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THE RÔLE OF HEREDITY IN THYROID PATHOLOGY.

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THE pathology of the endocrine glands is one of the most recent conquests of medicine. This branch of knowledge, which 50 years ago was practically unexplored, originated with the discoveries of Claude Bernard and Brown-Séquard. The thyroid body and the suprarenal capsules were the objects of the earliest research of clinicians and investigators; but despite the interest aroused by new ideas the field of research was confined, for the first syndromes recognised were strictly separated in compartments. Addison's disease, myxoedema, and exophthalmic goitre had long been known, but no connexion was perceived between these three distinct affections. No association of disturbances of the thyroid and those of the capsules was considered possible; hence myxoedema and exophthalmic goitre were needs attributed to failure or excess of thyroid secretion. But dangerously simple theories could not long prevail over new interpretations born of increasingly exact observation of facts and of more perfect knowledge of physiology. Numerous animal experiments, and knowledge gained at autopsies, enabled research workers to establish the fact that lesions of a single gland were rare—that usually several internally secreting glands were attacked, either simultaneously or successively. It might have excited remark that in an organism whose several organs function in harmony, only the endocrine glands could be isolated one from another; and from that idea arose the more recent and truer conception of multi-glandular syndromes to which French workers, Claude and Gougerot particularly, made important contributions. Only thus were to be explained many contradictory symptoms, description of which must be sought in vain in classical works. By this theory, whose value lies in its being based on carefully observed facts, it was possible to ascertain that a gland cannot function separately, but that there exists between one gland and the others a connexion of action and reaction, implying a complexity which sets in a new light the symptoms observed clinically.

The Concept of Dysthyroidism.

Thus one learns that when a lesion is produced by any one gland, the glandular limits are often overstepped; it is known, for example, that Addison's disease and Basedow's disease may be observed in the same patient. Similarly, the distinction between myxoedema and exophthalmic goitre is not so clear as has often been thought; the two diseases are bound up not strictly with a failure or excess of thyroid secretion, but rather with imperfect function. Thus because of the numerous intermediate forms assumed by thyroid affections, we prefer to use the general term "dysthyroidism." Observation has shown that even in cases apparently clear, where Basedow's disease or myxoedema is concerned, there is often an association of symptoms indicating at one and the same time an excess and a failure of thyroid secretion.

Garnier showed that thyroid lesions were very frequent in the course of acute infections, but that histological control was necessary to disclose them. Hutinel and Tixier observed the frequency of infectious diseases in youth (measles, scarlet fever, whooping-cough, rheumatism, chorea, mumps) to be in striking contrast with the rarity of exophthalmic goitre. Syphilis is at present one of the most evident

causes of thyroid affections; Hutinel—and later Schulmann and R. Barthélemy, one in his study of syphilitic exophthalmic goitre, the other in his work on the endocrines and hereditary syphilis—have insisted upon this fact; but the same objection may be raised—i.e., the discrepancy between the extraordinary frequency of syphilis and the relative rarity of exophthalmic goitre and myxoedema. It must be recognised that whilst in many cases the rôle of syphilis is established, in many other cases it appears very doubtful—for example, where syphilis remains unrecognised or where it is only indicated in descendants by the appearance of dystrophic trouble. Thyroid affections are sometimes anterior to the appearance of syphilis, which only serves to aggravate them; frequently, moreover, syphilis and infectious disease have merely assisted the development of previously latent thyroid disorder. Similarly, thyroid affections are observed in women at certain periods of their reproductive existence—puberty, menstruation, pregnancy, confinement, lactation, and menopause—in the same way as keen emotion or traumatism may develop such disorders, otherwise latent. The apparently rapid onset of exophthalmic goitre is frequently only the lighting up of a condition previously unsuspected.

Glandular Heredity.

In the writer's opinion heredity ranks prominent amongst the obscure causes of thyroid affections. Its rôle has been the subject of much debate; nervous heredity was thought to be indicated, but to-day we know that glandular heredity is to blame. If the nervous predisposition exists, it is much more frequently the effect than the cause of thyroid disorder. The sympathetic nervous system certainly comes into consideration, but its rôle is apparently secondary; nervous disorder is only manifested as a sequel of thyroid disorder. In no case of glandular trouble has an autopsy revealed a lesion of the sympathetic mechanism. Strong emotion, however, which by itself seems incapable of producing Basedow's disease, may "revive or aggravate certain more or less latent manifestations of Basedow's disease such as tremor and tachycardia" (Souques). The facts concerning thyroid heredity are still imperfectly known; but it is recognised that a mother suffering from Basedow's disease may bear children who later—after strong emotion, traumatism, or some illness—will present some of the signs of that disease. This fact proves hereditary transmission of thyroid weakness, whatever the cause of the latter. Thyroid defect exists in the family, preparing a soil in which syphilis, infectious disease, traumatism, and emotion will act with particular efficacy. I consider that if syphilis has a *selective* action on the thyroid it is frequently on account of an hereditary predisposition, of which the origin is not always demonstrably syphilitic. This thyroid weakness is not always isolated, being frequently associated with general glandular weakness; it is not as easily shown in the thyroid as in the liver or kidney—no one contests the existence of hereditary hepatic or renal debility—but there is no reason to doubt its existence. Yet heredity cannot account for everything, and its rôle must not be exaggerated. In my thesis devoted to this subject I have reported the frequent but not invariable discovery of a connexion with heredity in 150 observations, collected from French and other literature and noted in patients under Dr. Apert at the Hôpital des Enfants Malades.

The familial and hereditary theory of thyroid disorder has existed for 60 years, principally amongst French writers on the subject. Trousseau was one of the first to mention it in his clinical work. Landouzy

and Déjerine contributed several conclusive pieces of work—the latter's being a remarkable thesis on nervous heredity and the connexion of Basedow's disease with nervous affections. Charcot derived nervous heredity from the fact of hereditary degeneration. Later, Dieulafoy, and still more recently Apert, L. Lévi, and H. de Rothschild, made special studies of thyroid heredity itself, and of hereditary degeneration. It is curious to observe that though the rôle of heredity has long been recognised in exophthalmic goitre, the hypothyroid conditions were completely ignored. Myxoedema was known, but its familial character was entirely unsuspected. Two workers, Brissaud and Hertoghe (one French, the other Belgian) first described familial myxoedema in 1899; but the facts of familial and hereditary hypothyroidism and dysthyroidism—doubtless because of their apparent rarity, since they had not been investigated—remained little known and were even doubted altogether. In 1918 Hutinel aroused new interest in their importance and in that of the different methods of transmission of glandular debility. The present writer determined to show that besides the heredity of exophthalmic goitre and hypothyroid conditions there exist hereditary changes not only nervous but glandular—changes capable of involving most of the endocrine glands.

Heredity, "Similar" and "Dissimilar."

Thyroid heredity may be manifested in two ways—i.e., similar or dissimilar heredity. The term "similar" heredity is applied to instances in which are found, in direct or collateral descent, one or more subjects presenting indisputable signs of Basedow's disease. The latter may appear in several children of one female and may persist for several generations; it is often complete—i.e., the various subjects may present all the signs of the disease. Again, similar heredity is sometimes incomplete, in the sense that in the family of a subject of Basedow's disease modified conditions of the same disease—cases of hypothyroidism or nervousness—may be observed, which may be clearly connected with thyroid defect. The most useful observations on this subject which I have found are, in France, the works of Dieulafoy, Souques and J. Lermoyez, Harvier, and Schulmann; and abroad, those of Cantilena and Oesterreicher.

True myxoedema may appear in several children of the same family but apparently cannot be hereditarily transmitted, as women suffering from typical myxoedema are generally sterile; but modified myxoedema and thyroidism can be so transmitted. The following is a case of obvious familial myxoedema observed by the writer: M. R., aged 40; very nervous, pulse 108. The whole family examined Dec. 27th, 1920, also found to be very nervous—father and five children, all boys. The mother had had a four months' miscarriage. The eldest boy, aged 15, appeared to be 8; myxoedema had appeared about the age of 2 and he had had long treatment, but did not grow, was incapable of learning anything and suffered from migraine. One boy, aged 11, was normal, one aged 8 also normal, one aged 5 in hospital with myxoedema, and one aged 13 months in hospital for the same reason.

In other and more frequent cases the mother was observed to be obese, very sensitive to cold, and constipated, with scanty hair and eyebrows and infiltration of the face—all signs of hypothyroidism clearly established by Lévi; one child may have retarded growth or may remain infantile, whilst others present the dry skin, scanty hair, thick lips, slow movements, and diminished vitality of the myxoedematous. Many children are considered lazy or backward because they are feeble, apathetic, and have no aptitude for work; in reality they are often the subjects of disease which it is possible to cure, or at least to ameliorate, by means of thyroid treatment to which recourse should always be had, particularly if the maternal antecedents indicate the true condition.

Lévi, Hutinel, and Apert have published numerous observations of familial thyroidism and of dysendocrinism. Some curious features have been described by an Italian writer, Spolverini, who has seen infants

born of healthy parentage becoming myxoedematous after having been nursed by women with goitre. Thus, milk can, in certain cases, be an agent of transmission of thyroid poison. The rôle of heredity may be difficult to affirm, for the defect may remain latent for a very long time, only being revealed in adolescence or in adult age; but in congenital myxoedema the hereditary influence is more evident. Simple goitre, attributed to polluted water, is often a thyroid disorder, which may be transmitted to an infant under the form of Basedow's disease and myxoedema. Schiasi observed a manifest case of hyperthyroidism in a patient who was the son of a woman suffering from goitre; as the result of a wound of the neck this man presented testicular trouble at the same time as turgescence of the thyroid. Thus, in brief, are the facts of similar heredity which it is here possible to mention.

Dissimilar heredity is at least as frequent, but seems at first more difficult to admit. It might excite surprise to find subjects of well-defined exophthalmic goitre giving birth to myxoedematous children. One child may develop Basedow's disease, and another child of the same family may develop myxoedema. More infrequently may be found in one child hyperthyroidism, in another hypothyroidism. Those reactions in opposite directions may be observed, not only in the same family, but in the same individual; this latter condition may be called individual dysthyroidism, as opposed to familial dysthyroidism. The writer has observed amongst several patients of this type presenting contradictory signs a girl of 15 with exophthalmos and pronounced goitre; the pulse was 150, and tremors were present, but there was no psychic trouble or excitement; the patient, on the contrary, was apathetic, fat, and devoid of all hair.

Again, a boy of 13 was observed, in whom typical myxoedema appeared when he was 6; he still presented distinct signs of myxoedema, but his eyes were bright and clear, he was well-grown, with perfectly normal intelligence. Sometimes these patients present modified signs of hypothyroidism (migraine, oedema, scantiness of hair and eyebrows, cold and cyanosed skin) but display—at intervals of hours, weeks, or months—attacks of diarrhoea, increase of temperature, great excitement, swelling of the neck, and tremor, which are distinctly ameliorated by corpus luteum and thyroid extract. These crises are exactly described by Lévi and Rothschild, under the name of "thyroid instability." The present writer has observed several well-defined cases where a mother with goitre and hyperthyroidism has borne a child presenting hypothyroidism; in other cases the child presented congenital myxoedema.

Involvement of Other Glands.

Dissimilar heredity does not always involve only the thyroid. Other glands may be affected at the same time and play a part in the hereditary factor. Thus, obesity is frequently noted in familial hypothyroidism. Pituitary changes are often observed together with thyroid affections, and may occasion important disorders in the individual and in the offspring. In several observations acromegalous parents have been noted as having myxoedematous children. Barthélemy has instanced the case of a syphilitic father, one of whose children was acromegalous, the other myxoedematous. The connexion between the thyroid and the ovaries is sufficiently well known, and the reciprocal action of these glands may affect the offspring. The liver—a gland, like the testicle and the ovary, both of internal and external secretion—is similarly connected. Biliary lithiasis is often associated with thyroid disorder in the individual or the offspring. Knowledge of the rôle of the thyroid in the metabolism of calcium and in the general development of the skeleton enables us to understand the connexion between the thyroid and bone affections. Bone disease is frequently observed in children of subjects showing dysthyroidism. Lastly, achondroplasia and mongolism have occurred in families with Basedow's disease and myxoedema; and certain skin conditions (ichthyosis, scleroderma) are also seen in families displaying hypothyroidism.

Present Position Concerning Thyroid Pathology.

These ideas concerning thyroid pathology are not simply theoretical; they are based on numerous clinical observations made by many writers. Doubtless diagnosis in aberrant cases is not always easy, and it must be recognised that so far the great stumbling-block of endocrinology has been the impossibility of bringing sufficient scientific exactitude to bear on diagnosis. True, attempts have been made to estimate by humoral reactions the vitiation of thyroid secretion. R. Porak observed that injections of pituitary extract which in normal subjects provoke acceleration of the pulse give rise to no such acceleration in myxoedematous subjects, whilst in patients with Basedow's disease they produce marked bradycardia. Claude and his pupils, using adrenalin, have also observed in their subjects acceleration of pulse in normal health, intense and lasting bradycardia in Basedow's disease, and no modification in myxoedema. The results of biological tests are interesting, but unfortunately the reactions vary too widely with the subject for absolute confidence to be placed in them. Attention must, then, be devoted to the clinical signs and to the effects of treatment, which permit a certain degree of suspicion as to the predominance of action of this gland or that; the thyroid, however, is known to be one of those glands which give the best results, being capable of influencing lesions not always strictly limited to itself. It is chiefly due to experimental observation (the work of many writers, of whom the principal in France are Lortat-Jacob, Richoud and Jeandelize, Claude and Rouillard) that the facts of thyroid heredity possess a scientific value. It has been shown that thyroid disorder of parents determines in their offspring certain conditions such as rarity of birth, poor development, malformations of bone, shortness of life, and lastly, myxoedema; the successful result of thyroid treatment has also been demonstrated.

Conclusion.

This knowledge of the rôle of heredity in lesions of the thyroid has, above all, a prophylactic interest. It permits at times of diagnosis of disorders in the parents which enables treatment of their children to be directed against the real cause of disease. However, the thyroid condition of the parents is no indication of the degree of thyroid weakness in the offspring; a modified form in the mother may give rise in the infant to a clearly characterised syndrome, and vice versa. It is, then, important to treat parents showing even the least signs of thyroid affections. In treating the nursing mother, one probably gives treatment also to the child, since products of thyroid secretion probably pass over in the milk. Wet-nurses should be examined from this point of view. Maternal lactation is not contra-indicated unless a recrudescence of symptoms of thyroid disorder is observed in the mother or unless signs of excitation appear in the infant. Treatment must be carried out with prudence and perseverance.

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THE TREATMENT OF WAR INJURIES OF THE SPINAL CORD.

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TRIFLING concussion of the spinal axis, such as that due to the wind of a bullet, or to the repercussion on the spine of the shock of a projectile passing more or less near to it, will be excluded from this study. Such concussion, whose clinical picture is now well known, generally runs a favourable course without need for surgery; but it is otherwise in the case of grave lesions of the spinal cord—that is to say, complete or incomplete section, serious contusion, compression, and certain violent disturbances which, in the great majority of cases, produce a clinical syndrome of total section. The treatment of these conditions constitutes one of the most perplexing problems of war surgery—subtle as regards its indications, restricted in technique, deceptive in its results—and therefore all the more urgently demanding improvement.

The series of complications determined by physiological section due to traumatism are often of an importance disproportionate with the gravity of the causal lesion. These complications constitute disorders demanding separate treatment; thus it is necessary to consider the treatment of (1) the medullary lesion, and (2) each of the complications. Unless this distinction is made, the therapeutics of serious medullary injuries is confused and incomplete.

1. Treatment of Lesions of the Spinal Cord.

The evolution of the majority of cases of these spinal injuries points to the inability of the spinal cord to recover after section or violent traumatism. At least, the slowness of the process of regeneration, histologically observed,¹ is such that no sign of it has appeared before the patient's death. This fact, held to be indisputable before the war, led the majority of surgeons to consider wounds of the spinal cord as hopeless; it is still generally believed that to intervene with any operation involving shock simply hastens the patient's death or at least leads to no beneficial result. But this inaction is contrary to the theory of immediate intervention after war injuries, and admits, moreover, of two important objections: (1) The leaving untouched of an intra- or a para-rachidian projectile; neglect to treat the seat of a vertebral injury is exposing the patient to the risk of various infectious processes which may complicate the situation. (2) Numerous observations have clearly shown that the clinical signs of spinal traumatism are in their initial phase frequently deceptive. It is known² that congestion and cedema of the meninges

¹ Roussy and Lhermitte: Annales de Médecine, 1915, No. 6.

² Sencert: Congrès de Chirurgie, 1909.