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THE TREATMENT OF ENDOCRINE DISORDERS.

A POST-GRADUATE LECTURE DELIVERED UNDER THE
AUSPICES OF THE FELLOWSHIP OF MEDICINE IN LONDON,
ON MONDAY, OCTOBER 17, 1927,

By SIR HUMPHRY ROLLESTON, Bt.,
K.C.B., M.D., D.C.L., &c.,

*Regius Professor of Physic in the University of
Cambridge.*

THE deviations from normal endocrine secretion naturally fall into (i) quantitative changes, (a) absence and diminution, for example athyroidism as in cretinism and some cases of myxœdema, and benign hypothyroidism, as in the minor degrees of myxœdema; (b) excess, as in hyperthyroidism and over-medicinal ingestion of thyroid.

(ii) Qualitative changes, the nature of the hormone being presumably altered; clinically it may be difficult to be certain of the distinction between an excessive secretion of the normal hormone and an excessive secretion of the hormone altered in character. But it is reasonable to believe that if the gland, such as the thyroid in Graves' disease, the anterior lobe of the pituitary in acromegaly, or the adrenal cortex in virilism, shows adenomatous change, the resulting secretion will be correspondingly modified, and exert an effect different from that of the normal hormone. Thus, Graves' disease, which is a dysthyroidism, differs in some respects from hyperthyroidism, and from toxic goitre in which there is absence of the eye symptoms, except sometimes exophthalmos.

To give examples of the effects of these variations in the secretion of the endocrine

glands: in the case of the thyroid, absence of secretion causes cretinism; excess hyperthyroidism and perverted secretion, exophthalmic goitre. Deficiency of the secretion of the anterior lobe of the pituitary causes obesity, genital hypoplasia, interference with skeletal growth, and a low temperature; these are the predominant symptoms in Fröhlich's adiposo-genital dystrophy, which, however, is not regarded as solely due to anterior lobe deficiency, for low blood-pressure, increased sugar tolerance, and lowered basal metabolism are ascribed to deficiency of the posterior lobe. Diminished supply of the hormone secreted by the posterior lobe of the pituitary and the adjacent hypothalamic region of the brain is responsible for diabetes insipidus. Excessive secretion of the anterior lobe underlies giant growth, and its abnormal secretion, acromegaly. Thus with regard to the pituitary—a compound gland—it is interesting to attempt a contrast between the well-marked clinical manifestations and the therapeutic utility of the two lobes; skeletal overgrowth and obesity due to changes in the anterior lobe are prominent clinical features, whereas comparatively slight effects are obtained, in man at least, from its therapeutic use. Except for diabetes insipidus there are few clinical symptoms that can be referred to the posterior lobe, though its extract is very effective in temporarily controlling the polyuria of diabetes insipidus and as a powerful stimulant to the smooth muscle of the intestine and uterus. The adrenal, composed of the cortex and the medulla, which, like the lobes of the pituitary, are distinct glands, is somewhat similar in this respect; the hormone adrenalin of the medulla has many therapeutic uses—arrest of hæmorrhage and in asthma—though its effect in Addison's disease is most disappointing; but apart from Addison's disease and Addisonism or the less definite evidences of adrenal insufficiency, the clinical phenomena due to changes in the medulla are not clearly defined; on the other hand adenomatous

hyperplasia of the cortex gives rise, like similar lesions in the anterior lobe of the pituitary, to striking changes in growth, to virilism, and hypertrichosis; but extract of the adrenal cortex has not been found to be useful, except perhaps in exophthalmic goitre.

I do not propose to go into the difficult problems of pluriglandular insufficiency, when two or more endocrine glands are diseased, and of disturbance of the endocrine balance when the secretion of one is altered.

THE THYROID.

Cretinism, sporadic or endemic, is likely to be complicated by tuberculosis. It is interesting to recall that there appears to be some antagonism between the thyroid and tuberculosis; tuberculosis very seldom occurs in exophthalmic goitre however emaciated the patients may become from the excessive metabolism, the thyroid is very rarely the site of chronic tuberculosis, and years ago thyroid medication was thought to do good to lupus vulgaris, a very chronic form of tuberculosis of the skin. Thyroxin is an activator of metabolism; when it is deficient in quantity fat accumulates, as in cretinism, myxœdema and hypothyroidism. Thyroid extract is often used in obesity, but there are many obesities: some cases are due to hypopituitarism—Fröhlich's dystrophia adiposo-genitalis in which administration of the extracts of both lobes of the pituitary has been said to do good, especially in combination with thyroxin, which stimulates the pituitary in diminishing the adiposity, especially around the hips. The most striking form of obesity is adiposis dolorosa or Dercum's disease, so-called after the dermatologist who described it; this it is that provides the gigantic fat women of shows; it has been thought to be due to a pluriglandular lesion, more particularly of the thyroid and of the anterior lobe of the pituitary; in a few instances the thyroid has shown calcification.

Benign hypothyroidism has been regarded as responsible for such a large number of minor ills that it is excusable if some scepticism has been expressed, and yet the therapeutic test, namely, improvement on thyroid extract, has been positive in conditions so apparently remote as flat-foot, rheumatic pains, constipation, subinvolution of the uterus, chilblains, pigmentation of the skin during, and loss of hair after, pregnancy, some skin diseases, especially those occurring at puberty and the menopause, enuresis and hypertrophy of the prostate. It might of course be argued that the therapeutic test is open to the common fallacy that the beneficial effects are due to auto-suggestion; this no doubt applies to the improvement which certainly sometimes follows the use of the very numerous endocrine preparations now on the market. The beneficial effect of thyroid medication on the prostate if correct, and I have known of cases in which this has occurred, is curious, for Vines and Grove report benefit from parathyroid which has an opposite influence to thyroid. Is it possible that in the cases benefited by thyroid there was some parathyroid in the thyroid administered?

Thyroid extract, like other efficient drugs, is powerful not only for good but for evil, and it is important to remember that the suitable dose must be determined for each patient, beginning with a small dose and, if this has not any effect in either direction, rapidly increasing it. Thyroid, as shown by the thyrotoxic heart of patients with Graves' disease, may exert definitely deleterious influence on the myocardium. A medical man with a senile heart was anxious to try thyroid for chilblains, and though not taking large doses dated the steadily progressive cardiac failure from this time. Patients should be kept under observation while taking thyroid. Nott has found that in patients who do not react to thyroid by improvement may do so if given permanganate of potassium per rectum or orally to diminish or remove intestinal intoxication which, it

is assumed, prevents the thyroid extract from exerting its influence.

PARATHYROIDS.

While the thyroid is concerned with iodine the parathyroid controls calcium metabolism; parathyroid insufficiency in early life is responsible for the group of conditions called spasmophilia, with a tendency to tetany, and for these manifestations of calcium deficiency the injection of calcium salts and the administration of parathyroid extract are indicated. Parathyroid extract has given extremely good results in sprue, and has been advocated in a number of chronic infections.

ORAL AND HYPODERMIC ADMINISTRATION.

Thyroid and parathyroid extracts, as everyone knows, act when given by the mouth; this has been explained on the ground that originally the secretions were poured into the alimentary canal, but this ingenious idea is invalidated by the failure of insulin when given by the mouth. It is doubtful if adrenalin, which is not destroyed by the gastric juice, is absorbed by the mucosa of the alimentary canal, but the allied ephedrin, a comparatively recent preparation, appears to relieve asthma when taken by the mouth just as efficiently as hypodermic injections of adrenalin have long been known to do. Pituitrin, the extract of the posterior lobe, is always given hypodermically, for very large quantities by the mouth have been found to be necessary to produce any effect. Of the value of pituitrin in overcoming intestinal paralysis in surgical emergencies and in temporarily removing the symptoms of diabetes insipidus there can be no question.

In connection with the substitution treatment of glandular insufficiency, such as thyroid extract in cretinism and myxoedema, insulin in diabetes mellitus, and pituitrin in diabetes insipidus, it is clear that there is not a cure, for the treatment must be continued. It has naturally been hoped that the admin-

istration of insulin by resting the islands of Langerhans would enable them to recover, and so a cure would result; although there are a few encouraging results, it seems to be generally true that such a cure cannot be expected.

HYPOTHYROIDISM AFTER DYSTHYROIDISM.

In a certain number of cases of exophthalmic goitre there is a curious sequence of events, namely, that after the disease has passed into abeyance, which fortunately occurs eventually in the great majority, the signs and symptoms of myxœdema appear; thus the condition of dysthyroidism, in which there is an excessive and abnormal secretion by the thyroid, may be followed by hypothyroidism, as if the gland had undergone atrophy or exhaustion as a result of the morbid process—adenomatous transformation—characteristic of Graves' disease. As a rule thyroid extract exaggerates the symptoms of exophthalmic goitre, but in these transitional states towards the opposite condition of myxœdema it may do good.

It may be interesting to recall other examples in which excessive and morbid activity is succeeded by atrophy; it is said that excessive and intensive muscular hypertrophy, as in "strong men," may be succeeded by rapid wasting of the muscles as if there was only a certain quantum of vitality available; in the greatly hypertrophied left ventricle of high blood-pressure or compensated heart disease, the eventual dilatation and cardiac failure is really an atrophic change in the myocardium. In acromegaly, due to adenomatous over-activity of the anterior lobe of the pituitary, a loss of secretion may supervene, so that although the bony changes induced in the earlier stages remain some of the changes seen in an uncomplicated form in the young from hypopituitarism—the dystrophia adiposogenitalis of Fröhlich—may appear.

A curious instance of two opposite diseases occurring in the same individual has been

pointed out by Christian,¹ namely, that the comparatively rare disease of erythræmia, in which the red blood-count and hæmoglobin are much increased, may be succeeded by pernicious anæmia; here the simple explanation that over-activity of the red bone-marrow in erythræmia leads to exhaustion and aplasia would not hold good, unless, as is not stated, the anæmia was aplastic. Christian indeed mentions a case of erythræmia with free hydrochloric acid in the gastric juice, which seven years later came under observation with pernicious anæmia and achlorhydria; the achlorhydria was therefore the apparent cause of the anæmia.

TREATMENT OF GOITRE AND SOME OTHER ENDOCRINE HYPERPLASIAS.

Simple goitre, due, as McCarrison's results show, to infection which may be derived from water of "goitre wells," is closely connected with a deficiency in iodine, and it has been thought that bacterial infection of the alimentary tract may interfere with the absorption of iodine. The occurrence of goitre in fish in regions where goitre is endemic is interesting, and boiling the drinking water is obviously desirable. Preventive treatment in the form of iodide of potassium, 5 gr. twice in the week for two separate months in the year, has been most successful. Lugol's solution (iodine 5 per cent. in a solution of 10 per cent. iodide of potassium) may be employed, and an ingenious method employed by Albert Kocher to insure the influence of iodine is to place in the bed-rooms, in china pepper boxes, iodide of calcium, which diffuses into the air. When iodides are given by the mouth small doses are essential, otherwise, as iodine is a stimulant to the thyroid, hyperthyroidism, or even well-marked increase in the size of the gland, may result. Iodine has been largely given in developed goitre, but here again careful supervision is neces-

¹ Christian, H. A., *North-West Med.*, 1925, xxiv, 531.

sary, for it has been thought, though this is disputed, that it stirs up a simple adenoma of the thyroid into such activity that it becomes a toxic adenoma or secondary exophthalmic goitre.

The difference between the treatment of deficient and excessive endocrine secretion is noteworthy; when deficient, as in myxoedema, the indication is simple, namely, to supply it; but when excessive or perverted, as in exophthalmic goitre, acromegaly, and the alteration of growth and of the secondary sexual characters seen in tumours of the adrenal cortex, medicinal treatment is not so effective; it is true that in hyperthyroidism and exophthalmic goitre iodine exerts a beneficial influence, but in Graves' disease it is found to be most useful in preparing the patient for operation. With excessive secretion it is reasonable to give belladonna, but its effects are not constant, neither in the case of exophthalmic goitre are those of adrenalin; the extract of the adrenal cortex, though recommended, has not been widely tried. The destructive action of X-rays has given good effects in many cases of Graves' disease, but it is attended by the disadvantage of producing adhesions which render operation more difficult. In acromegaly extracts of the glands alone, or combined with thyroid extract, have been much tried, but with little success, except perhaps in diminishing headache; removal of the adenomatous gland is a severe, but in expert hands a successful operation.

In the remarkable changes of growth and the secondary sexual characters seen in cases of adrenal cortical tumours no measure short of removal of the tumour, which has been done in a small number of cases with success, notably in those reported by Gordon Holmes, and quite recently by Murray and Simpson, is at present available.

ON THE ETIOLOGY AND TREATMENT OF ECZEMA.

A LECTURE DELIVERED BEFORE THE HARROGATE
MEDICAL SOCIETY

(Under the auspices of the Fellowship of Medicine.)

By W. GRIFFITH,

M.B., M.R.C.P.,

Physician and Joint Chesterfield Lecturer in Dermatology at the St. John's Hospital for Diseases of the Skin.

IN the first place I would like to thank the Harrogate Medical Society for the honour they have done me by inviting me to address them.

The subject chosen for discussion is the "Etiology and Treatment of Eczema," a subject in which, as a practising dermatologist, I am especially interested.

Harrogate has a traditional and well deserved reputation for the treatment of eczema and other skin diseases.

Many of my eczema patients tell me they have been to Harrogate and that they have been benefited or cured, and I hope to hear to-night at first hand some details of the methods which are practised here with so much success.

I have not come to teach, but to learn.

Many years' experience in a busy metropolitan skin clinic has convinced me that the usual textbook descriptions of eczema are lacking in completeness; they are based on the views of Hebra and the Vienna school of his day, which maintained that eczema was a condition due entirely to external irritants acting on the skin.

This gives no explanation of eczema due to a special susceptibility in certain individuals.

The action of an irritant on the skin of a normal individual does not produce the clinical manifestations which we call eczema.

If a simple irritant, say hot water as the most familiar, be applied to the skin of a normal individual, it causes pain, redness,