A British Medical Association Lecture

ON

ENDOCRINOLOGY FROM THE PHYSICIAN'S POINT OF VIEW.*

BY

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ENDOCRINOLOGY is a subject to which I lay no claim to speak with special authority, but as the ductless glands play their part, and a very important part, in all phases of physiology, a knowledge of their main functions is essential to the rational carrying on of our work, whatever the branch in which we may be particularly interested.

In no department of medicine has the output of literature been so profuse or voluminous during recent years as in that concerned with the ductless glands, but we are still in the dark as to the true functions of many of them. They, like the blood-forming tissues, are situate, with few exceptions, in inaccessible parts of the body, and the interaction of one with the other is so intimate, yet variable in different species, that the correct interpretation of results of experimental research presents great difficulty. Over-enthusiasm in the medical profession has been seized upon and absorbed by many of the manufacturing chemists, who have also rushed into print urging practitioners to add this or that extract to their armamentarium long before any therapeutic value could be rightly assigned to it, and this in turn has influenced the public—"My doctor prescribes so-and-so; I have great faith in him, and therefore it must be good stuff." Hence our great individual responsibility in the matter. Harvey Cushing said in 1921:

"We find ourselves embarked on the fog-bound and poorly charted sea of endocrinology. It is easy to lose our bearing, for we have, most of us, little knowledge of sea-faring and only a vague idea of our destination. Our motives are varied; some unquestionably follow the lure of discovery; some are earnest colonizers; some have the spirit of missionaries and would spread the gospel; some are attracted merely by the prospect of gain and are running full sail before the trade winds."

One island securely charted since that time is insulin, and many are now engaged in preparing a survey of the land. With changes in some of the glands—thyroid, suprarenal, pancreas, pituitary—we know certain diseases are associated, and we also know that extracts from these same glands and the parathyroids, administered by appropriate routes, produce definite physiological results. It would seem certain that the balance of the endocrine glands determines our growth, development, and general characteristics. Puberty and the menopause are but the outward and visible sign of the readjustment of the endocrine balance; but of what that adjustment really entails we have few facts though many fancies. It is the fashion nowadays to classify individuals according to their endocrine type: phrenology has been completely adopted by certain endocrinologists—the bumps and depressions no longer correspond to benevolence and veracity, but are dependent merely on the whim of the pituitary or thyroid. The isolation of the active principle of the endocrine glands presents great difficulties, and there is reason to suppose that each gland may contain more than one hormone. The chemical composition of adrenaline and thyroïdin has so far been determined, but extracts of the thyroid, pancreas, pituitary, parathyroid, and suprarenal medulla have a definite pharmacological action of the greatest interest to the physician.

THE PREDOMINANT FUNCTIONS OF THE INDIVIDUAL GLANDS.

The Pituitary Gland.

The anterior lobe of the pituitary controls skeletal and muscular growth; overactivity before the epiphyses join results in gigantism, after fusion of the epiphyses in acromegaly. A lesion of the pars intermedia in early life may be associated with Fröhlich's dystrophia adiposo genitalis syndrome. The posterior lobe is concerned with

sugar metabolism and possibly with that of salt and water. Adiposity, infantilism, somnolence, and impotence are consequences of underactivity of the gland. If the condition begins before adolescence the body fails to grow, though the child may increase in weight because of the deposit of fat in the tissues. Sexual development is interfered with and the secondary characteristics fail to appear. In boys the pubic hair does not extend up to the umbilicus; the beard does not develop, whereas the hair of the scalp grows profusely. The skeleton remains of the female type, and a broad pelvis, rounded limbs, and small feet and hands are often observed. Sugar tolerance is usually high, which may explain the adiposity, sugar being converted into fat. When hypopituitarism does not develop until after adolescence, dryness of the skin, loss of hair, obesity, and the tendency of the male to adopt certain of the female characteristics as regards build and distribution of hair may be seen.

The Pineal Body.

The pineal body is credited with the promotion of sexual development, and is opposed by the thymus, whose function would seem to be in some way concerned with the maintenance of the characteristics of childhood.

The Thyroid.

The thyroid is the great regulator of metabolic rate in general, exerting an influence on protein, fat, and carbohydrate. In overactivity of the gland the metabolic fires burn high, the basal metabolic rate is increased, and the clinical signs of tachycardia, tremors, "nervousness," sweating, loss of flesh, and perhaps fever, appear. In many infective processes we see a slight enlargement of the thyroid, possibly as an immunity reaction. Hyperactivity with the production of an abnormal secretion gives rise to the syndrome of Graves's disease—the hyperplastic toxic goitre. Underactivity, congenital or acquired, results in cretinism and myxoedema respectively. It is of interest to note that of the various glandular extracts, when given by the mouth, thyroid extract alone furnishes a true replacement, and the thyroid is the gland which used to discharge its secretion via the thyroglossal duct into the alimentary canal.

The Suprarenal Glands.

The suprarenal glands have two distinct functions. The cortex develops from the Wolffian body and is closely related to sexual development and masculine characteristics—witness the "infant Hercules" type of premature development associated with certain overgrowths of the cortex. The infant Hercules with congested dusky complexion is hairy, muscular, and rarely obese. In female children with cortical overgrowth the breasts hypertrophy, hair appears on the mons veneris, and menstruation may occur—the patient resembling a stout little woman. At the other end of the scale are those rare cases of progeria where we find side by side the signs of infantilism and of premature senility—baldness, shrunken wizened features, arteriosclerosis—"a decrepit old dotard at 5." In pregnancy the cortex becomes hypertrophied and it is ill developed in sexual deficiency. The development of the cortex cerebri is also bound up with the adrenal cortex; in anencephalic monsters this part of the gland may be wanting. It is apparently the cortex and not the medulla which is essential to life.

The medulla, the smaller part of the gland but more richly supplied with blood for its size than any other tissue in the body, arises as an outgrowth from the ganglia of the sympathetic cord. It is built up in the main of chromaffin cells—so called from the fact that their granules stain with chromic acid—which secrete adrenaline; these chromaffin cells are not confined to the suprarenal medulla but are scattered throughout the ganglia of the sympathetic system. Destruction of sufficient chromaffin cells leads to Addison's disease, characterized by asthenia, muscular weakness, low blood pressure, vomiting, and pigmentation. The last mentioned sign has its origin in the fact that adrenaline is formed from tyrosin, a product of protein metabolism; when tyrosin can no longer be converted into

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adrenaline owing to destruction of chromaffin cells melanin results, which is laid down in the skin and mucous membranes.

The Parathyroid Glands.

The parathyroids are intimately concerned with regulating calcium metabolism, and the recent work of Grove and Vines has focused attention on these small glands. In the normal individual calcium is present in the circulating blood in two forms—ionized and combined. After coagulation the calcium in the serum is all ionized. Vines found that in certain ulcerative processes some of the calcium in the serum was present in the combined form and that by administering parathyroid extract by the mouth the ionic calcium content of the serum was increased and healing of the process favoured. He concluded that a toxic substance produced by the ulcer in some way injured the parathyroids and the calcium balance of the blood was upset. Parathyroid administered by the mouth in suitable cases appears to strengthen the resistance of the tissue cells by restoring the normal calcium balance in the plasma. Destruction of the parathyroids, or their removal, leads in man and in experimental animals to tetany. This, fortunately, is a rare complication of operations on the thyroid gland. The inferior parathyroids are the larger and lie one on each side close to the posterior border of the lateral lobes of the thyroid near where the inferior thyroid artery divides before entering the gland. Dunhill has found the intravenous injection of 4 grams of calcium lactate in solution completely effective in the two cases in which he has seen tetany as a post-operative complication.

The Pancreas.

The pancreas is a compound gland, the acinous portion secreting the pancreatic juice, which is discharged by a duct into the duodenum and the islets of Langerhans, which pass their secretion into the portal vein. The islet tissue comprises only about one-hundredth part of the gland, and the islands, though embedded in, are completely shut off from, the acinous portion, having their own blood and nerve supply. The cells of the islands when resting contain granules which Allen has shown to have a close relation to carbohydrate metabolism. Feeding with carbohydrate causes the granules to disappear from the cells of the islets. These cells furnish insulin, whose special function appears to concern the storage of sugar in the liver and muscles. This internal secretion of the pancreas is inhibited by the pituitary; adrenaline interferes with the storage mechanism by causing the liver to turn out its store of glycogen.

The Sex Glands.

The internal secretion of the gonads exerts an important influence on the development of secondary sex characters, but rather as a stimulus to their growth than as the source of their origin. Blair Bell accords to the ovary the post of liaison officer between the needs of the reproductive system and the other endocrine glands. Gonad fatigue is made up for by overactivity of the thyroid and pituitary. Enlargement of the thyroid is common during pregnancy and at each menstrual period, especially at puberty—in the latter case as a temporary hyperplasia, subsiding between whiles, where the ovaries have not yet developed full activity and supplementary action is required to establish menstruation. This transient physiological enlargement associated with scanty menstruation must be distinguished from a primary pathological lesion not infrequently seen about the time of puberty in which the thyroid enlargement persists between the periods at which menstruation is often profuse; this colloid goitre may develop into the hyperplastic toxic goitre with its symptomatology of Graves's disease. As puberty in the female is so often associated with increased thyroid activity, so the menopause is not infrequently accompanied by atrophy of the gland—and a like condition may follow operative removal of the ovaries.

The transient swelling of the pituitary at each period may account in part for the headache to which some women are liable at this time; but it is not the only factor, for in pregnancy the anterior lobe increases in size, never again to

subside to the virgin state, and such enlargement is by no means always accompanied by headache. Pituitary headaches are supraorbital or temporal in distribution; I cannot vouch for the statement that they may be relieved by feeding with pituitary gland.

The claim of the interstitial cells of Leydig—polygonal epithelial-like cells, containing lipoid granules—to be the structures responsible for the influence of the testis on the development of the male sexual characteristics, though long supported by numerous pseudo-scientific facts, has been assailed recently by K. M. Walker. He maintains that the function of the interstitial cells is the storage of nutritive material for the use of tubular epithelium, that they are trophic rather than secretory, and that the internal secretion of the testis is produced not in the interstitial cells of Leydig but in special cells—the cells of Sertoli—in the tubules. The internal secretion of the testis is only one factor concerned in the regulation of the development of the secondary sex characteristics—the influence of the pituitary and suprarenal cortex has already been mentioned—and in many cases of eunuchoidism it is unlikely that the testis alone is involved, and too much must not be expected from treatment by testicular grafts. If the operation of grafting the testis into another part of the body is successful the seminiferous epithelium degenerates after a time, but the interstitial cells remain alive; this may account for the temporary "rejuvenation" effect of the Voronoff operation. Steinach's operation of ligaturing the vas, and so putting an end to spermatogenesis, has a limited sphere of usefulness in the treatment of high blood pressure.

THE REGULATION OF BLOOD SUGAR.

The interdependence of certain of the endocrine glands is well exemplified in the mechanism regulating the blood sugar. Except for the temporary rise after a meal containing carbohydrate, the blood sugar remains fairly constant between 0.08 and 0.12 gram per 100 c.cm. of blood; the total amount of sugar in the blood of a man weighing 10 st. is about 5 grams. There are four ductless glands concerned with the regulation of the blood sugar—thyroid, pituitary, suprarenal medulla, and pancreatic islands. An increase in the activity of the three former leads to a rise in blood sugar, a diminution in sugar tolerance, and perhaps glycosuria. The islets of Langerhans occupy the other pan of the balance, for decrease in function produces lowering of sugar tolerance and glycosuria. How these glands produce their action is still not fully understood. The injection of adrenaline causes an increase of blood sugar, and this explains how fear and anxiety may induce temporary glycosuria. Langdon Brown has pointed out that stimulation of the sympathetic nervous system produces a series of effects calculated to facilitate violent action in the direction of flight or fight. The pupil dilates, the blood pressure rises, and the pulse increases in frequency. The skin sweats to cool the body, and the blood sugar rises owing to turning out of glycogen from the liver, the better to feed the active muscles. Stimulation of the sympathetic excites the production of adrenaline, and adrenaline increases the sympathetic response. Adrenaline may be the active agent which keeps constant the amount of sugar in the blood, but how the supply of adrenaline is regulated is not clear. Graham suggests that the need for sugar reacts in some way on a centre in the brain from which impulses pass by way of the splanchnic nerves to the suprarenals, which furnish more adrenaline, which in turn causes the liver to turn out more sugar into the blood. The mechanism of the thyroid influence is less clear. In hyperthyroidism sugar tolerance is generally reduced, and in myxoedema there is a great increase in the sugar tolerance. The administration of thyroid extract lowers the sugar tolerance and may actually produce glycosuria if a large amount is taken. With regard to the pituitary, an increase of blood sugar and occasionally glycosuria may occur in the early stages of acromegaly—an affection of the anterior lobe—but this may be due to pressure on the floor of the fourth ventricle or on the posterior lobe; it will be remembered that the anterior lobe arises as an outgrowth from the roof of the pharynx, and just as portions of thyroid may occur in the neck anywhere between the

foramen caecum of the tongue and the thyroid isthmus, so groups of the pars glandularis of the pituitary may be found between the pharyngeal vault and the sella turcica. Destruction of the posterior lobe, which arises as a downgrowth of the floor of the third ventricle, increases sugar tolerance, and feeding with posterior lobe will reduce sugar tolerance. Graham has found that the blood sugar curves obtained when sugar is given to patients with hyperpituitarism resemble those of mild cases of diabetes mellitus.

DIABETES MELLITUS.

The introduction of insulin as the result of Banting's researches has altered the whole outlook of the patient with diabetes mellitus, and is the greatest contribution of the present century to medical science. But how best to use insulin, and for how long its administration must be continued, are questions which cannot yet be answered. It is clear that every case of glycosuria does not require it; cases of renal glycosuria in which the kidney threshold for sugar is low and in which the small quantity of sugar constantly present in the urine is uninfluenced by diet, and the elderly obese glycosuric whose sugar is easily controlled by restricting the carbohydrate intake, are examples.

In our treatment of diabetes mellitus our object should be to rest the damaged islet cells in the hope that they may recover their lost function, and, in the case of children, that new cells of growing islets may develop free from strain. There is reason to believe that these cells are stimulated by a high sugar content of the blood, and we should try, therefore, so to adjust the dietary and the dose of insulin that the blood sugar is maintained on the low side of normal—that is, not above 0.10 per cent. One effect of the injection of insulin is a lowering of the blood sugar, the maximum fall occurring from three to six hours after the injection, the effect passing off in from ten to sixteen hours. It is clear, then, that the fasting blood sugar will be at its highest level twenty-four hours after an injection, and as it is this highest level with which we are concerned in watching the progress of a case under treatment with insulin, in which one daily dose only is given before breakfast, blood for sugar estimation should be taken just before that meal. Though it is advisable to estimate the blood sugar immediately it is collected it is not essential; Graham has devised a means whereby the blood can be preserved for two or three days—5 c.cm. of blood is withdrawn by venepuncture and a pinch of powdered potassium oxalate added to prevent coagulation, and one drop of 40 per cent. formalin to prevent glycolysis. If the condition of the patient in general and his urine in particular are carefully watched frequent blood sugar estimations are not essential, though occasional estimations are of the greatest value as a check. The healthy kidney allows sugar to pass if the blood sugar rises above 0.19 or 0.20 per cent.; if the diabetic as a result of treatment is sugar-free throughout the twenty-four hours it is probable that at no time does the blood sugar rise above 0.19 per cent. But a blood sugar of 0.19 per cent. is believed to be stimulating the islet cells, and we have no means other than by direct estimation of telling how much below 0.19 per cent. the blood sugar may be. Treatment of a diabetic, other than in coma, should be started by an attempt to get him sugar-free by alimentary rest days and the ladder diet according to Graham's plan; meanwhile any septic focus should be sought for and efficiently dealt with. If in spite of rest in bed the patient does not remain sugar-free at the top of the ladder, which represents a diet containing 16 grams of sugar in the form of vegetables with a calorie value of 1,300, 10 units of insulin should be given before breakfast. If the dose is not sufficient, sugar will be present in all specimens of urine, and it must be cautiously and slowly increased until each specimen passed in the twenty-four hours is sugar-free. Symptoms of overdose of insulin—sweating, a fear of impending disaster, diplopia, great "slackness," aphonia, drowsiness, and eventually coma—appear to be due more commonly to rapidity of fall in blood sugar than to the actual decrease; if the reduction takes place slowly no symptoms may appear till it falls below 0.04 per cent. Symptoms, if mild, are speedily relieved by food of any sort—a tomato, for instance—but

if severe, a hypodermic injection of adrenaline (which turns glycogen out of the liver) or the giving of sugar by the mouth will be required.

Diabetic coma must not be mistaken for coma following an overdose of insulin. In the former sugar is present in the urine; in the latter there is no glycosuria. In diabetic coma the Rothera reaction and ferric chloride test for diacetic acid are strongly positive and the breath may smell of acetone; in "insulin coma" these tests are not strongly positive, and it is unlikely that the odour of acetone will be present in the breath. In diabetic coma the intraocular tension and blood pressure are low and the pulse small and weak; in insulin coma there is no fall in intraocular tension and the pulse is full and bounding. Diabetic coma is associated with deep respiration, possibly of the "air hunger" type, and the alveolar CO_2 is low; insulin coma has no such effect on the character of respiration.

The urine should be sugar-free for several weeks at the top of the ladder diet before further carbohydrate is added. The longer this period, within limits, the better for the patient, and especially if he can be kept in bed. When further carbohydrate is added it may best be given as 4 oz. of milk—spread over the day—and if this has no ill effect 1/4 oz. of bread is added, given as hot buttered toast at breakfast. The quantity of bread, or its equivalent in other forms of carbohydrate, may be cautiously increased every other day until sugar appears in the urine, or, better still, the effect on the fasting blood sugar is seen. When glycosuria occurs the bread should be cut down by at least half an ounce.

Insulin is seen at its best in acute cases and particularly in coma; in diabetes of long standing its effect is apt to be disappointing. In impending or developed coma all food should be stopped, the bowels opened by turpentine enemata and oil, and 30 units of insulin injected forthwith. Provided the urine is not sugar-free in three hours the dose may be repeated, and as much as 100 to 150 units may be required in the twenty-four hours.

Any minor ailments which may arise must be taken seriously—a cold, for instance, will cause a rise in blood sugar. The instability of the sugar-regulating mechanism in some diabetics is well illustrated by the case of a boy aged 18. His diabetes had an acute onset while he was convalescing from an abscess in May of last year. He was put on strict dietetic treatment six weeks later, during which time he had lost 1½ st. in weight. He has apparently responded well to diet and insulin; though he is now allowed only 4 oz. of milk and ¾ oz. of bread extra, his weight has increased by nearly 3 st. in the six months and he is leading an active country life. He travelled up to London during the recent railway strike for periodical overhaul and adjustment. The journey of 100 miles took him ten hours, some of which were spent waiting about at a station—and in a cinema—and he was thoroughly tired out on reaching the nursing home. The following morning before his injection of insulin and his breakfast his blood sugar was 0.17 per cent.; two days later it had fallen to 0.12 per cent., and two days later still to 0.106 per cent. On the strength of this it was decided that no addition should be made to his dietary or any decrease in the insulin for another three months. At one time he required 30 units of insulin a day, but for the last three months 10 units in the morning has sufficed to keep his blood sugar well within normal limits. Can this be taken as an indication that his islet cells are recovering their lost function? Much yet remains to be learned about the use of insulin in diabetes mellitus, and it is likely there are rocks ahead. One that is already casting a shadow concerns symptoms that may arise in the process of withdrawal, but of its nature it is yet too early to speak.

THE RELATION BETWEEN THE ENDOCRINE GLANDS AND THE NERVOUS SYSTEM.

The viscera are innervated by both subdivisions of the vegetative nervous system. These subdivisions are anatomically distinct and physiologically antagonistic, and are termed sympathetic and parasympathetic or autonomic respectively. The sympathetic proper consists of two chains of gangliated cords made up of cells and involuntary

nerve fibres which pass to glands, blood vessels, and non-striped muscle fibres. The autonomic system (or extended *vagus*) consists of nerve fibres with peripheral ganglia arranged in plexuses near the viscera to be supplied, the chief of which are the cardiac, solar, and hypogastric plexuses. Stimuli conveyed by the sympathetic and autonomic systems are mutually antagonistic; thus, for example, stimulation of the sympathetic increases pulse frequency, whereas stimulation of the *vagus* slows the heart; the *vagus* is motor and secretory to the stomach, and its stimulation causes an increase in the amount and acidity of the gastric juice, contraction of the stomach, and relaxation of the pyloric sphincter, whereas excitation of the sympathetic inhibits peristalsis and contracts the sphincter. It is the balance of these two sets of stimuli which regulates the functioning of the various organs. People may be divided into two groups according to the dominance of their sympathetic or autonomic sensitiveness; the autonomic or vagotonic person is staid and unemotional, with an infrequent pulse, small pupils, deep-set eyes, and cool skin. The sympathetotonic individual, on the other hand, is emotional and excitable, with frequent pulse, dilated pupils, and warm skin; they are specially sensitive to adrenaline, which intensifies these characteristics. Sympthetotonia may be relative owing to diminished activity of the vagotonic system, or actual from increased excitability of the sympathetic system, and in like fashion diminution of adrenal function induces vagotonia.

As the clinical syndromes of autonomic and sympathetic stimulation have many symptoms found in definite endocrine disturbance, it is perhaps justifiable to assume a close connexion between them, though it may not be possible to determine whether such symptoms are due to a disturbance which arises primarily in the endocrine glands or in the nervous system. Adrenaline intensifies sympathetic response, and the suprarenals help to maintain the normal activity of the sympathetic ganglia, whereas the autonomic or *vagus* system is activated perhaps by the post-pituitary and alimentary glands. It is of interest in this connexion to compare the physiological action of adrenaline and pituitrin. Adrenaline is more rapid in its action, but the effect is of shorter duration; both raise blood pressure; pituitrin strengthens the force without increasing the frequency of the heart beat, adrenaline accelerates the heart. Pituitrin constricts the coronary and pulmonary vessels, on which adrenaline has no effect. Pituitrin dilates the renal vessels and acts as a diuretic, whereas adrenaline constricts the renal artery. Pituitrin stimulates the intestine, bladder, and puerperal uterus; adrenaline inhibits. Pituitrin acts directly on muscle fibre; adrenaline stimulates the sympathetic nerve fibre. Pituitary secretion is increased by the injection of ovarian extract (Dixon).

It may be that many of the so-called functional diseases—that is, diseases in which no structural lesion is demonstrable with the means at our disposal—are due to disturbance of endocrine function; we are accustomed to speak of various “neuroses,” which term implies the idea of an underlying instability of the nervous system as the *fons et origo mali*. But is it the nervous system which is always primarily at fault? We are frequently called upon to treat “gastric neuroses”—cases of dyspepsia in which peptic ulcer, carcinoma, cholelithiasis, or chronic appendicitis can be certainly excluded. The outstanding symptom may be referable to disturbance in the motor, secretory, or sensory function. Vagotonia is associated with a high stomach, vigorous peristalsis, and hypersecretion; sympathetotonia with a low and often large viscus, delayed emptying, and hyposecretion. Gastric neuroses present varying clinical pictures, but in not a few of the hyperchlorhydric type evidence of vagotonia may be found if carefully looked for, whereas hypochlorhydria is not infrequently associated with thyroid deficiency, and such patients will derive benefit from small doses of thyroid extract given by the mouth.

Neurasthenia is not infrequently a sequel to an infective disease in which the suprarenal glands may have suffered damage with consequent lowering of function, or it may develop after a prolonged period of strain or anxiety which calls in the first place for increased production of adrenaline with subsequent adrenal exhaustion. The

irritant effect of air raids or of physical or mental trauma does not find expression in neurosis until endocrine exhaustion occurs—then obsessions, fears, and anxieties gain the upper hand, overflowing the lowered threshold of control; or in another group the adrenal check on the thyroid is lifted and Graves's disease ensues. The neurasthenic is unable to control the functions of the nervous system in a normal manner, and the recognition of disturbed endocrine activity helps in understanding the symptomatology, and restoration to health will coincide with the readjustment of endocrine balance. In many cases there is doubtless a psychic element also, to which great importance has been attached in some quarters, but the elimination of this feature by itself is but rarely sufficient to effect a cure.

THERAPEUTICS OF ENDOCRINE GLANDS.

The majority of extracts of ductless glands, as at present prepared, have no obvious effect when administered by the mouth. Animal experiment up to the present has shown that tissue extracts in general, when injected intravenously, have much the same effect as any other foreign protein, and, with few exceptions, are in no way specific. Glandular extracts which have a definite action when given by the appropriate route are thyroid, parathyroid, pituitary, pancreas, and adrenal; extracts of intestinal glands given by the mouth in cases of atonic constipation may be helpful. But of these, thyroid and pancreatic alone afford true substitution therapy. There is no evidence that any extract other than thyroid and parathyroid is absorbed as such from the alimentary tract; adrenaline, for example, is only employed by the mouth as an astringent or to inhibit peristalsis in the stomach in cases of haematemesis and vomiting, but no “substitution effect” in Addison's disease is obtainable by feeding with or injection of the gland. Yet in adrenaline we have a valuable remedy as a haemostatic in shock, in asthma, and other spasmodic affections such as cardiospasm, urticaria, and angioneurotic oedema. Pituitrin, when injected, in no way replaces hypofunction of the pars nervosa from which it is prepared, but of its value as a stimulant to the failing myocardium, especially in toxic myocarditis, all will bear witness. It is useful also in intestinal distension not obstructive in origin, in asthma, and above all, I am told, in the third stage of labour.

If any advance in therapeutics is to be made with glandular extracts of doubtful action the practice of giving multiple extracts as a sort of blunderbuss, in the hope that one among the many may hit the mark, must be checked. Before organotherapy is employed we must be sure of our target and spend time and thought in charging our gun.

THE DIFFERENTIAL DIAGNOSIS BETWEEN ACUTE THORACIC AND ACUTE ABDOMINAL LESIONS.*

BY

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It is well known that thoracic disease frequently causes pain which is referred to the abdomen, and most experienced practitioners will agree that there is no class of case which causes greater anxiety and difficulty in diagnosis than that in which it is doubtful whether the cause of an acute abdominal pain lies in the thorax or the abdomen. It is imperative to make the diagnosis quickly, for a few hours' delay may cost the patient's life, yet a wrong decision to operate may be equally fatal. The bacteriologist and haematologist are of little help at this stage, and the decision has to be made on clinical grounds.

The difficulty in diagnosis lies for the most part in discriminating between conditions immediately above and below the diaphragm—parietal or diaphragmatic pleurisy, pneumonia, cardiac or pericardiac disease on the one hand, and cholecystitis or a leaking duodenal or gastric ulcer on the other. Frequently appendicitis and other diseases arising

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