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Some Diseases Of The Thyroid Gland In Humans

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ABSTRACT

Background:*The thyroid gland is a small gland located in the front of the neck, and it is part of the hormonal system that plays an important role in regulating body function and maintaining hormonal balance. The thyroid gland produces important hormones called thyroxine (T4) and tri-thyroxine (T3). These hormones influence many bodily functions, including metabolic rate, body temperature, and tissue growth.*

Some diseases that may affect the thyroid gland include:

Hyperthyroidism (overactive thyroid): occurs when the thyroid gland produces an excess amount of hormones, which leads to an increased metabolic rate and symptoms such as weight loss, persistent fatigue, elevated heart rate, and excessive anxiety.

Underactive thyroid gland (underactive thyroid): It occurs when the thyroid gland produces an insufficient amount of hormones, which leads to a low metabolic rate and symptoms such as weight gain, fatigue, depression, and extreme cold.

Thyroiditis (Tyroiditis): It may be due to inflammation of the thyroid gland as a result of a viral or bacterial infection, and it can cause redness and swelling in the front of the neck and difficulty swallowing.

Thyroid tumors: Cancerous (thyroid cancer) or benign tumors (papillomas) can form in the thyroid gland.

Type 2 diabetes and thyroid: Hyperthyroidism can affect blood sugar levels and increase the risk of type 2 diabetes. If you suspect any of these diseases, you should see a specialist doctor to conduct the necessary tests and make an accurate diagnosis.

Treatment for these diseases depends on the type and severity of the disorder, and may include drug therapy, surgery, or radiotherapy. Always make sure to follow your doctor's instructions and take care of your general health to improve your quality of life and avoid possible complications.

Keywords: Thyroid Gland, Hyperthyroidism, Tyroiditis, diseases.

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INTRODUCTION

The thyroid gland is positioned within the visceral region of the neck, near the larynx, and below Adam's apple (Garner and Chen, 2017). The thyroid gland weighs 10 to 15 grams in a normal adult. It is an organ that contains dense blood vessels and consists of two lobes on both sides of the trachea and connected by the isthmus, which represents a narrow passage of tissue that connects the two lobes, which leads to the production of the appearance of a butterfly. The isthmus and glandular lobes contain many follicles in the form of small, spherical, and globular sacs (Van Nostrand, 2016), as shown in Figure (1).

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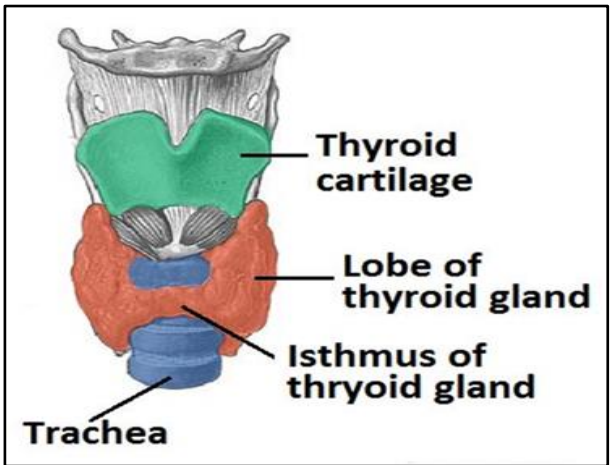

Figure (1): Shows the anatomy and structure of the thyroid gland.

Histological Structure of the Thyroid Gland:

A thin connective tissue capsule encases the thyroid gland and penetrates the lobes, dividing the gland into irregular lobular units. Each lobule of the gland contains a cluster of functional and structural units of the thyroid gland known as follicles (Figure 2) (Benvenga et al., 2018).

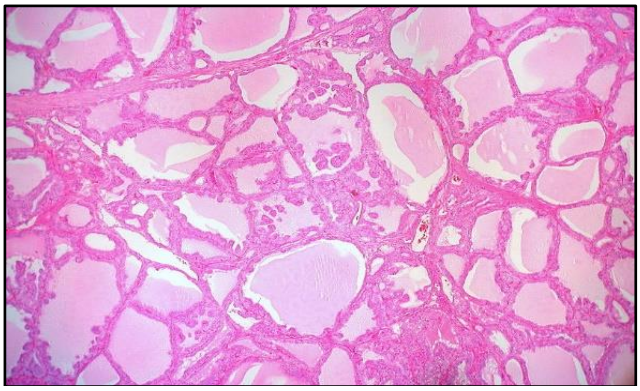

Figure (2): Functional and structural units of the thyroid gland.

The follicles forming the thyroid gland are surrounded by a thin stroma of connective tissue, which is supplied with lymphatic and fenestrated capillaries. The composition of the follicular epithelium is an epithelium of a group of squamous, columnar or cuboidal cells and the type of cells depends on the levels of activity of the follicle. The cuboidal and low columnar cells appear when the follicle is active, while the squamous cells emerge when the follicle is inactive (Arrangoiz et al., 2018). Thyroglobulin protein is an inactive type of THs produced by thyroid follicular function. Parafollicular cells, often known as C (clear) cells, are another kind of thyroid cell. Calcitonin is also produced by these cells Figure (3) (Malcomson & Nagy, 2015).

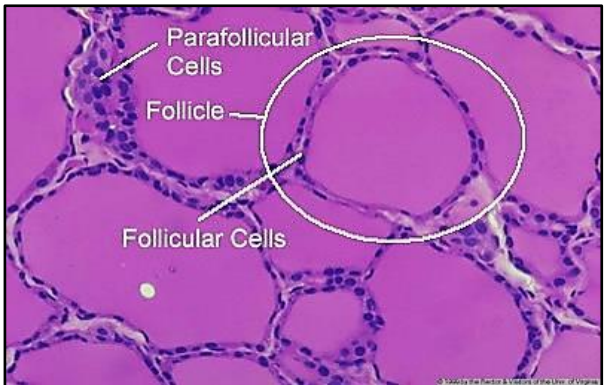

Figure (3): Histological anatomy of the thyroid gland.

Follicular cells line the follicles, which are filled with a colloid fluid, which includes the prohormone thyroglobulin. Follicular cells take precursors of amino acids and iodine on their basal surface and release the final products into the bloodstream. Follicular cells are known for their ability to produce and store thyroglobulin as a semi-solid colloid in the lumen of the follicle (Benvenga et al., 2018).

Thyroid Regulating

The hypothalamic-pituitary–thyroid (HPT) axis controls the amount of TH in the bloodstream. The anterior pituitary gland produces TSH in response to hypothalamic thyroid-releasing hormone (TRH). The hypothalamus constantly and accurately monitors the levels and concentrations of T3 and T4 in the blood. The hypothalamus often responds precisely to low T3 and T4 in the blood by releasing concentrations of TRH (Malcomson & Nagy, 2015). The anterior pituitary gland has special receptors that facilitate the binding of TRH to it, causing TSH to be produced and circulated in the bloodstream before binding to receptors on follicular cells, resulting in T3 and T4 release (Z. Zhang et al., 2018). To fine-tune the HPT axis, continuous negative feedback is employed. When the target organ responds

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cellularly or when there are sufficient concentrations of the hormone in the circulation, negative feedback is a key control mechanism for maintaining homeostasis; these data are transmitted back to the source of the key regulatory factors that stimulate the processes of hormone synthesis and release. The feedback mechanisms enhance cell stability and prevent overstimulation of target tissues (Figure 4) (Chou, 2019).

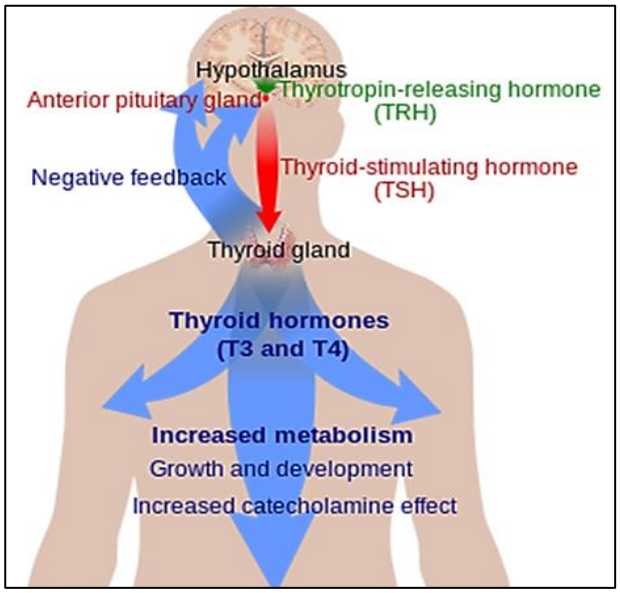

Figure (4): Thyroid system.
The hypothalamus detects an increase of T3 and T4 levels in the bloodstream, which reduces the anterior pituitary gland's secretion of TSH and TRH. It thus reduces the release of T4 and T3 secretion, which ultimately leads to the stabilization of the HPT, which ensures relative stability for metabolic rate (Bianco et al., 2019) .

Thyroid Hormone

The two most common thyroid hormones are T3 and T4 (Spence, 2016). The importance of hormones is because they are responsible for regulating metabolism. Follicular cells contain the essential enzymes for the synthesis of thyroglobulin and the release of THs from thyroglobulin (Braun & Schweizer, 2018).

The cells reabsorb thyroglobulin from the colloidal follicular lumen and cleave it into T3 and T4 when THs are urgently needed, and then release other hormones into the circulation (Bilal et al., 2017). It has become known today that iodine is an essential element for the thyroid gland health and is an element involved in the synthesis of both T4 and T3 (Videbeck, 2020). Iodine may be found in seaweed, vegetables, salt, and seafood (P. M. Gupta et al., 2018). Reduced iodine consumption can lead to iodine shortage and reduced TH synthesis. Iodine deficit can lead to hypothyroidism, myxedema coma, goiter, and cretinism (Videbeck, 2020).

Iodine is often absorbed in the small intestine through an active transport mechanism controlled by a co-transporter protein in the thyroid follicular cells' basolateral membrane (P. M. Gupta et al., 2018). Iodine concentrations inside follicular cells are 20-50 times higher than in the plasma due to active transport. Thyroid peroxidase attaches Iodine to thyroglobulin proteins in the follicular colloid, allowing T3 and T4 to be synthesized (Coscia & Taler-Verčič, 2021). T3 and T4 are carried across the body by coupled to plasma proteins such as thyroxin-binding globulin (TBG), transthyretin, and Albumin due to their limited solubility in the plasma's aqueous environment (Arrangoiz et al., 2018). The liver is responsible for synthesizing the prior three plasma proteins, TBG proteins having the highest affinity for binding (J. Knight, 2021).

Because triiodothyronine has three atoms of iodine in its structure, it has been given the abbreviation T3 to signify this (Yamauchi, 2016). TH affects virtually all cells of the body, resulting in rapid, potent and short-lived increases in cellular metabolic rates (Cicatiello et al., 2018). Although T3 is produced in smaller quantities than T4, it is primarily responsible for the reported TH effects and is approximately four times more influential than T4; nonetheless, T3 levels in peripheral tissues range from 10% to 15% (Magne et al., 2021). Deiodinases are enzymes found in the kidneys, liver, and other organs that convert T4 to T3. T4 conversion in the peripheral tissues accounts for around 85-90% of T3 hormones reaching their intended cells (Bayse et al., 2020). T3 has a half-life of approximately 2.5 days (Madan & Celi, 2020). Because thyroxin has four atoms of iodine in its structure, it has been given the abbreviation T4 to signify this (Yamauchi, 2016). T4 is synthesized in

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enormous quantities by the thyroid gland approximately 20 times more than T3 (Persani et al., 2019). T4 binds to globulins significantly more firmly than T3 and is not cleared from the blood as fast by target cells, and the half-life of T4 is approximately 5-6 days (Figure 5) (Madan & Celi, 2020).

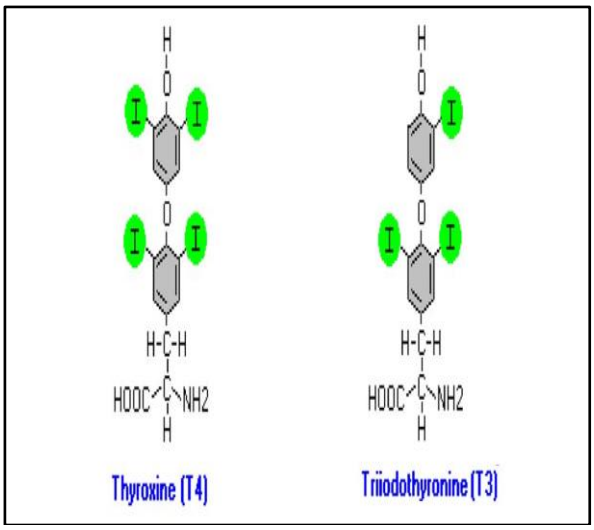

Figure (5): T4 and T3 Chemical Structure.

Physiologic Effects of Thyroid Hormones

Hormones of thyroid have a significant impact on numerous physiologic processes, including development, metabolism, and growth, and a lack of THs is incompatible with typical health (Mallya & Ogilvy-Stuart, 2018).

Metabolism: Most tissues' metabolic activity is stimulated by THs, resulting in an increase in metabolic rate. Increased ATP hydrolysis rates and oxygen consumption appear to be one effect of this activity (Weiss & Refetoff, 2016). The following are some instances of THs' particular metabolic effects:

Lipid Metabolism: Fat mobilization is stimulated by increasing TH levels, resulting in higher plasma fatty acid concentrations, it also promotes the oxidation of fatty acids in various body tissues, and TH levels are inversely associated to plasma triglyceride and cholesterol concentrations. Thyroid hormones, particularly T3, aid the liver in processing and removing the body's extra cholesterol (Sun et al., 2021).

Carbohydrate Metabolism: THs activate carbohydrate metabolism, including gluconeogenesis, glycogenolysis, and insulin-dependent glucose (Cicatiello et al., 2018).

Thyroid hormones have an important role in hemodynamic regulation. As a result, glomerular filtration, electrolyte management, and renal hemodynamics are all affected(Ayesha Ammar et al., 2021).

Growth: THs are required for children's growth, as indicated by the growth retardation seen in thyroid insufficiency; the effect of THs on growth is inextricably linked to that of growth hormone, and substantial evidence that various endocrine controls are necessary for complicated physiologic processes such as growth (Kucharska et al., 2021).

Cardiovascular System: THs increase cardiac output, cardiac contractility, and heart rate. They also cause dilation of blood vessels, which increases blood flow to various organs (Al-Makhamreh et al., 2022).

Development: Adequate TH levels are required for the brain development of neonates and fetuses (Moog et al., 2017).

Central nervous system: Both low and high TH concentrations cause mental changes, low concentrations of TH lead to mental lethargy, while high concentrations of TH lead to nervousness and anxiety (Núñez et al., 2017).

Reproductive system: Normal reproductive behavior and physiology require generally normal amounts of TH. Infertility is frequently linked with hypothyroidism (Silva et al., 2018).

Thyroid Diseases

Hyperthyroidism and hypothyroidism are prevalent disorders that can have serious health repercussions for people all over the world; thyroid disorder is widespread, easily recognized, and treated (Schellack et al., 2020). Thyroid disorders are divided according to the endocrine gland that causes the disease, classified as primary or secondary. Primary thyroid disease means a problem with the thyroid gland itself. While thyroid disease is the second type denotes anterior pituitary

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disorders that have an indirect effect on thyroid activity (Beynon & Pinneri, 2016).

The thyroid gland produces a lot of T4 and T3 in primary hyperthyroidism. Secretion of TSH from the anterior pituitary is suppressed by inhibiting negative feedback. It was observed that in cases of primary hypothyroidism, the thyroid gland produces insufficient concentrations of T3 and T4, which leads to a decrease in the inhibition of negative feedback and an increase in TSH synthesis (Garmendia Madariaga et al., 2014). In secondary hyperthyroidism, the anterior pituitary gland produces high concentrations of TSH, which stimulates the secretion of THs in high concentrations by the follicular cells (Bao et al., 2021). For the vast majority of individuals with suspected thyroid disease, TSH is the first-line test for diagnosing the disease (LeFevre, 2015). T3 and T4 can help evaluate primary and secondary thyroid disease. It is worth noting that TSH, T4, and T4 levels in the blood are employed in standardizing thyroid function tests because they are significant in discriminating between primary and secondary thyroid diseases and identifying thyroid disorders. A parallel shift in TSH concentration with T4 and T3 indicates a secondary disorder in the anterior pituitary gland. In contrast, a reverse shift in TSH concentration with T4 and T3 means a problem with the thyroid gland itself (MEMS, 2019).

Hypothyroidism

Hypothyroidism is widespread all over the world. Hashimoto's thyroiditis and iodine deficiency are the most prevalent causes of primary hypothyroidism. Hypothyroidism affects 1 to 2% of the population in countries where iodine is plentiful. Hypothyroidism is ten times more common in women than in males (Nemdis, 2013), and it may be brought on by several factors, including:

Hashimoto thyroiditis: is the most common autoimmune thyroiditis (AIT). It produces long-term inflammation of thyroid tissue. About 20–30% of patients have hypothyroidism (Nemdis, 2013; Halawani et al., 2018). AIT occurs 4-10 times more frequently in women than males (Halawani et al., 2018).

Environmental risk factors and hereditary susceptibility are thought to have a role in Hashimoto thyroiditis (Liontiris & Mazokopakis, 2017). The immune system usually defends the body against external invaders that might cause sicknesses, such as bacteria and viruses. However, in autoimmune disorders, the body's organs and cells are attacked by the immune system, particularly in Hashimoto's disease, causing inflammation of the gland and undermining its ability to synthesize THs. A hallmark of histological AIT is follicular destruction, and fibrosis and atrophy of the thyroid may be stimulated as a result of this destruction (Figure 6) (Liontiris & Mazokopakis, 2017).

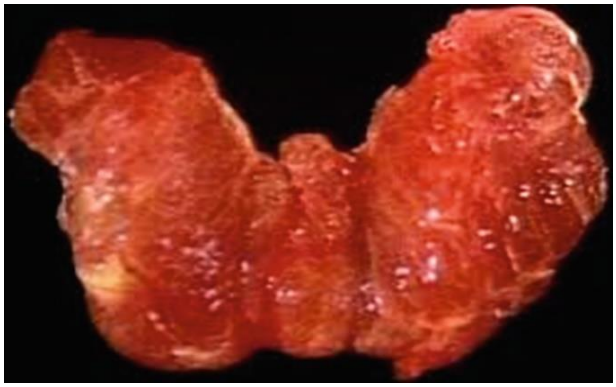

Figure (6): Hashimoto's disease, causing inflammation in thyroid gland.

Thyroiditis: Infection of the thyroid gland is uncommon as it is surrounded by a dense blood supply and substantial lymphatic drainage. Thyroid infection usually occurs in the chronically elderly and immunocompromised patients (Bostan et al., 2021). Gram-positive bacteria such as Streptococci, Staphylococci, Mycobacteria, and fungi, including pneumocystis, are the most prevalent culprits in immunocompromised patients (Alfadda et al., 2014). One of the primary sources of infection is mainly hematogenous or congenital defects, such as pyriform sinus, which is common in children. Respiratory tract infections are commonly associated with it and is thought to be caused by a viral infection, while definitive proof is lacking (Abbas et al., 2016). Thyroiditis causes the thyroid gland to release stored TH, which raises hormone levels in the blood. When TH levels are excessively high,

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hyperthyroidism develops and lasts for 1-2 months before the thyroid is fully recovered; the majority of patients suffer hypothyroidism (Bansi & Gauwerky, 2017).

Subclinical Hypothyroidism (SCH): The term SCH refers to an asymptomatic patient with increased TSH and T4 levels. The hypothalamus pituitary-thyroid axis must be intact for this description to be correct, there is no current or recent serious sickness, and the pattern can be repeated over time (Biondi et al., 2019). Subclinical hypothyroidism affects as much as 10% of the population, being particularly common among older people and women; indeed, in the absence of thyroid illness, older people with modestly raised blood TSH are not at risk of increased morbidity and death (Kim & Park, 2014). There are a variety of clinical disorders that might cause a rise in TSH levels that are unrelated to primary thyroid illnesses; they include thyroid lobectomy for malignant or benign thyroid nodules, sever illness, obesity, TSH receptor gene alterations, untreated adrenal insufficiency, medications like lithium and neck radiotherapy (Biondi et al., 2019). After a thyroid lobectomy and more than a year after the operation, up to 60% of individuals might develop persistent hypothyroidism, usually asymptomatic (Park et al., 2017).

Congenital Hypothyroidism: Some newborns are born with an underdeveloped or malfunctioning thyroid gland. Congenital hypothyroidism can cause development failure and mental disability if left untreated. Hypothyroidism affects roughly 1 per 4000 babies and can be prevented complications with early therapy. This condition may be temporary, mainly if the mother has used anti-thyroid medicines, but in most cases, persistent hypothyroidism develops (Wassner, 2018). Hypothyroidism, on the other hand, is a slow-developing condition, and many individuals are unaware of its symptoms. Symptoms specific to Hashimoto's disease include a feeling of throat fullness and a goiter (Saint & Chopra, 2018).

Treatment for Hypothyroidism

Iodine deficiency can be treated by eating iodized meals or using iodized salt. The thyroid gland, pituitary gland, or hypothalamus can all fail or be damaged, resulting in hypothyroidism. T4 pills, a kind of hormone replacement therapy, raise TH levels in certain circumstances (Ventura et al., 2017).

Hyperthyroidism

Hyperthyroidism is a kind of thyrotoxicosis caused by excessive TH production and secretion by the thyroid. Thyrotoxicosis therapy necessitates an accurate diagnosis (Samsam, 2020). Thyrotoxicosis is a clinical condition caused by abnormally high TH action in tissues, which is caused by abnormally high tissue TH levels (Bains et al., 2019). Several medical conditions may induce hyperthyroidism, including:

Graves' Disease

The immune system targets the thyroid gland in this disorder. Graves' disease is a genetic disorder; if one family member gets Graves' disease, it's possible that others in the family may have the condition as well, and it affects more women than men (Kahaly et al., 2018). The exact cause of Graves' disease is unknown; however, it most often strikes women between the ages of 20 and 50 and tends to run in families. Another factor contributing to an increased chance of having this disease is smoking. Graves' disease is the most frequent reason for hyperthyroidism, accounting for around 85% of all cases (Figure 7) (Akram et al., 2020).

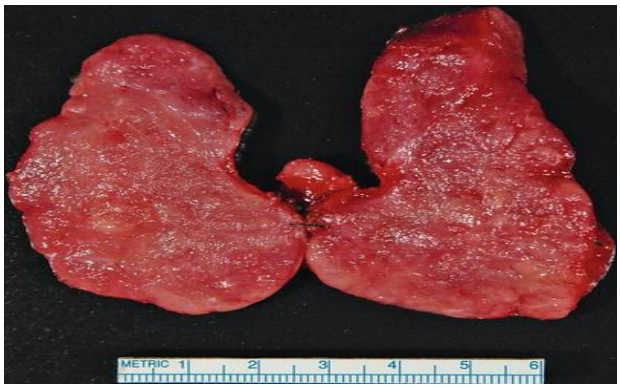

Figure (7): Graves' disease demonstrates hyperthyroidism as nodules.

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Thyroid Nodules

Thyroid nodules are cellular growths in the thyroid gland, which can create more hormones than the body requires, and cancerous thyroid nodules are uncommon (Fisher & Perrier, 2018). If nodules appear in the thyroid gland, it becomes overactive, and this condition is less common. Although nodules are generally benign, they may include thyroid tissue, leading to the synthesis of too many THs. It's unclear why some people get thyroid nodules, although they're more common in those over 60 (Figure 8) (Zou et al., 2020).

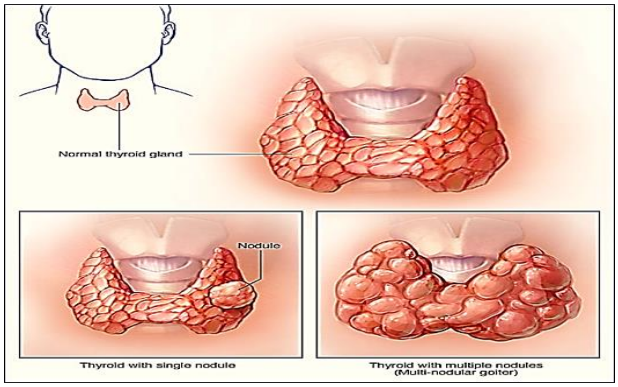

Figure (8): Shows the thyroid gland with single and numerous nodules.

Thyroid nodules can occur as a result of several disorders, including:

Thyroid Gland Hyperplasia: is a term for an excess of normal thyroid tissue. It's not apparent why this happens (Gharib et al., 2016).

Thyroid cyst:

The most prevalent cause of fluid-filled cavities is a kind of thyroid adenoma called degenerative thyroid adenoma. Thyroid cysts often combine solid and liquid components. Cysts usually are not malignant, however they can sometimes include solid malignant parts (J. Ren et al., 2019).

Thyroid Chronic Inflammation: Thyroid inflammation caused by Hashimoto's disease can result in nodules enlargement (Z. Li et al., 2020).

Iodine deficiency: Thyroid nodules can occasionally be caused by a of iodine shortage in the diet (B. A. Knight et al., 2017).

Thyroiditis

It is an infection that occurs in the thyroid gland, which causes swelling and inflammation, which may be painful or painless and can cause extra THs to be produced; the thyroid may be difficult to heal after experiencing thyroiditis (Figure 9) (Kopp, 2016).

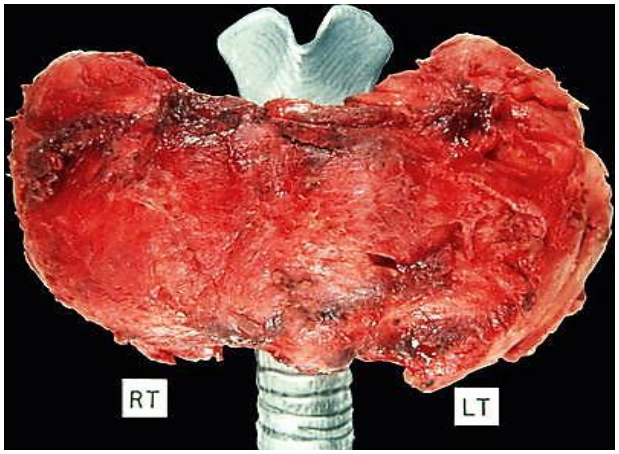

Figure (9): Swelling of thyroid because of thyroiditis (Reference).

Hyperthyroidism, as well as high iodine ingestion through drugs or food, can induce the thyroid to create more TH.

Consuming Excess Iodine

Hyperthyroidism, as well as excessive iodine consumption by medications or diet, can induce the thyroid to create more TH, Iodine is a mineral that the thyroid utilizes to produce TH; getting iodine dye intravenously can cause hyperthyroidism. There are several medications that contain iodine that may induce hyperthyroidism, such as Amiodarone (Ross et al., 2016).

Thyroid Cancer

Thyroid cancer is defined as the uncontrolled proliferation of thyroid gland cells, which diffuse to the surrounding tissue as well as other parts of the body. Anyone of any age can develop thyroid cancer. The medicines that are currently available can cure the majority of patients (La Vecchia et al., 2015).

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Thyroid tumors and growths can take several forms. The majority of them are non-cancerous, but some are cancerous (Patel, 2020). The production of THs can be affected by malignant thyroid tumors. Hyperthyroidism and thyroid cancer are a rare combination, as low TSH levels can prevent differentiated thyroid cancer cells from growing and developing (Figure 10) (Brito & Hay, 2019).

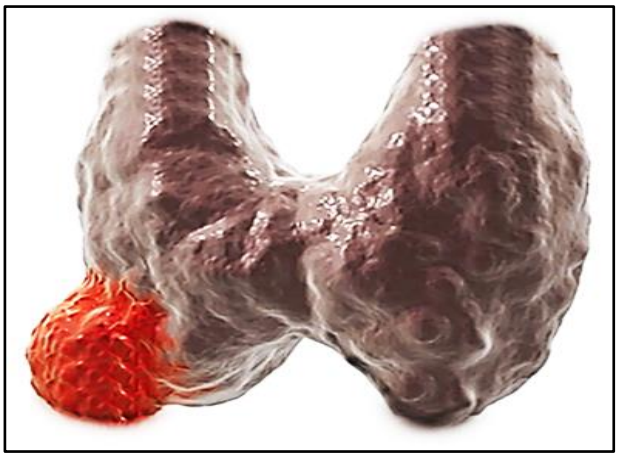

Figure (10): Cancerous cells proliferate in the thyroid gland (Reference).

The cause of cancer in the majority of patients is never found (Haugen et al., 2016). However, the following risk factors are well known:

- Pre-existing thyroid condition: It is somewhat more prevalent in people who already have a thyroid problem such as Hashimoto's thyroiditis or multinodular goiter; however, most thyroid malignancies manifest as a solitary nodule in the thyroid (Kline & Sadrzadeh, 2017).

- High-dose radiation: If the thyroid has already been subjected to radiation at a high dose, the chance of non-cancerous nodules as well as cancerous thyroid rises (Secretan et al., 2016). People who have had radiation or who have survived atomic blasts or accidents are high-risk populations. Patients who have received neck radiation as a cancer treatment should have frequent thyroid examinations, according to experts (Y. Zhang et al., 2015).

Age: Thyroid cancer is more common as people get older (Trimboli et al., 2020).

Obesity: thyroid cancer cases caused by overweight (Trimboli et al., 2020). Family history and genetic factors: More malignancies are discovered than would be predicted by chance in a limited number of families (Kamani et al., 2022).

Hyperthyroidism Treatment

There are several hyperthyroidism therapies available and the optimal course of action is determined by the severity of the problem, personal choice, the source of hyperthyroidism, health situation, and age (Chaker et al., 2017). Among the several treatment possibilities are:

- Radioactive iodine: Oral ingestion of radioactive iodine results in the thyroid gland's absorption of the substance, which causes the gland to become smaller. Within a few months, the symptoms usually disappear. Unnecessary radioactive iodine is excreted from the body within weeks to months. This treatment may produce hypothyroidism, necessitating daily thyroxin replacement medicine (Duntas & Jonklaas, 2019).

- Anti-thyroid Medicines: These drugs progressively alleviate hyperthyroidism symptoms by preventing the thyroid gland from generating excessive levels of hormones. They include propylithiouracil and methimazole. Although anti-thyroid medication therapy often continues for at least a year, normal improvement of symptoms typically occurs within a few weeks to months (Burch & Cooper, 2018).

- Beta blockers: Even though these drugs are often used for hypertension treatment and have no impact on thyroid levels, they effectively reduce the symptoms of hyperthyroidism, such as palpitations, rapid heartbeat, and tremors. As a result, doctors may prescribe them to help patients feel better until their thyroid levels return to normal (Jackson et al., 2019).

- Thyroidectomy: Although this is only a possibility in a few circumstances. During a thyroidectomy, the doctor removes the majority of the gland. There is a possibility that this operation might cause harm to the patient's voice cords or parathyroid glands, which are anatomically composed of four tiny glands found underneath the thyroid gland that aids in

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calcium regulation (Lee et al., 2018). Furthermore, lifelong medication with synthroid, levoxyl, and others is required to supply the body with appropriate levels of TH. If the parathyroid glands are removed as well, medication will be required to maintain normal levels of blood calcium (Ayers et al., 2015).

REFERENCES

- **Malcomson**, R. D. G., & Nagy, A. (2015). The Endocrine System. In Keeling's Fetal and Neonatal Pathology (pp. 671–702). Springer International Publishing.
- **Benvenga**, S., Tuccari, G., Ieni, A., & Vita, R. (2018). Thyroid Gland: Anatomy and Physiology. In Encyclopedia of Endocrine Diseases (2nd ed., Vol. 23, Issue 23, pp. 382–390). Elsevier.
- **Arrangoiz**, R., Cordera, F., Caba, D., Muñoz, M., Moreno, E., & de León, E. L. (2018). Comprehensive Review of Thyroid Embryology, Anatomy, Histology, and Physiology for Surgeons. International Journal of Otolaryngology and Head & Neck Surgery, 07(04), 160–188.
- **Zhang**, Z., Boelen, A., Kalsbeek, A., & Fliers, E. (2018). TRH Neurons and Thyroid Hormone Coordinate the Hypothalamic Response to Cold. European Thyroid Journal, 7(6), 279–288.
- **Chou**, K. (2019). Endocrine System and Endocrine Disruptors. In Reference Module in Biomedical Sciences. Elsevier.
- **Bianco**, A. C., Dumitrescu, A., Gereben, B., Ribeiro, M. O., Fonseca, T. L., Fernandes, G. W., & Bocco, B. M. L. C. (2019). Paradigms of Dynamic Control of Thyroid Hormone Signaling. Endocrine Reviews, 40(4), 1000–1047.
- **Braun**, D., & Schweizer, U. (2018). Thyroid Hormone Transport and Transporters. In Vitamins and Hormones (1st ed., Vol. 106, pp. 19–44). Elsevier Inc.
- **Bilal**, M. Y., Dambaeva, S., Kwak-Kim, J., Gilman-Sachs, A., & Beaman, K. D. (2017). A Role for Iodide and Thyroglobulin in Modulating the Function of Human Immune Cells. Frontiers in Immunology,8(NOV),1–13.
- **Videbeck**, S. L. (2020). https://t.me/MBS_MedicalBooksStore.
- **Spence**, A. W. (2016). Thyroid hormones. British Medical Journal, 1(5123) , 706 –708.
- **Gupta**, P. M., Gahche, J. J., Herrick, K. A., Ershow, A. G., Potischman, N., & Perrine, C. G. (2018). Use of Iodine-Containing Dietary Supplements Remains Low among Women of Reproductive Age in the United States: NHANES 2011-2014. Nutrients, 10(4), 422.
- **Coscia**, F., & Taler-Verčič, A. (2021). Cryo-EM: A new dawn in thyroid biology. Molecular and Cellular Endocrinology, 531(May), 111309.
- **Knight**, J. (2021). Endocrine system 3: thyroid and parathyroid glands. Nursing Times, 117(7), 46–50.
- **Yamauchi**, K. (2016). Thyroid Hormones. In Handbook of Hormones (pp. 493-e93-2). Elsevier.
- **Cicatiello**, A. G., Di Girolamo, D., & Dentice, M. (2018). Metabolic Effects of the Intracellular Regulation of Thyroid Hormone: Old Players, New Concepts. Frontiers in Endocrinology, 9(SEP), 1–7.
- **Magne**, F., Vliet, G. Van, & Delvin, E. E. (2021). Biochemical and Molecular Basis of Pediatric Disease. In Biochemical and Molecular Basis of Pediatric Disease. Elsevier.
- **Bayse**, C. A., Marsan, E. S., Garcia, J. R., & Tran-Thompson, A. T. (2020). Thyroxine binding to type III iodothyronine deiodinase. Scientific Reports, 10(1), 15401.
- **Madan**, R., & Celi, F. S.(2020).combination Therapy for Hypothyroidism: Rationale,Therapeutic Goals,and Design .Frontiers in

 Copyright © The Author(s)

Endocrinology,(July),1-11.

- **Persani**, L., Cangiano, B., & Bonomi, M. (2019). The diagnosis and management of central hypothyroidism in 2018. Endocrine Connections, 8(2), R44–R54.
- **Mallya**, M., & Ogilvy-Stuart, A. L. (2018). Thyrotropic hormones. Best Practice & Research Clinical Endocrinology & Metabolism, 32(1), 17–25.
- **Weiss**, R. E., & Refetoff, S. (2016). Thyroid Function Testing.In Endocrinology: Adult and Pediatric (Seventh Ed, Vols. 2–2,pp. 1350-1398.e11). Elsevier.
- **Sun**, X., Chen, L., Wu, R., Zhang, D., & He, Y. (2021). Association of thyroid hormone with body fat content and lipid metabolism in euthyroid male patients with type 2 diabetes mellitus: a cross-sectional stu Garner dy. BMC Endocrine Disorders, 21(1), 241.
- **Ayesha** Ammar, Kahkashan Bashir Mir, Sadaf Batool, Noreen Marwat, Maryam Saeed, Adnan Saeed, & Shazia Fatima. (2021). Assessment of decrease in renal function associated with hypothyroidism. World Journal of Advanced Research and Reviews, 12(1), 275–286.
- **Kucharska**, A. M., Witkowska-Sędek, E., Rumińska, M., & Pyrżak, B. (2021). Thyroid Hormone Changes Related to Growth Hormone Therapy in Growth Hormone Deficient Patients. Journal of Clinical Medicine, 10(22), 5354.
- **Al-Makhamreh**, H., Al-Ani, A., Alkhulaifat, D., Shaban, L., Salah, N., Almarayaty, R., Al-Huneidy, Y., & Hammoudeh, A. (2022). Impact of thyroid disease in patients with atrial fibrillation: Analysis from the JoFib registry. Annals of Medicine and Surgery, 74(December 2021), 103325.
- **Moog**, N. K., Entringer, S., Heim, C., Wadhwa, P. D., Kathmann, N., & Buss, C. (2017). Influence of maternal thyroid hormones during gestation on fetal brain development. Neuroscience, 342(07), 68–100.
- **Núñez**, A., Bedregal, P., Becerra, C., & Grob L., F. (2017). Alteraciones del neurodesarrollo en pacientes con hipotiroidismo congénito: Recomendaciones para el seguimiento. Revista Médica de Chile, 145(12), 1579–1587.
- **Silva**, J. F., Ocarino, N. M., & Serakides, R. (2018). Thyroid hormones and female reproduction. In Biology of Reproduction (Vol. 99, Issue 5, pp. 907–921).
- **Schellack**, N., Schellackb, G., & Esterhuizena, A. (2020). Shifting the paradigm in the management of conditions affecting the thyroid gland. Journal of Endocrinology, Metabolism and Diabetes of South Africa, 25(1), 28–34.
- **Beynon**, M. E., & Pinneri, K. (2016). An Overview of the Thyroid Gland and Thyroid-Related Deaths for the Forensic Pathologist.AcademicForensicPatholog y,6(2),217–236.
- **Garmendia** Madariaga, A., Santos Palacios, S., Guillén-Grima, F., & Galofré, J. C. (2014). The Incidence and Prevalence of Thyroid Dysfunction in Europe: A Meta-Analysis. The Journal of Clinical Endocrinology & Metabolism, 99(3), 923–931.
- **Bao**, L. H., Duc, N. M., Chien, P. C., Tra My, T.-T., Thang, T. V., & Nam, T. Q. (2021). Central Hyperthyroidism due to Thyroid-Stimulating Hormone-Secreting Pituitary Microadenoma in an Adolescent Boy: Case Report and Review of the Literature. Case Reports inEndocrinology,2021(30),1–7.
- **LeFevre**, M. L. (2015). Screening for Thyroid Dysfunction: U.S. Preventive Services Task Force Recommendation Statement. Annals of Internal Medicine, 162(9), 641–650.
- **Malaysian** Endocrine And Metabolic Society (MEMS). (2019). Clinical Practice Guidelines: Management of

Copyright © The Author(s)

Thyroid Disorders. Clinical Practice Guidelines, 07(Cdc), 1–6.

- **Nemdis**. (2013). Hypothyroidism National Endocrine and Metabolic Diseases Information Service What is hypothyroidism? 94(6), 1–8.
- **Halawani**, M. S., Nughays, R. O., & Altemani, A. F. (2018). Causes, Diagnosis and Management of Hypothyroidism. The Egyptian Journal of Hospital Medicine, 71(1), 2250–2252.
- **Liontiris**, M. I., & Mazokopakis, E. E. (2017). A concise review of Hashimoto thyroiditis (HT) and the importance of iodine, selenium, vitamin D and gluten on the autoimmunity and dietary management of HT patients.Points that need more investigation. Hellenic Journal of Nuclear Medicine, 20(1), 51–56.
- **Bostan**, H., Sencar, M. E., Calapkulu, M., Hepsen, S., Duger, H., Ozturk Unsal, I., Ozbek, M., & Cakal, E. (2021). Two Important Issues in Subacute Thyroiditis Management: Delayed Diagnosis and Inappropriate Use of Antibiotics. European Thyroid Journal, 10(4), 323–329.
- **Alfadda**, A. A., Sallam, R. M., Elawad, G. E., AlDhukair, H., & Alyahya, M. M. (2014). Subacute Thyroiditis: Clinical Presentation and Long Term Outcome. International Journal of Endocrinology, 2014, 1–7.
- **Abbas**, P. I., Roehm, C. E., Friedman, E. M., Athanassaki, I., Kim, E. S., Brandt, M. L., Wesson, D. E., & Lopez, M. E. (2016). Successful endoscopic ablation of a pyriform sinus fistula in a child :case report and literature review. Pediatric Surgery International, 32(6), 623–627.
- **Bansi**, H. W., & Gauwerky, F. (2017). Hyperthyroidism--hypothyroidism. Deutsches Medizinisches Journal, 19(22), 794–800.
- **Biondi**, B., Cappola, A. R., & Cooper, D. S. (2019). Subclinical Hypothyroidism.JAMA,322(2),153.
- **Kim**, Y. A., & Park, Y. J. (2014). Prevalence and Risk Factors of Subclinical Thyroid Disease. Endocrinology and Metabolism, 29(1), 20.
- **Park**, S., Jeon, M. J., Song, E., Oh, H.-S., Kim, M., Kwon, H., Kim, T. Y., Hong, S. J., Shong, Y. K., Kim, W. B., Sung, T.-Y., & Kim, W. G. (2017). Clinical Features of Early and Late Postoperative Hypothyroidism After Lobectomy. The Journal of Clinical Endocrinology & Metabolism, 102(4), 1317–1324.
- **Wassner**, A. J. (2018). Congenital Hypothyroidism. Clinics in Perinatology, 45(1), 1–18.
- **Saint**, S., & Chopra, V. (2018). The Saint-Chopra Guide to Inpatient Medicine. In S. Saint & V. Chopra (Eds.), The Saint-Chopra Guide to Inpatient Medicine. Oxford University Press.
- **Ventura**, M., Melo, M., & Carrilho, F. (2017). Selenium and Thyroid Disease: From Pathophysiology to Treatment. International Journal of Endocrinology, 2017(32), 1–9.
- **Samsam**, M. (2020). Hyperthyroidism. In Epidemiology of Thyroid Disorders (pp. 121–145). Elsevier.
- **Bains**, L., Bhatia, S., Kaushik, R., Jain, S. K., Singh, C. B., Mandal, S., & Kaur, D. (2019). Pre-sternal thyroid swellings: a case of rare aberrant site recurrence and review of literature. Thyroid Research, 12(1), 12.
- **Kahaly**, G. J., Bartalena, L., Hegedüs, L., Leenhardt, L., Poppe, K., & Pearce, S. H. (2018). 2018 European Thyroid Association Guideline for the Management of Graves' Hyperthyroidism. European Thyroid Journal, 7(4), 167–186.
- **Akram**, S., Elfenbein, D. M., Chen, H., Schneider, D. F., & Sippel, R. S. (2020). Assessing American Thyroid Association Guidelines for Total

 Copyright © The Author(s)

Thyroidectomy in Graves' Disease. The Journal of Surgical Research, 245(23), 64–71.

- **Fisher**, S. B., & Perrier, N. D. (2018). The incidental thyroid nodule. CA: A Cancer Journal for Clinicians, 68(2), 97–105.
- **Zou**, B., Sun, L., Wang, X., & Chen, Z. (2020). The Prevalence of Single and Multiple Thyroid Nodules and Its Association with Metabolic Diseases in Chinese: A Cross-Sectional Study. International Journal of Endocrinology, 2020(3), 1–11.
- **Gharib**, H., Papini, E., Garber, J. R., Duick, D. S., Harrell, R. M., Hegedus, L., Paschke, R., Valcavi, R., & Vitti, P. (2016). American Association of Clinical Endocrinologists, American College of Endocrinology, and Associazione Medici Endocrinologi Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules - 2016 Update Appendix. Endocrine Practice, 22(5), 1-60.
- **Ren**, J., Baek, J. H., Chung, S. R., Choi, Y. J., Jung, C. K., & Lee, J. H. (2019). Degenerating Thyroid Nodules: Ultrasound Diagnosis, Clinical Significance, and Management. Korean Journal of Radiology, 20(6), 947.
- **Knight**, B. A., Shields, B. M., He, X., Pearce, E. N., Braverman, L. E., Sturley, R., & Vaidya, B. (2017). Iodine deficiency amongst pregnant women in South-West England. Clinical Endocrinology, 86(3), 451–455.
- **Ross**-Munro, E., Kwa, F., Kreiner, J., Khore, M., Miller, S. L., Tolcos, M., Fleiss, B., & Walker, D. W. (2020). Midkine: The Who, What, Where, and When of a Promising Neurotrophic Therapy for Perinatal Brain Injury. Frontiers in Neurology, 11(October), 1–22.
- **La** Vecchia, C., Malvezzi, M., Bosetti, C., Garavello, W., Bertuccio, P., Levi, F., & Negri, E. (2015). Thyroid cancer mortality and incidence: A global overview. International Journal of Cancer, 136(9), 2187–2195.
- **Patel**, A. (2020). Benign vs Malignant Tumors. JAMA Oncology, 6(9), 1488.
- **Brito**, J. P., & Hay, I. D. (2019). Management of Papillary Thyroid Microcarcinoma. Endocrinology and Metabolism Clinics of North America, 48(1), 199–213.
- **Chaker**, L., Bianco, A. C., Jonklaas, J., & Peeters, R. P. (2017). Hypothyroidism. The Lancet, 390(10101), 1550–1562.
- **Duntas**, L. H., & Jonklaas, J. (2019). Levothyroxine Dose Adjustment to Optimise Therapy Throughout a Patient's Lifetime. Advances in Therapy, 36(S2), 30–46.
- **Burch**, H. B., & Cooper, D. S. (2018). Antithyroid drug therapy: 70 years later. European Journal of Endocrinology, 179(5), R261–R274.
- **Jackson**, J. L., Kuriyama, A., Kuwatsuka, Y., Nickoloff, S., Storch, D., Jackson, W., Zhang, Z.-J., & Hayashino, Y. (2019). Beta-blockers for the prevention of headache in adults, a systematic review and meta-analysis. PLOS ONE, 14(3), e0212785.
- **Ayers**, R. R., Tobin, K., Sippel, R. S., Balentine, C., Elfenbein, D., Chen, H., & Schneider, D. F. (2015). Does levothyroxine administration impact parathyroid localization? Journal of Surgical Research, 198(2), 360–365.

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