REVERSE T_3 AND T_3 IN PROCESS OF AGEING

THESIS

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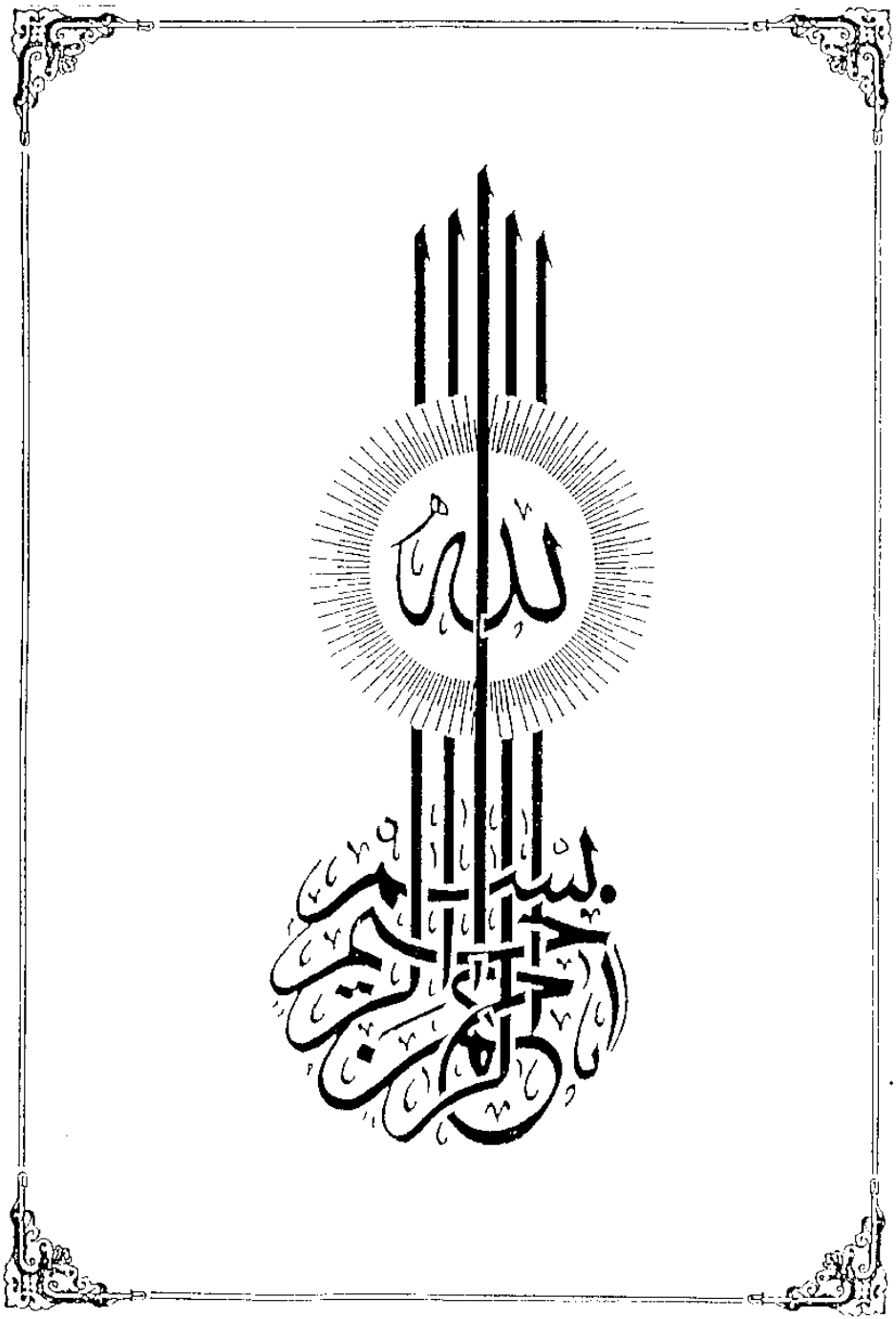
C O N T E N T S



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AIM OF THE WORK

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It was observed that in acute febrile illness, starvation, diabetic ketoacidosis, myocardial infarction, chronic respiratory, renal and hepatic diseases, there was a decrease in serum T_3 and increase in reverse T_3 concentration, (Kaplan et al, 1977and Havard, 1981).

The apparant shunting of T_4 from conversion to highly potent T_3 to production of calorigenically inactive reverse T_3 may reflect a defense reaction of the body attempting to protect sick tissues from excessive metabolic stimulation, (Chopra et al, 1975).

The aim of this study is to prove whether the changes in reverse T_3 in the elderly are due to illness or due to age alone. Therefore, we shall exclude presence of any illness in our selected persons.

Reverse T_3 , T_3 and T_4 will be measured by radioimmunoassay and their relation to each other will be evaluated.

ANATOMY OF THYROID GLAND

The thyroid gland is a highly vascular organ, situated at the front and sides of the lower part of the neck, opposite the fifth, sixth and seventh cervical vertebrae. It is ensheathed by the pretracheal layer of the deep cervical fascia and consists of right and left lobes connected across the median plane by a narrow portion, termed the isthmus. Its weight is somewhat variable, but is usually about 30 gm. It is slightly heavier in the female, in whom it becomes enlarged during menstruation and pregnancy.

The lobes are conical in shape, the apex of each being directed upwards and laterally and reaching the level of oblique line of the thyroid cartilage; the base is on a level with the fifth on sixth tracheal ring. Each lobe is about 5 cm long; its greatest width is about 3 cm, and its thickness about 2 cm.

The posteromedial part of each lobe is attached to the side of the cricoid cartilage by a ligamentous band. The lateral, or superficial, surface is convex.

Outside the sheath of pretracheal fascia, this surface is closely covered with the sternothyroid and it is the insertion of this muscle into the oblique line on the lamina of the thyroid cartilage which prevents the upper part of the lobe from extending forwards on to the thyrohyoid muscle. More superficially, this surface is covered with the sternohyoid and the superior belly of the omohyoid muscls, overlapped below by the anterior border of the sternomastoid. The medial surface is moulded over the larynx and trachea. Above it is in contact with the inferior constrictor of the pharynx and the posterior part of the cricothyroid muscle, which intervenes between the gland and the posterior part of the lamina of the thyroid and the side of the cricoid cartilage. The external laryngeal nerve passes deep to this part of the gland on its way to the cricothyroid muscle. Below, it is related to the side of the trachea, in front, and to the recurrent laryngeal nerve and (particularly on the left side) to the oesophagus, behind. The posterolateral surface is related to the carotid sheath and overlaps the common carotid artery. The anterior border, which is closely related to anterior branch of the superior thyroid artery, is thin and inclines obliquely from above

downwards and medially. The posterior border, which is blunt and rounded, intervenes between the posterior and the medial surfaces and is closely related below to the inferior thyroid artery and an anastomosing branch which connects that vessel to the posterior branch of the superior thyroid artery. In addition the parathyroid glands are related to this border, although they may be found in association with the posterior surface.

The isthmus connects together the lower parts of the two lobes; it measures about 1.25 cm transversely, and the same vertically and usually covers the second, third and fourth rings of the trachea. Its situation and size present, however many variations. Anterioly, it is separated by the pretracheal fascia from the sternothyroid muscles. More superficially it is covered by the sternohyoid muscles, the anterior jugular veins, the fascia and the skin. An anastomotic branch uniting the two superior thyroid arteries runs along its upper border; at its lower border the inferior thyroid veins leave the gland.

A third lobe, of conical shape, called the pyramidal lobe, frequently extends from the upper part of

the isthmus or from the adjacent portion of either lobe, but more commonly the left, to the hyoid bone. It is occasionally quite detached or may be divided into two or more parts.

A fibrous or muscular band is sometimes attached, above, to the body of the hyoid bone, and below, to the isthmus of the gland, or its pyramidal lobe; when muscular, it is termed the levator glandulae thyroeideae.

Vessels :

The arteries supplying the thyroid gland are the superior and inferior thyroid arteries, sometimes there is an additional branch from the innominate artery or the arch of the aorta, which ascends upon the front of the trachea. The arteries are remarkable for their large size and frequent anastomoses.

The veins form a plexus on the surface of the gland and on the front of the trachea; from this plexus the superior, middle and inferior thyroid veins arise; the superior and middle end in the internal jugular vein, the inferior in the innominate vein.

The capillary blood vessels form a dense plexus in the connective tissue around the vesicles, between the epithelium of the vesicles and the endothelium of the lymph vessels which surround a greater or smaller part of the circumference of the vesicle.

Lymph Vessels :

The lymph vessels run in the interlobular connective tissue, not uncommonly surrounding the arteries which they accompany and communicate with a network in the capsule of the gland, they may contain colloid material. They end in the thoracic duct and the right lymphatic duct, (Warwick and Williams, 1973).

Nerve Supply:

The thyroid receives its nerve supply from both adrenergic and cholinergic nervous systems, the former from cervical ganglia and the latter from the vagus nerve.

Afferent fibres pass through the laryngeal nerves and regulate an active vasomotor system. It has been thought that the sole function of neurogenic stimuli is the regulation of blood flow to the thyroid (thyroid blood flow ranges from 4 to 6 ml/min/g).

In severe hyperplasia as in diffuse toxic goiter, blood flow rates is greater than 1 Liter/min.). Although acute changes in blood flow do not appear to alter the rate of hormonal release, the rate of perfusion influences the delivery of T.S.H., iodide and metabolic substrates and may eventually influence glandular function and growth.

Recent ultrastructural and autoradiographic studies have revealed, in addition, a network of adrenergic fibers terminating near the basement membrane of the follicular wall. This finding together with new evidence that adrenergic and other amines influence thyroid iodine metabolism in isolated thyroid cells and in Vivo, indicate that the adrenergic nervous system can influence thyroid function through a direct effect on the function of the follicle cell, (Ingbar and Woeber, 1981).

Histology:

With light microscopy, the gland is seen to be composed of closely packed sacs, called acini or follicles, which are invested within a rich capillary network. The interior of the follicle is filled with the clear, proteinaceous colloid, which normally is the major constituent of the total thyroid mass. The diameter of the

follicles varies considerably, even within a single gland, but averages about 200 μ. As might be expected, the iodine-accumulating function of each individual follicle varies with its surface area. The wall of the follicle is lined by a single layer of closely packed cuboidal cells, approximately 15 μ high. The cell height of the acinar epithelium varies with the degree of glandular stimulation, becoming columnar when active and flat when inactive. The epithelium rests upon a well-defined basement membrane that stains positively with reagents for mucopolysaccharides and separates the follicular cells from the surrounding capillaries. From 2o to 40 follicles are demarcated by connective tissue septa to form a lobule supplied by a single artery.

The function of an individual lobule may vary from that of its neighbours. With electron microscopy, the thyroid is seen to have many features in common with other secretory cells but some of which are peculiar to the thyroid. From the apical aspect of the follicular cell, numerous microvilli extend into the colloid. There is considerable evidence that it is at or near this surface of the cell that such crucial reactions as iodination and the initial phase of hormone secretion, namely colloid resorption, occur. The nucleus of the

follicular cell has no distinctive features.

The cytoplasm contains an extensive endoplasmic reticulum (ER) Laden with microsomes. The ER is distinctive in being composed of a network of wide irregular tubules which probably contain the precursor of thyroglobulin. The carbohydrate component of thyroglobulin is probably added to this precursor in the Golgi apparatus which is located apically. Membrane-limited dense granules, believed to be lysosomes, and mitochondria are scattered throughout the cytoplasm.

Upon stimulation by T.S.H., the follicular cell undergoes changes in its ultrastructure. These include enlargement of the Golgi apparatus, formation of pseudopodia at the apical surface, and appearance in the apical portion of the cell of many droplets that contain colloid taken up from the follicular lumen.

In addition to the follicular cell, the thyroid contains a population of other cells, variously termed parafollicular, light or C cells. They produce a calcium-lowering polypeptide, calcitonin, (Ingbar and Woeber, 1981).