THE INTERNAL SECRETIONS IN RELATION TO DERMATOLOGY.

BY

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NEARLY twenty years have passed since Byrom Bramwell reported to the Newcastle meeting of the British Medical Association (1893) the results which he had obtained in cases of psoriasis, lupus vulgaris, and acute eczema by the internal administration of thyroid extract.¹ This was the beginning of organotherapy in connexion with dermatology. Thyroid treatment had already been successfully used in myxoedema by G. R. Murray, Hector Mackenzie, Arthur T. Davies, and others; and it was now employed on an extensive scale in the therapeutics of skin affections. But, as was perhaps inevitable, it was administered with too little discrimination, and, though it found enthusiastic advocates, signs of reaction were not long in declaring themselves, and after a while it was neglected and almost forgotten. Of late years, owing in part to the light that has been thrown upon the physiology and pathology of the ductless glands by a multitude of investigators, there has been a revival of interest in the subject, and the more discriminating use of animal extracts in many chronic skin diseases has yielded results more favourable than those at first obtained. The time seems, therefore, to be appropriate for considering in some detail the influence of the internal secretions upon the skin and its appendages, and attempting an estimate of the value of organotherapy in the treatment of cutaneous affections.

HISTORICAL NOTES.

It may not be without interest first to note the chief landmarks in our knowledge, so laboriously acquired, of the internal secretions, one of the most obscure and complex, and at the same time one of the most fascinating branches of medical science. In his textbook of physiology, published in 1776, Haller² grouped together the thyroid, the thymus, and the spleen as glands which, though ductless, secrete fluids that find their way into the general circulation. Thenceforward the glandular character of the thyroid body was generally accepted, though it was not until many years later that any serious attempt was made to investigate the nature and function of its secretion. In 1844 Johannes Müller³ included among secretory as distinguished from excretory glands, the spleen, thyroid, suprarenals, thymus, and placenta. But it was in connexion with a gland that is not ductless that the action of an internal secretion was first experimentally proved. In 1849 A. A. Berthold, of Göttingen,⁴ published his famous experiments in the transplantation of the testicles of cocks, showing that after the transplantation the animals retained their male characters in voice, reproductive instinct, fighting spirit, and growth of combs and wattles. Thus he demonstrated the influence exerted through the blood upon the economy by an organ through which the blood stream circulates, and to him, as Biedl⁵ remarks, belongs the honour of having first proved the existence of an internal secretion and seized its immediate significance.

The demonstration, however, passed unheeded; the time was not yet ripe for a recognition of its far-reaching import. In the following decade came the classical investigations by which Claude Bernard⁶ proved that in addition to its external secretion—bile—the liver forms an internal secretion—glycogen—which, he held, passes into the blood stream as sugar. But it was reserved for Brown-Séquard⁷ to formulate (1869) the theory that all glands, whether furnished or unfurnished with ducts, contribute to the blood substances of physiological utility. Some years earlier,⁸ prompted by Addison's discovery of the connexion between the suprarenals and the disease which now bears that great physician's name, he had experimentally investigated the action of those bodies, and had come to the conclusion that in certain animals their extirpation caused rapid death, which could be postponed by the injection of suprarenal extract. Finally, in 1889,⁹ he related the experiments which he had been conducting for twenty years with the subcutaneous injection of

testicular extract, and thus, whatever view may be taken of the value of that series of experiments, became the founder of modern organo- or opo-therapy, so like, yet so unlike, the organotherapy of primitive medicine.

The importance of the thyroid was first revealed by the results of the operations undertaken by the Reverdins and by Kocher for the relief of goitre. The keen observation of Sir William Gull¹⁰ had already detected the resemblance to cretinism of the condition afterwards known as myxoedema, and he had characterized it (1874) as "a cretinoid state supervening in adult life in women"; and when (1883) the Reverdins and Kocher described the symptoms produced in goitrous patients by removal of the thyroid their identity with the symptoms described by Gull was recognized by Sir Felix Semon,¹¹ and the Reverdins styled the condition they had unwittingly created "*myxoedème postopératoire*." Next, it was found *post mortem* that myxoedema is associated with degeneration of the thyroid. The brilliant experimental work of Schiff, Sir Victor Horsley, G. R. Murray,¹² and many other observers that followed these discoveries has not, it must be admitted, finally solved the problems to which it was directed, partly because the gland functions differently in different animals, but also because at first the influence of the parathyroids was not recognized. These bodies were only discovered in 1880 by Sandström, and it was not until 1892 that their importance was insisted upon by Gley,¹³ whose view, elaborated by Vassale and Generali, is that their secretion is even more essential than that of the thyroid itself.

To the pituitary body, which has functional relations with the thyroid, a glandular character had from time immemorial been ascribed. It was the view of Galen, and long afterwards of Vesalius, that it secreted a mucous fluid, which escaped through the nose, while Magendie, in times nearer our own, held that its office was to collect the cerebral lymph and pour it into the circulation; but it was so recently as 1889 that Pierre Marie,¹⁴ by associating it with acromegaly, suggested the real nature of its function as influencing the development of the body and furnishing the explanation of gigantism, infantilism, and other abnormalities of growth.

Of the thyroid and its functions our knowledge is still defective. The most diverse views are taken of its relations with the parathyroids, and all that can be regarded as certain on this point is that the relationship is of the most intimate character. This inference would appear to be irresistible from the hypertrophy which the parathyroids undergo when the thyroid is extirpated, and the thyroid when the parathyroids are excised.

To these historical notes it may be added that it was Starling¹⁵ who proposed the term "hormones" (from ὁρμάω = I excite or arouse) for the chemical stimuli, or, to use his own expression, "chemical messengers," which are "carried from the organ where they are produced to the organ which they affect by means of the blood stream." The word met with general acceptance and is frequently used as a synonym for "internal secretions."

CUTANEOUS SYMPTOMS OF MYXOEDEMA.

How the thyroid and the other ductless glands influence each other and the body generally—whether the secretions elaborated from the blood and then, directly or indirectly, returned to it, stimulate metabolism and growth, or neutralize the toxins of metabolism, or exercise an inhibitory effect upon organs whose activity requires to be controlled, or whether there is a combination of these processes, is a question still involved in obscurity. Nor is the difficulty of determining the functions of the thyroid lessened by the interaction that takes place between this gland and others. But however the thyroid does its work, and whatever its relations with other glands, it is certain that degeneration of this organ is causally connected with the changes in the integuments which enter into the myxoedema syndrome. It is probable also, though the evidence is less conclusive, resting as it does upon purely clinical grounds, that in irregular functioning of the thyroid is to be found in many cases, though not necessarily in all, the explanation of cutaneous changes similar to those met with in myxoedema. In this disease the skin is cold, dry, and rough, seldom or never perspires, and may take on a yellowish tint; it presents swellings, and the mucous membranes

also may be swollen. There is a bright-red flush in the malar region, due to dilatation of capillaries and veins. Swale Vincent¹⁶ has found that the elements of the connective tissue of the derma are torn asunder, while the fibres are the seat of a hyperplastic process, and the cell nuclei and the fibrils of the gelatinous substance between the fat lobules are multiplied. The skin as a whole looks transparent, as though saturated with a semi-fluid substance. The hair of the scalp becomes scanty, the pubic and axillary hair, with the eyelashes and eyebrows, often falls out; in many cases the teeth are brittle and carious. As these signs disappear under the administration of thyroid preparations, there is *prima facie* ground for expecting benefit from the same treatment in conditions presenting more or less resemblance to them, but not associated with myxoedema, such as psoriasis, alopecia, ichthyosis, and xeroderma. That expectation has been abundantly justified by experience. So often, indeed, have I during the last two years found the use of thyroid extract followed by improvement in these and other conditions that I now make it a routine practice, in examining patients suffering from chronic skin affections of which the causation is not known, to palpate the thyroid. If the gland be smaller than usual a trial of thyroid extract is suggested; if there be marked hypertrophy, thyroid medication is contraindicated. It has, however, to be remembered that thyroid insufficiency may be due not to atrophy of the gland but to replacement of the vesicular substance by interstitial growth. Moreover, it is probable that thyroid hypertrophy is sometimes compensatory rather than morbid, the result of an effort to restore secretory equilibrium that has been disturbed by failure of some other ductless gland. Cases are recorded in which thyroid treatment has abolished cutaneous symptoms associated with thyroid excess; such cases are examples of what French authors designate *l'instabilité thyroïdienne*. It is necessary, therefore, to be on one's guard against hastily concluding that a moderate degree of thyroid hyperplasia is an indication against the use of thyroid extract.

ITCHING AFFECTIONS.

In no skin affection has thyroid medication given better results than in *psoriasis*. The failures that have been reported by myself and others are explained by the fact that formerly there were no data for determining the cases to which the remedy was appropriate. My recent experience has led me to the conclusion that one of the secrets of success in the employment of thyroid extract, as of other ductless gland preparations, consists in selecting for its administration cases in which the skin affection complicates other conditions in which this remedy is indicated. In obesity, in infantile wasting, in a certain type of chronic rheumatism, both articular and muscular, in osteomalacia, rickets, and delayed union of fractured bones, in haemophilia, etc., thyroid preparations are of proved utility, and whenever cutaneous affections are found associated with such conditions as these, there is a presumption in favour of thyroid treatment. The association may, of course, be fortuitous, but on the whole it is more likely that the morbid process in the skin is an expression of the constitutional condition. Thus I have found thyroid extract specially efficacious in psoriasis associated with adiposity. In the case of a woman aged 32, who also displayed the mental symptoms of myxoedema, under a course of thyroid extract and arsenic the psoriasis entirely disappeared, the adiposity diminished, and the mental symptoms and general health were greatly benefited. Arsenic alone had been employed without avail; there can be no doubt, therefore, that the improvement was due, mainly at any rate, to the thyroid extract. This is but one of a series of somewhat similar personal cases in which the treatment has proved to be successful. Léopold-Lévi and de Rothschild¹⁷ report cases of psoriasis associated with chronic rheumatism in which the psoriasis completely disappeared under thyroid treatment. In psoriasis generally my experience is that the treatment is more suitable for chronic than for acute cases; and I agree with Radcliffe Crocker and with C. E. Sajous¹⁸ that thyroid extract should not be exhibited until the eruption is fully developed. Stelwagon,¹⁹ while holding that it has but a limited sphere of usefulness in psoriasis, allows that it has

been of service in a few instances in which other agents had failed, and he regards it therefore as a reserve remedy for trial in rebellious cases. In one such case in which it was employed with little hope of success, Sir Clifford Allbutt was agreeably surprised to find that it produced rapid and complete cure. The effect produced consists not only in lessening or abolishing the irritation, but also, it would seem, in stimulating the epidermal layers, so that the degenerate epidermis scales off and is replaced by healthy epidermis.

This is not the only itching affection in which thyroid treatment has been used with success. Obstinate cases of *pruritus* have proved amenable to its influence. In *eczema* I am able to report most encouraging results. Unlike psoriasis, this affection responds to it not only in chronic but also in acute forms. The most responsive cases are those in fat subjects, and those, again, in which the eczema is associated with xeroderma. In cases belonging to both these groups I have found it to answer exceptionally well. Léopold-Lévi and de Rothschild record three cases of eczema associated with thyroid symptoms which were cured or ameliorated by thyroid treatment; they also refer to a case reported by Parhon and Papinian in which eczema complicating chronic rheumatism disappeared under the same treatment. Marbé²⁰ reports two cases of eczema cured by thyroid. Eason²¹ has successfully treated cases of eczema in young children with thyroid; and "I have employed it with advantage in such cases. In several cases of infantile eczema, especially in fat babies, I have had equally satisfactory results. Moussous²² has found the treatment answer well in seborrhoeic eczema of the scalp.

DYSTROPHIES OF THE SKIN.

Ichthyosis, a malformation of the epidermis, was one of the affections in which thyroid extract was used with advantage in the early days of cutaneous organotherapy by Byrom Bramwell and by Arthur T. Davies.²³ Darier²⁴ counsels its prudent use in such cases. Stelwagon can only say that it deserves a trial. My own recent experience has been distinctly more favourable. I have used this agent in a number of cases, and in none without benefit. One in particular may be cited because of its inveteracy. The patient was a lady of 25, who had long-standing xeroderma of the palms, elbows, and knees, with severe seborrhoea of the scalp, scanty hair, and dry skin, the general picture resembling that of myxoedema. Under a combined course of thyroid extract and arsenic all the symptoms, notably the seborrhoea of the scalp and the dryness of the skin, were much abated, and the general health strikingly improved. Favourable results are also reported by Weill, Mouriquand, and Barth.

In *Darier's disease* there is ground for believing that thyroid is indicated, since it is associated with cellular degeneration, and is not improbably, as Audrey and Dalous hold, an expression of dystrophy of the whole epidermis. Darier himself has suggested that this remedy be tried, though not to the exclusion of local measures.

In *scleroderma*, again, there is a presumption in favour of the efficacy of thyroid, for it has been held that the changes in the derma are the result of perversion of nutrition analogous to myxoedema, and Ehrmann has advanced the view that they are the response to an autoinfection commencing in the thyroid body, while Pedrazzini found that of 5 cases the thyroid was small and atrophied in 4. Sir William Osler, in 1898, did not go beyond saying, from his own experience in 6 cases and from results recorded by others, that thyroid treatment in this condition might "be tried without harm." Later reports are by no means unanimous, but there is a rather considerable body of testimony in its favour, among others from Lancereaux and Paulesco, Lustgarten, Ménétrier and Bloch, Picko, Jakimoff, Schamberg, and M'Master. Grünfeld and de Kornfeld have found thyroid treatment beneficial in scleroderma, even when associated with Graves's disease. Léopold-Lévi and de Rothschild explain this result by the suggestion that Graves's disease and scleroderma sometimes evolve upon a *terrain* of thyroid insufficiency. Of 9 cases of scleroderma which they themselves submitted to thyroid medication the treatment was finally successful in 5, but it had to be perseveringly applied.

C. J. White of Boston²⁵ has reported great improvement from thyroid treatment in a case of *acanthosis nigricans*.

This affection, of which the pathology is not understood, may be referred to here; for although it is sometimes included among new growths, it was first designated, by Darier, *dystrophie papillaire et pigmentaire*.

CHELOID.

Cheloid appears to have been first submitted to thyroid treatment in the United States, by J. William White, who observed a lessening of the growth under its influence. Stelwagon employed it in several cases, in one of which there was material diminution of the growth. In my experience, it is distinctly useful in this affection, and I have been especially struck by its influence in alleviating the pain which is not infrequently a symptom of cheloid.

WARTS, ACNE, AND RHINOPHYMA.

Occurring as they do most commonly in children, and tending to disappear at puberty, *multiple warts* are possibly an error of development. Whether this be so or not, I have repeatedly found them disappear under thyroid medication. *Acne vulgaris* is another affection of childhood or adolescence which, in my experience, responds well to thyroid extract. In one case, that of a boy of 16 who had overgrown his strength, after a month's treatment the acne was considerably less, while the accompanying seborrhoea of the face and scalp had entirely cleared up and the general health had much improved. I have had equally satisfactory results in a number of other cases. Thyroid treatment is obviously indicated in *acne rosacea* occurring as a result of flushing in what, for lack of a better designation, I may term the pseudo-myxoedema sometimes associated with the menopause in fat women, who become dull and lethargic and depressed. In such cases I have found that the adiposity, the mental symptoms, and the *rosacea* have all alike responded to the treatment. Léopold-Lévi and de Rothschild report several cases of *acne rosacea* and *acne vulgaris* which were cured by thyroid treatment. In one, in which the skin affection was associated with menstrual irregularity, corpus luteum extract was combined with the thyroid treatment. A remarkable case of cure of *rhinophyma* after three months' thyroid treatment is reported by Dyer of New Orleans.

CUTANEOUS TUBERCULOSIS.

Lupus vulgaris is one of the affections in which thyroid treatment was first employed by Byrom Bramwell. In 1898 Pearce Gould²⁶ exhibited to the Clinical Society of London a woman of 47 in whom long-standing lupoid ulceration of the face, with tuberculous lesions in other parts, had completely healed over after three weeks' administration of thyroid colloid. Radcliffe Crocker is another of those who have reported favourably of thyroid medication in lupus. Pringle²⁷ has declared that it produces results little short of marvellous. According to him the cases which make the best response are those in which there is marked hyperaemia or inflammation. Both in lupus and in tuberculosis of the skin (*scrofuloderma*) I am able to report favourably of the treatment.

CUTANEOUS SYMPTOMS OF GRAVES'S DISEASE.

In exophthalmic goitre, generally held to be due to excessive or perverted functioning of the thyroid, the cutaneous symptoms are the reverse of those met with in myxoedema: instead of coldness, dryness, and scaliness there are heat and moisture; pigmentary changes are not infrequent; and there may also be pruritus, factitious urticaria, and purpuric erythema; but in both conditions there may be loss of hair and atrophy of the nails. In Graves's disease thyroid treatment is, of course, contra-indicated; but there are cases on record in which cutaneous symptoms associated with some degree of overaction of the thyroid have been benefited by the judicious administration of thyroid extract. Those are cases, probably, of the "thyroid instability" referred to above, in which the thyroid makes an effort to compensate the defective action of some other gland.

AFFECTIONS OF THE HAIR.

The influence of the thyroid gland upon the growth of hair is unmistakable. In myxoedema, as already noted, the hair of the scalp becomes scanty, and the eyelashes

and eyebrows, the pubic and axillary hair, often fall out, while under thyroid treatment there is a return to the normal. Hertoghe²⁸ records a case of entire baldness in myxoedema, followed by complete restoration of hair after the use of thyroid. On the other hand, in cases of thyroid excess there is sometimes hypertrichosis, manifesting itself in superabundance of growth, exaggeration of length, and growth in unusual situations, although in Graves's disease the hair often falls out, as in myxoedema. The hair of the face also may be affected by thyroid irregularity; with thyroid insufficiency the hair of the beard and moustache may fall, or its development may be retarded; with thyroid excess, spontaneous or due to medication, there may be growth of hair on the face in women, or black hairs may appear in the light-coloured beards of men. The colour of hair, too, is influenced by the thyroid, as is proved by return to the normal under thyroid treatment in cases of premature greyness. Examples of the effect of thyroid treatment upon the growth and colour of the hair in such affections as chronic rheumatism, scleroderma, neurasthenia, migraine, and asthma, associated with various degrees of thyroid irregularity, are reported by Léopold-Lévi and de Rothschild.

There is reason to believe that the pituitary and the adrenals take part in the trichogenic function. Thus in hyperpituitarism there is marked hypertrichosis, while in hypopituitarism, though the hair of the scalp may not be affected, except in cases commencing in adult life, that of the axillae and pubes may be almost entirely lacking, or in males may conform to a feminine type of distribution. A case reported by Bulloch and Sequeira²⁹ seems to support the view that there is some relation, stimulative or inhibitory, between the functioning of the adrenals and the growth of hair. The patient was a girl of 11, who, normal up to the age of 10, then began to show precocious general sexual development, evidenced by increase in her size and bulk, by the onset of menstruation, by rapid maturation of the mammary glands, and by the growth of hair on pubis and face and axillae. All this time a tumour was growing in the abdomen, which was found *post mortem* to be a malignant hypernephroma. Their researches brought to light a number of similar cases, in which carcinoma or hypertrophy of the suprarenals was attended by precocious sexual development, and also cases in which suprarenal atrophy was associated with non-development or disappearance of pubic hair and by genital hypoplasia.

It has long been known that the growth of hair is also influenced, directly or indirectly, by the sexual glands. Arthur Keith,³⁰ in his masterly little book on *The Human Body*, remarks that in elderly women the withdrawal of the sexual secretion seems to allow the forces of growth to assert themselves: hence the growth of hair on the faces of elderly women. This ingenious suggestion finds support in the fact, observed by Aristotle, and confirmed by Sabouraud as the result of inquiries made in Constantinople and Cairo, that eunuchs do not become bald. Léopold-Lévi and de Rothschild incline to the view that the thyroid chiefly influences the hair of the scalp, and the sexual glands the pubic and axillary hair, and the beard. The whole subject needs much further investigation.

AFFECTIONS OF THE NAILS.

Both in myxoedema and in Graves's disease, and also in the intermediate degrees of thyroid disorder, the nails, as well as the teeth, undergo degenerative changes. Cases in which thyroid treatment exerted a favourable trophic influence upon the nails are recorded by Léopold-Lévi and de Rothschild. The new part of the nail, nearer the matrix, became normal in colour and thickness and texture, and, as is observed in convalescence from some acute affections, there was a furrow between the old part and the new. The number of such cases is not considerable, but they are sufficient to encourage the use of thyroid treatment wherever ungual affections not known to be of parasitic origin are associated with thyroid disturbance.

In hypopituitarism also there is dystrophy of the nails. They are frequently small, thin, and imperfectly developed; and Crowe has noticed that they do not show the crescents at their base.

PIGMENTATION.

There can be little doubt that the coloration of the skin is influenced by several of the internal secretions, and

also, it may be, by the liver and the abdominal sympathetic. It is significant that, as Rolleston³¹ has noted, the pigmentation in Addison's disease is an exaggeration of the normal, and occurs, therefore, on the face, the neck, the hands, the anterior folds of the axillae, the nipples, the perineum, and the genitals, while in more advanced cases the mucous membranes may become pigmented. There is pigmentation also in hyperpituitarism, but it is often accompanied with asthenia and low blood pressure, which suggests that it may be due to adrenal insufficiency rather than to excessive functioning of the pituitary. The familiar pigmentary signs of pregnancy suggest that the sexual secretions may be concerned in normal coloration. There is evidence also that the thyroid is not without influence in this process. One of the signs of myxoedema is the yellowish tint which the skin may present, and Lancereaux and Paulesco, and others, have found that abnormal pigmentation is beneficially affected by thyroid treatment. In leucoderma favourable results from thyroid treatment are recorded, but the negative results recorded by other authors suggest that a careful selection of cases is necessary. The treatment appears to answer best in diffused cases.

Indications are not wanting that the rôle of the thyroid in coloration is of a regulative character. Arbutnot Lane³² has described the pronounced pigmentation met with in cases of alimentary toxæmia, beginning in the eyelids and thence spreading gradually over the face. The neck becomes first brown and then almost chocolate-coloured. The skin of the abdomen, the thighs, the axillae, and that covering the spinous processes of the vertebrae grows progressively darker, and on these surfaces areas of a still darker staining may develop. This observer also calls attention to the changes the thyroid undergoes in cases of intestinal toxæmia. In one case, in which the patient had for eight years suffered from an enlarged thyroid, it was obvious a few days after resection of the large intestine that the gland was diminishing in size, and by the time she left the hospital it was but little larger than usual. The case does not stand alone, for he had noticed the complete disappearance of symptoms of thyroid excess in other patients after operation for intestinal stasis. Such cases suggest that the thyroid may hypertrophy in its effort to antagonize the intestinal toxins to which in these cases the abnormal pigmentation is probably due. Possibly it is in this way that the effect of thyroid medication in improving the complexion is to be explained.

THYROID DOSAGE.

So powerful an agent as thyroid extract must obviously be used with great caution, and its effects closely watched. As a rule I begin with a 2½ grain tabloid, to be taken at bedtime, and after a few days double the dose; then, if the remedy be well borne, a tabloid of the same strength is taken, in addition, after breakfast, and, later, another after dinner, and so gradually a maximum of 10 grains per diem is attained. For infants I begin with ¼ grain a day, increased to ½ grain, and occasionally to 1 grain. Experience is proving that small doses are as efficacious as the larger doses formerly given, and it is obviously desirable to run no avoidable risk of evoking symptoms of thyroïdism, such as rapid pulse, nausea, headache, lumbar pain, restlessness. On the appearance of such symptoms the treatment must be at once suspended or the dosage diminished.

In cases treated with thyroid in which arsenic would be used, as in psoriasis, I usually employ the two agents together, and have found the combination answer admirably. I am glad to find myself in agreement on this point with Ewald and with Gauthier.

THE PITUITARY BODY AND THE SKIN.

That the skin and its appendages are subject to the influence of other ductless glands than the thyroid might have been anticipated from the interaction that has been proved to exist between these bodies, as well as between them and certain organs of external secretion—the testis and the ovary, for example—which also form internal secretions. As the result of this interaction there may be simultaneous functional disturbances in several organs of internal secretion, and thus may arise the clinical picture which has been designated pluriglandular or polyglandular insufficiency. In seeking for the causes of cutaneous affections the dermatologist must be prepared to take account

of the pituitary body. The thyroid is so often and so greatly affected in acromegaly, and the pituitary in myxoedema and after experimental thyroidectomy, as to suggest not merely a complementary relation between these glands when either is the subject of disease, but even some measure of normal interaction—a suggestion which finds support in their histological resemblances. Harvey Cushing,³³ in considering the relations between the pituitary and the thyroid, points out that definite alterations in the thyroid have been reported by many observers in animals from which the hypophysis had been experimentally removed, and that in 24 acromegalics Furnival found only 5 thyroids that were normal, while Schöneman, in 85 cases of goitre, observed marked alterations of the pituitary in 84. In acromegaly there is increase in the size of the hair follicles and of the papillae, and, as the result of enlargement and abnormal activity of the secretory glands, the skin becomes moist and greasy. There is also hyperplasia of the connective tissue of the subcutis, which may involve the muscles, and while the process of hyperpituitarism is active there is, as is mentioned in an earlier paragraph, an unusual degree of hypertrichosis, strikingly exemplified in one of Cushing's illustrated cases. The transition from hyperpituitarism to hypophyseal insufficiency is attended by a very slow but unmistakable retrogression of the cutaneous symptoms. Just as the condition of the skin in Graves's disease is the exact reverse of that in myxoedema, so in primary hypopituitarism the cutaneous changes are the opposite of those in acromegaly. Cushing found that in all his patients affected with primary hypopituitarism, except the older ones, the skin was "smooth, transparent, and notably free from moisture." In some it had an infantile smoothness, such as might suggest a subcutaneous oedema, though there was no pitting on pressure.

In connexion with the pituitary I may refer to the rapid growth of the long bones which often follows typhoid and many other infections in young adolescents, and which comes under the notice of the dermatologist, because of the patellar and other striae produced by the tension to which the skin is subjected. In one of my own cases—that of a girl of 15, who had had scarlet fever—there were linear streaks on the thighs, abdomen, and breast, suggesting a general skeletal overgrowth. Jean Chanal³⁴ has suggested that the skeletal over-development is due to bacillary stimulation of the epiphyses, but I agree with Cushing that it is more likely to be the result of a functional hyperactivity of the pituitary, which sets free in unusual quantity the hormones that stimulate growth.

THE THYMUS AND THE SKIN.

In view of the relation subsisting between the thymus gland and the sexual system, it is possible that to irregularity in the functioning of this gland may be due some affections of the skin that occur specially in childhood and adolescence. There is now reason for believing that the thymus continues to function regularly until puberty, and it has been found that in castrated animals the gland does not at puberty undergo hypoplasia. Although its secretion has not been definitely isolated, there is much to be said for the view that the thymus furnishes a secretion which is of service to the economy while the reproductive organs are undergoing development. Some cases of acne, therefore, may possibly be due to insufficiency or excess of its secretion. Similarly there appears to be some connexion, as Sabouraud has suggested, between large and active sebaceous glands and over-activity of the testicle; this may account for the frequency of seborrhoea in virile and hairy men and its rarity in women, who, when the subjects of it, are generally of the masculine type. It is significant that acne in women often coincides with the menstrual periods.

THYMUS, PITUITARY AND SUPRARENAL EXTRACTS IN SKIN DISEASES.

Neither thymus nor pituitary nor suprarenal preparations have yet been extensively used in dermatology. But I have employed thymus gland extract with advantage in acne associated with enlarged thyroid and rapid heart, and have had encouraging results from pituitary gland extract, and also from suprarenal extract, in *persistent urticaria* and *angio-neurotic oedema*, conditions in which Ravitch and other French authors report improvement

under thyroid treatment. I have also found benefit to follow the use of suprarenal extract in *lupus erythematosus*, possibly owing to its influence upon the vasomotor centres. This condition is amenable to physico-therapeutic methods—to radium and carbonic acid snow; but it is not a merely local affection, and when the lesions disappear under local treatment there is always the possibility of recurrence to be reckoned with. It is desirable, therefore, that further trial be given to any agent which holds out the promise of beneficially affecting the constitutional condition.

UNSOLVED PROBLEMS OF DERMATOLOGY.

The influence which the thyroid, the pituitary, the thymus, and other glands exert on metabolism and growth, and so on the nutrition of the integuments and their appendages, suggests that further knowledge of their nature and functions will help to solve some of the many perplexing problems of dermatology. Bacteriology has accounted for not a few skin diseases, and vaccine-therapy and serum-therapy have now a recognized place in dermatological therapeutics; but there is still a disconcertingly long list of skin affections of which the cause is unknown and the treatment purely empirical. May it not be that of some of these the explanation will be found in overaction or underaction of glands that form secretions at once so potent and so difficult of analysis? The facts that animals from which the hypophysis has been partially removed betray diminished power of resistance to infections, and that pituitary hyperplasia has been found associated with bacterial intoxications, may possibly prove to be charged with significance. It is conceivable that irregularity of this or of other organs of internal secretion may be the direct cause of certain obscure skin diseases, and that in others it may induce the predisposing condition which is the opportunity of bacterial or other pathological influences. Thus, too, may possibly be explained the tendency of so many skin affections to recur after the lesions have disappeared under empirical treatment.

I will not pursue these speculations, tempting as they are. But I venture to think that the results yielded by organotherapy in a considerable number of skin affections are sufficient to warrant a more extensive use of this method of treatment in dermatology. It was by the experimental use of thyroid extract, for example, in such affections that we acquired the knowledge that now enables us in some measure to select the cases suitable for its exhibition, and only by the further use of this and other preparations in the same spirit, guided largely by the principle of analogy, will our knowledge be extended. That animal extracts must be employed with circumspection need not be said; but their effects are now tolerably well understood, and those who are practised in their use will be at no loss to recognize the conditions in which they are contraindicated.

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THE late Surgeon-General Sir Colvin Colvin-Smith, Honorary Surgeon to Queen Victoria, King Edward, and King George, an Indian Mutiny veteran, left estate valued at £10,708.

A Lecture

ON

SOME POINTS IN THE EARLY DIAGNOSIS OF CANCER OF THE STOMACH.

DELIVERED AT THE CANCER HOSPITAL, BROMPTON,

BY

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It may possibly seem to some that as my contribution to this course of lectures I have chosen to speak on an unattractive subject. "What is the good," it may be said, "when you have diagnosed cancer of the stomach? You have diagnosed an incurable disease." There are three important considerations, however, a proper appreciation of which shows the subject to be one of great consequence.

1. *The incidence of the disease is high.* Cancer of the stomach is a very common disease, and it is becoming more common still. Half of all cancers originate in the stomach, and in men a larger proportion even than this. Whether a disease is, in its ultimate issues, incurable or not, if it is a common ailment and if it entails much suffering, it is essential that we should study it minutely and be able to recognize it at its earliest inception.

2. *The question of curability is probably in large degree a matter of early diagnosis.* This consideration not only holds good to-day, when the radical treatment of all cancers is by their surgical removal, but will no doubt hold good if and when the treatment of cancer proceeds along other than surgical lines.

Whatever chemical, physical, or biological principles govern the future treatment of cancer, it will be as important to begin the treatment at the earliest possible moment as it is now important to subject the patient at the earliest moment to a surgical operation.

3. *The differential diagnosis between cancer of the stomach and some other important, but less serious, maladies is often extremely difficult.* The thorough investigation of a case of suspected cancer of the stomach provides the best possible exercise of the clinician's powers, because of the large number and the great variety of observations that must be passed in review.

I do not intend to deal to-day with purely pathological points, such as the morbid anatomy or the histology of the disease, nor shall I treat of the help in diagnosis derived from chemical investigations made upon the stomach contents after giving a test meal. I shall confine myself to the purely clinical aspects of the disease—to the symptoms and signs that can be made out without the aid of special apparatus.

Briefly put, the problem is usually as follows: A man, about 40 years of age, consults us on account of dyspepsia. What are the conditions of his illness which lead us to suspect, and eventually to diagnose, gastric carcinoma?

I. HISTORY OF THE PRESENT CONDITION.

In the history there is one very material point that quite often emerges: it is that the dyspepsia has arisen, as it were, in the midst of health. The man is not, as a rule, a chronic dyspeptic. This is rather a striking fact. There seems no doubt at all in many situations as to the predisposing effect of chronic irritation in causing cancer; but chronic gastritis does not seem to lead to new growth in the stomach. Certainly, for one case in which this sequence is observed there are a dozen in which it is absent. The rule is that patients developing gastric carcinoma have, until the beginning of the disease, enjoyed good digestion. The exception that proves the rule is the passing of a chronic gastric ulcer into carcinoma, but this, though definite enough at times, is not at all a common event. A close analogy exists between this fact in the history of cancer of the stomach and a fact so often seen in the study of intestinal cancer—the difficulty with the bowels complained of by patients with this disease is very frequently their first experience of constipation. Chronic constipation does not lead to cancer, despite the theorists