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Thyroid Gland and Its Rule in Human Body.

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ABSTRACT

Thyroid gland is a part of the body's endocrine system. It is the largest organ specialized for endocrine function in human body. The gland is essential to normal body growth in infancy and childhood. It absorbs iodine from the diet and releases thyroid hormones -iodine- containing compounds that help govern the rate of body's metabolism (its total processes),controlling body temperature, and regulating protein, fat and carbohydrate catabolism in all cells.
Keywords: thyroid, endocrine gland, human body.

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Thyroid Gland

Thyroid gland is a part of the body's endocrine system. It is the largest organ specialized for endocrine function in human body. It is a butterfly - shaped gland Fig (1). It is an organ with many veins, anchored around the front of th e throat near the voice box [1].

The gland is essential to normal body growth in infancy and childhood. It absorbs iodine from the diet and releases thyroid hormones -iodine- containing compounds that help govern the rate of body's metabolism. Its total processes ,controlling body temperature, regulating protein, fat and carbohydrate catabolism in all cells.

Thyroid keep up growth hormone release, skeletal maturation, and heart rate ,force and output· It promotes central nervous system growth and stimulate synthesis of many enzymes, Thyroid is necessary for muscle tone and vigor·To a high degree, metabolism is regulated by the hormone thyroxine, which can be made by the thyroid if enough organic iodine is available [2].

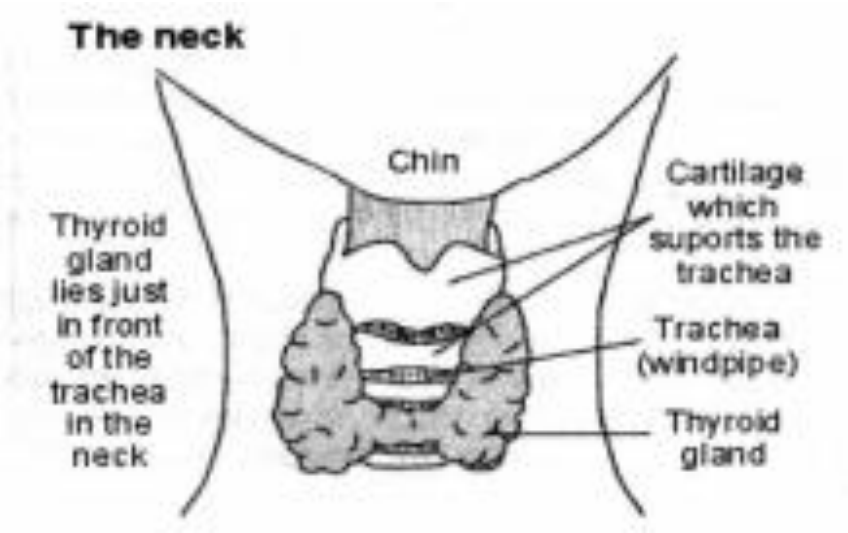

Figure (1): The thyroid gland

Thyroid hormones

Thyroid contains two hormones, L-thyroxine (T4, tetraiodothyronine) and Ltriiodothyronine (T3), Thyroid hormones are synthesized in the thyroid gland by iodination and coupling of two molecules of the amino acid tyrosine, a process that is dependent on an adequate supply of iodide (Fig 2).

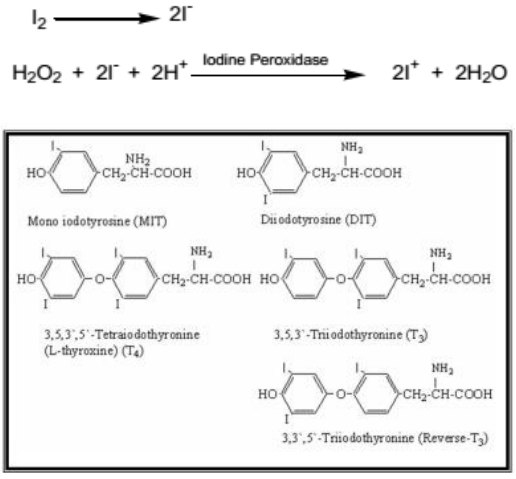

Figure (2) chemical structure of thyroid hormones and precursors. (3)

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Iodine is an indispensable component of the thyroid hormones, comprising 65% of T4's weight, and 58% of T3's. The thyroid hormones are the only iodine containing compounds with established physiologic significance in vertebrates [3].

The most obvious overall effect on metabolism is to stimulate the basal metabolic rate (BMR), but the precise molecular basis of this action is not known.

The only known action is that controlling the basal metabolic rate which depends on the conversion rate of T4 to T3in health individuals.

These two hormones are acted through entering the cells and binding to specific receptors in the nuclei, where they stimulate the synthesis of a variety of species of mRNA, thus stimulating the synthesis of polypeptides including hormones and enzymes in the cytoplasmi, they also increase the sensitivity of the cardiovascular and nervous systems to catecholamine [4].

The activity of the thyroid gland is predominantly regulated by concentration of pituitary glycoprotein hormone, thyroid stimulating hormone (TSH) [5].

The normal plasma concentrations of T4 and T3 are 60-150 nmol/L and 1.0-2.9 nmol/L, respectively. More than 99% of plasma T 4 and T3 is protein bound, mainly to an α-globulin, thyroxine- binding globulin (TBG), and to less extent to albumin and thyroxine-binding prealbumin. The free unbound fraction of both hormones are the physiologically active forms which regulate TSH secretion from the anterior pituitary [6].

T3 and T4 are released into the circulation, approximately 10 □g of T3 and 100□g of T4 are released into the blood stream, and about 25□g of T3 are produced daily by conversion of T4 into T3 in peripheral tissue [7].

The conversion of T4 to T3 takes place in a number of locations in the body, the main place is the liver, T3 is derived when the enzyme deiod inase removes one iodine atom from T4 [8].

Effect of thyroid hormone on specific bodily mechanisms in human body [9] :

- Stimulation of carbohydrate metabolism.
- Stimulation of fat metabolism.
- Stimulation of protein metabolism.
- Effect on plasma and liver fats.
- Increase requirements for vitamins.
- Increase basal metabolic rate (BMR).
- Effect on cardiovascular system.
- Excitatory effect on the central nervous system.
- Effect on sleep.
- Effect on other endocrine glands.
- Effect on sexual function.

Regulation of thyroid hormones secretion:

The right amount of thyroid hormones must be secreted at all times to maintain normal levels of metabolic activity in the body, to achieve this, specific feedback mechanisms operate through the hypothalamus and anterior pituitary gland to control the rate of thyroid secretion by a specific mechanism Fig (3). TSH (thyroid stimulating hormone) is also known as thyrotropin. It is a hormone from the anterior pituitary gland which increases thyroid secretion. TSH is a glycoprotein with a molecular weight of about 28.000 Dalton.

The secretion of TSH from the anterior pituitary gland is controlled by:

- Circulating concentration of thyroid hormones. (7)
- Thyrotrophin-relasing hormones (TRH).

The effect of thyroid hormones is to reduce TSH secretion by negative feedback were T3 which binds to anterior pituitary nuclear receptors. In the anterior pituitary gland most of the intracellular T3 is derived from circulating free T4. Therefore this gland is more sensitive to changes in plasma T4 than T3concentrations.

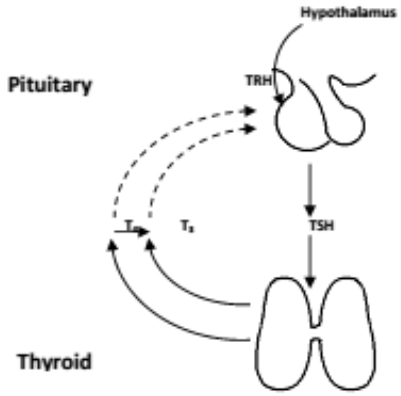

Figure (3): Secretion and control of thyroid hormones. (6)

Thyroid-stimulating hormone (TSH):

The history of TSH began with the discovery of thyroid-stimulating activity in the pituitary gland. Edward Uhlenhuth from the University of Maryland Medical School was the first to demonstrate that the anterior lobe of the pituitary gland secreted a thyroid stimulator [10] using several species of salamanders (Amphibiaus), He showed that injection of bovine pituitary extracts caused a clear histological stimulation of thyroid gland. In 1929 Leo Loeb and Max Aaron working independently confirmed Uhlenhuth's results using guinea pigs (mammals). These initial findings were followed in the 1960s by the purification TSH [8] and in the early 1970s by the determination of the primary structure of the TSH subunits. In the 1980s, the cloning of the human δ-subunit and TSH δ-subunit genes, were the important milestones in studying TSH expression, regulation, and action from the basic science stand point [11-12], another major breakthrough occurred in 1994 with the elucidation of the crystal structure of the closely related human Chorionic Gonadotropin (CHG) [13,14], which indicated that the glycoprotein hormones belong to the super family of Cystine-Knot Growth Factors (CKGF).

Then in 1966 it was found that TSH exerts its biological effects by binding to a protein on the thyroid cell plasma membrane [15].

TSH is a glycoprotein synthesized and secreted from thyrotrophs (basophile cell) of the anterior pituitary gland(19). TSH is a member of the glycoprotein hormone family that includes Follicle stimulating hormone (FSH), Lutenizing hormone(LH) and (CHG) [17,18].

Specific effects of TSH on the thyroid gland:

Effects on the thyroid gland is increases the secretion of thyroxine and triiodothyronine by the thyroid gland. Its specific effects on the thyroid gland are as follow:

- Increased proteolysis of the thyroglobulin that has already been stored in the follicles, with resultant release of the thyroid hormones into the circulating blood and diminishment of the follicular substance itself.
- Increased activity of the iodide pump, which increases the rate of "iodide trapping" in the glandular cells, sometimes increasing the 9 ratio of intracellular to extracellular iodide concentration in the glandular substance to as much as eight times normal.
- Increased iodination of tyrosine to form the thyroid hormones.

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- Increased size and increased secretary activity of the thyroid cells.
- Increased number of thyroid cells plus a change from cuboidal to columnar cells and much in folding of the thyroid epithelium into the follicles [19].

Disorders of the thyroid gland:

The metabolic manifestations of the thyroid disease related to either excessive or inadequate production of thyroid hormones (hyperthyroidism and hypothyroidism, respectively).

Hyperthyroidism (Thyrotoxicosis):

An abnormal condition of the thyroid gland resulting in excessive secretion of thyroid hormones characterized by an increased metabolism and weight loss [20].

The major causes and clinical features of hyperthyroidism are: (4)

- Grave's disease
- Toxic multinodular goitre (Solitary toxic adenoma thyroiditis
- Exogenous iodine and iodine-containing drugs,e.g. amiodarone
- Excessive T4 or T3 ingestion
- Ectopic thyroid tissue,
- e.g. struma ovarii
- functioning metastatic thyroid cancer HCG dependent
- e.g. choriocarcinoma, pituitary tumour (very rare)
- Clinical Features
- Weight loss (but normal appetite)
- Sweating, heart intolerance
- Fatigue
- Palpitation: sinus tachycardia or atrial fibrillation angina, heart failure (high output)
- Agitation, tremor
- Generalized muscle weakness,
- Proximal myopathy
- Diarrhoea
- Oligo menorrhoea, infertility
- Goitre
- Eyelid retraction, Lid lag

Hypothyroidism:

Table (2): Causes and clinical features of hypothyroidism(4)

Hypothyroidism	
Causes	**Clinical features**
* atrophic hypothyroidism (this condition may represent the end-stage of Hashimoto's disease) * autoimmune hypothyroidism (Hashimoto's thyroiditis) * post surgery, radioactive iodine, anti-thyroid drugs (e.g carbimazole) and other agents (e.g lithium) Congenital Dyshormonogenic Secondary (pituitary or hypothalamic disease) Iodine deficiency	Lethargy, tiredness, cold intolerance dryness and coarsening of skin and hair Hoarseness weight gain Slow relaxation of muscles and tendon reflexes many others including anaemia, typically macrocytic, non-megaloblastic but pernicious in 10% of cases. Dementia, psychosis constipation Bradycardia, angina, pericardial effusion Muscle stiffness carpal tunnel syndrome infertility, menorrhagia, galactorrhoea.

There are many causes of primary hypothyroidism table (2). Hypothyroidism, like hyperthyroidism, probably is initiated by autoimmunity against the thyroid gland, but immunity that

destroys the gland rather than stimulates (9). Clinical diagnosis is confirmed by the finding of a high plasma TSH concentration (Unless the condition is secondary to hypopituitarism) and low free T4 (FT4) concentration (4).

Albumin

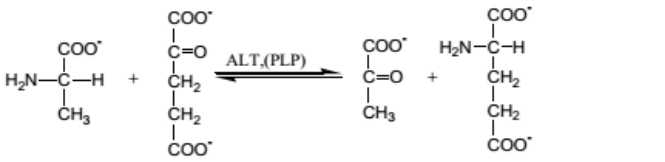
Albumin is the most abundant protein found in the plasma, making up 55 -65% of the total protein (reference range 35-50 g/L)[21]. Albumin is a small, highlysoluble, protein with a molecular weight of 69.000Da [22], It has a single polypeptide chain of 580 amino acids with 17 intrachain S-S bonds [23].

It is synthesized primarily by the hepatic parenchymal cells (24). Albumin functions include regulation of osmotic pressure [22], and nonspecific transport, as it binds many non-polar compounds such as bilirubin, long-chain fatty acids and a number of drugs[21]. It has specific binding sites for copper ion(22), it also functions as a reservoir for a number of hormones.Albumin is also an important component of plasma antioxidant activity [23,24], primarily by binding free fatty acids, free ions, hypochlorous acid (HOCl), and bilirubin [23], because of its copper-binding ability, it is a powerful continue on the albumin surface and damage it [25,26], but there is so much albumin present, therefore the damage is biologically insignificant, and more important targets are protected [27]. So albumin is required as a sacrificial antioxidant [22,24,27].

Albumin also reacts with HOCl [28], this acid damages the albumin, but this is again probably biologically insignificant in view of albumin's high concentration and rapid turnover [22].Albumin may scavenge peroxy radicals [29], also it can bind free fatty acids and protect them from peroxidation [30-32].

Alanine transaminases (GPT) (EC2.6.1.2)

Also called serum glutamate-pyruvate transaminase (SGPT). Having molecular weight approximately 101000 Dalton catalyze the reaction according to this equation:



L-Alanine **α-ketoglutarate** **pyrovate** **L-Glutamate**

This reaction goes to the right to provide a source of nitrogen for the urea cycle, the pyruvate is available for entry into the citric acid cycle.

Whereas glutamate is deaminated (catalyzed by glutamate dehydrogenase), yielding ammonia and δ-keto glutarate [31] . GPT is present in high concentration in liver to lesser extent in skeletal muscle, kidney and heart [32], measurement of GPT activity in serum used an indicator of hepatocellular damage [33].

It is used as a part of enzymes to establish whether liver damage has occurred [31].

Aspartate transaminase (GOT) (EC2.6.1.1):

Also called glutamate oxaloacetate transaminase (SGOT), present in high concentration in the heart, liver, skeletal muscle, kidney and erythrocytes. Damage to any of these tissue may increase plasma GOT levels [32]. GOT catalyses the following reaction:-

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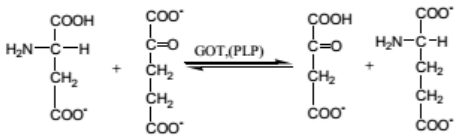

L-Aspartate α-ketoglutarate Oxaloacetate L-Glutamate

The reaction goes to the right [31]. There are two form of GOT. The mitochondrial and the soluble forms. The major diagnostic application used GOT activities are the investigation of myocardial infarction, liver disease and muscle disease [33-36].

CONCLUSION

Thyroid gland plays a master rule in body metabolism. The right amount of thyroid hormones must be secreted at all times to maintain normal levels of metabolic activity in the body, to achieve this, specific feedback mechanisms operate through the hypothalamus and anterior pituitary gland to control the rate of thyroid secretion.

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