HORMONAL STUDIES ON THE PATHOGENESIS OF PUBERTY GOITRE

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C O N T E N T S

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AIM OF THE WORK

It is well known that the thryroid gland may enlarge in some subjects at the age of puberty. This enlargement occurs most commonly in girls, usually the gland does not exceed twice its normal size and the patient is functionally euthyroid.

The aim of this thesis is to examine the incidence of puberty goitre in a sample of population and to study the hormonal background which may contribute in the pathogenesis of this goitre.

Measurement of serum thyrotropin (T S H). serum thyroxine (T_4), and serum triiodothyronine (T_3) for these subjects will be done by the radioimmunoassay method (RIA) in a trial to explore the possible underlying pathogenesis and to suggest a reasonable line of treatment.

INTRODUCTION

THE NORMAL THYROID GLAND

The thyroid is the largest endocrine gland in the adult. It is classically described as a flat-appearing, bilobed, pink structure of about 15-25 g in weight in the adult, lying on either side of the trachea at a level lateral and inferior to the thyroid cartilage. The thyroid gland is enclosed in a sheath of pretracheal fascia, which is attached to the arch of the cricoid cartilage and the oblique line of the thyroid cartilage superiorly; the gland moves therefore with the larynx in all its movements.

Each lobe is conical in shape, and has a convex superficial surface which is covered by the sternohyoid, sternothyroid, andomohyoid muscles, and is overlapped by the anterior border of sternomastoid. The medial surface is moulded inferiorly on the trachea and oesophagus with the recurrent laryngeal nerve between them, while superiorly it is fitted to the cricoid and thyroid carilages. The posterior surface is applied to the prevertebral muscle and overlaps the medial part of the carotid sheath. The parathyroid glands are embedded in its posterior surface. The dimensions of each lobe vary around 4-7 cm in length, 2-5 cm in width, and 1.75 cm. in depth. An isthmus connecting the two lobes lies anterior to the trachea just below the cricoid cartilage. It is square in shape, 2 cm^2 in area, and from 0.2 to 0.6 cm in depth.

The thyroid gland receives its blood supply from two superior thyroid arteries which arise from the external carotidartery on each side, two inferior thyroid arteries which arise from the thyrocervical trunk on each side which in turn arises from the first part of the subclavian artery. An occasional small artery (thyroidea ima) may arise from the brachiocephalic trunk, or the left common caratid artery or the aortic arch.

The venous drainage of the gland occurs thraugh three pairs of veins.

The superior thyroid vein arises near the upper end of the lobe and joins the internal jugular vein or the facial vein. The middle thyroid vein is very short and joins the internal jugular vein. The inferior thyroid veins arise from the network on the isthmus and each ends in the corresponding brachiocephalic vein close to the junction of these veins.

The nerve supply of the gland is from branches from the cervical ganglia of the sympathetic trunk and from the cardiac and laryngeal branches of the vagus. (Cunningham's Manual of Practical Anatomy). As far as embryogenesis is concerned, the human thyroid anlage is first recognizable at about 1 month after conception, when the embryo is approximately 3.5 to 4 mm in length.

The primordium begins as a thickening of epithelium in the pharyngeal floor which later forms a diverticulum. with continuing development, the median diverticulum undergoes relative caudal displacement and the primitive stalk connecting the primordium with the pharyngeal floor undergoes elongation (thyroglossal duct). During its caudal displacement, the primordium assumes a more bilobate shape coming into contact and fusing with the ventral aspect of the fourth pharyngeal pouch. Normally, the thyroglossal duct undergoes dissolution and fragmentation by about the second month after conception, leaving at its point of origin a small dimple at the junction of the middle and posterior third of the tongue, the foramen cecum. Cells of the lower portion of the duct differentiate to thyroid tissue forming the pyramidal lobe of the gland. Complex interconnecting cord-like arrangements of cells interspersed with vascular connective tissue replace the solid epithelial mass. These transform to tubule-like structures at about the third month of fetal life, and shortly thereafter follicular arrangements devoid of colloid appear, followed by colloid filled follicles.

Functional differentiation of the gland occurs concomitantly with anatomical development. Iodide concentrating ability appears first, at a time when primitive follicles have not yet formed.

Organic-binding reactions appear when the earliest follicles are evident. In man, the ability to accumulate iodide appears at about 12 weeks and anteceds the appearance of organic-binding mechanisms. The latter functions, including synthesis of thyroxine and triiodothyronine, are well established 14 or 15 weeks (Chapman et al., 1948; Yamazaki et al., 1959).

Microscopic Structure:

Thyroid tissue is composed of follicles consisting of usually cuboid epithelium arranged in a single layer surrounding spherical spaces containing a gelatinous substance, the colloid. Follicles may reach a diameter of 0.9 mm. The gland is covered by a loose connective tissue capsule which sends septa into the parenchyma. These septa become gradually thinner and reach all of the follicles, separating one from another by fine irregular connective tissue composed mainly of reticular fibres.

The thyroid is an extremely vascular organ, presenting an extensive blood and lymphatic capillary network between the follicles. The endothelial cells of these capillaries are fenestrated, as commonly occurs in the capillaries of endocrine glands. This disposition may perhaps facilitate the passage of the hormone to the blood capillaries.

The morphologic aspect of the thyroid follicles varies (polymorphism) according to the region of the gland and its functional activity. Thus, in the same gland larger follicles full of colloid and having a cuboid or squamous epithelium may be found along side smaller ones lined by prismatic epithelium.

The thyroid epithelium always rests on a basal lamina. The ultra structure of the follicular epithelium presents all of the characteristics of a cell which at the same time synthesizes, reabsorbs, and digests proteins. Thus, the basal part of these cells is rich in granular endoplasmic reticulum. The nucleus is generally round and situated in the centre of the cell.

The apical pole represents a discrete Golgi apparatus and secretory granules with the staining characteristics of follicular colloid.

Abundant particles, 0.5-0.6 um in diameter, and some (usually) large vacules containing a clear fluid are also found in this region.

These are believed to be lysosomes. The cell membrane of the apical pole contains a moderate number of microvilli.

Mitochondria are dispersed throughout the cytoplasm, and some free ribosomes are found.

Small isolated clusters of light cells are frequently found between the thyroid follicles. These are known as parafollicular cells. or C cells (clear cells). Evidence has been presented that these cells are responsible for the synthesis and secretion of the hormone calcitonin that promotes a reduction in the concentration of calcium in the blood. (Junqueira, L.C. and Carneiro, J. 1978).

PHYSIOLOGICAL CONSIDERATIONS

The normal thyroid secretes mainly an iodinated amino acid, thyroxine together with much smaller quantities of other iodinated amino acids.

Among these is 3, 5, 3 - **triiodothyronine** whose metabolic potency is severalfold greater than that of thyroxine.

These iodinated amino acids are stored bound to thyroglobulin in the colloid. The thyroid cells performs two parallel functions in producing its horomones: one is the synthesis of the protein substrate, thyroglobulin;the other is the accumulation of iodide from the very small amount present in the blood. This is followed by iodination of tyrosine residues in thyroglobulin, and conversion of these into iodothyronines.

THYROGLOBULIN AND ITS SYNTHESIS:

The thyroid follicular cells make a distinctive protein, thyroglobulin, which plays a central role in hormone production. Iodine and the thyroid hormones are intimately associated with this protein from the beginning stages of iodination to the final stage just prior to secretion into the blood. It contains more than 90% of thyroidiodine. It is the major protein secreted by the cell. (Kondo. Y., et al, 1968).

The term thyroglobulin is applied to this major component :
a glycoprotein with a molecular weight of 660,000 and sedimentation rate of 19s. (Robbins, J., et al 1960) and (Edelhoch, H., et al, 1964).

Thyroglobulin does not display an unusual amino acid composition, but it is unique among body proteins in its content of iodinated amino acids. Its tyrosine content of' approximately 3% is not unusual, but roughly 25 of the 140 tyrosyl residues are iodinated. The pattern of iodination is effected by the location of these tyrosyls, about two thirds of which are on the surface and susceptible to in vitro iodination. (Rall,J.E.,et al 1964) and *(Edelhoch, H., et al., 1965).

IODINE METABOLISM AND HORMONE PRODUCTION

Iodine is present in the environment in limited quantities, compared to the amount needed for normal thyroid hormone production. As a consequence there is a highly efficient mechanism for accumulation and conservation of this