THE THYROID GLAND.*

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PHYSIOLOGICAL CONSIDERATIONS.

The principal function of the thyroid gland is to control the oxidative processes of the organism, i.e., the metabolic rate, and to maintain it at its proper level. This is accomplished through the medium of its internal secretion, the active principle of which, thyroxine, is elaborated from iodine. The thyroid hormone is manufactured by the epithelial cells of the follicles and stored in the colloid. The iodine content of the gland varies with the amount of colloid present and inversely with the degree of hyperplasia. Great advances have been made lately in the chemistry of thyroxine. Kendall in 1916 announced that he had isolated a crystalline compound containing 65% of iodine, which produced the same pharmacological effects as desiccated thyroid. In 1926 Harington determined its structure and in 1927 Harington and Barger synthesized it.

The important function of the thyroid in controlling metabolic processes can be judged by the effects of its removal in animals or human beings or by feeding thyroid extract. All bodily activities are influenced. Particularly noticeable are the effects on growth and sex development in the young individual and on the activity of the bone marrow. The thyroid secretion probably also increases the irritability of the sympathetic nervous system and sensitizes in some way the tissues innervated by it so that they are more susceptible to stimulation by adrenalin. The main function of the thyroid, however, is undoubtedly that of metabolic control and this conception seems adequate to account for the obvious effects of thyroid absence or excessive activity.

An important recent advance in thyroid physiology has been the recognition of a close relationship between the thyroid and the anterior pituitary. In fact, there is evidence that the thyroid secretion is under the control of one of the principles of the anterior pituitary—the thyro-tropic hormone. It has been known for many years that marked hypertrophy of the anterior pituitary occurs in individuals with endemic goitre; also that hypertrophy of the anterior pituitary follows thyroidectomy. The first proof, however, of a pituitary hormone regulating thyroid activity followed the demonstration by Allen and Smith that hypophysectomy caused atrophy of the thyroid and Smith's later demonstration that implantation of fresh pituitary restored such atrophic thyroids to normal or even increased activity. Experimental evidence and clinical findings are in harmony though the exact significance of the anterior pituitary control of thyroid function is not yet understood.

PATHOLOGICAL CONSIDERATIONS.

The thyroid gland is endowed with a great capacity for increasing and decreasing its functional activity and thus provides a means for varying the rate of metabolism to meet the changing demands of the organism. Chiefly as a result of Marine's work, it is now well established that a deficiency of iodine,

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relative or absolute, results in a work hypertrophy or hyperplasia of the gland or simple goitre. Marine has described the cycle of changes which occurs in the gland under these circumstances. If iodine supplies fall below 0.1%, hypertrophy commences but can be prevented by giving iodine. If iodine supplies remain insufficient, hypertrophy progresses to hyperplasia. Subsequently either involution to the colloid type of gland or exhaustion atrophy supervenes. This cycle of hypertrophy, hyperplasia, involution, as a result of iodine deficiency, may be repeated many times provided exhaustion atrophy does not occur.

The essential cause of simple goitre, therefore, centres round the needs of the organism for iodine and the supply of thyroxine. As has been mentioned already, the iodine deficiency may be relative or absolute. A relative iodine deficiency may occur during times of physiological stress, for instance the sex events—puberty, pregnancy and the climacteric—and with infections and intoxications. At such times, the needs of the body for thyroxine are relatively greater. An absolute deficiency may result from a low iodine intake, the important ætiological factor in endemic goitre, or from interference with the absorption or utilization of iodine, the intake being normal, but little is known of the exact mechanism in the latter circumstances.

Simple Goitre.

The term *Simple Goitre* is used to signify any enlargement of the gland which is neither inflammatory nor a tumour and is not associated with toxic features. It would therefore include the diffuse colloid goitre, the nodular adenoparenchymatous goitre and the lymphadenoid goitre. The latter is the *gland of myxoedema* recently described by Williamson and Pearce and needs no further discussion at this point. Simple goitres have to be differentiated from the simple thyroid adenoma, which is essentially an encapsulated tumour developing from foetal cell rests and, as a tumour, does not fall under this heading. Foetal adenomata often occur in association with simple goitre and may persist without symptoms or degenerate with cystic formation or become toxic or occasionally malignant. They are isolated, round or ovoid, independent in structure and encapsulated, growing gradually.

There has been much discussion as to the unitary nature or otherwise of the two main types of simple goitre, diffuse and nodular, colloid and adenoparenchymatous. Though some authorities consider that they are separate entities, others hold the view that the nodular gland is only a later stage of the diffuse type, in which hyperplasia and the appearance of new gland tissue has resulted in addition to simple hypertrophy—evidence of a more prolonged and continuous functional strain. Clinical evidence would seem to support the unitary view. Moreover, recent investigations have shown that, whilst the foetal rest hypothesis may explain the simple congenital and encapsulated adenomata, the great majority of nodular glands are of the adenoparenchymatous type, arising from previously differentiated thyroid tissue and in their beginning due to the same physiological stimulus which produces the diffuse goitre in which they arise. Prevention of thyroid hyperplasia prevents the development of these so-called adenomata.

The chief differential features of the two main types of simple goitre are as follows:—

- (A) **Diffuse Colloid Goitre.** Smooth and avascular. Simple hypertrophy due to iodine deficiency. Colloid vesicles vary much in size. Clinically found in young adolescents at puberty and in adults during pregnancy, puerperium and at other times of physiological stress. Usually no symptoms apart from the goitre. Prophylactic treatment with iodine important. Therapeutic treatment with iodine cannot be expected to have any marked effect on the size of the goitre, if it has been present for more than a year or two but will prevent further hypertrophy.
- (B) **Adenoparenchymatous Goitre.** Nodular and avascular. Simple hyperplasia with new gland tissue laid down. Caused by sustained over-activity. Many new vesicles with areas of solid gland tissue. Later, fibrosis which further divides the gland up and causes nodularity.

After some time, liable to be associated with hypothyroidism or to become toxic (Secondary Graves' Disease).

Treatment: Thyroid Extract if hypothyroidism.

Toxic Goitre.

Three main forms can be differentiated:—

- (a) Primary Graves' Disease.
- (b) Secondary Graves' Disease.
- (c) Toxic adenomata.

The latter term should be used only in cases in which a true foetal adenoma has become toxic.

- (A) **Primary Graves' Disease.** The typical form in which thyro-toxic symptoms and goitre develop together.

Exciting factors: psychogenic or septic.

Predisposing factors: heredity in about 15%, and the sex events, especially in the female.

Pathology: Adenoid goitre in 100%. Changes affect the whole gland. No colloid. Invagination and proliferation of epithelial elements. Increased basal metabolic rate and loss of weight are important features. Shows a tendency to relapse as long as thyroid gland is left intact and a tendency to improve with pregnancy if it goes to full term. Risk of miscarriage and abortion.

Diagnosis of doubtful cases confirmed by basal metabolic rate.

Complications: cardiac and metabolic.

Treatment: importance of mental and physical rest; removal of septic foci; Iodine as a pre-operative measure. Difficulty in controlling primary Graves' Disease without operation. Good results with sub-total thyroidectomy. X-ray treatment a substitute for thyroidectomy in cases unsuitable for surgery.

(B) Secondary Graves' Disease. Toxic symptoms developing in existing simple goitre. The latter may either be of the diffuse colloid or adenoparenchymatous type. (Secondary thyro-toxæmia in the nodular adenoparenchymatous simple goitre has sometimes in the past been referred to as the syndrome of toxic adenoma). It seems better to reserve the latter term for the syndrome of thyro-toxæmia developing in true foetal adenomata.

Exciting factors: psychogenic and septic as in the primary form.

Pathological changes: part of the gland only affected, colloid remaining in parts; in others, typical changes as found in the primary form.

Onset tends to be insidious with gradual loss of weight, cardiac, or nervous symptoms; tendency to fibrillation; eye signs usually not prominent; rise in basal metabolic rate more gradual.

Clinical course more gradual and progressive.

Diagnosis: differentiation from primary form chiefly on clinical history.

Complications: cardiac or metabolic.

Treatment: as in the primary form but less responsive to medical measures. Surgery produces best results. Digitalis and Quinidine of value on development of fibrillation.

Less striking effects from pre-operative Iodine therapy in secondary cases.

Risks of recurrent hypertrophy after partial removal of diffuse glands (young simple goitres) with secondary Graves' Disease. In these cases, the preceding simple goitre has usually only been present for a few years. Recurrent hypertrophy seldom occurs after operation on the older and nodular types.