver and arsenic. During stagnation of normal blood in the skin, the blood loses more of its oxygen and becomes more venous, giving the skin a purple or cyanotic colour. This may be due to a protective closure of the superficial arterioles and capillaries against heat loss under external cold, or to general stagnation from a faulty circulation so characteristic of impairment of the right ventricle. Local colour variation due to circulatory changes may occur, as in nævus, or birth mark, in ecchymosis, and in rupture of the skin vessels, or bruising.

General State of the Skin.—The state of the normal skin depends on a variety of conditions of which the most important are the blood and nerve supply, and the secretory and endocrine activity, all of which are necessary if the skin is to perform its functions adequately. Obviously if the blood supply is cut off the skin will become dry and its nutrition will be impaired. In gangrene the skin is involved with the rest of the part to which the blood supply is reduced, and the speed with which varicose ulcers in the leg heal as soon as the circulation to the part is improved by raising the limb indicates the importance of blood supply in this relation. Similarly, heavy people who have to lie in bed for long periods are specially apt to develop sores.

The trophic influence of the nervous system on the skin is as important as it is in relation to muscle and in chronic nervous disease, especially in injury to the spinal cord, the prevention of bed sores is a test of good nursing. A water bed, air cushions, hardening of the skin by applications, *e.g.*, of spirit, and frequent changes of position if the condition permits, are the preventive measures usually taken.

The thyroid plays an important part in relation to the general nutrition of the skin. In myxœdema, in which the internal secretion of this gland is insufficient, the skin is extremely dry and brittle, and the hairs fall out. Still more striking is the somewhat gelatinoid degeneration of the subcutaneous tissues which gives the puffy appearance from which the disease takes

its name. This condition of the skin must, however, be clearly distinguished from œdema (page 403) or mere adiposity. In the former, the tenseness and the pitting on pressure are as characteristic as the inelasticity in myxœdema. Adiposity is to be recognized by its distribution and the normality of the skin colouring. People suffering from this condition frequently require considerable persuasion before they believe that their complaint is such a simple one, as an increase in girth may be the only feature noticed. I have known a patient imagine she had an abdominal tumour when in reality the distance of the skin from the abdominal muscles, which can be felt if made to contract, and the deep umbilicus, showed clearly that the increase of girth was really due to subcutaneous (and no doubt also omental) fat.

The secretion of sweat gives the body surface its characteristic moist feeling. The secretion is, however, quite independent of temperature, as is seen in the cold sweat of fear. The latter must be differentiated from the cold sweat which is experienced after excessive sweating, often due to the administration of drugs such as salicylates. This makes it important that when such drugs are given care should be taken to avoid excessive chilling of the body in the early hours of the morning when the action of the drug has worn off and the sweat is still upon the skin. The same applies to the taking of toddy at bedtime. Mention may perhaps be made of the old wives' cure of sweating out an incipient cold by taking, warmly clad, a brisk walk. The beneficial effects of the exercise, provided it is not excessive, depend on the resulting general dilatation of the vessels and invigoration of the circulation, especially of the respiratory tract.

Excessive sweating is generally looked upon as the result of sympathetic stimulation. This occurs in toxic goitre and after an overdose of ephedrine, a sympathetic stimulant administered in asthma. Very severe and unexplained sweating sometimes occurs, and the patient may literally drip sweat while at rest. The condition may be localised to the hands. The dry skin of myxœdema and icthyosis is the opposite condition, and may be associated with slow pulse, asthma, and other signs of over-activity of the parasympathetic.

It is very difficult to decide whether the skin is of any importance as an excretory organ in a normal person. It is certainly capable of excreting substances, such as urea, normally eliminated by the kidney, but these may simply be carried out in the sweat necessary for heat loss. On the other hand, it is evident that

drugs, such as bromides and iodides, are definitely excreted by the skin, and may cause irritation during the excretion. Elimination by the skin is important in the case of alcohol. A man may be quite sober in a warm room where the rate of the excretion of alcohol keeps pace with the absorption from the intestine. On going out into the cold the skin capillaries at once close down to conserve heat and the excretion of the alcohol is much reduced. The concentration in the blood increases as the absorption continues and the individual becomes narcotized. The large excretion by the skin no doubt accounts for the fact that in hot countries large quantities of alcohol may, so far as the nervous system is concerned, be ingested with impunity. Although, however, the arterial concentration does not become high, the concentration in the portal system through which the alcohol is absorbed may be very great and sooner or later affects the liver, bringing about those signs and symptoms associated typically with the " climate of the East."

In renal disease excretion by the skin becomes more important. Mackenzie used to relate the instance of a lady seriously ill whom he upbraided for powdering her face, only to find that the appearance was caused by the excretion of salts from her abnormally active skin. Advantage is taken of skin secretion by the physician in treating kidney disease in which the skin is kept active by special measures. These have already been dealt with.

Reaction to Stimuli.—The reaction of the skin to stimulation has been extensively studied by Lewis and his co-workers. If the skin of a large proportion of normal subjects is lightly stroked, there results a sharply outlined white line limited to the area stimulated. This is due to capillary constriction. Heavier stroking produces the triple response described by Lewis: (1) After a short period a red line develops as a result of capillary dilatation, and often on either side, where the stimulation has been less, a pale area of constriction; (2) outside, a little later, there is a general flush which can be shown to be due to arteriolar dilatation brought about by an axon reflex. The proofs of these explanations have been fully given by Lewis. (3) The skin of some persons gives the above response to light stroking, and in these a wheal develops in the site of the red line. This is due to increased permeability of the capillaries believed to be brought about by the production of histamine or a histamine-like substance in the skin (Lewis). Histamine injected into the skin produces

a typical triple response, and so also does practically anything which injures the skin. Further proof that a histamine-like substance is formed in the skin is the occasional flushing of the face like that which occurs when a small dose of histamine (·06 mg.) is injected subcutaneously. Such an injection causes a secretion of gastric juice, and it is probable that in these facts lies the explanation of the great liability to gastric ulcer after severe burns which produce histamine in the skin.

We have already studied the general effect of histamine on the circulation in relation to shock.

Morbid Eruptions.—Lewis suggests that it is possible to divide morbid eruptions of the skin into three categories: (1) those due to the local liberation of an "H substance," and characterized by a dull red or purple colour, a crisp margin, and the fact that it may be temporarily massaged away but is refractory to stimuli; (2) those due to the opening up of arterioles and characterized by a general scarlet flush, the rise of skin temperature, and by the fact that they are blanched by a stimulus such as stroking or adrenaline. Separately, these two types may be considered to correspond to the macular or measly rash on the one hand and the scarlatiniform on the other. The poison responsible for the rash may be considered to act either on the sensory nerve endings, so bringing about an axon reflex, or on the arterioles; (3) together the arteriole and capillary dilatations correspond to the urticarias which consist of wheals surrounded by a more or less widespread erythema.

The macule is regarded as representing a reaction of the first type but less acute and more prolonged than the urticarial lesion. In the raised macule œdema is added.

The blister, which is a common feature of burns, of many skin diseases, and of herpes, is looked upon as being the result of a simple release of an H substance and, like the wheal, the result of increased permeability. It is suggested by Lewis that the duration of the stimulus is a factor determining the production of a blister. This is borne out by common experience. The bed sore is probably produced in a similar manner, but often its production may be facilitated by nervous injury.

CHAPTER XLII

HYPERSENSITIVITY AND ALLERGY

By hypersensitivity is meant the state in which the body is abnormally sensitive to the entrance of certain foreign substances. Few abnormal conditions give the physician more trouble. He has good reason to believe that, given unlimited time, he might discover the causal agent when it is not easily discoverable, but very often the time factor makes a complete enquiry quite impossible. The chief among these are asthma and conditions of the skin which may amount to urticaria, pruritus, and prurigo, or eczema, but there may also occur in some circumstances œdema, vomiting, adenitis, diarrhœa, or the production of gas in the intestine. It is suggested by Cranston Low that many of the rashes of the exanthemata, many other skin diseases and other reactions to bacterial infection are really of a similar nature, although they are not usually classed as such. Death from shock rarely occurs.

It is convenient to divide hypersensitivities into local and general, but it must be understood that there is no hard and fast line between the two.

Local Hypersensitivity.—This is probably the easiest variety to elucidate and is commonly exemplified by dermatitis or eczema produced by local applications of a sensitizing agent, the so-called dermatitis venenata. The substances which produce such inflammation of the skin may be of infinite variety, and not always proteins. Even cold may suffice in suitable persons.

The dermatitis may be a purely local reaction: for example, the hands and arms of a baker may become sensitive to flour, but not the rest of the body. It seems probable that some cases of asthma and hay-fever may be a result of a similar local irritability of the respiratory tract and may be purely local conditions. It has been pointed out by Barber that an eczematous reaction from whatever cause always indicates an epidermal sensitization, whereas an urticarial reaction is a neuro-vascular response.

Once an area has become hypersensitive, a reaction may be

produced by an application at a distance. An example is given by Barber, who rubbed mustard gas on his arm and produced a local dermatitis. Later he rubbed it on the other arm, and not only obtained a dermatitis but also a focal reaction on the arm on which it had been previously applied. In some of the drug hypersensitivities, *e.g.*, atropine, the skin reaction is the most marked, but with others, *e.g.*, aceto-salicylic acid (aspirin), the nasopharynx may also be affected or an attack of asthma precipitated.

General Hypersensitivity.—The most striking example of hypersensitivity is seen in anaphylaxis, which is best seen in the guinea-pig but may be observed to a lesser degree in most animals and in man. The animal is injected subcutaneously with minute amounts of a simple foreign protein, such as egg albumin, and is apparently none the worse, but ten days or more afterwards if a similar injection is made, the animal, if a guinea-pig, dies of asphyxia produced by acute constriction of the bronchi. It is of interest that the animal dies with its chest full of air which apparently cannot be expired, a condition of acute emphysema. If the uterus (Dale) is placed in suitable saline solution or the bronchi perfused (Thornton), it may be shown that there has been a sensitization of the smooth muscle cells, for if brought into contact with egg albumin they at once contract.

What appears to be a true anaphylaxis in man may occur after the injection of the second dose of a foreign serum such as is used in diphtheria. The characteristic symptom is a rash which may be accompanied by joint pains and œdema, especially of the eyelids. The rash may simulate the exanthemata. In a few rare cases, usually asthmatics, there is dyspnœa and death.

The exact nature of anaphylaxis is still a matter of discussion. It appears certain that as a result of the first injection the body manufactures some substance which reacts violently with the second dose. The fact that the serum of a sensitized animal will render sensitive the uterus of a normal guinea-pig suggests that the anti-substance is circulating in the blood, but its exact nature and site of formation are not finally decided although many theories have been put forward.

Anaphylaxis is commonly associated with certain blood changes, diminished coagulability, eosinophilia, leucopœnia, and the common occurrence of one or more of these in asthma, urticaria, and pemphigus, suggests that these diseases are essentially anaphylactic in nature. There is also evidence of increased

irritability of the autonomic nervous system, especially of the vagus. The reactivity to pilocarpine and to adrenaline is increased. How far the symptoms are produced by the heightened nervous irritability is of the greatest interest and importance.

To include all the phenomena of sensitization which may not amount to a typical anaphylaxis as seen in the guinea-pig, the term " allergy " has been introduced.

The evidence is complete that an allergy may be produced by a foreign protein which may gain entrance to the body by way of the respiratory tract in the case of the emanations of animals or by the alimentary canal. To what extent a really normal, as distinct from an inflamed, respiratory tract will permit foreign proteins to enter the blood has not been determined. That unchanged protein may be absorbed by the alimentary canal is certain, for certain individuals develop attacks of asthma, urticaria, or eczema when they take certain specific proteins, and the absorption of abnormal proteins has been shown in the blood of animals and of man by the precipitation test. A further interesting proof is the Prausnitz-Rustner reaction. If into the skin of a normal person a small quantity of serum from, say, a lobster-sensitive person is injected and, twenty-four hours later, a meal of lobster is given, preferably on an empty stomach, the area of skin injected with the sensitive serum will probably swell up into an urticarial wheal.

There is experimental evidence that some disturbance of the normal processes of the alimentary canal must be present before any such absorption of foreign protein may take place. But some observers have found evidence that foreign protein is normally absorbed.

Cranston Low suggests that the time of the initial sensitizing doses of foreign protein may be traced to digestive disturbances at teething or to an attack of gastro-enteritis, while the hypersensitivity to certain articles of diet which are only eaten at certain seasons suggests that at some period excessive quantities may have been eaten of those foodstuffs, *e.g.*, strawberries. Once the patient is sensitive, minute quantities bring about a reaction. On the other hand, in many instances no initial sensitizing dose can be discovered, and it has been suggested that heredity is somehow responsible.

It is generally agreed that asthma and the allied allergies run in families, but how far this is a matter of true heredity is an interesting subject of discussion. In deciding whether the

condition is truly hereditary, *i.e.*, conveyed in the germ-plasm and not infectious like tuberculosis or due to causes operating generally in families, like rickets, great care must be taken, for many of us remember when the hereditary element was considered the most important in both tuberculosis and rickets. If the disease is truly hereditary, *i.e.*, depends on an abnormal anatomical or chemical make-up, we know that in hereditary diseases a real cure is practically impossible, although we may cause a cessation of symptoms by continued or intermittent treatment.

The work of Barber and Oriel suggests that the primary fault is hepatic, the liver being unable to deal with protein as it ought. This is suggested by the finding that the normal ammonia-urea ratio is upset. The beneficial action of glucose in some cases of asthma is explained, as an effect on the liver, the detoxicating action of which is improved.

It has also been suggested that the tendency to alkalosis as indicated by the increased alkali reserve of the blood is of importance in asthma, and this, supported by the fact that starvation (Adam), ammonium chloride, aspirin in non-sensitive persons, and muscular activity, all of which tend to cause an acidosis, bring about an amelioration of symptoms. Thornton has demonstrated that slight increase of the hydrogen ion concentration of perfused isolated bronchi brings about bronchodilatation. Similarly, the lowered blood potassium when present in asthma may be related to the bronchial contraction, for it has been shown that normal calcium in the absence of normal potassium causes the bronchi to contract.

That some sensitized persons should develop asthma and some skin conditions seems to demand a local influence. An attack of bronchitis may be such an influence, and, in relation to the skin, Low suggests trauma, even a severe towelling, when the abnormal protein is circulating. The evidence is now fairly complete that the irritability of the vagus which constricts the bronchi is increased in sensitization, and it has been shown that the vagus may be stimulated reflexly from the nose (Brodie and Dixon). Hence it is that a number of asthmatics may benefit at least temporarily from nasal treatment. It would seem possible on general principles to assess the nervous element in asthma by the injection of full doses of atropine, but no work appears to have been done on this point. The fact that the asthma is liable to come on at night or at the week-end is no doubt related to the lessened sympathetic and increased parasympathetic activity at

such times, and is indicated by the reduced heart rate and size of the pupil. Similar facts also explain the disappearance of asthma when the patients take up active lives. It is of interest that a sharp run may completely abort an asthmatic attack.

Even when it is suspected that a certain condition of the skin or a case of asthma is due to protein absorption, it may be an extremely difficult matter to determine the exact protein responsible, although, given an intelligent patient who is willing for a limited period to keep a diary of his food and activities and not leave all to the doctor, much can be done. When a temporary change of residence is associated with cessation of symptoms local conditions other than diet should be suspected. In some instances, unfortunately, the hypersensitivity has been shown to be bacterial in origin, say from a condition of the teeth or the lower bowel.

The cutaneous test in which the foreign proteins are applied to scratches in the skin, as in vaccination, may be of assistance in diagnosis. The " taking " of a vaccination itself is an example of skin sensitivity of bacterial origin, as is also the von Pirquet for tuberculosis, and many others. The common proteins may be tried, but the very large number which may be responsible make it almost a question of luck whether the cutaneous testing will be of value or not. Moreover, the patient may be sensitive to several proteins.

If a specific protein is found to be responsible, desensitization may be brought about by the injection of minute quantities of the offending protein, or, more drastically, by giving large doses of the protein with adrenaline to ameliorate symptoms. The fact that adult human beings are not hypersensitive to bovine protein is no doubt the result of the extent to which we consume products of bovine origin. In children, on the other hand, milk is one of the commonest causes of allergic symptoms. It is stated that French visitors to England often suffer from a mutton rash at the beginning of their visit until they have become accustomed to this article of diet (Pickering).

Even when a specific protein cannot be found, a great deal can still be done in dealing with sources of animal emanations, *e.g.*, pets and feather pillows, and in bringing the alimentary canal into a state of reasonable normality.

Dietetic treatment has probably received more general recognition than any other. Apart from the elimination of certain articles of diet, much of the advice given on the subject has little or no scientific foundation, but of recent years Adam and

Harrington have, in relation to asthma, set forth definite *régimes* in which normality may be considered to be the production of normal hunger and the call to stool after breakfast. Adam and others emphasize the importance of a diet in which there is no excess of carbohydrate or fat, which we know is liable to upset protein digestion. It has been established that many asthmatic children have a deficiency in protein digesting power as indicated by a hypochlorhydria, and much benefit accrues in some patients, especially children, from the administration of acid and pepsin (Bray).

Non-specific desensitization is really still in the experimental stage. Peptone, milk, autohæmotherapy, and tuberculin have all been found satisfactory in different cases, both of asthma and skin conditions. There is still a great field for investigation to determine the nature of the reaction caused by such substances. A large number of treatments of asthma in vogue, notably adrenaline, are merely palliative and consist in stimulating the sympathetic. Any condition which causes fever or tissue destruction or histamine production therefore causes an abatement of symptoms. It should, however, be remarked that it is probable that the inhalation of fumes, although temporarily beneficial, leaves the bronchi more irritable.

It is generally agreed that in asthma and even urticaria and the prurigos there may be a considerable psychological element. The patient develops the *habit* of having an attack under certain circumstances. If sensitive to a rose he may be seized with a spasm if he is shown an artificial rose, just as a dog which has frequently been caused to vomit by the injection of apomorphine may vomit on seeing a syringe. The recognition of the point is important, as attacks of asthma may continue in such circumstances even after desensitization unless the patient believes that the treatment will benefit him.

The production of asthmatic attacks as a result of purely local conditions in the bronchi has already been discussed on page 231.

MENSTRUATION

Few functions of the human body give rise to so much misery as menstruation ; yet it is remarkable that until recent years—largely under the stimulus of Marshall—little research has been made into its physiology. Unfortunately, the sexual life of the ordinary laboratory animals is quite different from that of women

in that menstruation is absent, and there is, during the year, limited periods of sexual activity, in which there are œstrous or heat cycles, the number of which varies in different animals.

In woman the menstrual cycle may be divided into four stages : a resting stage of about twelve days, a constructive stage of about five days during which the uterine mucous membrane becomes congested, a destructive stage of four or five days during which there is menstrual flow, and a stage of repair of about seven days.

Some of the higher monkeys menstruate, but in most of the lower animals the characteristic period is that of heat or œstrus, only during which the male is received. Immediately prior to œstrus is a pre-œstrus period when the uterus and vagina become congested and a vaginal smear shows epithelial cells and possibly blood. When œstrus is at its height the vagina becomes dry and faintly staining or eosinophil flakes (shed epithelial cells) appear in the smear.

It has long been known that both menstruation and œstrus depend on the ovaries, since removal of these organs brings about cessation of these functions. An actual hormone, known as œstrin, capable of producing œstrus at abnormal times, has now been extracted from the ovary (Parkes). It also stimulates uterine growth and hyperæmia. A second hormone has been extracted from the corpus luteum, *i.e.*, the glandular body which grows within the Graafian follicle after the extrusion of the ovum, but it has not yet been purified to the same extent as œstrin. Several names have been applied to this hormone, *e.g.*, corporin, progestin, but lutein seems to be the best.

There is direct evidence that the corpus luteum is responsible for the hypertrophic changes which occur in the uterus and mammary glands during pregnancy and pseudo-pregnancy. The latter state is produced by mating a female rabbit with a sterilized male and is the result, probably, of the action of the anterior lobe of the pituitary upon the corpus luteum. If the ovary is excised the changes do not occur. A pseudo-pregnancy associated with amenorrhœa and breast changes has been described in the human and is probably also due to psychic or nervous stimuli.

Further, it is known that the corpus luteum continues to grow during pregnancy, and if the ovary is removed, pregnancy comes to an end. This, however, is not true of the guinea-pig, and Allen and Doisy have discovered cases which suggest that

it may not be true for the human female—certainly after the fourth month of pregnancy.

It is quite definite, however, that the active corpus luteum may be over-ridden by the action of œstrin, which, if injected, produces œstrus in a pregnant animal. On the other hand, in pregnancy the increased luteal activity causes œstrin to be excreted in the urine.

It would thus seem that when a pregnancy has begun, the corpus luteum prevents the occurrence of a second pregnancy simultaneously. In the human it is known that the degeneration of the corpus luteum coincides with the onset of menstruation, while the experiments of Loeb indicate that the corpus luteum is largely responsible for sensitizing the wall of the uterus to respond to the stimulus of a foreign body in its interior. The uterus will form an " artificial deciduoma " if a glass bead is placed in the uterus, but will not do so if the corpus luteum is absent.

It has now been established that the anterior lobe of the pituitary body is intimately concerned with the functional activity of the genital organs ; in fact it appears to be the motor of the sex and reproductive cycles. There are probably two gonadotropic hormones of the anterior lobe of the pituitary, the rho 1 and rho 2 of Wiesner. The first stimulates the follicular phase of the ovary, causing growth of the follicles and increased œstrin production, the other stimulates the luteal phase and the secretion of lutein. The uterus is affected secondarily, the œstrin causing hypertrophy and hyperæmia, and the lutein producing proliferative changes in the endometrium. The gonadotropic hormones are tremendously increased in the blood during pregnancy, and also appear in the urine in large amount. The urinary hormones are called Prolan A and B, and there is reason to believe they are not exactly the same as the true pituitary ones. It is uncertain whether the prolans are pituitary gonadotropic hormones altered in their passage through the kidney, or whether they are manufactured elsewhere, perhaps in the placenta.

The presence of prolan in the urine forms the basis of the Aschheim-Zondek, and Friedman pregnancy tests. In the former urine is injected into infantile female mice, and a positive reaction is given by the appearance of hæmorrhagic follicles (Blutpunkte) and, or, corpora lutea in the ovaries. These corpora lutea frequently show the abnormality of containing an undischarged ovum. The test is positive at least seventeen days after fertile coitus (Kennedy). The Friedman test employs female

rabbits which have been isolated for over a fortnight : intravenous injection of pregnancy urine produces ovulation in sixteen hours.

In women suffering from disease of the pituitary, in which even in the later stages of acromegaly there may be loss of pituitary function, menstrual flow and sexual activity cease. A similar state is found in myxœdema, and in almost any state in which metabolism generally is greatly reduced.

It has not been definitely decided what phase in the œstrus cycle corresponds to human menstruation. It is generally agreed that human ovulation takes place about mid-way between the menstrual periods. In some women changes in the mammæ occur at this time, and occasionally " Mittleschmerz," and traces of vaginal hæmorrhage, or intermenstrual staining ; but details of the ovarian cycle in woman, if it exists, are not available. In view of this it is difficult to decide the exact significance of menstruation. It may correspond to the pre-œstrus stage in the lower animals, and this is suggested most strongly by the production of menstruation in the monkey by the injection of œstrin. On the other hand, from what has been said of the action of the corpus luteum in preparing the uterus for pregnancy, it may be that menstruation is luteal or post-œstral and, as Halliday Croom used to put it, represents " tears of disappointment," the casting off of the unrequired decidua. The latter view is generally held by clinicians, but it fails to explain the fact that monkeys can menstruate without previous ovulation or why menstruation should be produced by œstrin, unless we consider the normal œstrin of the ovary brings about menstruation as soon as it ceases to be held in check by the disappearing corpus luteum. A persistent corpus luteum then conveniently explains the amenorrhœa of pregnancy.

It has been possible to compare the menstruation in the ovulating and non-ovulating baboon, and it seems that when ovulation has not taken place and there is no corpus luteum, menstruation takes place from an undeveloped resting endometrium. This suggests that the factor responsible for the breakdown in the uterus is not the disappearance of the corpus luteum, although coincident with it in time. The evidence of Allen and of Hartman indicates that the pituitary body is concerned, since œstrin is not effective if this body is removed. Parkes suggests that menorrhagia is probably due to the necrosis factor functioning unduly. In view of what has been said regarding pseudo-pregnancy, the evidence emphasizes the possible importance of a psychic element as, indeed, many clinicians main-

tain, the more so as menorrhagia is often accompanied by great congestive changes in the mammary gland.

Marshall more recently has suggested that menstruation is both post-œstral and pre-œstral, but this view is also not without objection (Parkes). Until more human evidence is available the problem is difficult to decide. Various beneficial results have been claimed by the use of œstrin or extracts of ovary without corpus luteum in conditions such as amenorrhœa, dysmenorrhœa, menopausal symptoms, and the like. On the other hand, corpus luteum is used, it is claimed with success, in patients subject to miscarriage, with a view to promoting fixation of the ovum, but the difficulty in obtaining reliable extracts is very great. The use of prolan in this connection would seem to be more hopeful, as it enables the ovary to produce its own lutein, and good results have been reported by Johnstone.

CHAPTER XLIII

THE ACID-BASE EQUILIBRIUM OF THE BODY

UNDER normal conditions the body is constantly being subjected to states which tend to alter the reaction, or hydrogen ion concentration, of its fluids. Those who are not familiar with the term hydrogen ion concentration of the blood and the mechanism by which the gases are carried by the blood are advised to read now the section at the end of this chapter.

The food ingested may be acid or alkaline or may be made so as the result of digestion and metabolism. In exercise large amounts of carbonic and lactic acids are produced, while in digestion alkali and acid are poured out. Tissues are very sensitive to change of reaction. A very small increase of acidity is incompatible with life, although alteration to the alkaline side is more easily tolerated. A general idea of the neutrality of the body is furnished by the blood which keeps the different parts at equal hydrogen ion concentration. According to Sörensen's nomenclature, neutrality is expressed by *p*H 7·0 for reasons explained on page 447. In this nomenclature the reaction of the blood is 7·4, which is just on the alkaline side. Life is possible between *p*H 7·0 and 9·0, although such variations have never actually been demonstrated in man. This range is extremely small and several factors combine to maintain the reaction in the neighbourhood of 7·4. These are : the blood salts, the respiration, the liver, the kidneys, and the intestines. All these factors are interdependent, so that if one fails more strain is thrown on the others. Further, when it is considered that the normal hydrogen ion concentration of the blood is equivalent to 1 gramme of hydrogen in 32 million litres of water, it will be realized how extremely delicate these vital mechanisms are. No scientific apparatus yet designed has approached anywhere near their sensitivity.

The Blood.—The addition within moderate limits of acid or alkali makes little or no difference to the reaction of the blood. This is because of its " buffer " salts (the original word used by Fernbach and Hubert was *tampon*, and, translated into German,

"*Puffer*") which, as it were, soak up the hydrogen or hydroxyl ions. The buffer salts are sodium bicarbonate ($NaHCO_3$) and alkaline sodium phosphate (Na_2HPO_4). Suppose, for example, hydrochloric acid is added to the blood: then we have interactions—

(1) $NaHCO_3 + HCl = NaCl + H_2O + CO_2$ and
(2) $Na_2HPO_4 + HCl = NaH_2PO_4 + NaCl$.

In each instance there are formed a salt and a weak acid or an acid salt. It will further be seen that the carbon dioxide can react with the phosphate, and supply more bicarbonate, thus—

$$Na_2HPO_4 + CO_2 + H_2O = NaH_2PO_4 + NaHCO_3.$$

As the chief store of alkaline phosphate is in the red blood corpuscles, the reaction takes place in two stages, thus—

$$CO_2 + H_2O + NaCl = NaHCO_3 + HCl.$$

The acid passes at once into the corpuscles to reform potassium chloride according to the equation

$$NaKHPO_4 + HCl = KCl + NaH_2PO_4.$$

The phosphates, although playing an important part in buffering, do not leave the corpuscles unless in excess.

The same reactions occur when carbon dioxide is added to the blood by muscle activity. The importance of this reaction in the body, when there are conditions which tend towards an accumulation of carbon dioxide, is evident. Further, if carbon dioxide is added in the body, sodium bicarbonate is formed at the expense of the sodium chloride of the plasma, the hydrochloric acid entering the corpuscles and combining with the phosphates, as shown above. It also combines with the alkali set free by the oxyhæmoglobin when the latter is reduced to hæmoglobin in the tissues. (See "The Carriage of Carbon Dioxide.") A small amount is carried as acid in solution. This is balanced by the amount of the (alkaline) bicarbonate in the blood. We may consider the reaction of the blood to be proportional to

$$\frac{H_2CO_3 \text{ (carbonic acid)}}{NaHCO_3 \text{ (sodium bicarbonate)}}.$$

Actually, the venous blood contains about 56 c.c. of carbon dioxide, of which about 3 c.c. is in solution. The ratio is then, normally, one-twentieth.

The reaction of the blood will then be changed by adding carbonic acid or removing bicarbonate. The former is brought about by exercise, the latter by the addition of acids, such as lactic acid in exercise and β-hydroxybutyric in diabetes. In both instances, provided the addition is not excessive, the balance is maintained by the excretion of carbon dioxide from the lungs. For example, if bicarbonate is reduced, an additional amount of carbon dioxide must be got rid of to maintain the normal ratio. This is brought about automatically by the response of the respiratory centre. For most purposes, then, the essential factor in the maintenance of the neutrality of the blood is a store of alkali; this is called the *alkali reserve.* In practice this is taken to be the carbon dioxide fixing power of the blood under certain conditions. In the first instance, alkali for the formation of bicarbonate is set free by the reduction of the oxyhæmoglobin to hæmoglobin; more is set free by the phosphates; and in emergency the tissue cells, tissue fluids (Henderson and Haggard), and, according to some authorities, protein may be called into use to take up acid.

At first sight, if conditions in the body are considered to be identical with those which can be reproduced in a test-tube, it might be thought that a diminution in the alkali reserve of the blood necessarily indicated the addition of an abnormal acid to the blood. As has been emphasized by Haldane and by Yandell Henderson, a compensatory fall in the alkali reserve may also occur in an alkalosis. Thus, if for any reason, such as excessive sensory stimulation or oxygen want, the sensitivity of the respiratory centre be increased, an excessive amount of carbon dioxide may be lost. In such circumstances there is a compensatory reduction of the blood alkali which may be mistaken for an acidosis, when in reality it indicates an alkalosis. Usually the urine will show the exact nature of the case.

Liver and Kidney.—These organs play an important part in the neutrality of the blood. The kidney is of particular importance in the excretion of acid. We have seen that if acid is added to the blood the alkaline phosphate is converted into acid phosphate, thereby releasing alkali. This acid phosphate is got rid of by the kidney, and indeed this is the normal process. The acid phosphate is the chief acid constituent of the urine. On the other hand, if there be excessive acid loss, as, for example, when the respiratory centre has been over-stimulated and carbon dioxide is washed out of the lung, then little or no acid phosphate will be

found in the urine and excessive phosphate, if there is any, will be got rid of as an alkaline salt, and cause the urine to be alkaline. It is obvious, then, that should the kidney be diseased, there will be a reduction of the normal excretion of acid phosphate, as is seen in nephritis. Respiration is stimulated to get rid of acid as carbon dioxide. This is an important factor in the production of the typical dyspnœa seen in uræmia. The acids take up some of the available alkali, and the carbon dioxide combining power of the blood may be markedly reduced. This we know as a diminution in the alkali reserve, or acidosis as it is commonly called. It must, however, be admitted that much of the clinical evidence on this point is unconvincing.

The liver is the organ chiefly responsible for the production of urea. By the de-amination of the amino-acids resulting from protein digestion, large amounts of urea are produced. Some of the amino-nitrogen forms ammonia which unites with acids and is excreted as ammonium salts. Thus, the more the ammonia required to combine with acid, the less will be the urea excretion, and *vice versa*. How and where the actual process takes place are by no means clear. There is evidence which suggests that urea may be first formed, and that the kidneys subsequently break it down again into ammonia if this is necessary. Probably also some of the ammonia unites directly with acids as it is formed in the de-amination. It is quite clear that ammonia is made use of to get rid of acids and so conserves base, *e.g.*, Na for the body. For example, if the breathing is depressed or in asphyxia, an increase of ammonium salts in the urine is demonstrable, while after a period of forced breathing there is a corresponding reduction in the excretion of ammonium salts. This has been dealt with already in relation to the urine.

Respiration.—This has already been considered, but from what has just been written it is evident that it is also of first importance in the maintenance of the normal reaction of the body and of the ratio

$$\frac{H_2CO_3 \text{ (carbonic acid)}}{NaHCO_3 \text{ (sodium bicarbonate)}} = 1/20.$$

The slightest increase of numerator (or a decrease in the denominator) will increase this ratio. Such a state of affairs will tend to occur if an acid is added to the blood, carbonic acid being set free in solution in the plasma. This carbon dioxide will stimulate the respiratory centre, and the increased breathing will

bring the ratio to normal. Should the respiratory centre be capable of responding sufficiently to accomplish this, the condition is known as a *compensated* acidosis. If not, and the ratio is permanently increased, the condition is known as *uncompensated* acidosis. Similarly, the respiratory mechanism is of importance in the retention of acid which is dealt with in relation to the significance of alveolar carbon dioxide.

The Intestines.—Apart from the fact that alkaline phosphates are excreted by the intestines, we have little accurate information regarding this excretion. It is, however, a well-authenticated fact that a sharp purgative is frequently of value in a threatened acidosis. How the improvement is brought about is not clear, but in some way the excretion of acid products is facilitated.

ALVEOLAR CARBON DIOXIDE AND ITS SIGNIFICANCE

The comparative ease with which an analysis of carbon dioxide and oxygen in alveolar air may be made and the fact that normally there is almost equilibrium between the blood and alveolar air suggests at first sight that analysis of the alveolar air would be a very valuable index of the carbon dioxide in the blood and be of use in diagnosis. The principle of the method is to obtain a sample of the air breathed out at the end of a deep expiration. This may be done by Haldane's method, in which the patient expires deeply through a tube which is provided at its proximal end with a branch through which the sample can be withdrawn. Dodds has introduced the simple and reliable method of asking the patient to whistle rapidly through the lips; when the note begins to fall off, the nozzle of a 10 c.c. syringe is pushed into the aperture between the lips and a sample of the air in the mouth collected. In each instance the sample is rapidly transferred to a gas analysis apparatus in which the carbon dioxide is measured by determining the diminution in a measured volume which occurs on exposure to potassium hydroxide. Unfortunately the estimation is not so valuable as might be expected because individual cases differ so much. It might be supposed, for example, that a fall of carbon dioxide would result from the excessive breathing in consequence of stimulation of the respiratory centre by abnormal acids, and that the method would be a means of diagnosing the presence of such acids in the blood. Unfortunately, breathing is stimulated by so many other things which not infrequently complicate conditions in which there are

abnormal acids influencing the respiratory centre that alveolar carbon dioxide can only be of confirmatory value in diagnosis.

A broad generalization can, however, be made regarding changes in the alveolar carbon dioxide.

A *rise* in this gas occurs whenever there is an increase of it in the blood without any other complication and provided it can reach the alveoli from which the sample is taken. We consider this occurs normally in exercise. It is also increased when there has been an excretion of acids (Dodds), *e.g.*, hydrochloric acid, in the early part of digestion. Respiration is then depressed as the result of removal of acid, and carbon dioxide is allowed to accumulate in the blood and alveoli in order to keep up the hydrogen ion concentration of the blood to normal. The presence or absence of this temporary rise of alveolar carbon dioxide may be taken as indicating under- or over-secretion of gastric hydrochloric acid. In cases of hypersecretion the alveolar CO_2 has been found to be as high as 15 per cent (Dodds). A similar rise of carbon dioxide in alveolar air will result if quantities of bicarbonate are taken (Haldane), as the gas has to be retained to maintain the ratio $\frac{H_2CO_3}{NaHCO_3}$ normal. There will also be a rise where there has been faulty replacement of alveolar air from one of several causes (see page 214). The existence of such a rise, however, will be obvious without actual analysis being made and, indeed, in such circumstances, it may be difficult to get a sample.

A *fall in alveolar carbon dioxide* results whenever the respiratory centre is stimulated other than by increased carbon dioxide production. This stimulation is of two main types, one of which is an acidosis, in which the chemical state of the blood is the cause of the abnormal respiration, and the other in which there is direct stimulation of the respiration.

The first state occurs when abnormal acids exist in the blood, as in diabetes and uræmia, and the second may be due to a great variety of conditions. In the latter category are conditions in which the sensitivity of the respiratory centre to the normal carbon dioxide of the blood is increased, as in oxygen want, and as is common in excitement or sensory stimulation of various kinds. In these cases the carbon dioxide has been washed out of the body as the result of the excessive action of the respiratory centre, and an alkalosis, with diminished hydrogen ion concentration of the blood, is produced.

From a study of the mechanism for the maintenance of body neutrality it will be evident that the two classes are similar only so far as the carbon dioxide in the alveolar air is concerned. In the case of the addition of abnormal acids the body attempts to get rid of the acid by the urine as acid phosphate and increased ammonium salts, urea being reduced. On the other hand, in the case of increased sensitivity of the respiratory centre or of nervous stimulation, the body attempts to compensate for the excessive loss of carbon dioxide by the excretion of an alkaline urine with a reduction in the ammonium salts and a relative increase in the urea excreted. It is not quite clear why in the case of the addition of abnormal acids to the blood, as in diabetes, the respiration should be so excessive that the alveolar CO_2 actually becomes reduced, for it might be expected that the reduction of the carbon dioxide in the blood which results would prevent the breathlessness. Nor can it always be shown that there is an actual increase in the hydrogen ion concentration of the blood, even in diabetic coma. It may be that the abnormal substances produced, *e.g.*, acetone, have a specific stimulating effect on the respiratory centre (Hurtley and Trevan), but the breathlessness may also be due to a purely local stimulation of carbon dioxide in the respiratory centre, since the acid-carrying power of the blood may be appreciably reduced. The author has shown that in animals the extent to which the respiration is influenced by the impulses which pass up the vagi (see " Hering-Breuer reflex ") may be profoundly altered by conditions affecting the general sympathetic-parasympathetic balance. The evidence suggests that the sensitivity of the respiratory centre to the gaseous content of the blood may be related to the autonomic nervous system. An increased sensitivity so brought about would certainly explain the hyperpnœa referred to above.

The " alkali reserve " of the blood plasma can be determined by van Slyke's method. The plasma obtained by centrifuging oxalated blood is exposed to the normal alveolar air of the investigator or other gas mixture which contains 5–6 per cent of CO_2. One c.c. of the sample is then transferred to van Slyke's apparatus, and the CO_2 is evolved by addition of dilute sulphuric acid and measured. Normally 100 c.c. of plasma have a CO_2 capacity of 55–75 c.c. In acidosis the figure is much reduced. The method is a reliable test for acidosis, if controlled by estimation of the alveolar CO_2 and titratable acidity of the urine (see p. 442).

HYDROGEN ION CONCENTRATION

Of recent years much attention has been paid to the " reaction " of the body fluids. With the advancement of physical chemistry, it has been shown that the older terms acidity and alkalinity were merely relative and approximate. The advent of the ionic theory set up a new order of things in this matter. In other words, the idea of acidity and alkalinity is now put on a quantitative basis. This is expressed by the word " reaction," meaning the degree of acidity or alkalinity which exists in a given solution. Most salts, acids, and alkalies are dissociable bodies, that is, they break up on solution in water into separate components known as ions. It is now known that the chemical, and therefore the physiological, properties of a solution depend largely on the extent to which ions are present. For example, urine is not composed of sodium chloride, phosphate, sulphate, etc., but of sodium ions, sulphate ions, chloride ions, phosphate ions, and so on. The question of acidity or alkalinity is, in principle, a matter of the degree of abundance or scarcity, as the case may be, of hydrogen ions. It is the presence of these which gives the reactions and characteristics of various solutions. Hydrochloric acid, for example, dissociates into chlorine ions and hydrogen ions, while sodium hydroxide breaks up into sodium ions and hydroxyl ions. The extent of the dissociation is dependent on several factors : the nature of the solvent, the temperature, and the strength of the solution. Some of the solute always remains undissociated, and the amount dissociated can be expressed as a percentage for a given temperature and strength of solution. That is, if a solution of hydrochloric acid is 97 per cent dissociated, it means that at any given moment 3 per cent of the molecules are in (temporary) union. A few minutes later 3 per cent are still united, but they are not the same 3 per cent as before. In other words, temporary unions and divorces are continually being made. The state of affairs is a kinetic one, and so can only be expressed in a statistical way. Even water dissociates into H and OH ions, but only to a small extent. Of course, the numbers of each of these ions are equal. It should also be mentioned that the ions are electrically charged, the charges on each ion being equal and opposite.

When the number of H and OH ions in a solution is equal, the solution is said to be neutral. If to this neutral solution a little acid is added, the number of H ions is thereby increased over the OH ions and the solution is " acid." Conversely, if a little caustic

soda is added, there is an excess of OH ions, and the solution is " alkaline." It should be noted that even in an alkaline solution H ions are present, though they are numerically less than the OH ions. The presence of the former is, of course, due to the dissociation of the water that is necessarily present.

It has been found possible to determine the number of hydrogen ions per unit volume in pure water. They amount to 0·0000001 gram per litre. This figure is known as the *c*H or the concentration of the hydrogen, *e.g.*, 10^{-7}. Alkaline solutions have fewer hydrogen ions, and acid solutions more, than pure water. It is now customary and at the same time very convenient to express the actual hydrogen ion concentration (*c*H) as a power of ten. A further simplification consists in using only the numerical value of that power (regardless of sign). This index, devoid of sign, is known as its *p*H (Sörensen). Neutrality is therefore expressed as *p*H 7·0 ; acid solutions have a *p*H ranging from 0 to 7·0 ; and alkaline solutions vary from *p*H 7·0 to 14·0. It must, however, be noted that the *p*H scale is a logarithmic one, so that *p*H really stands for—log [H], that is, it represents a negative logarithm. Hence as *p*H increases, the acidity decreases, and *vice versa.*

A normal solution of any acid contains one gramme of hydrogen per litre. Hence a decinormal solution of hydrochloric acid would contain 0·1 gramme of hydrogen ions per litre. This, however, is only true provided the whole of the acid has dissociated, which is not usually so. It can be shown that in such a decinormal solution the acid molecules are 91 per cent dissociated, and the *c*H is thus not 10^{-1}, but 91 per cent of 10^{-1}, that is, 0·091. Converted into *p*H, that is to—log [H], it becomes 1·04 (instead of 1·0). A weak acid or a weak base is one which ionizes but little ; good examples are those of lactic or acetic acid. A salt derived from any such weak acid or base is more highly ionized than the acid or base from which it has been formed. This is of importance in that if the free ion has a different colour from the un-ionized acid or base there will be a colour change on converting the acid or base into a salt. We shall revert to this again below.

Since the ionization is a matter of electrical charges and their attractions, it is clear that the fundamental way of determining the hydrogen ion concentration of a solution would be an electrical one. The reaction is actually determined from the electro-motive force set up between a hydrogen electrode and the free ions in solution. The electrode is really a piece of platinized wire surrounded by an atmosphere of hydrogen and just dipping into

the solution whose reaction has to be found. This is an elaborate and highly technical way of finding the *p*H, and in practice one requires a more rapid and simple means of so doing. By using the principle mentioned above, namely, that a free ion may have a different colour from the un-ionized acid or base from which it is formed, a very much more convenient way of determining the hydrogen ion concentration of a solution may be devised. This colorimetric method is dependent on the use of salts such as just mentioned and known as "indicators." Large numbers of them are now in use, each having its own "range of action." For example, phenolphthalein is colourless in acid solution, the degree of acidity being not less than *p*H 8·0 or thereabouts, while in an alkaline solution it becomes pink. Therefore 8·0 is a transition point, and the mere addition of a little of this indicator to a solution will immediately show whether or not the reaction is of a *p*H greater or less than 8·0. To obtain more detail one must have a set of such indicators, whereby it is possible gradually to narrow down the range of action until the *p*H within narrow limits can be stated quite definitely.

Some of the more usual indicators are phenol red (6·8 to 8·4), yellow to red ; methyl orange (3·1 to 4·4), red to yellow ; Congo red (3·0 to 5·0), red to blue ; thymol phthalein (9·3 to 10·5), colourless to blue, and thymol blue in its acid range (1·2 to 2·8), changing from red to yellow, while in its alkaline range (8·0 to 9·6) it changes from yellow to blue. A few drops of any of these indicators may be added to a fluid of unknown reaction and the colour compared with a standard series of solutions of known and graded hydrogen ion concentration. By this means it is possible to determine quickly the *p*H of a solution. To give some idea of the nature of the results obtained, the following is a list of the usual *p*H values of some common biological fluids : Gastric juice, 1·77 ; urine, 5·5 to 7·0 ; human milk, 7·0 ; saliva, 6·9 to 7·4 ; blood plasma, 7·4 ; pancreatic juice, 8·3.

A certain amount of technical skill is required if the *p*H is to be found accurately. This is more particularly true in determining the reaction of blood. For details the reader must consult special textbooks.

ACIDOSIS AND ALKALOSIS

If an excess of fixed acid is produced or retained in the body the alkali-reserve is diminished. If the increased respiration is able, by increased output of carbon dioxide, to keep the H-ion concen-

tration of the blood plasma from rising unduly, the acidosis is said to be compensated, as already explained. If the accession of acid to the blood is too great or if the protecting mechanism fails, the acidosis is said to be uncompensated and the H-ion concentration soon rises and may reach a dangerous level. Evidently the dividing line between compensated and uncompensated acidosis is a somewhat arbitrary one and the terms are used chiefly with reference to the matter of urgency.

The term acidæmia has been favoured of late, to replace the word acidosis. There is no special advantage in either term, so long as the user of the term is clear as to what he means when he uses it. Acidæmia would appear to indicate an uncompensated acidosis, whereas compensated acidosis would be called a "tendency to acidæmia."

Clinically, acidosis occurs chiefly in severe diabetes mellitus and in certain forms of nephritis. In diabetes the production of β-oxy-butyric and aceto-acetic acids lowers the alkali reserve, but it appears probable that the enolic form of aceto-acetic acid is more likely to be the cause of diabetic coma than the mere acidosis which is present, and the condition is more properly called ketosis. Attention has been drawn in an earlier chapter to the importance of the desiccation which accompanies diabetic coma. In addition to coma and dyspnœa, the circulation is enfeebled through desiccation and the blood pressure and intra-ocular tension are low. Ketosis is a striking accompaniment of cyclical vomiting in childhood. Acidosis is probably the chief factor in the genesis of uræmic dyspnœa, and is then due in part to defective renal excretion of acid sodium phosphate, in part to the failure of ammonia formation by the kidney. Acidosis accompanies certain cases of infantile vomiting and diarrhœa; in other instances alkalosis may result and the exact result depends to some extent on the balance between the salt and water loss (Maizels and M'Arthur). If salt loss is excessive the kidney holds back alkali to keep up the vital osmotic pressure of the blood plasma, so that alkalosis results, whereas if more water is lost than salt the reverse occurs, and acidosis follows. Other factors are probably also concerned such as ketosis which is so readily produced by starvation in infants. A therapeutic acidosis can be induced by the administration of ammonium chloride as in the treatment of tetany. The NH_3 is converted into urea, leaving the HCl to combine with base, and so lower the alkali reserve. Acidosis occurs physiologically after severe muscular exercise,

from the liberation of lactic acid into the blood ; an analogous condition is found after epileptic and other convulsions.

Alkalosis may result from ingestion of massive doses of sodium bicarbonate at a rate with which the renal activity cannot keep pace. A dangerous alkalosis may in this way result in infants during the treatment of pyelitis, and for this reason potassium citrate is preferred to bicarbonate of soda, because the citrate radicles are steadily oxidized to bicarbonate, and a more graduated alkalinization of the urine is obtained. Excessive breathing causes CO_2 to be swept out, and provided, naturally, that this is not due to acidosis, alkalæmia results, as in certain cases of heart failure (although in others retention of CO_2 causes an acidosis) and in conditions of panting due to high external temperature.

Alkalosis may also result from increased retention or formation of bicarbonate within the body, quite apart from increased respiration or abnormal ingestion of alkali. Thus, when an excess of HCl is lost in the vomit, especially in cases of pyloric stenosis due to ulcerative cicatrization, the alkali reserve increases, and as explained under " Acidosis " and " Vomiting " respectively, diarrhœa and obstruction of the small intestine may have the same result quite apart from simple loss of HCl. It is widely believed that alkalæmia is the cause of gastro-intestinal tetany, and that it acts by diminishing the effective or ionized fraction of the serum calcium, the non-ionized fraction being increased at the same time. The total calcium concentration is not diminished. The possibility that alkalæmia may act directly on the nerve centres should not be forgotten. Tetany, as is well known, results also from lowering of the total serum calcium, as in advanced rickets and after extirpation of the parathyroid glands. Whichever type of tetany is present, whether hypocalcæmic or alkalæmic, the value of therapeutic acidosis, such as is produced by ammonium chloride, and of calcium and parathyroid injections in relieving the symptoms is not disputed.

Frank tetany is characterized by tonic spasms affecting principally the hands and feet (carpo-pedal spasm). The spasms last from a few minutes to an hour or more and put the hands into the " accoucheur " position, while the feet are dorsiflexed and inverted. The condition when it is severe is painful. Between the spasms, and in the prodromal period before a sufficient degree of biochemical change has developed for them to arise spontaneously, they can be brought on by encircling the limb with a constricting band (Trousseau's sign). Other signs of " latent tetany " are Chvostek's

(irritability of the facial nerve to percussion) and Erb's (hyper-excitability of the nerves to electrical stimuli). Tetany is most commonly due to rickets, and rickety children are apt also to have attacks of laryngeal spasm. This laryngismus stridulus is to be carefully distinguished from catarrhal spasm of the larynx or laryngitis stridulosa.

CHAPTER XLIV

THE AUTONOMIC NERVOUS SYSTEM

In various chapters we have considered examples of the sympathetic-parasympathetic activity, but, with a broader outlook in physiology, the time has come when we may no longer consider the body as a collection of units, but as an integrated whole. This is true not only in health but also in disease.

It is essential to understand that the so-called autonomic nervous system is really part of the general nervous system with which it is intimately related. It is commonly considered separately as it controls parts of the body over which the control is not voluntary, and it has certain anatomical and pharmacological relationships. For example, the autonomic nervous impulses pass through ganglia, while certain drugs bring about actions comparable to those which occur when parts of the autonomic system are stimulated. The nerve fibres which carry impulses from the organs supplied are not so differentiated but are considered part of the general nervous system.

In studying the heart rate we have noted the balance between the sympathetic and vagus nerves. It is now becoming clearly established that a similar balance exists not only in a great number of individual organs but also between large groups of organs associated with similar functions. The vagus is but one of the group of nerves arising from the central nervous system which we know as the *cranio-sacral autonomic or parasympathetic.* The group includes the third nerve which constricts the pupil, the chorda tympani (responsible for salivary secretion), and the sacral outflow which gives rise to the *nervi erigentes* or pelvic nerves supplying the pelvic organs. The term *sympathetic* is now restricted to those fibres with their associated ganglia and connections which issue from the spinal cord between the first thoracic and third lumbar segments. The sympathetic and the parasympathetic, together with the *enterosympathetic,* which is the intimate nervous supply of the intestine, make up, according to the Cambridge nomenclature, *the autonomic nervous system.*

The functions of the sympathetic and parasympathetic are

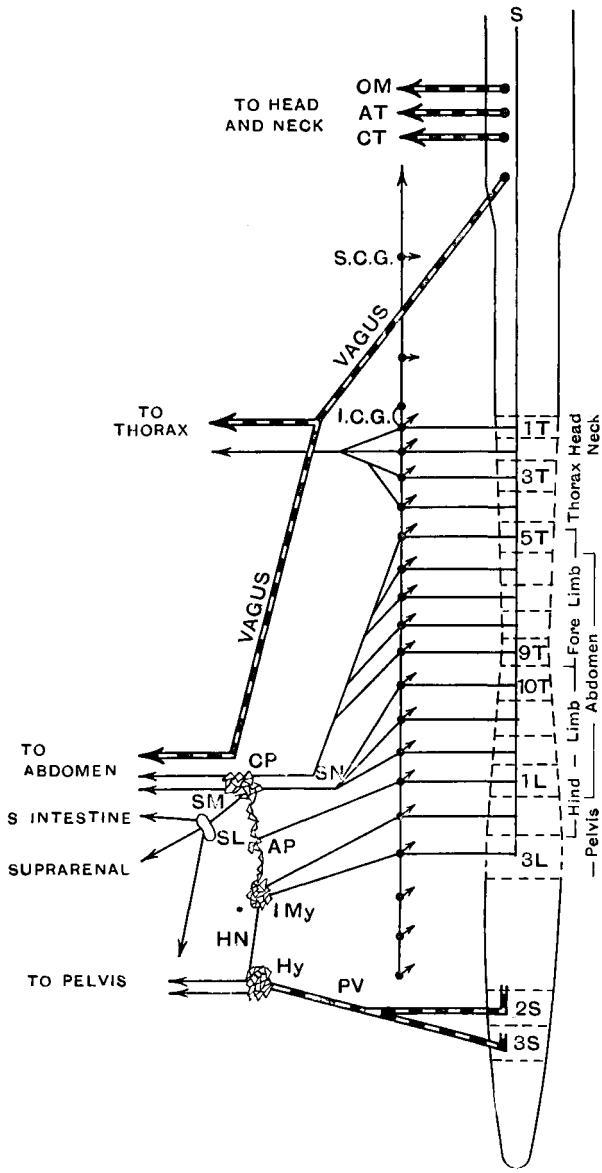


FIG. 11.—Diagram of the Autonomic Nervous System, showing its origin from the Central Nervous System.

The small arrows from the ganglionic chain indicate branches to limbs, trunk, etc.

essentially different and opposed, and are probably best realized in the changes which occur in that physiological adaptation which

occurs in the life of every animal, namely, exercise. The sympathetic is essentially concerned and brought into activity in circumstances in which the animal is called upon to do increased external work. The activity of the parasympathetic shows itself during conditions of bodily and mental rest, but it is probable that its activity is increased during exercise but is masked by the greater action of the sympathetic, although it also assists in preventing damage from over-action of the sympathetic.

During muscular exercise every effort is made to provide the muscle with additional supplies of fuel and oxygen. The circulation, as we have seen, becomes appreciably more rapid from a variety of causes, and clinically this is evident in the increased heart rate. As sufficient oxygen is not stored in the body, respiration becomes more efficient, a greater lung area being brought into use and the renewal of alveolar air more frequent. If the exercise is severe or is associated with mental activity, the pupils dilate and, in the lower animals, the hair bristles.

The additional supply of blood to the muscles necessitates the shutting down of activity in other regions, for the amount of blood available is limited. The intestinal or splanchnic area contains a large proportion of the blood, and this so-called venous reservoir is made use of in maintaining maximum physical activity. All activity associated with digestion is reduced or entirely stopped. This is made possible by the fact that adequate fuel is stored in the body as glycogen. In this form it is readily available for transformation into glucose. Less immediately available stores exist as fat.

We can, therefore, understand why in the general circulation the sympathetic is associated with activity or katabolism, and the parasympathetic with anabolism ; their functions are reversed, however, in the alimentary canal. We may, however, look upon the processes of digestion and assimilation as anabolic or building-up processes so far as the body as a whole is concerned. The parasympathetic provides the motor supply to the alimentary canal, and in the main controls the digestive secretions. The action of the sympathetic, on the other hand, causes closure of the sphincters, and so prevents the passage of food from one section of the alimentary canal to the other ; if the action of adrenaline can be taken as an indication, the sympathetic also inhibits the general intestinal movements.

The Nature of the Autonomic Balance.—It is common to talk about the sympathetic-parasympathetic balance as the term

gives an idea of a state in the individual organs, but it is very problematical how far a true balance actually exists. Neither side of the balance is essential.

Cannon has shown also that the sympathetic may be largely destroyed and the animal retain normal health. A bitch may, for example, rear puppies.

It has been shown by Sharpey-Schafer and also McSwiney, that animals with the vagi cut survive in an apparently normal way provided, as pointed out by Sharpey-Schafer, care is taken to prevent pneumonia from paralysis of the vocal cords. The stomach will empty without the action of the vagus, but animals used for such experiments are in confinement and have lived normal lives. It is, therefore, more correct to consider this balance as associated only with an active physical life. For this there is considerable experimental evidence—by McSwiney in relation to the alimentary canal and by the author in relation to circulation and respiration. The former suggests that the action of the vagus is regulative rather than essentially motor.

The term " balance " is, however, convenient in relation to the autonomic nervous system because of the effect on individual organs such as the heart. Normally both the vagus and sympathetic in the resting animal restrain and accelerate the heart respectively ; therefore the rate of the heart can be considered to be determined by the extent to which one activity balances the other.

There seems little doubt that the different parts of the system can act separately—for example, a constricted pupil can be associated with an accelerated heart. The two sides, however, commonly act as a whole. This is seen in sleep and narcosis, *e.g.*, by morphia or chloral, until the narcosis is sufficient to bring about asphyxia from depression of the respiratory centre.

The evidence suggests that periods of excessive external activity should be followed by periods of rest, and this alternation is common amongst wild animals. The disinclination for activity after a meal is common experience, and the disadvantages of disregarding it is obvious on radiological examination of the stomach or on a study of its contents, as has been done at Guy's Hospital and elsewhere. If severe exercise be taken, there is considerable delay in the emptying of the stomach. It is interesting to note that this delay is enhanced if the individual has no opportunity of conversation during the exercise, while mental perturbation has been shown experimentally to delay

emptying. It may be presumed that the sympathetic stimulation and reduction of vagal tone which take place to facilitate the supply of fuel and oxygen to the muscles at the same time prolong the period of evacuation of the stomach which is normally hastened by the vagus. The parasympathetic is also largely responsible for such general digestive secretions as the salivary, gastric, and pancreatic, and in consequence of diminished parasympathetic activity these will also be reduced. This diminished secretion will be further emphasized during severe exercise by increased water loss in the sweat.

In ordinary life it is accepted that those who " run and snatch " their lunch generally suffer from indigestion. Different mental states may have a similar effect. It has been noted that the heart rate is already increased by the anticipation of exercise, and this may be taken as indicative of an alteration in the sympathetic-parasympathetic balance. When we consider, too, the enormous influence which the appreciation of food plays in digestion, we need not seek far to understand why individuals who habitually continue work or mental exertion at meal times suffer from gastric complaints.

The same principle, however, may be carried still further into disease if the sympathetic-parasympathetic balance is likewise affected, as in the anæmias. In pernicious and in simple achlorhydric anæmia the indigestion may, however, be the primary condition and due to the achlorhydria. It is aggravated by arsenic and cured by hydrochloric acid. In acute disease, impairment of digestion is well recognized and is no doubt due to similar reasons, although in such conditions there is diminished secretion from excessive water loss, as in exercise, as well as diminished vagal activity. In fevers the more easily digested foods are given.

The possible effects of nicotine on the balance have already been referred to in relation to the heart. There is no reason why, as Patterson has emphasized, paralysis of the sympathetic or parasympathetic synapses should not affect the nervous control of the alimentary canal. The action of various toxæmias on this balance and their influence not only on the circulation and nervous system, but also on digestion are indicated by modern work which in the near future ought to throw a considerable light on the subject. It is possible, for example, that the substances absorbed in constipation and intestinal toxæmia may affect the balance and thus account for the indigestion which accompanies these conditions.

The Function of the Vagus.—The evidence is now fairly complete that the activity of the vagus is related to the requirements of exercise. Normally the vagus is constantly active and restrains the heart, but this restraint is best seen in those who take large amounts of exercise, both men and animals (Clark, Crawford). It would seem that the vagus centres are stimulated during exercise but that their activity is counteracted by the simultaneous sympathetic activity. Once the exercise is over, the vagus activity makes itself apparent.

Experimentally a rise of pressure in the aorta causes impulses to pass up the depressor nerve to the vagus centre, and the heart is slowed. Similar impulses pass up from the carotid sinus, at the division of the common carotid, by way of the glossopharyngeal. This may indicate a protective function of the vagus, but since the high blood pressure which occurs in exercise does not appear to be harmful, it seems more likely that the reflexes indicate the mechanism by which the vagus centre is stimulated during exercise. When vagus restraint is good, a rise of venous pressure will not cause the amount of cardiac acceleration it otherwise would, and a trained heart is allowed all the more time to fill. Undue cardiac acceleration by shortening the diastole might prevent the heart from filling to a maximum, and the benefit of an efficient cardiac muscle would be lost.

It seems reasonably probable that what has been found in relation to the circulation exists also in relation to the other functions of the vagus, *e.g.*, its stimulating action on digestion and insulin production. We are familiar with the former, and Lawrence has shown that when exercise is being taken, less insulin is needed than when the diabetic patient is leading a sedentary life.

On general grounds it may also be considered that animals which are extremely active become automatically endowed with unusually active digestions so that the digestive power is adapted to the energy requirements of the individual.

The sympathetic-parasympathetic balance is also of great value because of the greater sensitivity it gives to nervous mechanisms and the reduction, as it were, of inertia. The response to the requirements of the body is therefore immediate, and may even anticipate the demand.

From what has been said it may be learned that **sustained sympathetic activity** is harmful to the organism, and although in the physical life it is limited by **fatigue**, which may therefore

be considered protective, the limit is less evident in mental work. Mills has recently compared the death rates amongst Americans of Northern States with those of the more relaxing Southern States and China. The evidence shows that diabetes mellitus, pernicious anæmia, toxic goitre, Addison's disease, and angina pectoris (taken as index of cardio-vascular disease) are very much more common in those Northern States where life is more hectic. He emphasizes the advisability of those living high pressure lives going for a holiday not to stimulating but to relaxing places where they may rest. All physiological evidence supports this view.

Adaptation to external circumstance may be brought about by the action of hormones or chemical messengers, some of which appear to come in on the sympathetic side of the balance and some on the parasympathetic.

Strictly speaking, **carbon dioxide,** which is a product of combustion in all tissues, may be considered not only as an excretion, but also as a hormone, and it has the characteristics of such substances. It is, for example, readily diffusible, specific in its action on the circulation and respiration, and produces no antibodies. The effects of small amounts of carbon dioxide on the circulation are exactly those produced by sympathetic stimulation.

Adrenaline.—Of special interest in this connection is the action of the extract of the medulla of the suprarenal known as adrenaline. Its actions are so completely identical with stimulation of the sympathetic that the probability of its being thrown into the circulation in conditions of emergency for the purpose of enhancing the action of the sympathetic and of carbon dioxide is getting beyond the realm of doubt. This is supported by a study of the development of the suprarenal medulla which is formed from that part of the primitive neural crest which gives rise to the sympathetic. It must be remembered, however, that under normal conditions adrenaline will presumably *not* act independently but in conjunction with the sympathetic and carbon dioxide. The importance of H-ion concentration of the medium in which the adrenaline is present has also opened up new ideas. On the whole, then, it is justifiable (as concluded by Sharpey-Schafer) to consider that the evidence is fairly satisfactory, and that there is a normal secretion of adrenaline into the blood, especially under conditions of mental or physical stress.

The effect of adrenaline, then, so far as the autonomic balance

is concerned, is similar to that of atropine (see below), although it effects the opposite side of the balance. Adrenaline is now extensively used in the relief of asthma, but it has not yet been taken up enthusiastically for its action upon the heart. Carey Coombes advocated its use in acute pulmonary œdema, due to heart failure. Injected intravenously it is, in virtue of its action on the sympathetic, the most powerful cardiac stimulant known. It increases both the rate and force of the heart and is extensively used for this purpose in experimental work. Lack of appreciation in clinical work is due to several factors. When it was originally introduced only solutions of adrenaline were available. These varied in strength, as the drug deteriorates rapidly in solution because of the ease with which it becomes oxidized. Subcutaneous injection is slow in its effect. On the other hand, when injected intravenously overdosing occurred, and it can be demonstrated experimentally that overdosing with adrenaline in this way will lead to a degree of sympathetic exhaustion which may be fatal through its effect not only on the heart, but also on the blood-vessels. Now, however, solid adrenaline is available from which solutions of accurate strength can easily be prepared, and there is a large field for the investigation of the proper methods of administration of the drug in the cardiac emergencies. Its efficiency is undoubted.

Adrenaline causes a cessation of the activities of the alimentary canal, inhibiting peristalsis while causing constriction of the sphincters and the muscularis mucosæ. The vessels of the skin and to a lesser extent those of the intestine are constricted, but in moderate doses the vessels of muscles, including those of the heart, are dilated.

Adrenaline also mobilizes the liver glycogen and raises the blood sugar. It antagonizes the action of insulin.

Addison's Disease.—It was formerly thought that the low blood pressure and certain other phenomena, such as asthenia, of this disease were the results of suprarenal *medullary* deficiency. Experimentally, it has, however, been found that it is the *cortex* of the adrenal which is essential for life. Swingle and Pfiffner have recently prepared a cortical extract which will maintain life and health in animals from which the adrenals have been removed. Such an extract has proved of service in the treatment of Addison's disease in man, although, as is so often the case in natural as opposed to experimental patho-physiological states, the original

pathological condition which destroyed the suprarenals, usually tuberculosis, may still kill the patient after the deficiency has been relieved. In experimental suprarenal deficiency the blood becomes markedly concentrated; it is possible that herein lies the explanation of the low arterial blood pressure found in Addison's disease and also of the great toxicity of histamine in carnivora deprived of their suprarenals. In both cases R. F. Loeb and co-workers have shown that there is a deficiency of Na in the blood. Loeb has pointed out that the administration of sodium chloride in large doses is of value in relieving the asthenia of Addison's disease. There is some evidence that the pigmentation of Addison's disease depends on destruction of the suprarenal medulla.

Histamine.—This substance has come into prominence of recent years largely as a result of the work of Dale and his co-workers, who have shown that it causes a profound dilatation of capillaries, and if injected may produce in an anæsthetized cat a condition like surgical shock (*q.v.*).

Histamine represents a group of amines which are derived from the breakdown of protein by bacterial and other influences. Histamine itself is formed by the loss of carbon dioxide from histidine —an amino-acid—a product of normal digestion. Similar, if not identical, substances are also produced by the growth of *bacillus coli*, and histamine is therefore a normal constituent of the intestine and may be absorbed (E. Mellanby). There is undoubted evidence that histamine stimulates indirectly the sympathetic side of the balance. It brings about a secretion of adrenaline (Dale and Burn), and this no doubt accounts for the fact that a small dose of histamine injected into the circulation dilates the bronchi, while if applied locally to bronchial muscle causes constriction. Since adrenaline inhibits the intestine, constipation may be brought about (see "Constipation").

This point has a bearing on the possible effects of the absorption of histamine from the intestine and elsewhere, for many ascribe high blood pressure to chronic absorption of such toxic products. It appears probable that the over-compensation by the arteries described as a first stage of histamine shock may in part account for high blood pressure of toxic origin.

On the other hand, the intestine and the kidney of some animals have been shown by Best and McHenry to possess an enzyme capable of destroying histamine. This must limit its absorption appreciably, but it may not do so entirely if it is in excess. This

enzyme is absent from the skin. If histamine is injected into man it causes whealing of the skin at the site of injection and a general flushing of cutaneous vessels (see "Skin"). It also causes a striking secretion of gastric juice, and it is found a useful test in cases of suspected achlorhydria.

Atropine.—By far the most important drug which affects the sympathetic-parasympathetic balance is atropine, which paralyses the endings of the parasympathetic. The use of preparations of belladonna, indeed, for this purpose, preceded our knowledge of the mechanism of their action. By paralysing the parasympathetic nerve endings in the third nerve the pupil is dilated from unopposed sympathetic action, and use is made of this fact when it is desired to examine the fundus of the eye or to keep the iris out of a corneal wound. Atropine is also extensively used to diminish secretion during operations, especially on the upper air passages. In catarrhal conditions which result from irritant conditions of the bronchi, whether they be due to gas or infection, and where the patient is liable to suffocation from excessive secretion and the associated spasm, atropine is most strongly indicated. As all glandular secretions are affected, it may also be of value in sweating or to reduce the secretion of milk, and in such instances local application is quite efficient.

Reference has already been made to the use of atropine to reduce the action of the vagus on the heart, which is exaggerated in the first stage of chloroform anæsthesia. In this respect it must be remembered that individuals of athletic habit are more likely to have greater vagal tone than others. As the parasympathetic is the motor supply of the alimentary canal in general, atropine is indicated in a large variety of intestinal spasms or colics where morphine is considered unnecessary. The same may be said of the use of atropine in asthma. The motor nerve to the bronchi is, as shown by Brodie and Dixon, the vagus, and the sympathetic brings about dilatation, although the actual pathways have not yet been traced. When the bronchial muscles go into spasm they may be obviously dilated by paralysing the vagus with atropine or by stimulation of the sympathetic with adrenaline. Experimentally, atropine is very efficient and its action prolonged, but clinically the excessive dryness of the mouth, after atropine, is intensely disagreeable, while adrenaline usually acts long enough to relieve the spasm. Stramonium, which is a common ingredient of asthma smoking mixtures, has a similar action to atropine, but on general principles

it is doubtful whether such inhalation does not itself irritate the mucous membrane and make it more sensitive. Belladonna is often used in cases of incontinence of urine in children and reduces the normal tendency of the bladder to empty itself automatically when it is but partially filled. For similar reasons it is used in vesical spasm from any cause. Some rare individuals suffer from toxic symptoms after small doses, so that large doses should not be administered without previous knowledge of the patient.

Pilocarpine.—Pilocarpine, by stimulating the endings of the parasympathetic, has an action directly opposed to that of atropine. In view, then, of its action on the heart its use is obviously limited. By its action all glandular secretions are increased, and because of its stimulating action on the sweat glands preparations of jaborandi are given to activate the skin in kidney disease. Its most common use is by local instillation to constrict the pupil so as to facilitate absorption by way of the filtration angle of the anterior chamber of the eye in cases of glaucoma.

Acetyl Choline.—This substance is produced in tissues by stimulation of vaso-dilator nerves (Dale and Gaddum) and probably also when the vagus is stimulated, and it is possible that these nerves act by producing the substance at their endings. It is by far the most active vaso-dilator known, but as it is extremely rapidly destroyed in the circulation it is very doubtful if it can be of any therapeutic value.

Nicotine.—The absorption of nicotine from tobacco may produce a large variety of effects, for, as shown by Langley and Anderson, it paralyses the synapses in the autonomic nervous system. Its effect on the heart has already been referred to, and it has been seen that although both the sympathetic and parasympathetic are paralysed, as the normal balance is in favour of the vagus, cardiac acceleration is produced. Its effect, however, will depend largely on the actual balance in the individual. It will be evident from what has been said in relation to vagus tone that young persons, especially athletes, are more liable to be affected than the old or sedentary. The general effect of nicotine is to limit the activities of both sides of the autonomic balance so that the individual, especially as regards his circulation, is less capable of adapting himself to conditions of physical stress. This is generally admitted in athletics, and in consequence smoking is avoided. How far it may similarly affect mental work is an interesting problem. Its paralysing effect may prevent such work

from having an unduly deleterious effect on digestion; indeed, an instance has recently come to the author's knowledge where a cessation of smoking was followed by indigestion. On the other hand, without the full bodily responses the best mental work may be impossible. The possible effect of the nicotine on the alimentary canal, especially the pylorus, has been referred to in relation to duodenal ulcer.

In consideration of the functions of the autonomic nervous system, one is reminded of the remark of a "philosophic physiologist" (quoted by Bayliss from Bernard) that "nature thought it prudent to remove these important phenomena from the caprice of an ignorant will." In the light of our further knowledge we are also driven to deplore the fact that civilization brings with it conditions with which even our delicate automatic mechanisms were never designed to deal. We look forward to the time when, with a fuller physiological knowledge, we shall lead our fellow-creatures to more physiological modes of life.

CHAPTER XLV

EXERCISE AND REST

THE EFFECT OF EXERCISE

ALTHOUGH it has long been considered that exercise is generally beneficial to the body, the lack of a definite scientific basis for this assertion has tended to bring about a disregard for it. In lay and even in many medical minds, exercise and fatigue are not clearly distinguished. Too often is the apparent impasse reached where the doctor finds himself, and rightly, advising exercise to a patient who feels physically tired at the end of the day.

Within recent years our knowledge of muscular contraction has enormously increased ; especially as a result of the War has it been possible for this generation to see the good effects of open-air life. Physical nonentities found themselves capable, under the proper stimulus, of carrying out an amount of work which no amount of persuasion could have made them believe possible but a few months before. We now see that there is involved the great biological principle that structure is determined by function, and that function depends on the necessities of existence. This principle, we believe, has been largely responsible for organic evolution, but it is no less applicable to the individual organs of our body. Under conditions of civilized life our physical selves become less and less of importance for our existence and we find that we differ from the lower animals most greatly in respect of our brain structure which has indications of being the most highly evolved. Whatever the nature of our occupation our bodies and minds adapt themselves to a greater or less extent to our requirements. It is then most physiological that these requirements should be reasonably constant. Otherwise excessive strain may be thrown on individual organs and cause breakdown. A sedentary brain-worker is no longer adapted to meet physical emergencies any more than is a physical worker capable of doing a mathematical problem which he could easily have done at school. In the latter instance we use the term " forgetfulness," but in the physical sense a similar term could quite correctly be

applied. Further, it is likely that the two processes, physical and mental, are essentially similar.

Whatever our occupation, however, there is a limit to physical unfitness, for not only does every life depend on physical necessities, but the body is liable to disease, and we shall see that by exercise the body creates a reserve which may be utilized—indeed, may be the deciding factor—in the maintenance of life under adverse conditions produced by many pathological states. The subject is now considered in more detail in relation to those tissues in which the physiological effect of exercise is most evident.

The Muscles.—The voluntary muscles we know to be bundles of muscle fibres. Each small group of fibres is capable of exerting its own tension independently (about 150 fibres are supplied from each anterior horn cell, p. 16). The actual arrangement of the fibres varies according to the situation of the muscle. Thus, if a wide range of movement is desired the fibres are long and more or less parallel ; whereas if a high tension is required, a large number of fibres are inserted into a raphe or raphes, running almost the whole length of the muscles, as in the rectus femoris or deltoid. Experimentally the number of fibres utilized depends on the strength of the stimulus, provided the amount of work to be done is constant. What is more important, however, is the fact recently shown by Fenn that the muscle adjusts itself to the work to be done after the contraction has already begun. In a manner not yet understood some local stimulus is set up by the load which causes the muscle to do more work. If the work is frequent, hypertrophy, *i.e.*, increase in the number of muscle fibres, occurs. It seems reasonable to believe that this is the result of the stimulus set up by the load referred to above when the work demanded is in excess of the normal. In doing light work there is excellent evidence, not only that all the fibres of the muscle are not used, but that those required are utilized in rotation. For example, a pound can be held up in the hand for a longer period than a stone (14 lbs.), and if the weight is heavier it can only be retained for a very short period. In view of the fact that fatigue of individual fibres comes on comparatively rapidly, we must presume that in holding up the light weight for a long time groups of fibres are utilized in turn. There must, therefore, exist some switch arrangement by which these groups are thrown out of or into action. The suggestion that such a mechanism does exist is supported by the existence of apparently similar processes in the capillaries, the alveoli, and the hot and

cold spots of the skin. Possibly the products of slight fatigue allow the stimulus to spread to the other fibres. It is not, however, until all the muscle fibres of the muscle are fatigued that the contraction is diminished and the sense of fatigue appreciated.

Fatigue.—In a biological consideration of muscular fatigue in man we must look upon the individual muscles of a certain group, say of the leg, as analogous to the relationship of the individual fibres to the muscle. We may fatigue certain muscles, or certain groups of muscles. Here we find ourselves faced with another factor, namely, muscular adaptation, not only to certain movements but to a certain speed of movement. We are familiar with the fact that a slow walk with an invalid is much more fatiguing than a more rapid one. Similarly, a Marathon runner is by no means necessarily an efficient walker. Indeed, he finds running much less fatiguing than walking. He has, in other words, an optimum rate of contraction of muscle, and it can be demonstrated that at this rate less oxygen is required for the work. In average persons this is approximately at the rate of two steps per second, and it is interesting to note that the army authorities, from experience and quite independently, at an earlier date arrived at 120 paces per minute as the optimum rate of marching. There is, no doubt, an appreciable individual variation in this respect, as the performance of a Marathon runner suggests. Greater facility in co-ordinating muscle groups no doubt also plays an important part. The department from which this volume was written has the misfortune to be on the third storey, and some 120 steps from the ground floor, and it is common experience that although at first or after vacation it is a difficult matter to hurry up the stairs, in a few weeks the exercise becomes appreciably easier and is no longer accompanied by circulatory or respiratory distress, although actually after a vacation one may be much more physically fit in a general sense. It is obviously a matter of co-ordination of muscle.

These facts are of considerable importance in relation to training in general in that special training is necessary for a particular sport or exercise. It is a well recognized fact that the long-distance runner is seldom an efficient sprinter, and *vice versa*. In the treatment of obesity, too, these facts have to be remembered, as walking, in an individual accustomed to this form of exercise, ceases to be a method by which large stores of energy can be got rid of.

Fatigue may be a purely local phenomenon, but it is seldom so, for it is found that if a voluntary movement is continued until it cannot be carried out any longer, the muscles concerned can still be stimulated electrically, directly or through their nerves. The fatigue is then in part the result of changes in the central nervous system. It may be that there is actual exhaustion of nerve cells, but on the other hand it may be that the fatigue which appears to be essentially central is really the result of impulses which pass up from the muscles themselves and inhibit the centre. That such impulses may exist is suggested by the "lengthening reaction." If the limb of an animal in decerebrate (extensor) rigidity (see page 63) is forcibly bent it is felt "to give way" suddenly as a result of the inhibition of the extensor tone. It is now considered that normally we cannot use our muscles to a maximum because of this reflex from the muscle spindles by which excessive and possibly harmful tension of the muscles is prevented. The abnormal strength of lunatics and others in unusual circumstances is explained as a temporary disappearance of this protective reflex, the stimulus to the voluntary movement being prepotent. It is easily possible to fatigue certain muscles and yet not receive the beneficial effects of exercise. Healthy exercise is general in the muscles it involves and can only be held to be taken when the muscular movement has been sufficiently extensive to cause increased activity of the circulatory and respiratory systems. In an ideal exercise all the muscles of the body are used to a moderate extent and a sense of pleasant fatigue, not localized to any special group of muscles, should be experienced.

Now it has been shown by Krogh that in exercising a muscle a large number of capillaries previously closed become opened up. This must result in a washing-out of the products of metabolism and in the utilization of stores of energy which give a sense of freshness and fitness in the muscles comparable to that experienced when one washes one's face in the morning. The blood-flow through a part in use is also increased by means of the Lovén reflex, by which the sensory impulses bring about dilatation in the organ from which they proceed. This reflex, which is quite clearly established (Bayliss), appears to be of the nature of an axon reflex (page 51). The impulse passes up by the afferent fibre towards the posterior nerve root, but at some point the stimulus passes to the outgoing vaso-dilators which accompany the sensory nerves.

Massage and electricity bring about essentially the same thing,

and they are often possible when exercise is not, as after injury. In this latter respect there can be little doubt that bed exercises are not sufficiently utilized to maintain general fitness during confinement to bed. Movements against resistance can readily be made even in the recumbent position and the majority of the body muscles can be so exercised. Electricity has many fashionable adherents and may act in several ways. It may actually stimulate the muscles to contract, as in the Bergonié chair treatment, or, by the sensation it produces, cause the patient to contract muscles, or it may stimulate vaso-dilators if it is of a certain quality, as the experiments of Bowditch and Warren suggest.

Exercise must then be in proportion to the musculature of the body. In our cities thousands of individuals leading active mental lives have little exercise and apparently do not suffer. The truth is that the general musculature is small and less exercise is required. Thus a person accustomed to much exercise suffers appreciably if compelled to lead a more sedentary life. Many felt this on returning from military service after the War. Gradually, however, the muscles degenerated to their civil requirements and there was no longer the same necessity for exercise, a moderate amount sufficing to give a sense of physical well-being. Unfortunately, in the same way, it is possible for an individual to feel well with little or no exercise, and he is led into a false sense of security as he becomes less and less efficient physically and also less capable of resisting disease. Not only do the skeletal muscles become reduced but also the efficiency of the other systems, especially the circulatory and respiratory, which are essentially the servants of the muscular system. Recent work goes to show that the circulatory, respiratory and autonomic nervous systems are primarily designed to serve the physical needs of the body, especially in relation to the supply of oxygen and elimination of carbon dioxide. But what is more important, should any breakdown occur in the tissues or mechanisms responsible for the supply and elimination, Nature uses the mechanisms primarily designed for exercise to make up for the deficiency. For example, should the blood become inefficient, the circulation becomes more active, or if the circulation fails, the respiratory movements increase. The less the margin kept utilized by exercise, the more liable is the individual to be overwhelmed by an acute breakdown, although when the latter is less acute the body may get time to mobilise its defences. This will be seen to be specially true in relation to the circulation.

The Nervous System.—The effect of exercise on the autonomic nervous system has already been alluded to above, and as a large number of the skeletal nerves are used we may presume that they are benefited, although we know little about the mechanism of nerve conduction in this respect. There is indication, however, that hypertrophy of muscle brings about also hypertrophy of nerve. It is also clear that by the frequent use of certain paths in the nervous system the resistance in these paths becomes appreciably reduced and the movements concerned become easier to perform. This is particularly true in relation to reflexes (see page 51), which play an important part in muscular exercise. To the sedentary brain-worker probably the most important effect of physical exercise on the nervous system is the mental relaxation which is produced and which is often so difficult to obtain. Not only does the relaxation occur during the exercise itself, but sleep is promoted, which is essential to active life of any kind.

Just as physical exercise is of benefit to the body generally, so mental exercise benefits the brain, and it is a well accepted fact that, within physiological limits, the more mental work an individual has to do, the more he finds himself capable of doing. It is a common experience that the results of examinations are better in the heavier terms than in the light ones, and we are often surprised at the amount of work those whose time appears to be already much occupied "find time" to do. As yet, we are quite unable to understand how this occurs, but from general biological principles, especially the fact that the brain of man has developed a surface much in excess of that of any other animal, even allowing for differences in size, we may assume that it "hypertrophies" with mental exercise just as does any other tissue. We do not know the nature of this hypertrophy, which obviously cannot be an increase in bulk, although it may be conceivably an increase of surface at the expense of the less used areas.

It is probable that the term exercise as applied to the nervous system requires some definition. The nervous system is activated by the stimulation of all sensory nerves, and on general principles it would seem desirable that all sensory nerves should be utilised. The usual conditions of civilized life appear to be against stimulation of the great sensory area, the skin. The benefits of general massage and of baths which have been recognized since antiquity probably depend largely on skin stimulation, as also does the beneficial effect on women of reduction in the weight of the clothing. The cooling of the skin has been shown to cause

adrenaline secretion and increased metabolism, both of which indicate general tonic effects.

Of the nature of fatigue of the nervous system we have little exact information except that it is probably fatigue of cells rather than of nerves, since the latter are not fatiguable in the ordinary sense. It is, however, of interest that fatigue of the nervous system occasioned by overwork, difficulties, or worry, is commonly associated with a general loss of nervous activity as indicated by digestive disturbance, loss of alimentary motility often with loss of gastric tone, and general muscular flaccidity. The recognition of the primary cause where there are digestive symptoms is of first importance.

Circulation.—The effect of exercise on the circulation is to increase the amount of blood passing from the lungs to the tissues in a given time, and thereby the supply of oxygen. The mechanism by which this is brought about has already been described. Exercise, for various reasons, produces an increased venous flow and pressure, and, by increasing sympathetic and diminishing vagal tone, increases the cardiac rate. These, together with the increased inflow, cause an enormous increase in cardiac output and rise of blood pressure. As with the skeletal muscles, the heart, if the exercise is habitual, adapts itself to the increased work, and if necessary hypertrophies to deal with the greater load. One of the aims in athletic training is to produce an increased cardiac efficiency. A similar hypertrophy of one or more chambers of the heart occurs in valvular disease. Here the increased work is brought about not by the increased filling but by increased resistance and deficient emptying. This latter, added to the normal filling, brings about the same effect as increased filling would do. The muscular hypertrophy is compensatory, and it is evident that a greater margin of compensation may be produced by carefully graduated exercises. This has been considered in relation to cardiac efficiency, and is the basis of modern treatment in cardiac disease. As with skeletal muscle, exercise is necessary to keep the cardiac muscle efficient. In cardiac disease too often does the patient take excessive care of himself.

The beneficial effects of exercise are then evident, provided the exercise is adjusted to the capabilities of the individual. Exercise also increases the vaso-motor tone and vagus restraint of the heart.

While it is true that many lead very inactive lives without any apparent harm, it is just as true that many patients have died of circulatory failure who might not had they taken more exercise.

Exercise makes use of those parts of the body which are made use of in disease. Should, for example, the oxygen-carrying power of the blood be reduced, the lungs fail as respiratory organs, or the liver or kidney cease to play their part in acid excretion, the heart rate is increased and the circulation is hastened to make up for the deficiency, the blood making, as it were, more journeys in a given time. The capability of the heart to respond depends on how much it has been used. No doubt it is the resilience on the part of the heart in active young people which makes it less likely that in them there will be cardiac failure in pneumonia.

The effect of the anticipation of exercise on the circulation has been discussed in relation to the rate of the heart.

Respiration.—Exercise, by causing an increased production of carbon dioxide and utilization of oxygen, necessitates a great increase in the efficiency of the respiration (Chapter XXIII.). When the exercise is habitual, however, there is a permanent increase in respiratory efficiency. The chest and lungs become larger and there is, in consequence, not only an increased respiratory surface, but also a more efficient replacement of alveolar air, as indicated by the increased vital capacity and chest expansion (page 216). In other words, an increased amount of blood can be aerated in the lungs in a given time without undue hyperpnœa. In disease, should any pathological condition arise which would lead to breathlessness, the normal margin of reserve is taken up, but it will be obvious that the more exercise has been taken the greater reserve there is to fall back upon. Hence we see the value of strenuous games at an age while the thorax can still grow. Similarly, breathing exercises and gymnastic exercises which enlarge the chest are of value and are often more possible for children insufficiently robust to play games such as football. The latter, however, must be considered a much more physiological method of increasing the respiratory reserve than so-called breathing exercises, as the latter, although they may enlarge the chest cavity and possibly the lungs, cause a washing-out of the carbon dioxide from the body, which is quite an opposite state to that produced by exercise in that it tends to depress the circulatory and respiratory mechanisms. Normally, increase in respiratory efficiency should be accompanied by increased cardiac efficiency, which latter does not occur with breathing exercises alone. Respiratory fatigue has already been dealt with.

Digestive and Other Organs.—Exercise must also be beneficial

to all organs responsible for metabolism, as the essential *raison d'être* of metabolism is the provision of energy for transformation into external work. The matter need not be dealt with in detail, but we are all familiar with the stimulating effect of exercise on our food consumption and digestion. Important, too, is the beneficial effect of exercise on the bowel movement, although how this is caused is not quite clear. There is, however, evidence that during exercise both the sympathetic and the parasympathetic are stimulated, but the sympathetic predominates, while after the exercise the parasympathetic activity continues (McDowall). Such an increased parasympathetic action is proved in relation to the circulation, and the available evidence suggests that by a similar action in relation to the digestive tract, the efficiency of the digestion is adapted to the energy requirements of the individual. No doubt also the increased action of the abdominal muscles plays a part. Whenever any organ is used, it increases its efficiency and, if necessary, its size. The exact stimulus to such local growth is not known, but it seems that whenever work is thrown on an organ to an extent that all its available reserve is used, hypertrophy occurs to provide a reserve and so to make it possible for different parts of the organ to rest, since, as we know, intermittency of action may be considered a law of Nature.

Exercise also, by producing carbon dioxide and lactic acid, brings into operation the mechanisms responsible for the maintenance of the normal acid-base equilibrium of the body. Indeed it may, with justification, be considered that these mechanisms have attained their full perfection because of the necessity for severe exercise in the preservation of life, as in animal flight and pursuit. As acid-base equilibrium is of considerable importance in disease it has been considered in a separate chapter.

THE EFFECT OF LACK OF EXERCISE

To appreciate the beneficial effects of physical exercise is but to appreciate the deleterious effects of lack of such exercise. We have noted that structure is dependent on function. It is a further biological principle that disuse leads to degeneration, and in an attempt to adjust organs to the requirements of the individual, disease may be brought about. Every tissue may suffer to an extent which is not fully appreciated. A most striking instance of this came to the notice of the author recently. It was the almost complete disappearance of calcification from

the spinal column of a monkey which had been closely confined for several years. The vertebræ could be cut easily with an ordinary knife.

With disuse the various systems gradually become less efficient. This we readily appreciate in relation to the muscles when we take part in any unaccustomed game. The muscles become stiff and painful, presumably from an accumulation of the products of the exercise which have not been adequately removed because of temporary inefficiency of the local circulation, and which cause an infiltration of fluid into the muscles. The pain must be considered to be caused by tension probably so produced.

There seems to be little doubt that those who have developed a large amount of muscle from special exercises are specially liable to feel the effect of lack of exercise.

Large areas of tissue must become relatively stagnant so far as circulation is concerned. This general feeling of lassitude is probably due in some part to the substances produced as the muscle degenerates from lack of use. Specially important is the fact that similar degeneration tends to take place in cardiac muscle which has become hypertrophied as a result of valvular disease if the individual does not lead a moderately active life. Fatty degeneration and infiltration may also take place in a previously normal heart. In each case, there is an increasing possibility that the organ may become filled with more blood than it can pump out and may fail in attempting to do so.

Other parts of the vascular system also suffer. The power to regulate body temperature becomes, we know, seriously impaired by wearing excessive clothing. The extent to which human beings can use their skin as protection against cold is indicated by the fact that the inhabitants of Patagonia wear practically no clothes, although their climate is more severe than that of the British Isles. Another instance of the loss of the function of the vaso-motor system is that of the caged rabbit, which, if the confinement has been prolonged and close, may die of cerebral anæmia if held up by the ears. This failure of the circulation to adapt itself to posture is also demonstrated if for any reason we are confined to bed even for a few days. Not only do we lose the power of accurate walking from some loss of power to co-ordinate, but there is a sensation of "light-headedness" which is exaggerated in changing from the horizontal to the erect posture. What has been said of the vaso-motor system is probably true of the nervous system as a whole, and even of mentality.

In surgery it is now realized that the inefficiency which may result from the prolonged lack of use due, for example, to a fracture, may be as important as the injury itself, and every attempt is made to maintain the condition of the soft parts by massage and movement.

The ventilation of the lungs also becomes reduced in those who take little active exercise, while we know that mental sloth is the forerunner of mental inefficiency. In industry it is recognized that skilled workers are less efficient than normal on Mondays, although it is agreed that a week-end break promotes general efficiency—indeed, is essential.

Any dole-without-work system for relieving unemployment is obviously fundamentally unsound, through no fault, necessarily, of the recipient. There can be no doubt that the physical capacity to work becomes appreciably reduced and, until this capacity is regained, work is found to be extremely irksome. Any of us may undergo a similar experience if we embark upon an unusually energetic holiday and it is a recognised matter for consideration in the training of Army recruits. In the more leisured classes games, possibly even dancing, form a convenient method of providing exercise. There can be little doubt that their increasing popularity amongst women has largely reduced the number of minor ailments which were the fashionable accompaniments of leisure in the Victorian era.

If insufficient exercise is persisted in there is inevitably a tendency to adiposity if the energy intake continues, and the laying down of fat in the various tissues, especially in the muscles and heart, leads to a still greater inefficiency and disinclination to work. Motor-cars have undoubtedly lessened the amount of exercise taken, and one has only to observe the general proportions of many of the occupants of cars in a fashionable district to appreciate this fact. Many doctors are similarly affected. Although cars save so much time, they are often a curse in disguise in eliminating the need for exercise. The matter is dealt with more fully in relation to body weight.

Added frequently to lack of exercise is the effect of monotony, although clearly the two conditions may occur quite independently.

In concluding this subject we must note how often retirement from an active occupation is soon followed by death. Such a sequence must be considered quite unphysiological. Retirement should be gradual. As the flexibility, which is necessary in prac-

tically every walk of life, becomes reduced, less responsible occupations should take the place of the more serious, although even flexibility can be prolonged by exercise. The proof of such conclusions is that those who live longest are those who either never retire at all or those whose occupations are of such an easy nature that retirement is more nominal than actual.

THE NECESSITY FOR REST, SLEEP, AND INTEREST

Fatigue is the inevitable result of severe work. Rest is necessary as the physiological sequel to ensure recovery. No tissue in the body is constantly in use, and the more detailed physiology we know the more evident it becomes that this is true.

The need for rest may be restricted to an individual muscle, but if the requirement is more generalized, sleep tends to be induced. Of the nature of sleep we know little. That there is usually a cerebral anæmia and an increase of limb volume, and that there is a greater distribution of blood to the limbs, is undoubted, and such anæmia would tend to bring about unconsciousness (page 5). These changes, however, may be the result rather than the cause. Although they appear to be the common corollary they are not essential, as has recently been shown by McWilliam, who brought evidence to suggest that the cerebral pressure may, in dreams and the like, become appreciably in excess of normal. There can be no doubt, however, that conditions which tend to bring about cerebral anæmia facilitate sleep, as is seen when we sit down in front of a fire after dinner, or where there is a minimum of external stimulation. Similarly, a monotony of stimulation has the same effect. This may be produced in two ways: the nerve endings may become adapted and cease to send in impulses to the central nervous system (Adrian), or there may be a fatigue in the central nervous system. This is well seen in the effect of monotonous sounds on blood pressure. Quite commonly persons who live in the country find it difficult to sleep in a city hotel because of the noise, but in a few days the difficulty passes. Similarly, we cease to notice the ticking of a clock. Most suggestive recent work on the subject of sleep has been that of Pavlov, whose experiments appear to indicate that inhibition, hypnosis, and true sleep are essentially similar phenomena of varying degrees of magnitude, and may be produced experimentally. He brings forward evidence which suggests that sleep is an inhibition of certain parts of the cerebral cortex and may be very localized. It has been found possible, for example, to produce an inhibition of

the motor cortex in a dog so that the animal, although hungry, may not partake of food. There is much evidence which suggests that in sleep all mental processes are not closed down and the reverse possibility that certain individuals are often only " half awake " may have a scientific foundation.

The Nature of Sleep.—Since the above was written, Hess, of Zurich, has brought forward evidence that sleep is essentially a parasympathetic phenomenon associated with a depression of the sympathetic. He finds that sleep is produced by the injection of ergotamine (the well-known sympathetic paralysant) into the third ventricle, and may also be caused by the application of special electric currents in this region. His results are certainly dramatic and in no way contradict the view of Pavlov, for we know that the autonomic nervous system may be profoundly influenced by conditioned stimuli. The results of Hess emphasize the importance of the prevention of sympathetic stimulation in the promotion of sleep.

Whatever its nature, it is generally agreed that sleep is essential to promote bodily rest, and during sleep all the functions are reduced to a minimum provided it is undisturbed by dreams. For the average person eight hours' sleep is ample, but it is evident that the more exhausting the occupation the more sleep is necessary. It is well known that some of our most active public men require a least nine or ten hours' sleep and have exceptional faculties for sleeping when not actually at work. Sleep, however, is a matter of habit and the more we have the more we want. It is possible to accustom oneself to extraordinarily little sleep, and some appear to be capable of doing with comparatively few hours. Edison, the inventor, is stated to have been one of these.

Sleeplessness is one of the curses of our civilization and it is specially evident in those who have insufficient or excessive bodily or mental exercise. Excessive bodily fatigue, which is painful, may result in sleeplessness ; similarly, late suppers to those unaccustomed to them, strange beds, and all conditions, *e.g.*, pain or the discomfort of a full bladder, which, in virtue of the stimulation produced, bring about vaso-motor states preventing cerebral anæmia, which, although not necessarily the cause of sleep, is a common, if not essential, concomitant of it. Cold, for example, is probably one of the commonest and acts in this way. The skin vessels become constricted as a protective action against excessive loss of body heat, and in such instances the effects of a hot drink, preferably milk (as it also allays gastric acidity) and a

hot-water bottle are often marvellous. Excessive mental activity, especially when associated with an impaired vaso-motor system, such as may be brought about by arterio-sclerosis or mere lack of use, is also a common cause of sleeplessness. Worry is perhaps the most difficult cause to treat, and in the milder cases, light reading at bedtime to take the mind off more serious topics is often found useful. Alcohol, too, has many advantages in this respect. Its vascular action and the sense of well-being it promotes both induce sleep. This sense of well-being is of more importance in relation to sleep than is often at first sight supposed, as not infrequently sleeplessness is at least made worse by the fear of sleeplessness, or lack of confidence in being able to sleep. The tendency to form an alcohol habit frequently contraindicates its being advised, and in such cases the more disagreeable hypnotics, *e.g.*, paraldehyde, are prescribed. In no instance, however, should drugs be prescribed until the physician has considered the cause of the sleeplessness in the individual case and, if possible, dealt with it. Psychotherapeutic measures are of much value.

When, however, there is excessive energy output it may not be possible to obtain sufficient sleep for complete recovery. Each day's work is begun before the fatigue of the preceding day has worn off and complete fatigue slowly supervenes or a degree of inefficiency is produced which reduces the amount of work possible. This may occur as the result of excessive physical or mental work or both combined. The former was not uncommon in war-time, when not only were there occasions of great physical output of energy but the opportunities of sleep were often very limited. In civil life excessive nerve strain in this way is common. The nervous exhaustion may be purely local, as is seen in the condition of writer's cramp, which results from excessive writing, and once established the condition may be extremely difficult to get rid of. More commonly there is a general breakdown in which the individual is quite incapable of working or standing the mental strain any longer, and Nature enforces rest. Not infrequently such insidious fatigue is associated with monotony, as indicated above. A holiday is the natural and physiological antidote to such fatigue ; even cessation of the usual work at the week-ends is of enormous value, and there can be little doubt that the moral obligation of keeping the Sabbath is really based on a physical necessity. The efficiency of skilled workers is reduced on Mondays or after the holidays. On the other hand, without that holiday there is a gradual diminution in the total output per

week. The holiday must, however, be suited to the needs of the individual and is quite distinct from that necessary to relieve monotony. A visit to an Exhibition may be of value to those who suffer from the latter, but it is of no use for those who require rest, just as rest is insufficient if revival of stimulation is required. Each case must be judged on its own merits.

More and more attention is now being paid to the alleviation of industrial fatigue which we may look upon as a mixed variety of fatigue. The elimination of unnecessary movements, the introduction of rhythmical and alternative movements, the provision of rest pauses, are all of value in preventing actual fatigue of muscles, but, as we shall see, the mental state also must be studied.

The Necessity for Variety or Interest.—We are creatures of our own physical environment, and although sometimes apt to forget that this is so, we are quite conscious of the effect of environment on others. In some of the earlier chapters we have seen how many of our actions and thoughts became purely reflex and adapted to our daily needs. Structure adapts itself to function, and, in the biological world in general, we see how plants and animals have become altered to suit the conditions under which they live.

Throughout all this adaptation there is one requisite factor, namely, stimulation. The plant is stimulated by its environment, and variation is brought about. In the same way, however original we may imagine ourselves to be, everything we say or do is the result of stimulation in some form or other. The primitive animal concerns itself chiefly with the necessity of preservation of the individual or the race, and, in doing so, a utilisation of energy is necessary which, in return, necessitates a supply in proportion to the activity of the life.

Under many conditions of civilised life, however, stimulation is reduced to a minimum. Consider an extreme case : an individual in a factory who sprays pieces of toys with enamel. The picture is a drab one when considered as a form of human existence. A small chamber, partitioned off to prevent the enamel flying about, everything in front and at the sides black with enamel, the skin probably also coated ; on one side a heap of pieces finished and on the other a heap to be done. The story of Dickens in his factory may still be seen daily, although conditions are admittedly somewhat improved to-day. In what sense can such a life be considered physiological ? Only in so far as it is a

means of supplying energy in the form of food which is essential to life. A minimum of mental and physical exercise is required. All the senses are used to a minimum. A change of posture is now advised and made possible, but full advantage is seldom taken of this provision. The workers become mere automata. Such an existence cannot be compatible with the physiological functions of organs, and it is indeed marvellous that the body can become adapted to such a life at all.

An extreme example has been given, but more and more evidence is accumulating that monotony of stimulation is an important factor in everyday life. An interesting experiment by Thompson, who has shown that the continued playing of the same gramophone record causes a fall of blood pressure but a change of the tune at once caused a rise. To continue working for long periods, especially at high pressure, or under conditions of anxiety, inevitably breaks down the health of those who attempt it. The value of holidays is proved and the more the holiday differs from the normal mode of life, the more efficient is it likely to be. A holiday is not altogether a matter of rest. Inland dwellers benefit from a visit to the seaside and *vice versa*. Town dwellers enjoy the country, but those who live in the country go for holidays to the town. The value of " a change of air " has long been appreciated by physicians and public alike since the days of Hippocrates.

Holidays, however, should not be prolonged except after special strain, and it will be generally agreed that the first fortnight of a holiday is always more efficient in its recuperative power than any succeeding period.

Monotony is prevented by congenial occupation. Those who find real pleasure in their work are able to work extremely hard without any harm accruing. Indeed, the work promotes health, provided it permits of a reasonable amount of physical activity. The workers are the most happy, contented, and usually the most successful amongst us, and also the most physiological. It is a noticeable fact that the most eminent men of our time are amongst the longest lived, and long life is the final test of physiological living. Consider further the condition of life of that section of society, country ministers and farmers, which heads our vital statistics, and we see the essentials of a physiological life : lack of worry, lack of monotony, and moderate exercise.

In two classes of society monotony is extremely difficult to relieve. The unemployed, both rich and poor, suffer from similar

complaints. For the former, social excitements, travelling, and games may give a temporary relief, but, if not continued, often exaggerate the monotonous conditions of home life. The provision of an occupation, preferably involving a reasonable amount of physical exercise, is the ideal treatment in both instances.

The provision of work which gives interest to the individual workers is one of the most difficult social and economic problems of to-day, and there can be little doubt that the general tendency for workers to eliminate competition and pride of work amongst themselves has reduced appreciably the interest in a large number of occupations. Far be it from the intention of a physiologist to attempt to solve such problems, but on purely physiological grounds, the introduction of greater interest into labour by giving the workers a real share in the result of their work seems a step in the proper direction.

It is evident that *monotony* is quite different from fatigue in the ordinary sense. Mere rest in bed and plenty of sleep are not the efficient remedies for monotony that they are for overwork. An analogous, if more localized condition, known as " staleness," is well recognized in athletics. Walter Hagen, speaking of an American golf team, said that he would rather put his faith in an insufficiently trained team than a team stale through overtraining. There is no actual fatigue, but the zest has gone and the maintenance of training becomes a mental weariness ; at the same time efficiency is markedly reduced. If we may take an analogy again from golf, " Bobby " Jones considers that he plays his best game when he is keyed up to the situation, and, as we say, " feels nervous."

It may be that there is too little variety of sensory stimuli, or that there is localized exhaustion of nerve cells responsible for the too-often repeated motor movement or mental work. The fact that a change of occupation is as beneficial as a rest, indeed often more so, suggests the former cause, as does also the fact that in the condition there is often a considerable degree of mental languor, and that in a change of occupation the nerve cells, previously overwrought, may get some degree of rest.

The only explanation of the effect of monotony put forward has been that if there is insufficient interest there is insufficient circulatory reaction which may be essential for the best performance of work. We can hardly imagine that the high blood pressure which occurs in mental stress is entirely useless. Evidence for this from different sources is accumulating.

There seems to be little doubt that the mental state is the most important, since if two people have a similar occupation, they are not necessarily both affected by its monotony. Interest prevents its ill effects and interest depends on the mental state, especially on the mental outlook.

A great deal undoubtedly can be done by studying mental and physical make-up, and by allowing a person to follow his or her natural bent. Psychologists indicate how many of the apparently trivial matters of childhood may awaken interest along certain lines, and industrial psychologists emphasize the importance of finding the occupation to which the individual is best suited.

Therapeutically, if the physical circumstance cannot be readily altered, much can be done to improve the mental outlook by teaching that content is the true philosophers' stone which can convert the lead of misery into the gold of happiness.

The Sense of Well-being.—In the scientific sense this is difficult to define, although we appreciate what it means. It may be described as a sense of physical and mental fitness which makes one at peace with the world. Most of us experience this if we go for a sharp and not too fatiguing walk in clear frosty air on a sunny day, but the exhilaration produced by bathing, massage, electric treatment, and the like are probably of the same order. It is claimed that sponging the body alternatively with dilute acid and dilute alkali produces similar effects.

It is remarkable that all these procedures bring about a considerable amount of sensory stimulation, especially of the skin, while conditions which have the opposite effect do not. How the passage of a large number of impulses into the nervous system promotes this sense of well-being is a very interesting problem.

Geoffrey Evans emphasizes that the doing of anything superlatively well is specially valuable in producing the sense of well-being, and we know that nothing is more healthful or is more successful than success.

CHAPTER XLVI

PROTECTION AGAINST DISEASE

It is one of the greatest indictments against civilization that under its influence the natural defences of the body against certain classes of organisms are not fully maintained. One has only to be acquainted with life in some communities exposed to infection to realize how far we are deficient. I have in my mind as a striking example one of the most ancient cities of the East, where the water supply comes from a well by the city, runs down the filthy streets—for there are few real gutters—to an ancient and practically stagnant walled pool. This water the inhabitants put to all the purposes for which water may be used and are apparently none the worse; they have natural immunity against water-borne disease. It must be confessed, however, that natives are quite prone to many of the common infectious diseases, although they are seldom exposed to infection. In war-time we saw clearly that even our attenuated resistance to infection could be appreciably increased by an active and open-air life. It became possible to withstand a degree of exposure almost inconceivable in peace-time, while it was found in the near East that a considerable immunity to bowel infections occurred after a few years of association with conditions which at first could not be tolerated.

Our resistance may conveniently be divided into two categories, that by which the entrance of bacteria into the body is prevented and that by which the body defends itself against bacteria and their toxins when they have entered. These protective mechanisms must be considered physiological, as they are normally present in all animals, although their study has mostly been carried out by bacteriologists and pathologists.

Skin and Mucous Membrane.—In the first category are the skin and mucous membranes which act as a mechanical protection, for the mucous membrane of the alimentary canal is quite as much exposed to bacteria as the skin. Especially is this the case in the large intestine where bacteria are of normal occurrence and in the lower animals take an essential part in body economy as in the breaking-down of cellulose.

The protective value of the skin depends on the fact that the upper layers are tightly packed together and are impervious. In the event of injury, also, the skin has an exceedingly rapid power of repair which is best where the circulation is good, but less rapid where it is liable to be impaired, as in the legs, a point of great practical importance. Thus, in ulcers of the leg, the circulation and process of repair are greatly improved by raising the limb. The skin may, however, become infected by way of the hair follicles and sebaceous glands, especially if subjected to abrasion, or if the general power of resistance is reduced.

Should the skin protection fail, and bacteria enter the subcutaneous tissue, they are at first held up by the immigration of the **leucocytes,** which process is facilitated by increased vascularity of the part, as the result of which we have the well-known characteristics of inflammation—heat, redness, pain, and swelling. Usually, if the infection is mild, the invasion may remain local, as a papule, a boil, or carbuncle, according to its size and depth. This sequence is not, however, invariable, for, as in tetanus, there may be little or no local reaction, while the toxin produced in the wound may be of great consequence.

The next line of defence is the **lymph glands** which are aggregations of lymphoid tissue and the home of the lymphocytes. In some diseases the effect on the lymph glands may be really more important than the local reaction, as in plague, where there is no evidence necessarily of the entrance of the bacilli, although their presence is made clear in the characteristic bubo. In certain regions, normally liable to infection, the lymphoid tissue may be situated immediately under the mucous membrane as a special safeguard. The naso-pharynx is protected by the lymphoid tissue in the tonsils and neighbourhood. Clinically, these are of importance, as such adenoid tissue may become the seat of inflammation and chronic enlargement under conditions which suggest excessive demand on their function. Similarly, we have, at the lower end of the small intestine, aggregations of lymphoid tissue known as Peyer's patches, which, according to Barclay Smith, protect the small intestine from the invasions of bacteria from the colon. These too, however, may be overcome by bacteria and their toxins, as they are in typhoid fever, in which the patches become the main seat of the disease.

The upper part of the alimentary canal is, apparently, protected by the digestive secretions, and this no doubt accounts for the comparative immunity from infection, apart from that associated

with gross lesions, in this region. It has been shown experimentally (Cornwall) that injections of bacteria which in animals produce no marked effects if introduced into the stomach, bring about severe infections if introduced into the ileum. There is, however, a definite limit to the protection, as may be adduced from the tenets of public health. Thus, water which contains *bacillus coli* (this bacterium being used as an indication of possible infection), in ·5 c.c. would be considered unsafe, while if the organism is not readily demonstrable in less than 10 c.c. of water this might be considered safe, if otherwise suitable. Obviously, the underlying principle of these considerations is the concentration of bacteria which can normally be dealt with, and the immunity of natives to bowel complaints may be due to the benefits conferred by a simple diet which does not overtax their digestive mechanisms. All the main ducts of glands which open into the alimentary canal are well supplied with digestive secretions ; occasionally these ducts may become infected, causing inflammation in such as the bile passages or the pancreas, the latter more rarely, no doubt in virtue of the digestive properties of its juice.

Kidney.—Once bacteria have gained access to the blood-stream there is good evidence, such as that of Kidd and of Chalmers Watson, that they may be eliminated by the kidney. There can be little doubt that, if proper culture media are used, the occurrence of a sterile urine is much less common than has been usually supposed. It is considered that should the kidney be overstrained in this respect, the organ itself may be attacked and become the seat of disease, which will vary with the bacteria concerned. The existence of such an eliminating mechanism is supported by the fact that the kidney may become the seat of blood-borne disease which does not necessarily exist in any other part of the body.

Reticulo-endothelial System.—More recently it has been shown that the Kupffer cells of the reticulo-endothelial system, especially in the liver (see " Bile Formation "), have the power of ingesting bacteria which are excreted in the bile, a fact possibly of importance in relation to infection of the biliary passages.

Immune Bodies and Lysins.—These substances are produced in the blood to operate against bacteria which they kill by a process of solution or lysis. It is, however, interesting to note (Muir) that these substances are not themselves capable of destroying bacteria, but act as sensitizers and make it possible

for the substance known as *complement or alexin*, normally produced in the serum, to attack the bacteria. The immune bodies are, however, specific, that is, they can deal only with special classes of bacteria or special antigens. The sensitization is developed also towards foreign blood corpuscles (should they be injected into an animal), and this fact is of considerable importance, for such corpuscles may be utilized as a test for complement in an unknown serum. If the complement has been fixed it is no longer capable, as in normal serum, of causing the lysis of sensitized corpuscles. The application of these principles is a basis of the Wassermann test. Thus, if an unknown serum is added to a syphilitic antigen plus complement and when, added to the sensitized corpuscles, is found to have its complement fixed, this is evidence that the unknown serum contains an immune body which has been intended as a protection against syphilis.

Opsonins.—In many respects these substances are like immune bodies, but they can act in the absence of complement. They are specially important because they lead to the phagocytosis or destruction of bacteria by the leucocytes, which can be seen to ingest and apparently to digest the bacteria. In the absence of the opsonin the phagocytes cannot attack the bacteria and its presence is therefore most important in rendering the body resistant to bacterial invasion, and its absence would be of grave significance in disease. Reference has already been made to the fact that an insignificant leucocytosis in conditions where a large one is expected, indicates that the bacteria are obtaining the mastery. Endeavours have been made to estimate the body resistance by the number of bacteria ingested by the phagocytes under suitable conditions *in vitro*. This estimation of the "opsonic index," as it is called, has not, however, been generally useful, largely owing to the difficulty of obtaining standards. What exactly causes the opsonins to be formed is unknown, nor is it yet understood by what mechanisms enormous numbers of leucocytes are caused to assemble in diseased or injured areas, although as the word chemiotaxis indicates, we suspect an attraction of a chemical nature.

Antitoxins.—At the same time as immune bodies and opsonins are dealing with the bacteria the toxins of the latter are being neutralized by antitoxins and rendered innocuous. In some instances, as in diphtheria and tetanus, the toxins produced are extremely powerful and produce dire results. Fortunately these

organisms, especially the former, also cause powerful antitoxins to be formed, not only in man but in other animals. Thus it is possible to inject the toxin made from killed bacteria into an animal (such as the horse) and subsequently withdraw some of the blood of the animal to obtain a serum which is rich in antitoxin, and which may be injected into man to combat the disease. Not only are the toxins thereby neutralized, but the bacterial growth itself is inhibited so that an antitoxin may be utilized as a prophylactic.

The immunity thus conferred is known as *passive immunity*, for though the tissues of the individual are rendered immune they play no part in producing the immunity. Where, however, the antitoxin, together with the lysins and opsonins, are formed as a result of the reaction of the individual, the term *active immunity* is used. Thus, in diphtheria antitoxin, active immunity is produced in the horse. Such immunity takes more time to produce, but lasts appreciably longer and is part of the natural cure of bacterial disease.

It is important to remember that for the production of an active immunity it may not be necessary to inject living bacteria, since the toxins of bacteria, grown and killed *in vitro*, bring this about, and it is thus possible to control the amount of toxin injected.

On these physiological principles vaccination and inoculations are based. The vaccines ingested are dead or attenuated bacteria and their toxins and they are intended to set up an active immunity, either as a prophylactic, as in typhoid or small-pox, or therapeutically where it is considered that an infection, possibly because it is shut off by the local reaction it produces, does not produce a general reaction. It will be obvious that, therapeutically, it is important, in view of the specificity of anti-substances, that the bacteria or toxins should be of the same variety as those concerned in the infection. Where there is doubt of this, autogenous vaccines, *i.e.*, vaccines produced from cultures of bacteria taken from the actual patient, are necessary, but stock vaccines of a more " blunderbuss " type are commonly used.

It must be remembered that the injection of vaccine does throw some strain on the reserves of the patient, and, if the response is not good, may actually do harm. Harm may be indicated by excessive reaction which may be local, *i.e.*, at the site of the injection, focal, *i.e.*, at the site of the lesion, or general. Any one of these indicates a reduction of the dose or a lengthening of the interval between the doses. Such reactions, especially the

local and focal, show that temporarily the bacteria have got the upper hand, and may extend the lesion. Hence, the imperative necessity of their avoidance. There is, as emphasized by Philip, little doubt that failure in vaccine therapy has in a large measure been due to neglect of this precaution and to the routine practice of giving standard doses at stated intervals irrespective of the response of the patient.

These local reactions have been utilized for diagnostic purposes. Thus, in von Pirquet's test for tuberculosis, tuberculin is applied to the scarified skin. The application of Moro's tuberculin ointment to the skin may be similarly used, though, in the latter instance, it may be first necessary to increase absorption by the application of a fomentation. In the Schick test, too, in which a little diphtheria toxin is introduced intradermally, use is made of a similar reaction in determining whether or not individuals exposed to infection should be given prophylactic doses of diphtheria antitoxin.

Finally, when the body gets the upper hand, bacteria may settle down in the tissue but give rise to very little general reaction. Locally, there is the formation of granulation tissue, of which the tuberculous nodule is a well-known example, or the formation of fibrous barriers. In the abdomen, the localization of infection is facilitated by adhesions of peritoneum and the coagulation of the lymph. In this way an abscess may be completely shut off, and finally absorbed. Unfortunately, it is not possible to predict the extent to which the individual will react, and surgical evacuation of the abscess is a much more certain method of bringing about recovery. When the bacteria become enclosed in granulation or fibrous tissue they lose their vitality and die. Only a fibrous nodule remains. Occasionally, the fibrous tissue is assisted by the deposition of lime salts.

Unfortunately, there occur instances of what Mackie calls " a non-sterilizing immunity," as exemplified by the convalescent carrier who, although he may himself be immune from acute infection, will pass on a virulent organism to another person. The treatment of such a carrier, *e.g.*, of diphtheria in the nasal passages, typhoid bacilli in the intestines or gall-bladder, is often extremely difficult, even if the carrier himself can be found, a matter of difficulty, as such carriers may be apparently normal people.

Precipitins and Agglutinins.—These substances are found in serum on the injection of an antigen and appear to be of the

nature of anti-substances, although their exact significance in relation to immunity is uncertain. They are, however, important clinically in diagnostic methods.

A precipitin is so called as it causes a precipitate to be formed if it is added to the serum similar to that injected into an animal to cause its formation. Thus, if human blood is injected into a rabbit, a precipitin will be formed in the rabbit's serum which will cause a precipitate with human blood. This is made use of medico-legally to differentiate between human and other blood, the unknown blood being added to the previously obtained serum of an immunized animal.

Agglutinins have the peculiar property of causing clumping and sedimentation of bacteria where the latter are similar to those which have previously been injected into the animal. Thus they may be utilized for differentiating bacteria, and are made use of in the Widal Reaction. When positive in typhoid fever, the serum of the patient in appropriate dilution agglutinates the *bacillus typhosus*.

Body Temperature, Oxygen Supply, General Metabolism.—The fact that chilling of the body is liable to lead to infection is well known, and has been referred to in relation to the body temperature. Unless the latter is maintained invading organisms are likely to get the upper hand. The body possesses a mechanism to protect itself against cold. One of the initial effects of cold is the production of adrenaline from the suprarenal (Cramer, Crowden), which mobilizes the leucocytes and causes constriction of skin vessels.

The effect of cold indicates that local metabolism plays a distinct part in the protection of the tissues. This is further seen by other factors which affect metabolism. Thus, if the oxygen supply is diminished, *e.g.*, in venous congestion or anæmia, there is a special liability to local infection often difficult to clear up. If the fuel supply for the maintenance of local fire, as it were, is difficult, a similar state of affairs is seen, as in diabetes, where boils, gangrene, and tuberculosis are common complications. In myxœdema, prior to thyroid treatment, death from intercurrent infection was frequent. In this disease metabolism is extremely slow. Analogous, too, is the liability of a starved person to infection.

How this reduced local metabolism affects resistance is not clear. Possibly the production of antibodies and vascular reaction are reduced in such circumstances.

Open Air and Exercise.—The fact that people who live open-air lives are appreciably less liable to catarrhal affections of the respiratory tract was proved in war time. Exercise by increasing respiration increases evaporation from the respiratory tract and, in order to maintain the normal surface moisture and temperature, a considerable local circulation has to be kept up. If this protective circulation is not required, as in a sedentary worker especially in a humid atmosphere, the mucous membranes are more liable to infection.

Alcohol and Salicylates.—The belief that alcohol is of value in cutting short or protecting against catarrhal infections is too strong to be dispelled on negative scientific grounds. It does not appear to have been suggested that the benefit may be the result of hyperæmia of the respiratory tract during the excretion of the alcohol. That salicylates bring about an increased circulation through the pharyngeal mucous membranes is certain ; indeed in some persons this may be intensely disagreeable.

Vitamins.—There is increasing evidence that diets deficient especially in vitamins " A " and " B " may reduce the power of the body to withstand disease, and many instances of refractory cases of infection, even gastric ulcer, have benefited greatly from cod-liver oil and yeast. It will be interesting to see how far carrots (in view of the carotin which they contain, and which is inseparable from vitamin " A ") will replace milk and cod-liver oil in this respect, the more so as evidence is increasing that the giving of too much milk to children may be actually harmful in producing dyspepsia and adenoids, if not tuberculosis.

Chemical Protective Mechanisms.—When poisonous substances are taken into the body, if they are not in such doses as to produce fatal results, they are excreted by causing vomiting or diarrhœa or by being combined with harmless compounds and excreted in the urine. These are dealt with in the section on urine.

CHAPTER XLVII

PHYSIOLOGICAL PRINCIPLES IN THE TREATMENT OF CERTAIN EMERGENCIES

ILLNESS does not as a rule immediately endanger life, and the clinician has time to consider his procedure. In some emergencies, however, life is in immediate danger, and it is the duty of the clinician to be prepared for them. His action depends on his knowledge, in particular, of that which has been described earlier as the essentials of life. It must not be forgotten that on the speed of the action may depend the result, for every moment the heart is getting weaker. Essentially the heart is about to fail, and the physician has to consider immediate action to prevent this failure. It may be that the cause of failure of one of the factors on which heart-action depends is temporary, and artificial aid may be of value in tiding over the minutes of danger. But even when death in a few hours is inevitable, the prolongation of life to its utmost may be of the greatest importance, as in criminal cases.

A knowledge of physiology at once indicates the procedure to be adopted, but alas! the instances in which the cause of the failure is temporary are but few. Considerations of space make it impossible to deal with more than the common emergencies which threaten immediate death.

Primary Cardiac Failure.—Such an emergency occurs when the heart fails to expel its contents. This is usually the immediate result of strain put on it, by overfilling and increased peripheral resistance in the arteries, *e.g.*, in running to catch a train. The weaker the heart muscle, however, the more liable is the strain to be effective, and in a very weak heart what would be considered normal activity may prove too much for it. In toxæmic conditions, particularly diphtheria, the heart may not be able to stand the strain involved in the patient's sitting up in bed. Occasionally, as in *status lymphaticus*, there is sudden failure of the heart from stimulation of the inhibitory mechanism. Such a stimulus may be of a very trivial nature, such as a flip on the pomum Adami, or the stimulation may be of a more reflex nature,

such as fright, grief, joy, or the drinking of cold water when overheated, etc. This failure is particularly liable to occur in the early stages of chloroform anæsthesia, and for this reason many anæsthetists administer atropine as a routine prior to operation. The weakening of the cardiac muscle may be the result of acute poisoning, but more commonly it is progressive from chronic disease of the myocardium, or from excessive strain put upon it as the result of valvular disease. It is possible clinically to get acute dilatation of the heart as a result of rapid diminution in intra-thoracic pressure, such as may occur when large quantities of fluid are renewed from the chest. Such a condition is to be avoided rather than treated.

Whatever the cause, the chances against resuscitation, if the heart has actually stopped, are very great, especially when the failure is due to over-distension. Even in the ventricular fibrillation due to an electric current, recovery is possible. Cardiac massage through the diaphragm is the sole hope and only in a few thin people can this be done. Fortunately a certain number of cases, as indicated above, occur on the operating table and the surgeon may obtain rapid access to the lower aspect of the diaphragm. The heart is gently and rhythmically compressed. The assistance thus given to the myocardium may be sufficient to tide over the emergency. In such cases it is greatly to the disadvantage of the patient that he should be lying down, as this position tends to maintain the already high venous pressure, and to throw unnecessary strain on the heart.

Failure of Aortic Pressure.—The pressure in the aorta is dependent on three variables : the peripheral resistance, the blood volume, and the heart. A fall of aortic pressure, then, is both a cause and a result of cardiac failure. Where it is a result, nothing can be done except cardiac massage, since any attempt to raise the aortic pressure by pressure on the abdomen also raises the venous pressure, and throws a further strain on the heart. A primary failure in peripheral resistance is never sufficient to cause immediate death, but in conditions such as spinal shock it may indirectly hasten a fatal termination.

A sudden diminution of aortic pressure from hæmorrhage is an instance where physiological knowledge is of real value. The hæmorrhage has to be stopped and the blood volume restored. The application of a tourniquet, or efficient uterine massage in post-partum hæmorrhage, has saved the life of many a patient. One of the most insidious forms of blood loss is that in which the

individual bleeds, as it were, into his own vessels, which become excessively dilated. This may occur in severe accidents or after surgical operations.

In man the blood loss is evident from the pallor of the skin, which is brought about in an attempt to make up for the loss. In restoring blood volume we have to consider the chemistry of the blood (this is dealt with in detail on page 179), but in an emergency elaborate detail is impossible. The accurate adjustment of the saline content to 0·9 per cent sodium chloride is a secondary consideration, and the heat may be judged by the sense of touch. All that is required is a warm aseptic or mildly antiseptic saline, boiled sea water or boiled salt solution (half a teaspoonful of common salt to the pint) will fulfil immediate needs. With more time available gum saline or blood transfusion must be considered, and the practising clinician is well advised to have always available a litre of sterile salt solution. The physiology and dangers of the administration of gum saline and blood transfusion have been already considered.

Hæmorrhage, however, may be relative rather than actual, that is, the actual volume of the blood is not reduced but the capacity of the vascular system is enlarged. Such a condition occurs in secondary wound shock (in which there may be enormous dilatation of capillaries), in childbirth, and in the sudden withdrawal of fluid from the abdomen as in ascites, after which blood may accumulate in the splanchnic area, which, it is calculated, is capable of holding a third of the total blood in the body. In the latter instances the firm application of an abdominal binder is all that is required, but in secondary wound shock steps have also to be taken to make up the blood volume.

The use of drugs in circulatory collapse must be considered. The purified alkaloids of the digitalis series are of immense value, and still better is adrenaline which, even more than the others, constricts blood-vessels and assists in maintaining aortic pressure. Experimentally it is found to be of great value and, though its action is short-lived, it is often sufficient to bridge over a critical stage. By subcutaneous administration its action, however, is not so temporary as intravenous injection would lead one to expect. Many of the disappointments in relation to this drug when given intravenously are due to overdose. The drug is primarily a sympathetic stimulant, but, if the stimulus is too severe, a period of exhaustion follows ; in fact, large doses of adrenaline have been used to produce experimental shock and

cardiac failure. The writer feels it is a duty to warn the reader against the indiscriminate use of commercial pituitary extracts in cases of circulatory collapse. There is now ample evidence that many preparations cannot be relied upon to raise aortic pressure as they often contain depressor substances ; indeed, not infrequently in midwifery practice they have been found to lower it. The introduction of standards by the Medical Research Council will remedy this defect.

In acute cases of cardiac failure the apprehension of the patient requires as much treatment as his actual condition. He feels that the end is near, and under the influence of such extreme emotion the heart beats with great rapidity. This causes exhaustion, but the heart output is not necessarily increased. The wonderful effects of small doses of morphine accompanied by a cardiac stimulant or tonic administered hypodermically are now well known, and in some hospitals the injection of these is a routine when acute cardiac cases are admitted.

There can be little doubt that bleeding by lowering venous pressure gives an enormous relief to the heart even if it is scarcely sufficient to lower the arterial pressure (see page 135). Alcohol has also a great reputation in such cases. That it gives a certain amount of courage by paralysing higher cerebral centres responsible for fear is no doubt a factor, but it may be shown experimentally that it causes a profound fall of venous pressure. It seems certain that this little known fact has been overlooked by those who avoid its use on the ground that it has not been shown to be a stimulant of the isolated heart. Here indeed is an interesting example of clinical observation proving itself superior to inadequate experimental data.

When, however, the cardiac failure is secondary to toxæmia the venous pressure may not be high but low, as in shock from capillary dilatation at the periphery. The treatment of the shock may become as important as that of the cardiac condition. This is often true in pneumonia (Ritchie).

Failure of Respiration.—The supply of oxygen to the heart is dependent on the large variety of factors which are dealt with in the chapter on " Breathing." The sudden failure of respiration is commonly related only to a few of these factors, and on the immediate action of the clinician depends the life of the patient. The failure may be related to (1) the respiratory centre, (2) the respiratory passages and chest, but only those sources of failure in which real benefit can be obtained are dealt with here.

Sudden failure of the respiratory centre is commonly the result of the action of anæsthetics, or drugs such as opium and alcohol. In these cases the centre may rapidly lose its sensitiveness, and cease to act, the result being seen in the typical signs of carbon dioxide accumulation and oxygen want. Respiration must then be continued by artificial means, and this may be necessary for some hours if the heart continues to beat. If in narcotic poisoning consciousness is not quite lost, the carbon dioxide from muscular activity is the best respiratory stimulant.

Asphyxia is the cause of death in strychnine poisoning, and in tetanus, where the chest wall is thrown out of action. In some cases asphyxia may be due to actual obstruction of the respiratory passages, *e.g.*, a foreign body or water in the larynx. In asphyxia three stages are seen: in the first stage carbon dioxide begins to accumulate. Respirations are deep and laboured, ringing in the ears is complained of, the face is blue from venous engorgement and bears an anxious expression. There results a general rise of pressure in the vascular system from the action of the carbon dioxide on the blood-vessels and the stimulation of the secretion of adrenaline. Consciousness is soon lost, as the result of diminished oxygen supply to the brain, and in this, the second stage, the conditions are exaggerated. The sphincters relax, and there are convulsions from the action of diminished oxygen on the nerve cells. In the third stage there is general enfeeblement of respirations which become irregular and gasping. Convulsions become less, and more stretching in nature. Finally respirations cease, usually five minutes after the obstruction, but the heart continues to beat for a few more minutes and during these minutes there is still time for remedial action.

In cases of foreign bodies in the glottis, if these cannot be removed, immediate tracheotomy is necessary. In the case of hanging, the body must be cut down at once, and in drowning, special care must be taken to see whether any obstructing substance has been taken into the mouth during respiratory effort.

In **artificial respiration** an attempt is made to get the maximum amount of air in and out of the chest. The prone pressure method of Schafer is most effective. The patient is placed face downwards with a coat under his chest. This procedure is of advantage in cases of drowning as it facilitates the exit of water from the respiratory passages. The operator kneels beside the patient and places his hands on the lower ribs. Then by alternately lowering

and raising his body he throws his weight on the loins and thus alternately compresses and allows to expand the abdomen and, indirectly, the diaphragm. This procedure can be kept up by one person for hours. Compression of the chest is not attempted.

When a man is asphyxiated by drowning, laryngeal spasm may sometimes prevent the entrance of water into the lungs, and resuscitation has in these cases been known after very long periods of immersion. It is to be remembered that, although the person may fall into water, death may not be necessarily due to asphyxia, but to shock, concussion, heart failure, apoplexy, exhaustion, or injuries. It is not always possible to turn the patient into a prone position (as when on an operating table), and Sylvester's method is then used. Here the ribs are raised by traction on the pectoral muscles by alternately raising the arms of the patient from the sides and compressing them against the chest. The method may be supplemented by pressure on the abdomen (Howard), but the danger of injuring the engorged liver must not be forgotten.

There are also certain adjuvants of value. One of the most useful is rhythmical traction of the tongue, and in anæsthesia this may be sufficient to stimulate an indolent respiratory centre. Forceps which pierce the tongue cause much less subsequent pain than those which crush. Friction of the face and ribs, and smelling salts, are used to stimulate the respiratory centre, but carbon dioxide accumulated in the patient's blood is actually the best possible stimulant. The expired air of the operator blown into the patient's mouth may also be used to stimulate.

It has been pointed out by Yandell Henderson that failure of respiration during anæsthesia is not infrequently due to acapnia, *i.e.*, a washing-out of the carbon dioxide as a result of the over-ventilation which results from sensory stimulation. There is then a possibility that the heart may fail from lack of oxygen before sufficient carbon dioxide has accumulated to bring about stimulation of the respiratory centre, the sensitivity of which is reduced by the anæsthetic. To counteract this, carbon dioxide is now frequently administered with the anæsthetic. Prevention, however, is better than cure, and, since experimentally such acapnia can readily be prevented by causing the animal to rebreathe its own expired air, there seems to be room for the introduction of a method by which patients who are tending to over-ventilate can be easily made to do likewise.

Body Heat.—Loss of heat to an extent which will endanger life is not such a rare occurrence as might be supposed. The death of a healthy man in this way is certainly rare and occurs only after exposure to severe cold. Even in this country, however, it is estimated that 130 people die annually from exposure. Blood heat is as dependent on heat production as on heat loss (see page 413). Should heat production be much reduced, from malnutrition or exhaustion, the liability to a severe fall in blood heat may be brought about by comparatively mild degrees of exposure. This liability is still further increased if the individual is under the influence of a drug such as alcohol, which not only causes unconsciousness but also increases heat loss from dilatation of the skin vessels. The effect is to create a vicious circle, for a fall in body temperature itself diminishes metabolism and still further reduces heat. Death from exposure is therefore most likely to occur in the very old or young or those suffering from exhausted conditions whose heat production is low. For the same reason patients under an anæsthetic, whose heat-regulating centres are thrown out of order, are particularly liable to suffer from excessive heat loss. In all such cases the principle of treatment is obvious, but it is necessary to warn against the danger of burning in bed by the injudicious use of artificial heat.

In those suffering from exhaustion special care has to be taken in feeding, as, in those who have been starved, the power of digestion, like all other functions, is much reduced. Partially digested and easily absorbed foods are indicated so long as there is marked enfeeblement.

Danger of overheating is for the most part confined to hot countries. For those not acclimatized an air temperature of 100° F. in the shade may be excessive, while a very warm humid atmosphere prevents the normal loss of heat from the skin. In toxæmic and febrile conditions, when the heat-regulating mechanisms are thrown out of order, and sweating fails, there is also a tendency to overheating of the body. The symptoms of excessive temperature are chiefly referable to the nervous system, and death may ensue from failure of the respiratory centre. Emergency treatment is obviously the reduction of body temperature by cold applications, *e.g.*, by wetting and fanning the body. Such applications must be stopped when the temperature has been reduced to 100° F., since it will then continue to fall for a short period.

Bichat, in 1798, described what he called the Tripod of Life : the heart, lungs, and brain. The violent deaths in his time indicated that these organs were the most important. Increased physiological knowledge shows us the principles on which life is maintained, and, when life is in danger, indicates the lines along which our efforts to save it should be directed.

CHAPTER XLVIII

THE PSYCHOLOGICAL PRODUCTION OF SYMPTOMS

By Dr. N. D. Hardcastle

The symptomatology of psychological medicine is necessarily somewhat speculative because its ætiology is still the subject of debate between various schools of thought, and its morbid anatomy is conspicuous by its absence.

In spite of the somewhat nebulous state in which psychological medicine finds itself, it is, however, becoming definitely established. The Great War did much to stimulate the researches into psychological medicine and to consolidate the findings, and certainly psychotherapy, in its widest sense, proved to be a technique of profound curative value in dealing with those cases suffering from psychological traumata.

The Theory of Modern Psychology.—To understand the formation and structure of symptoms relative to psychological medicine it is essential to grasp the fundamental principles of the psychic content of the mind, quite apart from its neurological foundation and evolution since the birth of the individual.

The psychic content of the normal mind is similar to that of the sick person, the difference being only in degree, but in order to understand why a patient becomes ill psychologically we must consider the subject in a wide sense. In biology the activities of plants and animals are designed towards the preservation of the individual and the species and towards peace and harmony in a physical world. The activities of man are fundamentally directed towards the same end, his goal being peace of mind and harmony with his environment, any interruption of this relationship will result in the psychological symptom of anxiety in just the same way as a lack of adjustment between the physical body and the physical world will result in a physical symptom. As Hilton pointed out many years ago, pain is a danger signal which demands rest, and recovery will be the natural sequence.

In the most " normal " individual there are instances of what can be called psychopathic trends. He is not infallible, he may forget to keep an appointment which would be unpleasant to him,

by a slip of the tongue he may betray his true feeling when trying to be polite to an influential bore. These are superficial examples of what may be considered to be the dual working of the mind; the mind is not an unified entity and the more a person introspects (considers his own actions) the more he will find conflicting trains of thought, and the more he will see that his little slips are directed towards his own unreasoned infantile desire for tranquillity even if they must of necessity miscarry in the adult world.

A simple example of this split mentality can be cited from the shell-shock cases resulting from the war. It was obvious to the casual observer that these patients reacted with all the feeling which was normal to the war situation when they were confronted with quite harmless domestic ones in which there was a common factor, such as noise of traffic, or the backfire of a motor car; they either became anxious or reacted as though taking cover from an exploding shell. It would seem as though the anxiety or shock experienced during the war, when the individual was faced with an utterly intolerable situation, one which to him meant immediate extinction, *i.e.*, inhibition of the free play of the instinctual impulse of self-preservation was, unknown to the patient, in some way still active. He was unable to incorporate the experience into his psyche, and the experience, instead of being integrated into his mental make-up, was extruded or encapsulated as a foreign body. But as it was an actual experience which had happened to him, and was actually a part of his mental experience, though not recognized as such because of repression, he continually carried it about with him as something yet to be experienced.

The two essential features which characterize this condition are the patient's refusal to think about the war incidents together with his constant preoccupation with trivial affairs, as if to keep his mind otherwise occupied, and the anxiety which is elicited when the exciting causes are brought into consciousness, as when he is asked to talk about the war or has war dreams in his sleep.

It is thus clear that this act of forgetting, or repression, is one way to safeguard the individual's feeling of well-being, his peace of mind.

Now in this concept of a traumatic experience being repressed from consciousness and yet ever striving for recognition, as evinced by the fact that the shell-shocked soldier had war dreams and continually reacted as though the traumatic situation was

yet to be experienced rather than being a thing of the past, the mind of a child becomes evident.

The mind of the child may be considered from two viewpoints, (*a*) its neurological foundation, and (*b*) its mental functioning, *i.e.*, thinking, feeling, etc.

From what is known of the development of the cortex and association fibres, it is safe to assume that at birth the highest functioning neurological level corresponds to the paleopallium, and is predominantly thalamic in character. The process of the myelinization of the four primary sensori-motor fields of the cortex —olfactory, visual, acoustic and sensory—both afferent and efferent, commences about the time of birth. This process then spreads to the series of intermediate areas whose projection fibres serve to connect the primary cortical areas with the thalamus and the pontine nuclei.

The last areas to become myelinated are those made up almost entirely of association neurons whose axons cross in the corpus callosum, and those that extend to near and distant parts of the same hemisphere ; in all these latter myelinization is not completed until puberty.

In conformity with this development the highest functioning neurological level is continually shifting until the neopallium, as represented by the cortex, assumes complete control.

Two widely different examples may be quoted to indicate this developing function of the neopallium, and to support the theory, based upon the anatomical findings, that the type of mental functioning changes during the growth of the individual.

(1) Play of young animals and children.

(2) Psychological testing for the estimation of intelligence.

(1) It is generally accepted that play is a preparatory activity, of transient character, destined to help the animal or human acquire the total requirements necessary for him to survive in his world (environment). According to the increasing complexity of the brain, so this period of play is prolonged. The kitten and the puppy manifest activities which, though apparently purposeless, can be taken as preparatory to fitting them for the adult requirements. The hen, however, which never develops much plastic intelligence, but which exhibits rather stereotyped instinctive behaviour, does not play when young.

The human being when compared with the animals has quite a disproportionate length and complexity of play, but, on the other

hand, this length and complexity are proportionate with the complexity and relatively slow development of his cortex.

(2) The basis of intelligence testing is to sample the capacity of the individual to solve standardized problems, which are so devised that the solution of them does not necessarily depend upon acquired scholastic or cultural knowledge, but upon the abilities of memory, comprehension and power to integrate. These tests have been worked out empirically and graded from infancy up to eighteen years, after the age of eighteen no appreciable further development of mental capacity has been noted, but, of course, the individual continues to acquire knowledge and experience, but no further capacity, although he may benefit by practice.

Other examples could easily be cited, such as the elaboration of speech, which has been studied in detail by Head in relation to aphasia.

The Psychological Superstructure.—It is upon a nascent cerebral structure that the child receives his first impressions of the world and with it makes his adaptations to the new surroundings, an environment in which everything is new and for which he has no past experience to help, guide and comfort him. He has to orient himself to time and space, delineate his own boundaries and differentiate his mental attributes and volition from those of his mother or nurse.

It is difficult to conceive, even in the vaguest terms, what form the mental processes take in the infant mind. A great deal has been written on the subject which is still the centre of much controversy.

It may be assumed that the infant is endowed with certain instincts—innate reaction patterns—he will seek to be comfortable which entails being fed, kept warm, etc., and he will react to situations of discomfort, such as hunger and cold. His incomplete differentiation of the self from the non-self will prevent him from localizing these " pains " as within himself, and he will project, or externalize them, on to his environment.

Owing to his lack of past experience and the strong thalamic influence in the paleopallium, he must have immediate relief of tension, and he is unable to withstand any prolonged frustration, for it is only by building up from his past experience—the formation of a mental background—that he can look forward to the future and from this he can anticipate and reassure himself that the " pain," the discomfort of hunger, will be alleviated. Should

the baby be allowed to remain hungry or in a condition causing profound discomfort, he will first of all manifest annoyance developing into rage, which will show itself by lusty howling; then, if nothing occurs, fear will develop, which can be regarded as the emotion which results from thwarting of the instinct of self-preservation, and hunger can be definitely interpreted as a threat to his existence. Accordingly there are three distinct processes going on in the child's mind; he is hungry and wants food, he is angry and wants to howl, and he is afraid and wants to cry. The emotional tone and the natural channel of discharge of each of these is different. He can only deal with one situation at a time and therefore he has to repress those which are not relevant, and in this early stage of development **repression** can be regarded as an expelling or thrusting into the outside world the painful thing which is within him.

This is the same mechanism as was described when the soldier encountered an unutterably intolerable situation, which is dealt with in the same way, namely, by repression.

The concept can be formulated that the child from the very earliest divides his "world" into good things and bad things. The good he incorporates—takes into himself—and the bad things he expels. The mother's breast is the first thing that he perceives as the source of pleasure and that which dispels discomfort (*i.e.*, hunger), and gradually he learns to recognize that the breast is part of the mother. Then, later, he appreciates the mother as a person, and along with the identification of the individuality of the mother as a separate person apart from himself, he is able to carry this idea on to other people in his environment. His mother in particular he recognizes as his source of comfort and accordingly he resents her leaving him, and out of "being with him" and "not being with him" are built up, in his own primitive way, two images of the mother, the "one who gives comfort" and the "one who gives pain." He then develops in phantasy schemes for binding her to him and for punishing her for not being with him. And again in this way the child is confronted with two incompatible trains of thought, both strongly charged with affective tone, for when the mother is with him he cannot have those savage ideas about her which he evolved when she was away from him, and, in consequence, they are repressed. But ideas are to him real things, and out of the repressed material returns to him the fear that he will be punished, and the more vigorous are his ideas of punishing the mother

for leaving him the more harsh will be the punishment in return, which he dreads.

Weaning and toilet training are two periods in the early life of the child particularly fraught with frustration, where the child finds himself in conflict with the parent. Immediately following these, and out of the desire to keep the mother with him, will develop what is known as the Œdipus situation, where the child identifies himself with the father to possess the mother. In this relationship, it is claimed, the child manifests definite sexual feelings (using the term in a wide sense) towards his mother, which are again frustrated and leave him with a feeling of inadequacy, especially when he compares himself with his father and realizes that he imperils his life when in conflict with his father for his mother. For he feels that his father will retaliate and destroy him for wanting to steal the mother—here may be cited the earliest instance of the sex instinct being in direct opposition to the instinct of self-preservation, consequently the sex instinct is repressed. The child by this time is now able to direct his attention to other things in his environment and occupy himself with them. Each occasion where there has been repression of some painful train of thought—where the child has expelled it from himself—may be regarded as a psychological trauma, the same type of mechanism as was described above when the soldier encountered his utterly intolerable situation. The psychological mechanism of repression is the same in both instances, but, in case of the soldier the repression took place in the adult mind at the cortical level of neurological development, while in the child it may be assumed that the repression takes place at the then highest functioning neurological level which is responsible for consciousness, and which is sub-cortical in the adult. So in the further development of brain structure that psychologically repressed material is subjected to definite organic neurological repression.

Through this dual repression the return of this infantile material to the adult conscious mind in the form in which it was laid down is rendered impossible because the type of thinking characteristic of these two neurological planes is entirely different, and the connecting link between the two, *i.e.*, the transition from the one type of thinking to the other, has never been forged in the process of growth because of the initial psychological repression.

There remains, then, this isolated repressed but dynamic infantile material still demanding its expression or gratification,

totally unrecognizable at the adult level as belonging to the personality and only to be regarded as the residuum of a former existence.

A reaction which is commonly seen is the so-called *inferiority complex*, in which the patient is really suffering from excessive frustration. His reaction shows itself as an excessive timidity and avoidance of difficult situations. In some way, however, the conscious self refuses to acknowledge the inferiority and reacts violently in the opposite direction, producing an abnormal arrogance of manner. The mental attitude of certain emperors of former days is attributed to a reaction against physical disabilities, and girls who in the family have been made to feel their inferiority compared with boys commonly become aggressive spinsters. A superiority complex is really an over-compensated subconscious inferiority on frustration.

In the case of the soldier suffering from shell-shock, it was shown that memories of the actual experience were painful to him, that forgetting was an active process on his part, that the memories, on the other hand, were for ever demanding recognition, for it was obvious that all that was required to liberate the influence of the repressed material was a stimulus similar in form or in some way associated with that which produced the original trauma, and that the symptom of his psychological condition was his anachronistic behaviour, a normal reaction to something in the past but out of keeping with the present.

From this simple "diagrammatic" explanation symptom formation generally may now be discussed together with the other important contributory factors.

Contributory Factors.—As was stated earlier, the activities of man are directed towards peace of mind and harmony with his environment. In order to attain this he must shield his conscious conception of himself from harmful criticism, both by himself and by other people, and must make a compromise between himself and his environment, entailing reasonable and adequate excuses for his inefficiencies in order to avoid this criticism. That frequently used prescription for the "neurotic" patient, a sea voyage or change of air, is based upon a recognition that environmental factors play an important part in ætiology. The simpler the environmental demands, the less adaptation is required. But the average individual has to live in an average world, and the majority of persons manage this without apparent difficulty. What is it, then, in the environment that causes the difficulty

that some people experience? And why should it affect only these few?

The proportion of soldiers who were shell-shocked during the war was small; why did these fall ill and the others not do so? The answer is that there is something in the environment incompatible with the individual, something which is causing him "pain." The general behaviour of the shell-shocked soldier has not so far been discussed, but only his reactions to definite stimuli. He is found to have most of those indefinite symptoms which characterize the "neurotic" patient—headache, a feeling of exhaustion, vague feelings of apprehension, etc.; he complains of forgetfulness, he cannot concentrate, he is unable to sleep, and has many other symptoms. The main features to be commented upon here are exhaustion, forgetfulness, and insomnia. These are manifestations of his activity in maintaining his repression, for other things beside the war memories are repressed, and the patient forgets things generally. He cannot sleep because in sleep he relaxes that control of himself, and he is exhausted because he is expending energy the whole time in the maintenance of repression. As a result of this continual mental activity the patient is the less able to adapt himself to the difficulties which are in his environment, and out of this will arise, as a natural sequence, his irritability and other minor manifestations.

He readily appreciates his lack of efficiency and proceeds to invent plausible reasons to excuse himself; these may be either psychogenic or physiogenic, as described later. Once he has established a symptom, a reasonable excuse, he naturally does everything in his power to keep it and resists all effort directed towards its removal.

To understand why he becomes ill it is necessary to consider his constitutional and developmental history and his early environment from the time of his birth up to puberty, any other contributing factors and the situation which ushered in the illness. This group of considerations is the same as is usually applied to the understanding of the ætiology of physical illness.

The constitutional factor from the standpoint of psychological medicine may be taken as the degree of innate stability of the child against frustration, for upon this will depend his emotional equilibrium and all the physiological activities which are affected by it. As has been previously pointed out, the higher controlling powers of the central nervous system are as yet undeveloped, and in consequence the child as a whole reacts more violently to his

emotions—fear and rage—than does the adult, and in this way a vicious circle may be established at a very early age, in which emotional disequilibrium and its physiological concomitants act and react upon one another. The other important constitutional factor, described by Freud, is the degree of excitability of the primary erotogenic zones in the child, at birth and during the few succeeding years. As is well known, some babies at birth react vigorously, breathe without encouragement and take the breast well, while others seem to show, in spite of an otherwise quite normal birth, a disinclination for any independent activity, the initial breathing may be difficult, and they will not take the breast.

The reactions of babies to feeding differ, some will be satisfied and sleep, while others seem to demand greater satisfaction in spite of an adequate supply of milk.

Vomiting in the absence of any organic factor, such as pyloric stenosis or improper feeding, may be another indication of instability.

The bowel activities are not the same in all babies, some will be constipated, others will have loose motions despite all variations in feeding. And following on from this the wide variations in the ease with which some babies like pet animals can be toilet-trained may be noted, some seem to acquire the habit of cleanliness early and without difficulty, while others may be the despair of their mothers.

Infantile masturbation is another activity showing the widest variations. Many babies may never manifest this activity, while some may begin it in the first few months of life; the period during which it may last varies, and so does its frequency.

The foregoing may be taken as a rough outline of some constitutional factors found in the child. These may be inherited, for the neurotic patient often has a neurotic family history.

With this concept of the constitutional background and its wide variations, the concept of infantile repression described above and the rough "diagrammatic" conception of symptom formation in the shell-shocked soldier, the whole of early childhood development may be reconsidered in relation to susceptibility for falling ill later in life.

The child who is active at birth feeds easily, is satisfied, and falls asleep, does not suffer from frustration. He also induces in his mother a feeling of confidence, and she, in turn, is able to deal adequately with him. But, on the other hand, if for any reason,

either within the child or the mother, the feeding is not successful, or if the child vomits persistently, he fails to attain adequate gratification. He experiences hunger and discomfort. Crying, rage, and a feeling of being baffled lead to frustration, as previously described. The state of the infant has reactions on the mother, who becomes anxious about the child and, through this anxiety, less capable of dealing with him. The child, in his turn, is sensible of the mother's anxiety and reacts to it accordingly by the acquisition of anxiety on his part in relation to his own well-being. All these things painful to him can only be dealt with by repression, as he has no other means available. The child in this way will soon learn to dominate the mother by his cries, and she, in her anxiety, will acquiesce. Thus at a very early age definite reaction patterns are laid down which will be repeated by both child and mother all through childhood.

The handling of toilet training is another important phase in the mother-child relationship. This may be the first occasion when the mother definitely attempts to impose her own will upon the child. Should the child have suffered from frustration, possibly in association with feeding or weaning, he may violently resent her interference with his own freedom and the gratification which he obtains from the act of defæcation. Among the least harmful of the results of poor handling of such a child is an undue sense of shame and impropriety of the whole function of elimination. Constant wetting and soiling may be a method employed to obtain the mother's attention; this occurs specially in babies where there is a feeling of insecurity.

The theory has been advanced that infantile masturbation is a compensatory gratification especially where the normal oral gratification, in association with suckling, is insufficient, and that after the act the child will fall peacefully to sleep. Thumb sucking in children would come under this category of a compensatory gratification. Early masturbation usually causes the mother grave anxiety and her one desire is to break the child of it. Should the habit be dealt with severely and the child punished, and the idea of wrong-doing be harshly imposed, then there will be again that so frequently repeated sequence of denying the child—frustration—leading to anger and feelings of hate towards the mother, then repression and projection or externalization of the act which initiated this sequence.

It should be clear from this very brief and sketchy outline of the child's life during the first year or eighteen months that he

has acquired definite reaction patterns and accumulated a considerable amount of repressed material, and, unless any marked changes should occur in life from this period up to the beginning of puberty, it is certain that his relationship with his parents will not change, and, therefore, the patterns and repressions will continue to be laid down in the same form and reinforced by each new addition.

Under the heading of other contributing factors may be classified such things as happen to the child himself, illnesses and accidents which lessen his own feeling of self-assurance and increase his parents' anxiety about him. Also things outside himself, but which directly affect him, such as the birth or death of a brother or sister, or the loss of a parent, greatly affect him in his relationship with his parents. Again under this heading can be included any debilitating physical illness arising at the time that he falls *psychologically* sick, provided that there is an adequate external situation, otherwise the two may merge and becomes that external exciting cause situation which ushers in the illness.

The individual in the process of growing up learns to assess his own capacity, both physical and mental, in a vague and indefinite way, and he tends to keep within what he knows to be the limits of safety. In the same way that an experienced driver knows the capacity of his car, power of acceleration, efficiency of braking, optimum running speed, etc., he is aware that if he overstrains the mechanism, something may happen. But, as has been shown, the limits of safety are narrower for some individuals than for others, and some environmental factors may present insuperable difficulties. And here is the reason why the soldier fell ill with shell-shock. Before the war he was able to make an adequate adaptation to a simpler type of environment, but while in the army he had to adjust himself to discipline, grave dangers, etc., and the elasticity of his power to adapt was strained beyond the limits of his definite acquired reaction patterns of childhood. The feeling of security which he had constructed for himself in more recent years upon the infantile pattern of insecurity (fear of frustration, etc.), was broken down because the disturbing factors in the new environment had the same value for him then as analogous factors had had during infancy. The new factors reinforced the early repressed material, and brought to life again the emotional content of the long forgotten phantasies concerning the wild and savage punishment he had desired for his parents and the fears which he had for himself. In this way repression

was strained to its limits and the individual succumbed to anxiety and reverted to the former infantile type of reaction, namely, repression of the then present-day situation leading, as often was the case, to unconsciousness or complete loss of memory, and there seemed to be an inverse ratio between the loss of memory and anxiety. Both, however, were for him a symptom, which was of profound value for it excused him to himself and also prevented him from being returned to the front line.

The treatment of individual psychological symptoms is far beyond the scope of this chapter, and their structure can only be considered on the broadest principles. Anxiety, as has been pointed out, is the essential foundation, and the *rôle* of the symptom is always to mitigate it.

Symptoms with a Physiological Background.—Physical symptoms may arise as the direct outcome of anxiety by its action through the autonomic nervous system. The evidence is very complete that fear and anger cause increased sympathetic and probably adrenal activity, resulting in increase of blood pressure, of blood sugar, and of coagulability of the blood, dilatation of the pupils, and diminution of splanchnic activity. All this activity is a normal and natural response in the animal to a situation which demands activity—fight or flight—and after the situation has passed, the condition of the animal returns to normal. But, if there is a condition of persistent anxiety, then this natural transient response is apt to become a chronic state out of which arise disturbances of the alimentary function, indigestion and all that follows in its wake, of the circulation, tachycardia, arrhythmia and hypertension, and also breathlessness, tremors and sweating.

All these symptoms may be regarded as the direct outcome of sympathetic overstimulation. In addition there will be consequent exhaustion which aggravates the condition. Exhaustion from disease, *e.g.*, influenza, has a similar aggravating effect.

The group of symptoms above described in regard to the circulation are well known as the Effort Syndrome, and are particularly gratifying to the patient because they are far removed from any psychological implication, and, having a definite physical basis, they can be used without any fear of repudiation, shielding the patient from his own inadequacy and the rigours of his environmental demands.

Symptoms with an associated Organic Lesion.—The concept that has been so far formulated with regard to the structure of symp-

toms can now be applied to the wider understanding of symptoms generally found in " neurotic " patients. For example, with regard to pain with no organic cause, there may have been at one time a definite organic lesion causing pain. The original cause of the pain may have now completely cleared up and yet the pain persists, usually because certain movements have become associated with pain in the past. This pain has been called by various observers different names, such as habit pain, memory pain, conditioned pain, etc., but in spite of whatever it is called, it is for the patient a very real and definite pain which suggests organic disease and death. To treat the pain as a pain and nothing else, will be of no avail. It is essential to regard it in the light of a psychological symptom and to investigate the mental attitude of the patient and his environment, for the pain may be a convenient excuse for being unable to do something which for one reason or another he does not wish to do. It may provide him with an excuse to avoid attempts at doing something of which he is afraid lest he should fail or after he has failed being an invalid may appeal to him, because it excites sympathy, etc. There is also the fact that he may exact service from some of his relations to an extent which may amount to revenge. The advantages of being ill can be extended to an almost unlimited extent.

What the meaning of the pain was to the patient when he first had it must be considered, and also what his emotional reaction to it was. What value had it for him in terms of the past ? What infantile reaction pattern or instinctive gratification did it supply or fulfil ?

The onset of pain may have been associated with some very pleasurable or gratifying experience, one which the patient may continually yearn for, and the pain then may have for him a pleasurable feeling tone.

Conversely, the onset may have been traumatic, as in " shell-shock " railway-spine, etc. Where there was very violent emotional disturbance, laden with fear and anxiety—conditions which have been previously described—and pain is left as a symptom.

The pain in either case must still have a deeper significance, and may represent for the patient a form of punishment which he feels is due to him, this feeling proceeding from forgotten phantasies of violence towards those he loved. In the traumatic cases where there is a question of financial compensation, the desire for compensation may be regarded at the infantile level as a reassur-

ance of the parental love which was jeopardized by the phantasy of violence, and this would partly account for the speedy recovery of these patients after settlement. Many physicians, however, will regard the question of compensation as having a cruder and simpler, if less laudable explanation than that just outlined.

What has been said of pain may apply to any other symptom. The sight of an artificial rose may provoke an asthmatic attack in a patient sensitive to roses, the mere going on a boat may cause sea-sickness in a sensitive person, etc., etc.

Even a dog which has been several times injected with apomorphia may vomit when it sees a syringe.

Symptoms with a Psychological Significance.—Physical symptoms may occur through the intervention of either the central or autonomic nervous systems and have for the patient a definite psychic meaning, though this is not consciously recognized. The simplest examples can again be taken from the war cases. The most significant of these were those men who developed a very accentuated stooping gait, the back being very nearly horizontal with a compensatory extension of the neck. It is quite clear that this would be a safe gait when walking in a shallow trench which was being raked by machine-gun fire, and yet it would be disabling if the attitude were permanent, and certainly it did remain so for some years after the war. In this example the posture assumed fulfilled the two *rôles*. It was the agent by which the man was able to report sick and be removed from danger, and at the same time it was the natural reaction to the self-preservation instinct ; in so far as the situation allowed, the instinct was being gratified. Anxiety was thus reduced to a minimum. The man was quite unaware of the significance of his gait, repression having removed from his consciousness the memory of the circumstances under which the gait was assumed. The next interesting point to note in connection with this condition is that while the stooping attitude was allowed to remain, anxiety was at a minimum, but any attempt to get the patient to walk upright aroused extreme anxiety which diminished as soon as he assumed the old posture. This would agree with that which has already been discussed, that the symptom is a normal or compromise reaction to a past event, but carried over to the present in spite of the fact that the original environmental cause has ceased to exist.

There is an apparent similarity between the war psychoneuroses quoted and Pavlov's conditioned reflexes. In his investigations Pavlov chose the reflex secretion of saliva as his

subject of study because it is powerful, constant, and readily measurable ; the amount of saliva secreted was used as an indicator of what Pavlov calls the alimentary reflex. The alimentary reflex can be regarded as one aspect of the instinct of self-preservation, for it operates both in eating and in dispelling a noxious substance from the mouth. Any stimulus can be conditioned to one or other of these reflexes, provided that it is not in itself a threat to the animal's life.

The common factor, then, is the feeling tone associated with inhibition of the free play of the instinct of self-preservation in the war cases, and gratification or inhibition in the one or other of the two phases of the conditioned reflex. One of the difficulties in the way, however, of utilizing the concept of " conditioned reflex " in relation to human psychopathology is the unknown quality of the dog's past experiences, the animal's innate variations and its consequent uncertain temperament.

Disorders of the alimentary canal, such as hysterical vomiting, diarrhœa, constipation and soiling in children, can be regarded in the same way as the previous examples. In the face of environmental difficulty the patient regresses to an infantile mode of reaction, which, at a former time, had a specific value. In describing the early development of the child it was shown how he tried to incorporate the good things and cast out the bad. Vomiting and diarrhœa may be looked upon as the infantile type of reaction in the child in getting rid of something troublesome in the environment, or merely in attracting the mother's attention to him. The cases where a child deliberately soils himself immediately after the mother has changed him would suggest that he is employing this device to punish her. Constipation can be regarded as the effect of too severe a toilet training ; here there is established in the child's mind a definite fear of passing his motion, together with other infantile conceptions of the value of fæces, that he is losing something of value to himself.

Phobias, such as fear of closed spaces or of animals or even fear of illness, and obsessions must be mentioned. The mechanism of their causation follows the general principles.

In the case of phobias, the " thing " feared is either directly, or indirectly through the interplay of symbolism, linked up with some trauma of childhood, and every time the patient encounters it, the old emotion will be reactivated. For example, the fear of illness may depend upon the early recognition by the child of the mother's anxiety about its health, as previously described.

The obsessions are slightly different from the preceding group. They are of a reassuring character, the thing has to be done or the thought has to be repeated a certain number of times ; this mechanism is a definite regression to the animistic phase of development of the child, and it is carried out in order that some harm may not befall him, the harm being a symbol of a former harmful wish of his own directed against somebody else and then by projection returned to him.

The choice of a particular symptom may depend on a large variety of circumstances. It may be suggested to the patient by the illness of a friend, by a trivial sensation, by reading about the condition, etc., etc., or the symptom may, according to some, be symbolic of the condition causing it, *e.g.*, backache signifies oppression.

A few other examples may be briefly reviewed. The case of a man suffering from impotence may be examined. First of all there have to be considered his present-day attitude towards the act, his feeling towards the other person, and his fears, anxieties, etc., at the present-day level about the consequences. In addition to this system of ideas, the early infantile pattern is significant. This depends on early conflict over infantile masturbation, etc., with severe parental intervention, later conflict over the solution of the Œdipus situation with formation of phantasies portraying dire punishment by the father, and possibly, punishment for the later masturbation of childhood, or sex play with a small companion of either sex. Such a sequence as this, where the instincts of self-preservation and sex were in direct opposition, would lay down a pattern in the child's mind that sex actually was a thing to be avoided. (The memory, however, of the antecedents is, as in all the former examples, completely repressed.) In this example it is the avoidance of the activity of one instinct that allows free play for that of another, and this opens up the question of infantile frustration and the extent to which the free play of the instinct of self-preservation had been inhibited in the child at the time when he found these two instincts in opposition, and how this earlier repressed material had turned the balance and reinforced the instinct of self-preservation at the expense of the sex instinct.

Frigidity in the woman is frequently found to follow the same sequence of events ; the taboo of all things sexual in early childhood is often the crucial point in her psychosexual development.

Character can hardly be regarded as anything pathological, and

yet in dealing with psychopathology it may be given a place, especially in view of the statement made early in the chapter that the mental processes of the sick person only differ in degree from those of the apparently normal person. The character of a person is shown in his reaction to his environment, as has been previously pointed out this reaction represents the predominant feature of the sum total of his reaction patterns since early childhood. It represents the way in which he has been accustomed to meet difficulties, and, if carefully studied, a prognosis could be made as to how he would meet future difficulties, and to what extent he would be able to deal with them.

It is difficult to go into the question of why one patient develops one type of symptom and another quite a different one in view of the theory which has just been outlined, namely, that the symptom in all cases represents a compromise between infantile gratification and adult consciousness. Several factors have to be considered here. First of all the age at which the initial heaping up of frustration occurred and the extent of the infant's feeling of confidence, or the extent to which he had a rapport with his mother and those about him, and secondly, the attitude of his conscious self towards himself as a whole (it is interesting to note here that in the war there was a higher percentage of conversion hysteria among the men than among the officers, while the officers, on the other hand, suffered more from anxiety), and thirdly, the interplay between the environment and the sum total of the individual's responses.

This account of symptom formation can only be looked upon as the briefest possible outline of a most complex subject. It is based upon the modern dynamic conception of psychopathology.

Psychological Effects on the Symptoms of Organic Disease.—Nor is the effect of psychological states limited to the positive side of symptom production ; sometimes symptoms are caused to disappear. Even when a serious pathological condition is present the symptoms and even the signs may vary from day to day ; a change of doctor or of treatment may affect alleviation even when an incurable condition is present. It is well known that the general state of the patient may be much influenced by the visit of a friend, nurse or doctor.

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