A British Medical Association Lecture

ON

THE POSITION OF THE THYROID GLAND IN
THE ENDOCRINE SYSTEM.*

BY

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Few subjects in medicine have so powerfully stimulated interest and imagination of recent years as endocrinology. It provides the missing link between biology and psychology, and has profoundly modified our conception of disease. The internal secretions result from the specialization of the old chemical stimuli to which primitive animals reacted even before there was a nervous system at all. They reveal their antiquity in the way they cling to vestigial structures. Not infrequently when in the course of evolution a structure has become useless for its original purpose the endocrine system supplies it with a new tenant. Thus, the thyroid probably represents the Palaeostracan uterus, the parathyroids and thymus originate from the now useless gill-slits, the pituitary represents an invertebrate kidney, and the pineal an invertebrate eye. They remind us of the hermit crab that seizes on an empty whelk shell. And just as the hermit crab existed before it found an empty house, so the endocrine functions were in existence before they had a local habitation. This is particularly well seen in the primitive chromaffin material, which was originally widely diffused throughout the body of lower animals, before becoming concentrated in the adrenal medulla.

Internal secretions regulate instinctive behaviour. When the gonads of the queen bee reach a certain stage of development they render her strongly heliotropic. Hence the nuptial flight. The immediate effect of fertilization is to destroy this heliotropism, and she seeks the shelter of the nest. So with human beings. The instinctive behaviour of a young man in the presence of the opposite sex, whether shy or aggressive, depends mainly on the state of his endocrine system, and the unreasoning fractiousness of the climacteric woman merely reflects the chaos into which this system falls when its keystone is displaced. In this connexion it may be pointed out that the influence of these glands on secondary sexual characters is rather complex. The man with hyperthyroidism shows feminine traits, hyperpituitarism leads to virilism, hypopituitarism to feminism; and increase in the adrenal cortex, while producing premature sexual development in children, leads to marked virilism in women. According to Blair Bell, all the endocrine glands acting in harmony control metabolism in accordance with the needs of reproduction, and adapt the whole organism, physically and psychically, to this end. These few examples will illustrate what may happen when harmony is replaced by discord. The endocrines not only develop some characteristics, but they repress others. Without following Bolk to all his conclusions, I should agree that certain monkey-like traits are kept in abeyance by the pituitary. When this is diseased, as in acromegaly or osteitis deformans, the reversion to a monkey-like aspect is obvious. It is also known that when the pineal is diseased there is sexual precocity. Bolk suggests that the present function of the pineal is to delay sexual maturity in the interests of a more prolonged somatic development, for in the higher species the individual counts for more and fertility for less.

The activities of the endocrine glands are correlated to a large extent through the nervous system. We are so much more conscious of what goes on outside than of what occurs inside us that when we speak of the nervous system we are apt to think of it only in terms of the sensorimotor structures which keep us in touch with the external world. But for the maintenance of our vital functions we depend much more on the autonomic nervous system—and it is this system which has entered into an alliance with the endocrine glands.

THE AUTONOMIC NERVOUS SYSTEM.

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. The rhythm of life depends largely on the fluctuating balance between these two. The parasympathetic plays the chief part in the digestion and assimilation of food, the sympathetic spends the energy thus derived. In sleep the parasympathetic gains control, and the arrest of external manifestations of energy lasts until the balance is restored in favour of the sympathetic, when the subject awakens ready to expend energy again.

Each of these great divisions co-operates with a group of endocrine glands—the sympathetic with the adrenals, thyroid, and pituitary, the parasympathetic mainly with the glands of the digestive organs and their annexes. Possibly the parasympathetic co-operates also with the parathyroids. The autonomic nervous system is pre-eminently defensive in its action. In the primitive animal either the parasympathetic may be brought into play when the shock to which it is exposed is very great, producing immobility—the “shamming dead” reflex—or the sympathetic may be stimulated, violently activating the body for flight or fight. It is important to note that either this or that result follows without any attempt at compromise between the two, which Sherrington has shown is typical of reflex action in general.

But the sympathetic nervous system is a defensive mechanism not only against the external, but also against the internal foe. Fever is a response to bacterial invasion, and we now know that it is produced peripherally rather than centrally, since the cerebral vessels are remarkably impermeable to drugs and toxins so long as they remain intact. And this is carried out by the thyroid and adrenals, possibly with the aid of the pituitary. Fevers are known to be followed by changes in the adrenals and thyroid, but Cramer has been able to show that anything which calls for increased production of heat definitely increases the secretory activity of these glands. Mere exposure of a mammal, though not of a cold-blooded animal, to a low temperature will effect this. The injection of the drug known as T.H.N. will produce similar changes, together with all the phenomena of heat-stroke, and only exposure of the injected animal to cold will prevent a fatal issue. He has found similar changes in hyperpyrexia, and to a less degree in all fevers. He regards the heat regulation of the body as mainly effected peripherally, and points out what a profound effect climate must therefore have on the endocrine glands. Indeed, when one compares the brain, rigidly shut off in its bony box, with the peripheral apparatus in the skin, possessed of sensitive end-organs, responsive blood vessels, and sweat glands, together with the power of acquiring protective pigment, the case for a peripheral regulation of the temperature becomes so plausible as to cause wonder at its being overlooked so long. This was, no doubt, because it was so difficult to see how sufficient co-ordination could be obtained, as long as the close ties between skin, sympathetic nervous system, and endocrine glands were not appreciated.

Leonard Williams some twelve years ago called attention to the influence of climate in moulding racial character through the endocrine glands, but his conception was too much in advance of current medical thought then to receive the attention it merited. He pointed out that not only are there differences between the white man and the black, between Asiatics and Europeans, between the Latins and the Saxons, admittedly and even obtrusively climatic in origin, but that modifications through climate can still be seen at work. He says: “In illustration of the last point I need only mention the fair skin and the red hair which long residence in northern climes has conferred upon some Jewish families, and the stereotyping by the climate of the North American continent of the descendants of its widely dissemblant annual European recruits into the hatchet-shaped face and wiry frame of the Red Indian aborigines.” He suggests that the skin may be compared to a sensitive plate, stimulation of any portion of which will produce reflex activities in some distant organ, and he regards the formation of cutaneous pigment as protective against such stimulation becoming excessive. The distant organs mainly affected in this way he believes to be the endocrine glands, and it is obvious that the adrenals, for instance, play an important part in the pigmentary changes in the body. Recent observations show the pituitary must share directly in this, since tadpoles that had the anterior lobe of that gland removed became albinos. The unadapt-

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ability of albinos to climatic changes is well known. At the time the theory was put forward the close association between the sympathetic-endocrine system and the higher levels of the nervous system was not sufficiently recognized to make it acceptable. But I think we are now justified in saying that climatic environment can modify our psychic "make-up" through the endocrine glands.

HYPOTHYROIDISM.

These preliminary considerations will enable us to realize the position of the thyroid gland in the endocrine system. Says McCarrison: "The thyroid gland is to the human body what the draught is to the fire." It is a quickener of the whole metabolism. Recent studies of basal metabolism have shown that in hypothyroidism this is lowered by 40 per cent., while in hyperthyroidism it may be raised by an even greater amount. Although severe degrees of hypothyroidism, such as myxoedema and cretinism, are well recognized, there are minor degrees, as pointed out by Hertoghe, which are unfortunately often overlooked, although they are eminently amenable to treatment. In the adult these are characterized by the accumulation of material which should be katabolized. Headache, giddiness, somnolence, and a sense of fullness in the ears and nasopharynx, are not uncommon. A number of manifestations of hypothyroidism are attributed to rheumatism, although really due to myxoedematous infiltration of ligaments and fasciae, producing knock-knee, painful heel, flat-foot, and lordosis. The hand becomes lax and flabby, feeling, as Hertoghe says, like a glove stuffed with clay. A very helpful sign of hypothyroidism is the disappearance of the outer half of the eyebrows. The association of this with "rheumatic" symptoms should suggest the administration of thyroid extract. Nocturnal enuresis has been shown to be sometimes due to the same cause, partly because desquamation of the epithelium of the bladder renders it more irritable, and partly because of the deep somnolence. Infiltration of the nerve centres causes mental slowness, loss of memory, and difficulty in expressing ideas. Sometimes there are hallucinations of sight and hearing. It is rather surprising that acute mania should occur in myxoedema, but it does so occasionally. I recently saw an example in a middle-aged man whose myxoedema had improved extraordinarily under thyroid extract. Unfortunately he abandoned medical treatment and took up Christian Science. He became violently maniacal, and was removed to an asylum. Here they recognized that he was suffering from myxoedema, but at first they were afraid to give him thyroid extract because of his maniacal condition. But when they did so he again improved rapidly, and was soon able to give his medical history. He is now quite sane.

HYPERTHYROIDISM.

Turning to hyperthyroidism it is convenient, as McCarrison does, to classify the influences leading to it under the three heads of nutritional, toxic, and psychic.

(1) Nutritional.

Lack of vitamins leads to diminished thyroid secretion (McCarrison). Mellanby has suggested treating Graves's disease by cutting off the fat-soluble vitamin from the diet, but I have not been much impressed by the results of this method. Under the nutritional heading we may also include some part of the epochal changes in the gland, such as is so common in girls at puberty. In this connexion I should like to call attention to the importance of a small or twisted upper lateral incisor as evidence of gonadal deficiency. It is difficult to see the connexion until we recall that this condition of the incisor is the slightest degree of cleft palate. It is an atavistic stigma, and implies a difficulty in establishing adult development. This may explain why, as I have observed, such patients are liable to undue enlargement of the thyroid at puberty, since it is apparently more of a strain for them to achieve maturity.

(2) Toxic.

Two sources of toxæmia seem particularly apt to produce thyroid enlargement—namely, intestinal and oral. We can understand why intestinal toxæmia has this effect, since Kendall has shown that the active principle of thyroid secretion is an iodine compound of indol, a putrefactive decomposition product of the tryptophan in the protein molecule. It would appear as if the body provided in this way its own antidote, an increased production of indol necessitating and providing for more thyroid secretion. Quite as striking is the influence of oral, particularly

tonsillar, sepsis. It is hardly too fanciful to connect this with the fact that the thyroid gland originally discharged its secretion into the mouth through the foramen caecum at the base of the tongue. Since thyroid secretion is evidently increased by reaction to bacterial infections, an infection so near to the point at which this secretion was originally discharged might be expected to be specially potent in this direction.

A few weeks ago I had a case in hospital of recent and severe thyroid enlargement in a lad of 17. The gland formed a tense collar from the jaw to the clavicles, and his neck measured 20 inches in circumference. I was afraid that he might have sarcoma of the thyroid, but Mr. Dunhill, who kindly saw him with me, thought it was probably sub-acute thyroiditis. His tonsils appeared septic, but before they could be enucleated he had an attack of tonsillitis, after which the gland rapidly subsided, so that in a few days the neck measured only 17 in. The tonsils were then enucleated by Mr. Harmer. X rays were applied to the gland and he was given thyroid extract. He improved with remarkable rapidity. It should be added that he showed no ocular signs, tachycardia, or tremors. His increased thyroid secretion had apparently been needed to combat the sepsis.

Squier has commented upon the rapid subsidence of thyroid enlargement after an acute infection, which he attributed to diminution of secretion through post-infective sclerosis of the gland. Of course, other septic causes may induce thyroid enlargement besides these two, and I recently saw a case of Graves's disease following pericarditis. Indeed, Walter Edmunds speaks of the toxin of acute rheumatism as one of the recognized causes of Graves's disease. But, after all, there is a good case for regarding acute rheumatism as due to alimentary streptococci of altered virulence.

(3) Psychic.

While making full allowance for the influence of the other two factors, I am convinced that in Graves's disease the psychic factor plays a very large part. Happy people do not get Graves's disease. "But who is happy?" you may retort. True it is that it would be hard to find anyone who during the past seven years had not been subjected to some kind of unpleasant emotional strain, whereas only a limited number developed this disease. But in cases both of fully developed Graves's disease and in the *formes frustes* the history of shock, strain or psychic conflict is generally pronounced, even though the medical man is not able to obtain it for some time. Matrimonial causes frequently lie at the root of the trouble, and these are not reasons which the patient cares to parade. The factor of shock was shown repeatedly during the air raids on London, as it was after the San Francisco earthquake and the Kischineff massacres. As Coué has expressed it, the emotions rather than the will affect structure. Now, the emotions find their expression through the sympathetic nervous system, and it is the sympathetic that innervates the thyroid gland. Cannon's classical experiment on cats definitely proved that stimulation of the cervical sympathetic would cause exophthalmic goitre. Once the vicious circle is started it is hard to break, for the sympathetic stimulates the thyroid and thyroid secretion lowers the threshold to sympathetic stimulation. To my mind, operation, radium or x rays, operate merely as factors in breaking this vicious circle by diminishing the amount of thyroid secretion and thus allowing the balance to be restored. But the earlier and more efficient the medical treatment the less frequently will surgical interference be required. And for medical treatment to be efficient all those factors must be carefully investigated, remembering that it is when more than one of them is at work that Graves's disease is most likely to result. Treatment will consist of rest, psychotherapy in the widest sense, elimination of toxic factors, and administration of quinine hydrobromide for its sedative effect upon the sympathetic. Indeed, this drug has been used in America as a test for hyperthyroidism. For while it is generally well tolerated in this condition, patients with an adenomatous or compensatory enlargement of the thyroid gland will display symptoms of cinchonism fairly soon. I usually give it in 5-grain doses three times a day to men and in 2½ to 3-grain doses to women.

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THE INFLUENCE OF HYPERTHYROIDISM ON CARBOHYDRATE METABOLISM.

As is well known, glycosuria occasionally happens in hyperthyroidism, while lowering of carbohydrate tolerance is more common. What is not so clearly recognized is that the curve

of sugar in the blood after ingestion of carbohydrate is, as far as my observation goes, always abnormal. Usually the amount of sugar in the blood rises to a level at which glycosuria would normally occur, yet without the appearance of any sugar in the urine. There is also a delay in its return to the normal level. Since glycosuria does not occur, it would appear as if the kidney threshold for sugar had risen, presumably as a compensatory mechanism. This rise of blood sugar is the method by which the thyroid secretion provides for the increased heat production in fever. In other words, both in Graves's disease and in fever the thyroid contributes towards increased katabolism by mobilizing sugar into the blood stream, and the kidney holds it there by raising the threshold against its excretion. It is noteworthy that in several of my cases of this type transitory glycosuria has nevertheless occurred under emotional stress, or amenable glycosuria has come on as the hyperthyroidism became less acute. I would interpret this by saying that the threshold was lowered again before the carbohydrate plethora passed off. Conversely, in myxoedema the level of the blood sugar remains low, even after the ingestion of considerable amounts. In part, no doubt, these effects of the thyroid are due to its antagonism to the pancreas. This antagonism is expressed not only (1) in the high blood sugar which is common to increased action of the thyroid and diminished action of the pancreas; and (2) in the mydriasis following instillation of adrenaline into the eye, which occurs under similar conditions; but also (3) in the output of pancreatic diastase in the urine, which is diminished in hyperthyroidism.

INTERMITTENT SWELLING OF THE THYROID IN CERTAIN NERVE STORMS.

The close association between the thyroid gland and the emotional nervous system is seen in the following three cases:

CASE I.

A lady of 50 was brought to see me because she suffered from periods of depression followed by periods of excitement, tachycardia, and tremors, in which the thyroid swelled. Hysterectomy had been performed four and a half years before, and a cystic adenoma had been removed from her thyroid ten years ago. She had no glycosuria after 100 grams of dextrose, and, unlike an ordinary case of hyperthyroidism, her urinary diastase was rather high. This was not observed, however, during a period of excitement. The effect of quinine hydrobromide was to cut out the periods of excitement, but to leave the periods of depression as severe as ever. Careful search was made in this case for a toxic factor, without success.

CASE II.

A girl of 20 was admitted to hospital under my care with the history that some eight months previously her ovaries and tubes had been removed on account of tuberculous disease. After this she became distinctly fairer in complexion, and put on weight considerably. She suffered from hot flushes. Her thyroid had been rather full before the operation, but this had been less noticeable since, except during the attacks for which she was admitted to hospital. These occurred every three to four days. There was no aura, and consciousness was almost but not completely lost. She flushed and choked, while the pulse and respiration quickened very much. The attacks lasted about six minutes, and ended quickly, though the pulse rate subsided more slowly. The thyroid swelled noticeably in the attacks, and she passed a small amount of sugar then, but not at other times. Under bromide and opocaps of ovomammoid the attacks ceased completely—the last having occurred on September 4th. Her weight has fallen considerably, the hot flushes have ceased, and her general condition has greatly improved.

CASE III.

A man of 31, who had been subject to *petit mal* for three months following an accident thirteen years ago, had a recurrence of these attacks after another accident in 1917. In July, 1921, he had malaria, after which his *petit mal* assumed some new features; on recovering from a brief unconsciousness he became restless and excited, complained of difficulty in swallowing, and his thyroid swelled. On one occasion it was only the left lobe that enlarged. He is a man of great intelligence, and he expressed himself as feeling completely disorientated for about ten minutes by an attack. A curious feature was his bradycardia, the pulse rate varying from 48 to 52. Even when his temperature rose to 104° in an attack of malaria his pulse only went up to 64. Yet on vigorous exercise the pulse rate rose to 96 for a short time. I associate this bradycardia with his epilepsy.

It is interesting to note that the first two patients had their endocrine balance upset by the induction of an artificial climacteric, one in early life, the other shortly before the time when it would have normally occurred. I should like to call special attention to the benefit derived from the ovomammoid extract in apparently restoring endocrine

balance in the second case. In the third case no doubt the thyroid specially suffered in the outbreak of excitement because it was already irritated by an infection—namely, malaria. I have since heard that on quinine hydrobromide till free from malarial parasites, and then on potassium bromide, he has kept entirely free from attacks. I also learned he had matrimonial troubles, which, as I have said, so often have an effect on the thyroid gland. The absence of tachycardia with emotional excitement suggests that vagotonia played a part in this case. But all three cases illustrate the influence of emotional excitement on the thyroid.

Such cases should, I think, be distinguished from the condition of thyroid instability described by Leopold-Levi and Rothschild where there are spurts of hyperthyroidism occurring with a background of continuing hypothyroidism. This may be compared to a state of "irritable weakness." In one such case I saw these spurts were accompanied by tachycardia and tremors, yet her weight was rapidly increasing, and until small doses of thyroid extract were given she appeared to be developing acute myxoedema. Pituitary extract was first tried without benefit, but on thyroid the condition cleared up rapidly.

It may well be asked what are the points which should guide us in determining whether thyroid enlargement is compensatory for a deficiency of thyroid secretion, or whether there is genuine hyperthyroidism. I would say that if basal metabolism is increased, if there is wasting, pyrexia, continued tachycardia and tremors, with attacks of diarrhoea, and if there is any glycosuria, the case is certainly one of hyperthyroidism, and thyroid extract should not be given, but quinine hydrobromide is indicated. If these signs are lacking and the patient is putting on weight, thyroid extract should be given a trial.

THE CARDIO-VASCULAR COMPLICATIONS OF THYROID DISEASE.

Hypothyroidism.

(a) *Vascular*.—The liability of the subjects of hypothyroidism to chilblains is well known. A condition like Raynaud's disease is not uncommon. It will usually be found that there is then a well-marked intestinal toxæmia, usually the result of definite viscerotoposis, which often exhausts the thyroid while also affecting the vessels. Mr. Morley Roberts has suggested to me that histamine may be the product of putrefaction which damages the capillaries, and from some preliminary investigations I have made it seems to me this may be the case. Treatment should be directed to the condition of the bowel, such as by a Curtis support, Plombières douches and intestinal antiseptics.

(b) *Cardiac*.—I have seen a number of instances where patients with hypothyroidism and feeble flabby hearts have been labelled as suffering from "fatty heart." I agree with Leopold-Levi and Rothschild that thyroid extract benefits such cases greatly, but that great care is required in the dosage. Naturally some apprehension may be felt about giving such a drug in this condition, but half a grain twice a day has never, in my experience, produced any unpleasant symptoms.

Hyperthyroidism.

(a) *Vascular*.—Goodall and Rogers describe three stages in the reaction of the blood pressure to Graves's disease. First, a preliminary rise from the sympathetic irritation which has caused the thyroid enlargement, possibly from simultaneous stimulation of the adrenals. Next, a fall of pressure from the vaso-dilator effect of the excessive thyroid secretion, which they regard as the safest stage for operation. Thirdly, a rise due to reduction of this secretion, accompanied by some change such as cardiac hypertrophy.

(b) *Cardiac*.—Here again we are indebted to Goodall for a clear exposition of the position. Prolonged tachycardia may exhaust the myocardium. This leads to atony and dilatation with valvular incompetence. Then myocardial degeneration is apt to result, which may go on to auricular fibrillation. Quite lately I have seen three instances of this in the later stages of Graves's disease. Further, there is a danger of this fibrillation affecting the ventricles after operation, which is probably the cause of the sudden death which sometimes follows it, as unfortunately happened lately in a case under my care. There is a liability to a considerable rise of blood pressure after operation, which greatly adds to the work of an already overtaxed heart. Ventricular fibrillation is not compatible with life.

THE PARATHYROIDS.

These glands were first described as distinct entities by Sandström, while Gley was the first to attribute to them functions apart from the thyroid. But in 1907 Forsyth concluded that they were merely portions of the main thyroid gland which had not yet formed vesicles, and that all the intermediate stages between thyroid and parathyroid tissues occurred. Berry, as the result of 1,338 operations for the removal of goitre without the occurrence of tetany, altogether discredits any separate function for the parathyroids; but as he states he always leaves a piece of gland at the hilus, he presumably does not completely remove them. The consensus of opinion at the present time seems to be that the general effect of the parathyroids on metabolism is antagonistic to the thyroid, and that they play a special part in the fixation of calcium in the tissues. If the nervous system lacks calcium it becomes more irritable, and tetany is likely to occur. It is possible, however, as pointed out by Noël Paton, that it is the accumulation of methyl-guanidine which occurs after parathyroid removal that causes tetany, since injection of this substance will produce a similar effect. Parathyroid secretion may distoxicate methyl-guanidine. Korenchevsky has repeatedly produced tetany in rats by destroying their parathyroid tissue, which forms a distinct encapsulated structure in these animals, with the electric cautery. Clinical observations by Hurst, Cordier, and G. H. Clarke support the view that parathyroid disease causes tetany, tremors, and fibrillary twitchings, among other symptoms, which can be relieved by administration of parathyroid extract. That these glands have some effect in checking calcium loss has been shown by comparing the output of calcium salts on thyroid and parathyroid extract. Quite recently Vines has shown the value of parathyroid extract in promoting the healing of ulcers of the skin and stomach. He suggests that various chronic infections damage the parathyroids and thus prevent healing by diminishing the amount of ionizable calcium salts in the blood. Walter Edmunds has noted that after parathyroidectomy animals may be kept alive longer by an exclusive milk diet, with the addition of calcium lactate. He also quotes Eppinger, Falta, and Rudinger, who found that the removal of the parathyroids, one by one, tended more and more to favour the onset of glycosuria. This would suggest that the parathyroids work with the pancreas and fall into the anabolic group, while antagonizing the thyroid, which belongs to the katabolic group. It also raises the question as to whether the increased calcium loss in diabetes may be due to parathyroid deficiency.

CONCLUSION.

We are thus led to the conclusion that the position of the thyroid gland in the endocrine system is that of a powerful activator of metabolism. In this respect it co-operates with the adrenals and pituitary, and antagonizes the pancreas and parathyroids. On the nervous side it co-operates with the sympathetic nervous system, both being stimulated to increased activity by it and lowering the threshold to it. In this way it plays an important part both in external and internal defence. Externally it leads to greater manifestation of energy in the direction of fight or flight; internally it quickens the reactions to bacterial invasion. An important way in which it accomplishes this is by mobilizing the blood sugar. This increased supply of sugar may either be used for muscular energy in external defence or for heat in the febrile reaction of internal defence. As a provision against waste of this sugar the kidney threshold is raised to prevent its escape into the urine, so that despite hyperglycaemia there may be no glycosuria. Yet this blood sugar may exceed even this raised threshold, so that some escapes. This is particularly likely to occur during emotional excitement, when the gland is apt to enlarge. It interacts also with the gonads, and the undoubted fact that it plays a more active part in female metabolism may be due to its origin from the uterus of a Palaeostracan ancestor. This interaction may account for the disturbances which are so apt to occur in the gland after an artificial or natural climacteric. That in the former instance this is likely to take the form of intermittent hyperthyroidism may be due to the gland being still in full activity; in the latter instance hypothyroidism is more common, presumably because the gland is already undergoing retrogression. The combination of a distressing emotion of matrimonial origin with a toxæmia of alimentary origin is the most fertile cause of hyperthyroidism, and the biological consideration here presented may help to explain why this is the case.

RHEUMATOID ARTHRITIS DUE TO INFECTION
OF THE NASAL ACCESSORY SINUS.*

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In this ancient city of Bath which our medical colleagues have made renowned throughout the world, not as the Mecca of the rheumatic, for that it has been long before medical practice could be termed a science, but as a centre where exceptional clinical opportunity has been utilized for scientific research and post-graduate study, it is with a certain sense of diffidence that I chose for the subject of my address such a group of diseases as rheumatism, neuritis, and arthritis.

The recognition of the infective nature of a considerable percentage of clinical syndromes loosely designated rheumatism, rheumatoid arthritis, chronic articular fibrositis, neuritis, and so forth, has led to investigations directed to the many possible sources of such infection. While the teeth, gastro-intestinal and genito-urinary tracts have received due consideration, there lies in the nasal accessory sinuses a possible source of chronic systemic infection which merits more attention than has hitherto been accorded to this region. And if, as I hope to show, the nasal sinuses may contain the cause even in a percentage only of such intractable diseases, it is the more important that these nasal cases should be recognized inasmuch as it is relatively easy to determine the presence or absence of nasal sinus infection.

Why a nasal source of the infection in rheumatoid arthritis is so liable to escape attention, and how it is that the joint affection is more prone to arise in patients whose nasal symptoms are slight rather than in cases where there is profuse purulent rhinitis, I shall endeavour to explain below. Before doing so I submit brief notes of some cases which have benefited so definitely by treating the infection of the nasal sinus that it seems to leave no room for doubt that by such treatment the source of the joint disease was eliminated. Of three examples the first illustrates the earlier or slighter forms of articular fibrositis; the other two were typical cases of chronic rheumatoid arthritis (fibrositis) of long standing.

CASE I.

Miss E. R., aged 40, was referred by Dr. Mary Morris, of Bath, on account of chronic fibrositis, involving several finger-joints, gradually developing for two years; chronic rheumatic pains in the legs and feet, central frontal headaches, and an occasional subjective sense of foul odour. For four years she had noticed some post-nasal catarrh, and this led her medical attendant to suspect a nasal source, particularly as treatment for pyorrhoea had failed to relieve her. Furthermore, the patient, formerly of a bright and active disposition, was mentally repressed. Examination of the nose revealed no nasal discharge whatever, yet the history of post-nasal catarrh and the general condition of the patient was so suggestive of a latent infection of an accessory nasal sinus that exploration of the sinuses seemed warranted if only to eliminate such a source of infection as a cause of the serious disease that menaced her health. Exploration of the maxillary antra, sphenoidal sinuses, and the left posterior ethmoidal cells was made by means of my suction syringe, so as to obtain a "deep-sea fishing" from each cavity. No pus was obtained, though the left antrum and the left posterior ethmoidal cell yielded turbid contents. On bacteriological examination by Dr. Kay Mouatt, both the maxillary antra yielded cultures of *Staphylococcus pyogenes aureus*, and the left ethmoidal cell staphylococcus, together with a bacillus that "is frequent in influenza-like catarrhs"; the other sinuses were uninfected. A solution of 1 in 10,000 mercury binoiodide was injected into each cavity, and the diseased antrum was opened and drained. The patient rapidly improved and was further benefited by autogenous vaccines from the cultures. Not only did the rheumatic swellings largely resolve, but the general health improved and she regained her former cheerful disposition and betook herself actively to games.

The second example is of interest, not only on account of the very long history of the joint affection, but also as being one of the very large percentage of cases of appendicitis occurring in association with chronic infective rhinitis.

CASE II.

Miss B. D., aged 46, had suffered from rheumatism in the left knee from the age of 14 and in the right from one year later. This condition persisted without much change till, sixteen years later, the left wrist and finger-joints became involved; not very long afterwards she had an attack of neuritis in the left shoulder. Ten years before I saw her she began to suffer from pains and stiffness

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