Academic Science Journal

Thyroid gland: physiology and pathology

(A short review)

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Received: 1 February 2024 **Accepted: 30 May 2024**

DOI: https://dx.doi.org/10.24237/ASJ.02.03.857I

Abstract

One of the main parts of the endocrine system is the thyroid gland, it produces thyroid hormones, tetraiodothyronine, and triiodothyronine, which are important for general health. In this article, we review the most important thyroid hormones and the imbalance in these hormones. The thyroid hormones control various metabolic processes, involving expenditure of energy and growth, common thyroid dysfunction include excessive activity (hyperthyroidism) or limited activity (hypothyroidism) of the thyroid gland.

Keywords: Graves' disease, Hypothyroidism, and Thyroid hormone.

الغدة الدرقية وظيفتها وامراضيتها (مقالة قصيرة)

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الخلاصة

الغدة الدرقية هي أحد الأجزاء الرئيسية في جهاز الغدد الصماء، فهي تنتج هرمونات الغدة الدرقية (الثايروكسين، ثلاثي ايودين الثايرونين) وهي مهمة لصحة الجسم العامة . في هذا المقال نستعرض أهم هرمونات الغدة الدرقية والخلل في هذه الهرمونات وطرق تشخيصها. تتحكم هرمونات الغدة الدرقية في عمليات التمثيل الغذائي المختلفة، بما في ذلك استهلاك الطاقة والنمو، ويشمل الخلل الشائع في الغدة الدرقية النشاط المفرط والنشاط غير المفرط للغدة الدرقية ويؤثر هذا الخلل على وظائف الجسم بصورة عامة.

الكلمات المفتاحية:- مرض كريفز، قصور الغدة الدرقية، وهرمون الغدة الدرقية.

Introduction

The thyroid gland is butterfly or bow-tie like and composed of two-lobes, located between the cervical 5 and thoracic 1 vertebra in the position of the neck, just under the thyroid cartilage (Adam's apple) of the larynx (figure.1). The thyroid gland has two primary lobes (the right and left), which are joined by a smaller unit of tissue called the isthmus. About half of all people have an additional third lobe, known as the pyramidal lobe, which is often triangular in shape [1].

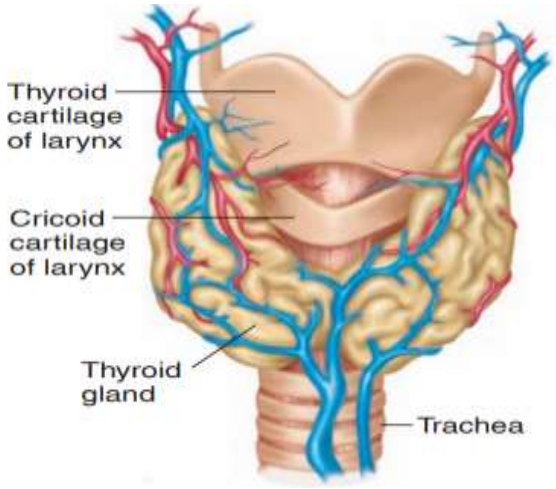

Figure 1: Thyroid gland [3]

On a microscopic level, the thyroid gland consists of numerous spherical hollow sacs called thyroid follicles (figure 2). These follicles are lined with a simple cuboidal epithelium composed of follicular cells that synthesize the principal thyroid hormone, thyroxine. The

interior of the follicles contains colloid, a protein-rich fluid. In addition to the follicular cells that secrete thyroxine, the thyroid also contains parafollicular cells that secrete a hormone known as calcitonin (or thyrocalcitonin). Triiodothyronine (T3) and thyroxine (T4) are hormones that have a variety of functions in the homeostatic regulation of essential physiological processes and organ development, including human body growth and energy consumption [2].

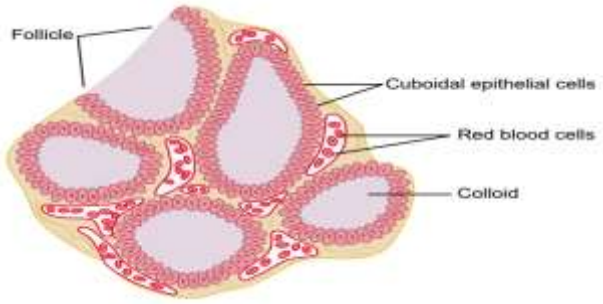

Figure 2: Microscopic appearance of the thyroid gland, showing secretion of thyroglobulin into the follicles

Thyroid Hormone

One of the many glands connected to the endocrine system called the thyroid gland, which produces and secretes thyroxine and triiodothyronine hormones [4]. Thyroxine makes up around 93% of the thyroid gland's released hormones with metabolic activity, and triiodothyronine makes up 7%. However, in the tissues, about all of the thyroxine is finally transformed to triiodothyronine, making both functionally significant. [5]. Over 99 percent of the thyroxine and triiodothyronine that enters the blood combines quickly with numerous of plasma proteins, which are all produced by the liver. They mostly bind to thyroxine-binding globulin, whereas prealbumin and albumin bind to thyroxine significantly less [6].

Thyroid Hormone Synthesis can be shown in the following steps

Thyroid hormone synthesis can be shown in the following steps (figure 3) [7-10].

- Active transport of iodide into the follicular cell via the sodium-iodide symporter (NIS). This is actually secondary active transport, and the sodium gradient driving it is maintained by a sodium-potassium ATPase.

- Thyroglobulin (Tg), a large protein rich in tyrosine, is formed in follicular ribosomes and placed into secretory vesicles.
- Exocytosis of thyroglobulin into the follicle lumen, where it is stored as colloid. Thyroglobulin is the scaffold upon which thyroid hormone is synthesised.
- Iodination of the thyroglobulin. Iodide is made reactive by the enzyme thyroid peroxidase. Iodide binds to the benzene ring on tyrosine residues of thyroglobulin, forming monoiodotyrosine (MIT) then diiodotyrosine (DIT).
- Coupling of MIT and DIT gives the triiodothyronine (T3) hormone and coupling of DIT and DIT gives the tetraiodothyronine (T4) hormone, also known as thyroxine.
- Endocytosis of iodinated thyroglobulin back into the follicular cell. Thyroglobulin undergoes proteolysis in lysosomes to cleave the iodinated tyrosine residues from the larger protein. Free T3 or T4 is then released, and the thyroglobulin scaffold is recycled.

T3 and T4 are the active thyroid hormones. They are fat soluble and mostly carried by plasma proteins – thyronine binding globulin (TBG) and albumin. While T3 is the more potent form, it also has a shorter half-life due to its lower affinity for the binding proteins. Less than 1% of T3 and T4 is unbound free hormone [11].At the peripheries, T4 is deiodinated to the more active T3. T3 and T4 are deactivated by removing iodine. This happens in the liver and kidney. As T4 has a longer half-life, it is used in the treatment of hypothyroidism over T3 as its plasma concentrations are easier to manage [12].

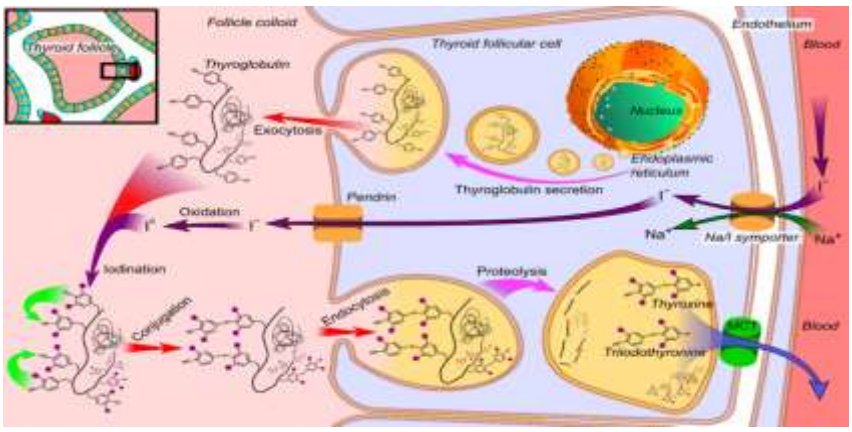

Figure 3: The production and storage of thyroid hormones

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Feedback regulation of thyroid hormones

The hypothalamic-pituitary axis regulates thyroid-stimulating hormone (TSH), that is generated by the anterior pituitary stimulates the thyroid to secrete thyroxine and triiodothyronine [13]. Thyrotropin-releasing hormone released from the hypothalamus induces the secretion of TSH. This simulation is balanced by thyroxine negative feedback inhibition, which decreases the anterior pituitary receptiveness to TRH activation. (figure.2). The anterior pituitary's thyrotrophs are stimulated to reals TSH by hypothalamic neurons, and TSH in turn stimulates follicular cells in thyroid gland to release T4 or T3 [14]. T3 is the active form of the thyroid hormone, even though it only accounts for 20% of the hormone produced, the common form of T3 is derived through the peripheral conversion of T4 to T3. It de-iodinates to create T3 when it is discharged into the bloodstream. The anterior pituitary can then encounter negative feedback from T4 and T3, with high T3/T4 levels reducing TSH secretion and low T3/T4 levels increasing TSH release [15].

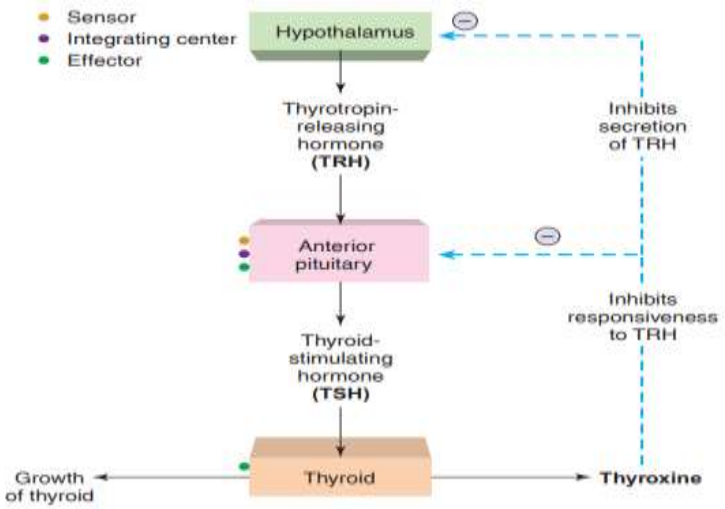

Figure 4: The hypothalamus-pituitary-thyroid axis (control system) [3]

Thyroid disorder

Thyroid disorders are the second biggest endocrine problem in society after diabetes. Environmental and genetic factors lead to the development of thyroid disorders [16]. An imbalance of thyroid hormones can lead to either hypothyroidism or hyperthyroidism [17].

Hyperthyroidism

The disease known as hyperthyroidism is caused by the uncontrolled synthesis of thyroid hormones, which can be carried on by thyroid hyper function, metabolic imbalance, or excess glandular hormone production. A dangerous side effect of hyperthyroidism is called thyrotoxicosis which results from an overt tissue exposure to excessive amounts of circulating thyroid hormones. It is characterized by emotional instability, intolerance to heat, tremor, sinus tachycardia, ionotropic effects and marked chronotropic, rise cardiac output (increased exposure to congestive heart failure), hypertension, systolic heart murmur, rise appetite and loss of weight [18]. The most frequent cause of hyperthyroidism is Graves disease (GD), followed by toxic multi-nodular goiter (MNG),In iodine-sufficient countries, GD accounts for 70–80% of all instances of hyperthyroidism, but in iodine-deficient nations, it accounts for 50% of all cases [19,20].

Hypothyroidisms

Hypothyroidism disease is known by a decline in secretion of thyroid hormone and dysfunction of thyroid gland. It results from, chronic thyroiditis disease (Hashimoto's), severe iron deficiency, absence of stimulation, follicle destruction caused by radioactive iodine, operation and pharmacological managers such as amiodarone and lithium, operation and pharmacological managers such as amiodarone and lithium, the latter of which is usually taken antidysrhythmics [21].

Hypothyroidism can also be caused by severe iodine deficiency because of the trace element iodine is necessary to synthesize of thyroid hormone [22]. Hashimoto thyroiditis, and chronic autoimmune thyroid disease, is the most prevalent cause of primary hypothyroidism in regions with abundant iodine. Because thyroid hormone is essential for many elements of a child's appropriate growth [23,24].

Symptoms

Hyperthyroidism

Symptoms: Most people with hyperthyroidism have one or more of the following symptoms which include anxiety, irritability, agitation, trouble sleeping, weakness – especially of the

upper arms and thighs which makes it difficult to climb stairs or get up from a chair, tremors of the hands, perspiring more than normal with difficulty tolerating hot weather, Rapid, forceful, or irregular heartbeats, fatigue, weight loss in spite of a normal or increased appetite, frequent bowel movement, In addition to that some women have irregular menstrual periods or stop having them [25-26].

Hypothyroidism

Symptoms depend on the level of the thyroid hormone and how quickly the level dropped. Some individuals have no symptoms and others have severe symptoms and even, rarely, life threatening symptoms. Symptoms can be very non-specific [27]. Usually, symptoms are milder when the hypothyroidism develops slowly.

General symptoms include (fatigue, sluggishness, weight gain, intolerance of cold temperature)., In addition to skin changes include (decreased sweating, dry, thick skin, coarse, thin hair, eyebrows may disappear, brittle nails, mild swelling around eyes) [28,29].

Diagnosis

Hyperthyroidism is typically diagnosed with blood tests. A thyroid scan can also be done to help determine the cause of hyperthyroidism [30].

- TSH level – this will be low.
- Free T4 and free T3 levels – these will be high [31].

Hypothyroidism can be diagnosed by blood tests.

- TSH level – this will be elevated if the thyroid gland is not functioning well.
- Free T4 and free T3 levels – these will be low.

Conclusion

The thyroid hormones control various metabolic processes, involving expenditure of energy and growth, common thyroid dysfunction includes excessive activity and lack activity of the thyroid gland.

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