A British Medical Association Lecture ON MINOR ENDOCRINE DISTURBANCES

AND THEIR METABOLIC AND PSYCHICAL
EFFECTS.*

BY

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THE last decade of the nineteenth century added greatly to our knowledge of the physiology of the ductless glands, while in 1902 Bayliss and Starling's discovery of secretin opened out the vista of a chemical control of the body, in which the nervous system merely acted as a trigger, firing off a series of reactions. This conception was elaborated until it bade fair to dethrone the nervous system from its supreme position, although Langley had already provided the antidote by his generalization that the action of adrenaline on any part was the same as that obtained by stimulating the sympathetic. But the far-reaching significance of that generalization was not yet appreciated. "The key to evolution lies in the continuous development of the nervous system," said Gaskell. Or, as Elliot Smith put it: "Man has developed and become the greatest of the primates because of his faithful dependence upon the development of the brain." Considering the struggle the central nervous system has had to obtain control, it is not likely that it would abdicate its suzerainty in favour of the more ancient dynasty of chemotropism.

We ordinarily think of the evolution of the nervous system as peacefully accomplished. A struggle for supremacy between two animals or between two species we recognize. But it would appear that a similar struggle accompanies the integration of the multicellular individual. Many apparently peaceful events in nature prove on closer analysis to involve a concealed struggle. Man is a gregarious animal, but he has not found it an easy task to adjust the desires of the individual to the needs of the community. Philosophers may lament this, theologians may attribute it to original sin, but it should lead the biologist to inquire whether the cells of which he is composed have always found it easy to sink their individuality in that of the organism. The thesis of a hostile symbiosis between the tissues of the body has been skilfully upheld by Morley Roberts. A strong central government is needed to keep order, and no high degree of differentiation is possible in the animal body without the control of a centralized nervous system, which has gradually acquired an increasing predominance. It is not too much to say that this control, though for the benefit of the body as a whole, may be resented by the individual tissues. Wilfred Trotter developed the argument of a hostility between nervous and somatic tissues, which is expressed in the way the former insulates itself.

Without defensive mechanisms no animal can survive in the struggle for existence, and no method of defence remains impenetrable, for, if it were, the species possessing it would multiply to the exclusion of others. As evolution proceeds the apparatus for defence comes under the control of a central nervous system. Some defensive mechanisms, such as nettle cells, never become so controlled, but are replaced by other methods as the nervous system evolves. Certain primitive motor apparatus, such as cilia, also never come under such control, though they persist even in the highest animals. In general terms, a central nervous system enables very rapid reactions to occur, and the need for such rapidity of response will first be experienced in the struggle for existence, when its advantage is at once manifest. G. H. Parker, in his book on *The Elementary Nervous System*, has brought new observations into relationship with previously known facts, and has impressed upon us afresh that a nervous system starts as a series of

independent receptors and effectors in the deeper layers of the skin, the cells of which sink in deeper and deeper, until they become concentrated into a central nervous system. Between the receptor and effector an adjustor mechanism develops, which is the germ of the whole associative apparatus. In the vertebrates these internuncial adjustor neurons compose the chief mass of the central organs. It is not too fanciful to compare the origin of the nervous system to a group of settlers on the coast, who gradually invaded the interior, first singly and then in an organized army, as in the nervous system of vertebrates which arises as a tubular invagination from the surface. Once established the invader assumes control over the indigenous inhabitants, fortifying itself as it goes and maintaining its protectorate by a system of rapid communication throughout the invaded areas. The biological and sociological parallel is remarkably complete.

A wise military occupation utilizes existing institutions, and the lowest level of the nervous system—that is, the autonomic or vegetative portion—enters into a close association with the older chemical methods of control. In my former lectures¹ I have emphasized the fact that the endocrines which represent the specialization of these older chemical methods reveal their antiquity in the way they cling to vestigial structures. Indeed, with the exception of the pineal, these structures would appear to be homologous, and can all be traced to modified nephridia.² In the course of evolution structural alterations have made them useless for their primitive excretory function and they have taken on a new function of internal secretion. Circumstances alter function. Thus we have hand in hand (1) an increasing concentration of the government in the hands of the central nervous system; (2) an increasing concentration of endocrine functions in glands which can no longer discharge their primitive functions.

I have also recalled the fact that the autonomic, vegetative, or visceral nervous system consists of two great divisions—the sympathetic and the parasympathetic or extended vagus. The former is katabolic, converting potential energy into kinetic and facilitating outward manifestations of that energy, while the latter is anabolic, directing energy inwards, where it is stored up. When these two are distributed to the same structure their action is always antagonistic, and when one is stimulated the other is inhibited. Each of these great divisions co-operates with a group of endocrine glands—the sympathetic with the adrenals, thyroid, and pituitary; the parasympathetic with the glands of the digestive organs and annexes. This is explicable since the former group are largely defensive, while the latter are concerned with obtaining energy from the food. The sympathetic is defensive not only against the external foe, but also against internal invasion by bacteria. Fever is a defensive mechanism largely controlled by the sympathetic through the ductless glands associated with it. This explains why (1) patients with endocrine defects stand infections badly; (2) infections may lead to endocrine exhaustion.

The endocrines are important regulators of metabolism. If metabolism is quickened up, hyperglycaemia usually results. This excess of sugar in the blood is normally used either to supply energy to the muscles or as a source of heat for the febrile reaction. Glycosuria does not necessarily result, for there are two factors concerned in this—the amount of sugar in the blood and the threshold of the kidney. In fever this threshold is raised, so that the sugar poured into the blood by the thyroid, pituitary, and adrenals is prevented from escaping before it can be utilized. This is not only the case in fever, but whenever activity of the endocrine glands associated with the sympathetic is exaggerated. Thus in hyperthyroidism I have always found a higher percentage of sugar in the blood even if there is no glycosuria, and it is well known that the basal metabolism—that is, the metabolism per unit surface of the resting, fasting body—is increased.

OBESITY.

If metabolism is slowed down fat and mucinoid material is deposited. Obesity is due to alteration in the balance between anabolism and katabolism. The commonest cause is taking more food or less exercise than the body requires,

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but this is not the whole story. Recent studies in basal metabolism show that it is lower in adults than in children, and in women than in men. It gradually diminishes with each decade. It is profoundly influenced by the endocrine glands, particularly the thyroid. A slowing down of basal metabolism means an increase of weight even though the intake of food is by no means excessive. It was clear during the food rationing of the war that a certain number of stout people did not lose weight as others did.

In *thyroid obesity* the increase in weight is not all due to fat. The heavy folds running from the nose to the cheeks, the bags under the eyes, and the supraclavicular pads are all very characteristic. The condition is really a minor degree of myxoedema, and presents a similar harsh dry skin with a malar flush. The mental lethargy is as marked as the physical.

In *pituitary obesity* the whole face is rounded, with a smooth, soft skin, while the colour is usually fresh or unduly high. I called it the "Dutch doll" type, and then found Fearnside had previously referred to it as the "pudding face." The amount of hair on the face and body is much reduced. Fat is specially deposited on the shoulders, breasts, hips, and thighs, giving the latter a "plus fours" appearance. The skin over the posterior borders of the upper arms and on the legs below the knees is a mottled red. The way this mottling stops abruptly just above the olecranon is very characteristic. These people bruise very easily and there is some polycythaemia. In women there is often amenorrhoea; but that is not the cause of the polycythaemia, as I found it in a typical case in a boy of 16. The mental outlook is often bright, active, and cheerful.

In *Dercum's disease* there are localized deposits of fat which are painful—they are particularly likely to occur on the posterior borders of the arms and the flexor aspects of the thighs. Here the mental condition is usually one of great depression, which is not merely due to the pain of the lumps, although this may be considerable.

In some cases of *pituitary tumour* there is both an insatiable appetite and great sleepiness; the patient awakes to eat, and having eaten falls asleep again. It is not easy to be sure what determines the bright alertness of one group of fat hypopituitarism and the profound somnolence of the other, but I suspect it depends on whether there is increased intracranial pressure or not. The fat boy in *Pickwick*—"Drat that boy, he's asleep again!"—is usually quoted as a classical example. A few years ago a very fat Jew, weighing 20 st., turned up at St. Bartholomew's Hospital at 11 p.m. complaining that he felt very sleepy. Fortunately he had a doctor's card with him, otherwise I cannot help thinking that a fat Jew complaining of sleepiness at 11 o'clock at night might have received more advice than treatment. It was a good thing he was admitted, for he had a syncopal attack soon afterwards. X-ray examination showed enlargement of his pituitary fossa. Under injections of 1/2 c.cm. of pituitrin three times a day he lost 2 st. in ten days and his general condition improved remarkably. Quite recently I advised two daily doses of 1/2 c.cm. in a similar case, with the result that 17½ lb. were lost in twelve days.

Thymic Obesity.—The thymus is an infantile organ; if it persists after it should have vanished we find it is antagonistic to the development of the gonads, and hence indirectly leads to the deposit of fat. The thymic type tends to have rather a long face, with clear skin and good features, marred by the precocious development of a double chin. It constitutes the lymphatic type of the older physicians, or status lymphaticus as we prefer to call it to-day. Such patients are liable to paroxysmal dyspnoea, the so-called thymic asthma, and they respond to infections badly.

Gonadal Obesity.—Recently I saw a girl of 22 who was very stout, and who presented some features of the pituitary and thymic type, and even some signs of thyroid deficiency. I noted that her upper lateral incisors were very small. She was surprised when I guessed that her periods began late. The guess was correct, for they did not start until she was 16½. One or both undeveloped upper lateral incisors are often associated with gonadal deficiency, and, her obesity showing signs of several endocrine glands

being implicated, it appeared to me probable that this was due to some common factor rather than to disease of each of these glands, of which, indeed, there was no other evidence. Now the gonads stimulate the thyroid and pituitary while antagonizing the thymus, so that it seemed to me the probable starting point of the obesity was gonadal deficiency. Indeed, I think that pathological obesity in early life, showing mixed endocrine symptoms, is very often due to delay in gonadal development. It may subside quite rapidly when adolescence is complete. To hark back for a moment to the undeveloped lateral incisors. If you see a girl with more than the usual enlargement of the thyroid at puberty together with this condition of the teeth, you are, in my opinion, justified in regarding the enlargement as probably compensatory and not of evil import. Her periods may establish themselves with difficulty, but the enlargement of the thyroid is likely to subside when this has been done. The process may be hastened by small doses of thyroid extract. Curiously enough, this association between the teeth and gonads appears to be a crossed one. Thus with an undescended right testis it will be the left lateral incisor which is small, twisted, or displaced.

THE ADRENALS.

Having considered some of the effects of the endocrine glands on general metabolism, I will turn to some other results of minor disturbances of these glands, with some reference to the psychological aspects.

It is clearly recognized that the medulla of the adrenals really represents the post-ganglionic element of the sympathetic nervous system, which explains Langley's generalization, to which I have already referred. The chromaffin cell and the sympathetic cell migrated out of the central nervous system together, and the chromaffin elements were originally much more widely distributed. The cortex, on the other hand, represents a group of nephridia, and still arises from the Wolffian body. It is very significant that it has the same origin as the interstitial cells of the gonads. To this we may trace the extraordinary effect that cortical tumours or overgrowth have in producing premature sexual development. In whichever sex they occur they tend to virilism. We shall see that each of the different endocrines has its own tendency to tip the balance towards virilism or feminism. What the advantage may be of this close association of two structures of such widely different origin we cannot say, but the persistence of the association in all animals above the level of fishes suggests that it is of great importance. Apparently, if this association fails to occur in foetal life the brain remains at the fish stage, the neopallium does not develop, and an anencephalic monster results.

Since adrenaline can raise blood pressure and excite glycosuria, it is tempting to assume that these combined symptoms occurring in later life are due to overaction of the adrenal medulla, produced by nervous strain of an emotional sort. But proof of this is lacking. The classical picture of underaction of the adrenal medulla is seen in Addison's disease, and it is possible that adrenal exhaustion may play a part in war neuroses and other functional states characterized by myasthenia, vasomotor instability, and low blood pressure.

I should like to say a few words on the psychological aspect of adrenal disturbances. Fear is really a perversion of a defensive mechanism. It is the intensification of the instinctive process called into activity by danger. But just as we cannot conceive that all the primitive sensations of a lower animal have the affective intensity of pain as we experience it, so we must not regard the emotional response of an animal to danger as having the affect of what we mean by fear. To do so would be to fall into the common error, as Parker says, of interpreting the activities of the simpler animals as though they were miniature human beings. The much scantier associative mechanisms in the nervous system of lower animals precludes such an idea. An imaginative writer, A. C. Benson, says:

"It is strange to note the perpetual instinctive consciousness of danger which besets birds in the open; they must live in a tension of nervous watchfulness which would depress a human

being into melancholia. . . . Do we realize what it must be to live, as even sheltered birds do, in a quiet garden, with the fear of attack and death hanging over them from morning to night?"

The best answer to this anthropomorphic view is that the behaviour of birds gives no suggestion of their being depressed into melancholia. Doubtless when the appropriate motor response is prevented the lower animal can feel both pain and fear; but that all its sensations and emotions are thus coloured is most improbable when we consider the much simpler structure of its nervous system. It might be argued, on the other hand, that as sensations of fear at once arise when the inhibiting mechanism is in abeyance—as in night terrors, in the induction of anaesthesia, or in exhaustion states—fear must be a primitive emotion of great strength and universally present in lower forms of life. But I would urge that it is only in the stage when the associative mechanisms have been evolved, and before these have been controlled by the higher levels, that this is the case; or as Carpenter puts it, "Fear only became a mental stimulus at the time of, or after the evolution of, self-consciousness." The behaviour of savages supports this view. Fear—whether of evil spirits, of magic, of the dark—panic fear dominated primitive man, and whenever our resistance is lowered by disease, by shock, or by psycho conflict, we betray our ancestry. That strange primitive being which lurks in the unconscious mind of us all peeps out. Elaboration of ceremonial and ritual is the first step taken by primitive man to counteract this; all religions pass through the "God-fearing" stage. Then with the higher development of the mind, and the recognition of the reality principle, comes release from such obsessions of fear. In the disintegrative process of disease this higher control fails and phobias develop which cannot be effectually exorcised by the ritual of a compulsion neurosis.

The adrenal medulla from its activating effect on the sympathetic is a fighting gland. And as the adrenal cortex tends to virilism, the owner of a well developed pair of adrenals is pugnacious and masculine in type, with plenty of drive, not to say aggression. If the adrenals are in defect we see a weakening of all these characteristics, with a tendency for the vagus to get the upper hand, which may precipitate such things as asthma. If the adrenals are in excess we find a liability to anxiety neurosis, and to phobias of all kinds. In such an individual the dominant emotion is fear.

THE PITUITARY.

That overaction of the anterior lobe produces acromegaly in adults is well known. It is also generally recognized that some lesion of this lobe plays a large part in the osteitis deformans of later life. Overaction of this lobe in early life when general growth is still possible produces gigantism. Minor degrees of increased action of the anterior lobe results in a tall hairy man, long in tooth and big in jaw, with large broad hands. He often has a good intellect, with an imaginative force which can be controlled and brought to the service of his active brain; he is often musical—in short, a practical visionary. Unfortunately the effect of an overactive anterior lobe is not always so balanced as to produce such a happy result. Thus in the following case the amount of pituitary disturbance was not great, though the effect on character was disastrous.

A young man of 23 was brought to see me who had been very late in learning to walk and talk. He showed me two photographs of himself taken at the age of 4 or 5; one of these looked like a normal child, while the other looked degenerate. By the age of 6½ he had developed the habit of lying. He grew rapidly to the height of 6 ft. 5 in. His palatal arch was very high, and his knuckles were very large. He was a confirmed liar and thief, and was suspected of deliberate and wilful arson.

Gigantism due to overaction of the anterior lobe before the epiphyses are united may be followed by degeneration of the gland. The fossa becoming too small for the gland the patient is apt to develop moral and intellectual inferiority, to suffer from compulsions and obsessions, and to lack inhibitions. As Berman puts it, such individuals are "pathological liars with little or no initiative or conscience. . . . As children they lie and steal, have enuresis, have poor control over themselves and a low learning

capacity." This patient showed all these points. But it is a little difficult to explain why even while the pituitary was actively stimulating growth there was a failure of the moral sense and intellect to develop. In the present state of our knowledge we can only say that there may have been a diversion of the pituitary action in one direction at the expense of others. Dr. Crichton Miller has suggested to me that it is rather due to failure on the part of other endocrine glands. In connexion with Berman's view that the posterior lobe is concerned with the affections, it is interesting to note that this youth had never shown the slightest affection for anyone. It had been suggested that he should be certified as of unsound mind. On that I wrote to his doctor as follows—and it happened to be just a fortnight before Ronald True's case:

"We are up against the difficulty which always arises between the medical and legal view of responsibility. I think that in spite of his plausible manner with strangers he has a criminal type of countenance; and I should never be surprised at his doing something to justify that harsh saying. But the law which gives the dog one free bite would certainly not allow him to be deprived of his liberty."

The sufferer from pituitary disturbances seems to compensate for his feeling of inferiority by craving for the limelight. The craving of the "fat boy in *Pickwick*" was to make people's "flesh creep."

The pars intermedia of the pituitary, which is developmentally part of the anterior lobe, is concerned with carbohydrate metabolism. If it overacts there is excess of sugar in the blood and sometimes frank glycosuria; if it underacts the blood sugar is low and carbohydrate tolerance is high—no doubt this plays a part in the obesity of hypopituitarism.

When the anterior lobe with the pars intermedia is in defect we have Fröhlich's syndrome—an abnormally fat patient, with little hair, smooth skin, and undeveloped sexually; in fact, an extreme degree of the type of pituitary obesity I have already described.

It has been said that the anterior lobe tends to produce virile characters, and the posterior lobe feminine characters. The flat-chested, long-toothed, large-jawed, clumsy-handed woman, fondly believed by the French caricaturists to be typically English, is certainly suggestive of an exaggerated anterior pituitary, and she is not remarkable for feminine characteristics. A little side issue of some interest occurs to me here: you are all familiar with the inseparable couple of women friends; one of the two usually adopts a somewhat masculine rôle, and I have been struck on several occasions to note the number of signs she presents of overactive anterior pituitary. Be that as it may, I am sure the pituitary plays some part in differentiating the secondary sexual characters.

We are on safer ground in asserting that the secretion of the posterior lobe stimulates plain muscle and is often found to be an excellent stimulant in a certain type of atonic constipation. I am convinced, too, that diabetes insipidus is generally due to defective action of the posterior lobe. Clinical and pathological evidence strongly supports this view, and injections of pituitrin will control polyuria. Apparently this is due to direct action on the kidney; but I must not stop to discuss this point.

Several recent observations have thrown considerable light on the influence of the pituitary on carbohydrate metabolism. Thus, Mackenzie Wallis⁴ has found the blood sugar curve to be the same in pituitary glycosuria and the glycosuria of pregnancy; Dixon has shown that ovarian extract increases the secretion of pituitrin into the cerebrospinal fluid⁵; while J. H. Burn has found that pituitary extract will inhibit the action of insulin in reducing the blood sugar. Therefore, in the glycosuria of pregnancy the gonads apparently stimulate the pituitary, which in turn inhibits the pancreas.

THE THYROID.

The thyroid is essentially a feminine gland, and it is developed from the uterus of the paleostracan ancestor. Its enlargement at puberty, marriage, and pregnancy, and its tendency to involution at the menopause, all point that way. It has been called the gland of creation. Some time ago Crichton Miller asked if anyone had ever heard of a

myxoedematous artist. Tredgold replied by citing a cretin in Zürich in the eighteenth century who was an artist of some repute. But possibly he was really only an achondroplastic. Crichton Miller has returned to his point, and asks for cases of subthyroidic creators—be it of works of art or of children. It is, of course, true that a subthyroidic woman may have children after she has had thyroid treatment. Crichton Miller further maintains that child-bearing and artistic creation are mutually exclusive, the storehouse of creative energy being unable to cope with both kinds of creation; and I think that though we can find apparent exceptions to this rule, it is very rare for both kinds of creation to be possible simultaneously. I went so fully into the question of the factors in hyperthyroidism in a previous lecture that I need only recall them briefly now. Various toxic influences may excite a reaction in the thyroid gland; of these, tonsillar and intestinal sepsis seem to be the most important, though others may play a part. Thus in a recent case the hyperthyroidism was much ameliorated by removal of septic teeth, but septic tonsils were apparently responsible for an intermittent auricular fibrillation which came on soon after this, and which could not be controlled by quinidine. But more and more I am impressed with the influence of emotion in causing Graves's disease, which is readily comprehensible in view of the sympathetic innervation of the gland. This is particularly likely to happen if the distressing emotion has a matrimonial origin, while it naturally adds considerably to the difficulty in detecting the cause, as this is not usually a matter of advertisement. I had the opportunity of watching the case of an unmarried lady who was entrusted with the care of her niece between the ages of 4 and 17. The girl's parents were Anglo-Indians, and when she grew up they sent for her to go back to India. The aunt was greatly distressed; her whole emotional life appeared to centre round the girl, and within six weeks of her departure the aunt, who had reached an age which precluded her from having children of her own, developed marked Graves's disease. Fear is another emotion which has a marked influence in exciting hyperthyroidism, as was well shown during the air raids on London. The air raids were almost an "acid test" of race. An uncontrollable impulse to flight from London or into the tubes was almost diagnostic of Semitic origin. More self-controlled people, who nevertheless suffered acutely, repressed their impulses from the motor to the vegetative level, and received their reward in hyperthyroidism, amounting in some cases to Graves's disease. That stimulation of the thyroid should normally be followed by vigorous action is shown by the way it produces excess of sugar in the blood, even though there may be no glycosuria.

I have nothing fresh to say about minor degrees of hypothyroidism, but I should like to reiterate my belief in the importance of the disappearance of the outer half of the eyebrows as an indication of this condition and of the frequency with which "rheumatic" pains are experienced by sufferers from it. Once the suspicion of hypothyroidism is aroused its detection and treatment are not difficult. The following case presents points of more interest:

A boy, the only child of a widow, had an attack of subacute rheumatism. Following this he grew very fat and completely paraplegic. He had been in this state for a year when I saw him. His appearance suggested hypopituitarism, but though not quite 14 signs of puberty were well developed. A skiagram showed a normal pituitary fossa. There were no signs of organic nervous disease. I came to the conclusion that the rheumatic poison had damaged his thyroid gland, and that while pain had for a time made movement difficult, the existing paraplegia was functional. Separation from his mother, administration of thyroid, massage, and re-education exercises led to a complete cure with loss of his obesity.

The psychic effect of hypothyroidism is interesting because it is by no means uniform. The commonest result is a stato which has been called "resigned melancholy," but sometimes the mental attitude is one of suspicion, which may result in delusions, and occasionally leads to acute mania. This is surprising in a disease usually characterized by lethargy. My experience is that mania in myxoedema should not deter us from giving thyroid extract.

THE PARATHYROIDS.

Most observers are now agreed that the parathyroids have separate functions from the thyroid. Their two recognized actions are (1) to destroy guanidine, a purin body which otherwise accumulates in the muscles, where it is believed to cause tetany; (2) to increase the ionizable calcium content of the blood. The first effect has been recently used by Vines to estimate the activity of preparations claimed to contain parathyroid secretion, and the second has been proved by the same observer by direct estimation of the calcium in the blood. Applying these facts to clinical observation Grove and Vines⁶ found in the case of lesions which could be watched, such as a varicose ulcer on the leg, that calcium was an important factor in their healing, that parathyroid extract was capable of influencing calcium metabolism, raising a deficiency in it to normal, and that with a normal calcium content healing speedily occurred. They then applied this method to internal lesions such as gastric or duodenal ulcer, with similar results. They believe that calcium deficiency is an index of the absorption of a toxin, and that in all the various diseases improved by parathyroid therapy the common factor is sepsis. It is suggested that the benefit is derived from a stimulation of the leucocytes, since the polymorph count rises, probably from an indirect effect of calcium on the blood plasma.

THE THYMUS.

As already stated, the activity of this gland is normally limited to the infantile period. It appears to act as a brake on the development of sexual maturity, presumably in the interests of somatic development. Since no internal secretion has been obtained from the thymus it is not easy to see at present how it antagonizes the gonads. Possibly this is achieved through its influence on the structure of the blood, for the appearance of the adult blood picture and the disappearance of the thymus are usually simultaneous. While the thymus exists the characteristic blood reaction is lymphocytosis, and it is only during this period that we meet with the condition known as pseudo-leukaemia, or "splenic anaemia of children," which is probably merely the reaction of infantile blood to various severe toxæmias. In status lymphaticus the enlargement of the thymus is simply a part of a general adenoid enlargement. It may be that this is a sign of an abnormal sensitivity to foreign proteins, which is a characteristic of those whose vague response is exaggerated. This would account for the liability to dyspnoea, syncope, and anaphylactic shock associated with status lymphaticus. When the adult blood picture is reached this lymphocytic reaction is replaced by a leucopenia in anaphylactic shock.

THE PANCREAS.

Both the external and internal secretions of this gland are anabolic in their effect. The external one prepares all the foodstuffs for absorption; the internal one is now proved to lead to the utilization of sugar by the tissues. It is the special merit of Banting's work that he has been able to isolate the active principle of this long-suspected and long-sought-for internal secretion. It would appear to act by changing glucose into another form, γ glucose, in which it can be used. When it is absent or diminished, more or less of the sugar in the blood remains in a non-assimilable form and is bound sooner or later to be excreted into the urine. How soon it appears will depend on the response of the kidney, which tends to raise its threshold when there is excess of sugar in the blood, thus allowing a longer time for the diminished pancreatic internal secretion to act. This internal secretion, insulin, is not confined to the pancreas. It is probably widely spread, and certainly appears to be present in yeast at a particular phase of its life cycle (Winter and Smith). This is not the place to discuss the therapeutic use of insulin, but it is already clear that it lowers blood sugar, diminishes ketosis, and raises the respiratory quotient. All these are different aspects of the same action. By converting glucose into a form in which it can be used it naturally prevents its accumulation in the blood. It is of great

interest to observe that the avidity of the tissues for this form of glucose is so pronounced that an overdose of insulin leaves insufficient sugar in the blood for immediate needs. Too little blood sugar is more disastrous than too much; the former immediately produces acute symptoms; the latter is compatible with fair health for years. The effect of insulin on ketosis is very marked, for even on a rigid protein and fat diet the diabetic may show no reaction for diacetic acid in the urine—another evidence of the oxidizing power of γ glucose. The rise in the respiratory quotient inevitably follows the more complete utilization of carbohydrate.

I may remark that while the discovery of insulin completely proves that the cell-islets of the pancreas form an internal secretion which promotes the assimilation of sugar, it does not prove that all diabetes is due to a pancreatic lesion. The fact that pituitary extract can antagonize insulin provides new support for the view that diabetes may be due to a more profound and subtle disturbance of metabolism than a lesion of one gland.

Swale Vincent has reminded us that organotherapy is often employed without any rational sanction. As he says, it would be difficult to mention a drug which is clearly and beyond doubt of value in the treatment of disease and yet which possesses no known pharmaco-dynamical effects. Yet many of the extracts in common use have not been shown to have any such action. Even some of those which do, cannot be satisfactorily used in substitution therapy. The early triumphs of thyroid medication tended to blind us to the difficulties surrounding the use of other glandular extracts in therapeutics. Yet the thyroid is exceptional in containing a definite reservoir of secretion and, by virtue of its duct originally opening into the alimentary canal, retaining the power of having its secretion absorbed by that route. It is perhaps fortunate that many of the preparations in use are inert, for otherwise damage might be done. Thus the injection of secretin by liberating an active pancreatic secretion may produce digestion of the intestine. It is just as well, therefore, that organotherapy lags behind endocrinology. But I feel sure that Swale Vincent, while rightly demanding more exact experimental methods in organotherapy, reaches too agnostic a position with regard to endocrinology. Here the careful study and comparison of abnormal types by clinical methods may be of considerable help. To that study I hope some of the foregoing observations may contribute.

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SOME HINTS FROM THE OLD PHYSICIANS.

AN ADDRESS DELIVERED BEFORE THE BRADFORD MEDICO-CHIRURGICAL SOCIETY, OCTOBER 17TH, 1923,

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HISTORY rightly occupies an important place in general education. It is not only a subject of great intrinsic interest but it is full of instruction for us. We cannot understand the present without some knowledge of the past out of which it has been evolved. History fosters judgement, chastens opinion, gives warnings, encourages research. This is true of history in general, and for us the history of medicine has special claims. We owe it to our profession to know something of the long and toilsome path which medical science has travelled before attaining its present position of influence and authority. We ought to know something of its pioneers, its seers, its heroes, and its martyrs. We can derive encouragement from their labours, sacrifices, and successes, warning from their mistakes and failures. We shall read with chastened feelings of false theories and

imaginary cures which long held the field, and we shall learn to be more careful in appraising every new medical doctrine and every new method of treatment which to-day makes its appeal to us. The past has much to teach us, positively and negatively. We shall learn that time is the great test and experience the only safe guide. The history of medicine is to-day coming into its own. There is now an International Society for the Study of the History of Medicine, which has already held three successful congresses. Chairs and lectureships in the history of medicine have been provided in various universities. The FitzPatrick Lectures at the Royal College of Physicians have produced many valuable monographs, and the time is near when some knowledge of the history of medicine will become a necessary portion of the medical curriculum.

Scientific medicine begins with the Greeks. They were the first to study medicine as a lay subject, to free it from superstition and priestly authority, to practise bedside observation on scientific lines, and to develop a sound therapeutic. Whether they owed much or little to Egypt, Babylonia, or Crete, we have no certain information. When the darkness which enshrouds early Greek history lifts, we find a cult of the God of Healing—Asclepios—and a society of physicians—the Asclepiadae. The chief centres of this cult were at Trikka in Thessaly, in the island of Cos, at Pergamos in Ionia, and at Epidaurus in the Peloponnese. The temples of Asclepios were practically hospitals and sanatoriums. They were usually placed in localities favoured with climatic and hygienic advantages, and often in the neighbourhood of mineral springs. The chief means of cure were physical exercises, baths, inunctions, purgatives, emetics, dietetic regulations, rest, and various modes of suggestion. It is instructive to note that in the very earliest times the Greek physicians understood and stressed suggestion. They knew well the great influence of mind upon body. In the temples of Asclepios one of the favourite methods of treatment was the temple sleep. In the silence of the night hours the physician, personating the God of Healing, visited his patients, soothed their fears, encouraged the hope of recovery, and no doubt favourably influenced the course of disease. Whether he taught them to say "I am feeling better and better every day" I am unable to affirm; history is silent on the subject, but if the formula was different, the method and design were the same. M. Coué would have felt quite at home in a temple of Asclepios, and I am not sure that Freud, Jung, Adler, and their numerous followers might not have found some of their views and methods anticipated by the disciples of Asclepios. The wheel has come full circle, and modern psychotherapy is reverting to the practice of Cos and Epidaurus.

Hippocrates is the first great figure in the history of medicine. He belonged to the great age of Greece, the age which saw such astonishing achievements in literature and in art. Born in the island of Cos in the year 460 B.C. of a family of Asclepiads, he travelled widely, acquired all the medical knowledge of his time, practised in various cities of Greece, and achieved great renown in his own time, and even greater fame in succeeding ages. Galen called him "the divine," and he is justly regarded as the Father of Medicine. His works cover the whole field of medicine, surgery, and obstetrics, and are an encyclopaedia of the best knowledge of his day. His *Aphorisms* is probably the only book of ancient medicine which is still frequently read. Much of it is obsolete, but there is hardly a page which does not contain evidence of shrewd observation and sound wisdom.

Hippocrates was the first great clinical physician and the founder of the bedside method. His anatomy was weak, his physiology weaker, and his pathology weakest, but he was an observer of the first order, and he had a sane and profound intellect. He studied disease objectively, without theory, and recorded his successes and his failures with equal impartiality. He relied upon experience. Hippocrates achieved three great objects: he freed medicine from superstition; he systematized and expanded the best medical knowledge of his day; and he gave physicians the highest ethical inspiration which medicine can possess. The famous Hippocratic oath is an ideal of medical practice which can never become obsolete. Hippocrates left descriptions of the epidemic fevers of Greece, phthisis, epilepsy, puerperal