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A Review on Thyroid Disease

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A B S T R A C T

The thyroid gland is one of the largest endocrine gland and consists of two connected lobes. The thyroid gland is found in the neck, below the thyroid cartilage. It participates in these processes by producing thyroid hormones, the principal ones being triiodothyronine (T_3) and thyroxine (sometimes referred to as tetraiodothyronine (T_4)). These hormones regulate the growth and rate of function of many other systems in the body. T_3 and T_4 are synthesized from iodine and tyrosine. The primary function of the thyroid is production of the hormones T_3, T_4 and calcitonin. Up to 80% of the T_4 is converted to T_3 by organs such as the liver, kidney and spleen. T_3 is several times more powerful than T_4, which is largely a prohormone, perhaps four or even ten times more active. Beta-blockers are used to decrease symptoms of hyperthyroidism such as increased heart rate, tremors, anxiety and heart palpitations, and anti-thyroid drugs are used to decrease the production of thyroid hormones, in particular, in the case of Graves' disease. The gland shrinks by 50-60% but can cause hypothyroidism and rarely pain syndrome, which arises due to radiation thyroiditis. It is short lived and treated by steroids.

Keywords: Thyroid Gland, Thyroxine, Triiodothyronine, Graves 'disease, Spleen and Kidney.

A R T I C L E I N F O

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1. Introduction

The thyroid gland is one of the largest endocrine gland and consists of two connected lobes. The thyroid gland is found in the neck, below the thyroid cartilage (which forms the laryngeal prominence, or "Adam's apple"). The thyroid gland controls how quickly the body uses energy, makes proteins, and controls how sensitive the body is to other hormones. It participates in these processes by producing thyroid hormones, the principal ones beingtriiodothyronine (T_3) and thyroxine (sometimes referred to as tetraiodothyronine (T_4)). These hormones regulate the growth and rate of function of many other systems in the body. T_3 and T_4 are synthesized from iodine and tyrosine. The thyroid also producescalcitonin, which plays a role in calcium homeostasis.Hormonal output from the thyroid is regulated by thyroid-stimulating hormone (TSH) produced by the anterior pituitary, which itself is regulated by thyrotropin-releasing hormone (TRH) produced by the hypothalamus.

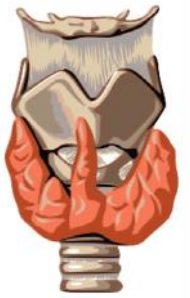

Figure 1: The thyroid gland as present on the human trachea

The thyroid gland is a butterfly-shaped organ and is composed of two cone-like lobes or wings, lobusdexter (right lobe) and lobus sinister(left lobe), connected via the isthmus. Each lobe is about 5 cm long, 3 cm wide and 2 cm thick. The organ is situated on the anterior side of the neck, lying against and around the larynx and trachea, reaching posteriorly the oesophagus and carotid sheath. It starts cranially at the oblique line on the thyroid cartilage (just below the laryngeal prominence, or 'Adam's Apple'), and extends inferiorly to approximately the fifth or sixth tracheal ring. It is difficult to demarcate the gland's upper and lower border with vertebral levels because it moves position in relation to these during swallowing. There is occasionally a third lobe present called the pyramidal lobe of the thyroid gland. It is of conical shape and extends from the upper part of the isthmus, up across the thyroid cartilage to the hyoid bone. The pyramidal lobe is a remnant of the fetal thyroid stalk, or thyroglossal duct. It is occasionally quite detached, or may be divided into two or more parts. The pyramidal lobe is also known as Lalouette's pyramid. On the posterior side, the gland is fixed to the cricoids and tracheal cartilage and cricopharyngeus muscle by a thickening of the fascia to form the posterior suspensory ligament of thyroid gland also known as Berry's ligament. The thyroid glands firm attachment to the underlying trachea is the reason behind its movement with swallowing. In variable extent, the pyramidal lobe is present at the most anterior side of the lobe. In this region, the recurrent laryngeal nerve and the inferior thyroid artery pass next to or in the ligament and tubercle. Between the two layers of the capsule and on the posterior side of the lobes, there are on each side two parathyroid glands. The thyroid isthmus is variable in presence and size, can change shape and size, and can encompass the pyramidal lobe. The thyroid is one of the larger endocrine glands, weighing 2-3 grams in neonates and 18-60 grams in adults, and increased in pregnancy.

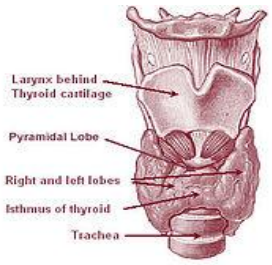

Figure 2: Isthmus showing pyramidal lobe

In a healthy patient, the gland is not visible yet can be palpated as a soft mass. Examination of the thyroid gland is carried out by locating the thyroid cartilage and passing the fingers up and down, examining for abnormal masses and overall thyroid size. Then, place one hand on each of the trachea and gently displace the thyroid tissue to the contralateral side of the neck for both sides while the other hand manually palpates the displaced gland tissue; having the patient flex the neck slightly to the side when being palpated may help in this examination. Next, the two lobes of the gland should be compared for size and texture using visual inspection, as well as manual or bimanual palpation. Finally, ask the patient to swallow to check for mobility of the gland; many clinicians find that having the patient swallow water helps this part of the examination. In a healthy state, the gland is mobile when swallowing occurs due its fascial encasement. Thus when the patient swallows, the gland moves superiorly, as does the whole larynx.

The thyroid is supplied with arterial blood from the superior thyroid artery, a branch of the external carotid artery, and the inferior thyroid artery, a branch of the thyrocervical trunk, and sometimes by the thyroid ima artery, branching directly from the subclavian artery. The venous blood is drained via superior thyroid veins, draining in the internal jugular vein, and via inferior thyroid veins, draining via theplexus thyroideusimpar in the left brachiocephalic vein.Lymphatic drainage passes frequently the lateral deep cervical lymph nodes and the pre- and paratracheal lymph nodes. The gland is supplied by parasympathetic nerve input from the superior laryngeal nerve and the recurrent laryngeal nerve.

2. Physiology:

The primary function of the thyroid is production of the hormones T_3, T_4 and calcitonin. Up to 80% of the T_4 is

converted to T_3 by organs such as the liver, kidney and spleen. T_3 is several times more powerful than T_4, which is largely a prohormone, perhaps four or even ten times more active.

T_3 and T_4 production and action:

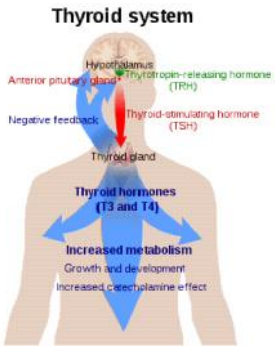

Figure 3: The system of the thyroid hormones T_3 and T_4

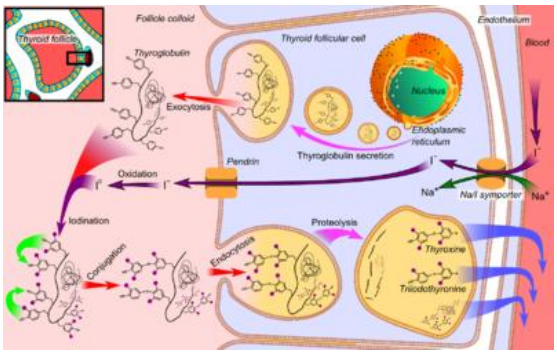

Figure 4: Synthesis of the thyroid hormones, as seen on an individual thyroid follicular cell.

- Thyroglobulin is synthesized in the rough endoplasmic reticulum and follows the secretory pathway to enter the colloid in the lumen of the thyroid follicle by exocytosis.
- Meanwhile, a sodium-iodide symporter pumps iodide actively in to the cell, which previously has crossed the endothelium by largely unknown mechanisms.
- This iodide enters the follicular lumen from the cytoplasm by the transporter pendrin, in a purportedly passive manner.
- In the colloid, iodide is oxidized to iodine by an enzyme called thyroid peroxidase.
- Iodine is very reactive and iodinates the thyroglobulin at tyrosyl residues in its protein chain.
- In conjugation, adjacent tyrosyl residues are paired together.
- The entire complex re-enters the follicular cell by endocytosis.
- Proteolysis by various proteases liberates thyroxine and tri iodothyronine molecules, which enters the blood by largely unknown mechanisms.

Thyroxine (T_4) is synthesized by the follicular cells from free tyrosine and on the tyrosine residues of the protein called thyroglobulin (Tg). Iodine is captured with the "iodine trap" by the hydrogen peroxide generated by the enzyme thyroid peroxidase (TPO) and linked to the 3' and 5' sites of the benzene ring of the tyrosine residues on Tg, and on free tyrosine. Upon stimulation by the thyroid-stimulating hormone (TSH), the follicular cells reabsorb Tg and cleave the iodinated tyrosines from Tg in lysosomes, forming T_4 and T_3 (in T_3, one iodine atom is absent compared to T_4), and releasing them into the blood. Deiodinase enzymes convert T_4 to T_3. Thyroid hormone secreted from the gland is about 80-90% T_4 and about 10-20% T_3. Cells of the developing brain are a major target for the thyroid hormones T_3 and T_4. Thyroid hormones play a particularly crucial role in brain maturation during fetal development, A transport protein that seems to be important for T_4 transport across the blood–brain barrier (OATP1C1) has been identified. A second transport protein (MCT8) is important for T_3transport across brain cell membranes.

Non-genomic actions of T_4 are those that are not initiated by liganding of the hormone to intranuclear thyroid receptor. These may begin at the plasma membrane or within cytoplasm. Plasma membrane-initiated actions begin at a receptor on the integrin alphaV beta3 that activates ERK1/2. This binding culminates in local membrane actions on ion transport systems such as the Na(+)/H(+) exchanger or complex cellular events including cell proliferation. These integrins are concentrated on cells of the vasculature and on some types of tumor cells, which in part explains the proangiogenic effects of iodothyronines and proliferative actions of thyroid hormone on some cancers including gliomas. T_4 also acts on the mitochondrial genome via imported isoforms of nuclear thyroid receptors to affect several mitochondrial transcription factors. Regulation of acting polymerization by T_4 is critical to cell migration in neurons and glial cells and is important to brain development.T_3 can activate phosphatidylinositol 3-kinase by a mechanism that may be cytoplasmic in origin or may begin at integrin alpha V beta3.In the blood, T_4 and T_3 are partially bound to thyroxine-binding globulin (TBG), transthyretin, and albumin. Only a very small fraction of the circulating hormone is free (unbound) - T_4 0.03% and T_3 0.3%. Only the free fraction has hormonal activity. As with the steroid hormones and retinoic acid, thyroid hormones cross the cell membrane and bind to intracellular receptors (α_1, α_2, β_1 and β_2), which act alone, in pairs or together with the retinoid X-receptor as transcription factors to modulate DNA transcription.

T_3 and T_4 regulation

The production of thyroxine and triiodothyronine is regulated by thyroid-stimulating hormone (TSH), released by the anterior pituitary. The thyroid and thyrotropes form a negative feedback loop: TSH production is suppressed when the T_4 levels are high. The TSH production itself is modulated by thyrotropin-releasing hormone (TRH), which is produced by the hypothalamus and secreted at an increased rate in situations such as cold exposure (to stimulate thermogenesis). TSH production is blunted by somatostatin (SRIH), rising levels of glucocorticoids and sex hormones (estrogen and testosterone) excessively high blood iodide concentration. An

additional hormone produced by the thyroid contributes to the regulation of blood calcium levels.Parafollicular cells produce calcitonin in response to hypercalcemia. Calcitonin stimulates movement of calcium into bone, in opposition to the effects of parathyroid hormone (PTH). However, calcitonin seems far less essential than PTH, as calcium metabolism remains clinically normal after removal of the thyroid (thyroidectomy), but not the parathyroids.

3. Clinical Significance

Thyroid disorders include

- Hyperthyroidism (abnormally increased activity).
- Hypothyroidism (abnormally decreased activity).
- Thyroiditis, inflammation of the thyroid.
- Thyroid nodules, which are generally benign thyroid neoplasms (tumours), but may be thyroid cancers.

All these disorders may give rise to a goiter, that is, an enlarged thyroid.

Hyperthyroidism

Hyperthyroidism, or overactive thyroid, is due to the overproduction of the thyroid hormones T_3 and T_4, which is most commonly caused by the development of Graves' disease, an autoimmune disease in which antibodies are produced which stimulate the thyroid to secrete excessive quantities of thyroid hormones. The disease can result in the formation of a toxic goiter as a result of thyroid growth in response to a lack of negative feedback mechanisms. It presents with symptoms such as a thyroid goiter, protruding eyes (exopthalmos), palpitations, excess sweating, diarrhea, weight loss, muscle weakness and unusual sensitivity to heat. The appetite is often increased.Beta-blockers are used to decrease symptoms of hyperthyroidism such as increased heart rate, tremors, anxiety and heart palpitations, and anti-thyroid drugs are used to decrease the production of thyroid hormones, in particular, in the case of Graves' disease. These medications take several months to take full effect and have side effects such as skin rash or a drop in white blood cell count, which decreases the ability of the body to fight off infections.

These drugs involve frequent dosing (often one pill every 8 hours) and often require frequent doctor visits and blood tests to monitor the treatment, and may sometimes lose effectiveness over time. Due to the side effectsand inconvenience of such drug regimens, some patients choose to undergo radioactive iodine-131treatment. Radioactive iodine is administered in order to destroy a portion of or the entire thyroid gland, since the radioactive iodine is selectively taken up by the gland and gradually destroys the cells of the gland. Alternatively, the gland may be partially or entirely removed surgically, though iodine treatment is usually preferred since the surgery is invasive and carries a risk of damage to the parathyroid glands or the nerves controlling the vocal cords. If the entire thyroid gland is removed, hypothyroidism results.

Hypothyroidism

Hypothyroidism is the underproduction of the thyroid hormones T_3 and T_4.

Hypothyroid disorders may occur as a result of

- Congenital thyroid abnormalities.
- autoimmune disorders such as Hashimoto's thyroiditis,
- iodine deficiency (more likely in poorer countries) or
- The removal of the thyroid following surgery to treat severe hyperthyroidism and/or thyroid cancer.

Typical symptoms are abnormal weight gain, tiredness, baldness, cold intolerance, and bradycardia. Hypothyroidism is treated with hormone replacement therapy, such as levothyroxine, which is typically required for the rest of the patient's life. Thyroid hormone treatment is given under the care of a physician and may take a few weeks to become effective.Negative feedback mechanisms result in growth of the thyroid gland when thyroid hormones are being produced in sufficiently low quantities, as a means of increasing the thyroid output; however, where hypothyroidism is caused by iodine insufficiency, the thyroid is unable to produce T_3 and T_4 and as a result, the thyroid may continue to grow to form a non-toxic goiter. It is termed non-toxic as it does not produce toxic quantities of thyroid hormones, despite its size.

Thyroiditis

There are two types of thyroiditis where initially hyperthyroidism presents which is followed by a period of hypothyroidism; (the overproduction of T_3 and T_4 followed by the underproduction of T_3 and T_4). These are Hashimoto's thyroiditis and postpartum thyroiditis. Hashimoto's thyroiditis or Hashimoto's Disease is an autoimmune disorder whereby the bodies own immune system reacts with the thyroid tissues in an attempt to destroy it. At the beginning, the gland may be overactive, and then becomes underactive as the gland is damaged resulting in too little thyroid hormone production or hypothyroidism. Some patients may experience "swings" in hormone levels that can progress rapidly from hyper-to-hypothyroid (sometimes mistaken as severe mood swings, or even being bipolar, before the proper clinical diagnosis is made). Some patients may experience these "swings" over a longer period of time, over days or weeks or even months. Hashimoto's is more common in females than males, usually appearing after the age of 30, and tends to run in families, meaning it can be seen as a genetic disease. Also more common in individuals with Hashimoto's thyroiditis are type-1 diabetes and celiac disease. Postpartum thyroiditis occurs in some females following the birth of a child. After delivery, the gland becomes inflamed and the condition initially presents with overactivity of the gland followed by underactivity. In some cases, the gland may recover with time and resume its functions. In others, it may not. The etiology is not always known, but can sometimes be attributed to autoimmunity, such as Hashimoto's thyroiditis or Graves disease. There are other disorders that cause inflammation of the thyroid & these include subacute thyroiditis, acute thyroiditis, silent thyroiditis and Riedel's thyroiditis.

Symptoms:

Hypothyroidism results in low levels of T_4 and T_3 in the blood. Not having enough T_4 and T_3 in the blood causes your metabolism to slow down.

- coarse and dry hair
- confusion or forgetfulness (often mistaken for dementia in seniors)
- constipation
- depression
- dry, scaly skin
- fatigue or a feeling of sluggishness
- hair loss
- increased menstrual flow (women)
- intolerance to cold temperatures
- weakness
- weight gain

If hypothyroidism isn't treated, the symptoms will progress. Rarely, a severe form of hypothyroidism, called myxedema, can develop. Symptoms of myxedema include:

- low body temperature
- dulled mental processes
- congestive heart failure, a condition where the heart cannot pump enough blood to meet the body's needs

Myxedema coma occurs in people with severe hypothyroidism that has been exposed to additional physical stresses such as infections, cold temperatures, trauma, or the use of sedatives. Symptoms include loss of consciousness, seizures, and slowed breathing.Hyperthyroidism results in high levels of T4 and T3 circulating in the blood. These hormones speed up your metabolism. Some of the most common symptoms include:

- increased heart rate with abnormal rhythm or pounding (palpitations)
- high blood pressure
- increased body temperature (feeling unusually warm)
- increased sweating
- clamminess
- feeling agitated or nervous
- tremors in the hands
- feeling of restlessness even though the person is tired or weak
- increased appetite accompanied by weight loss
- interrupted sleep
- frequent bowel movements, sometimes with diarrhea
- puffiness around the eyes, increased tears, sensitivity to light, or an intense stare
- bone loss (osteoporosis)
- stopped menstrual cycles

Graves' disease, in addition to the common symptoms of hyperthyroidism, may cause a bulge in the neck (goiter) at the location of the enlarged thyroid gland. It also might cause the eyes to bulge out, which may result in double vision. Sometimes, the skin over the shins becomes raised.

If hyperthyroidism is left untreated or is not treated properly, a life-threatening complication called thyroid storm (extreme overactivity of the thyroid gland) can occur. Symptoms include:

- confusion
- coma
- fever
- high blood pressure
- irregular heartbeat, which can be fatal
- jaundice associated with liver enlargement
- mood swings
- muscle wasting
- restlessness
- shock
- weakness

Thyroid storm, considered a medical emergency, can also be triggered by trauma, infection, surgery, uncontrolled diabetes, pregnancy or labour, or taking too much thyroid medication.

4. Pathophysiology

The thyroid gland is formed from the pharyngeal epithelium during the third week of fetal development; it then migrates caudally to its final position, which is posterior to the cricoid and arytenoid cartilages in the neck midline.During this process, the thyroglossal duct is formed(in the junction of the anterior two-thirds and posterior one-third of the tongue). The adult gland comprises a bilobular structure, which weighs between 15 and 20grams, and is connected by a 2-centimeter–wide isthmusthat is located anterior to the laryngeal cartilages. The isthmus varies greatly in position and size, making its palpation difficult in certain patients.

The gland, however, is palpable in most healthy adults. The internal anatomy of the thyroid gland consists of follicles that contain a mucinous colloid where the protein thyroglobulin is found. Thyroglobulin is the basic building block for the two main hormones produced by the thyroid triiodothyronine, or T_3, and thyroxine, orT_4. In addition to thyroglobulin, iodine is needed for T_3 and T_4 synthesis. Iodine is transported into the thyroid follicular cells and is combined with thyroglobulin to form the thyroid hormone precursorsmonoiodotyrosine and diiodo tyrosine. These precursors are transformed into T_3 and T_4 and later released into the bloodstream. T_4 is produced only in the thyroid, while T_3 also can be produced in extra glandular tissues. Once in the plasma, T_4 is bound primarily to T_4-binding globulin, or TBG, and less efficiently to T_4-binding pre-albumin (transthyretin) and albumin. Thyroid hormones influence the growth and maturation of tissue, energy metabolism, and turnover of both cells and nutrients. T_4 is at least 25 times more concentrated than T_3 and is deionized in the extra glandular sites to T_3 (about 80 percent of T_3 is produced in this form). Approximately 40 percent of T_4 is deionized to reverse T_3 in a similar manner. Reverse T_3 is not biologically active. T_3 is the main metabolic effector, with a 10-fold greater affinity over T_4 or nuclear thyroid receptor proteins. The action of this hormone at a molecular level includes the activation of genetic material (mainly transcription and formation of messenger ribonucleic acid) and translation to proteins coding for multiple hormonal and constituent tissues such as growth hormone;

thyrotropin- releasing hormone, or TRH; malic enzyme; myosin; and the calcium pump complex of the sarcoplasmic reticulum. Tissue-specific thyroid receptors have been described as α and β. α-receptors are found in myocardial cells, and β-receptors are responsible for hormone hemostasis and feedback mechanism. Thyroid function, like many hormonal somatic regulators, is controlled by feedback mechanisms (Figure), in which the thyroid hormones act as direct inhibitors of TRH, thus regulating their own production.

A deficiency of either T_4 or T_3 can affect adversely the growth and development of the infant and will decrease metabolic function in the adult. An overproduction or excess availability of thyroid hormones can cause serious and life threatening complications if not discovered and managed in time.

5. Diagnosis

Blood tests

a. The measurement of thyroid-stimulating hormone (TSH) levels is often used by doctors as a screening test. Elevated TSH levels can signify an inadequate thyroid hormone production, while suppressed levels can point at excessive unregulated production of hormone.
b. If TSH is abnormal, decreased levels of thyroid hormones T_4 and T_3 may be present; T_4 and T_3 levels may be determined with blood tests to confirm that their levels are decreased.
c. Auto antibodies may be detected in various disease states (anti-TG, anti-TPO, TSH receptor stimulating antibodies).
d. There are two cancer markers for thyroid derived cancers. Thyroglobulin (TG) for well differentiated papillary or follicular adenocarcinoma, and the rare medullary thyroid cancer has calcitonin as the marker.
e. Very infrequently, TBG and transthyretin levels may be abnormal; these are not routinely tested.
f. To differentiate between different types of hypothyroidism, a specific test may be used. Thyrotropin-releasing hormone (TRH) is injected into the body through a vein. This hormone is naturally secreted by the hypothalamus and stimulates the pituitary gland.
g. The pituitary responds by releasing thyroid - stimulating hormone (TSH). Large amounts of externally administered TRH can suppress the subsequent release of TSH. This amount of release-suppression is exaggerated in primary hypothyroidism, major depression, cocaine dependence, amphetamine dependence and chronic phencyclidine abuse. There is a failure to suppress in the manic phase of bipolar disorder.

Ultrasound

Nodules of the thyroid may or may not be cancer. Medical ultrasonography can help determine their nature because some of the characteristics of benign and malignant nodules differ.

Table 1: characteristics of a thyroid nodule on high frequency thyroid ultrasound:

Possible cancer	Benign characteristics
irregular border	smooth borders
hypoechoic (less echogenic than the surrounding tissue)	Hyperechoic
Microcalcifications	---
taller than wide shape on transverse study	---
significant intranodular blood flow by power Doppler	---
---	"comet tail" artifact as sound waves bounce off intranodular colloid

Ultrasonography is not always able to separate benign from malignant nodules with complete certainty. In suspicious cases, a tissue sample is often obtained by biopsy for microscopic examination.

Radioiodine scanning and uptake

Thyroid Scintigraphy, imaging of the thyroid with the aid of radioactive iodine, usually iodine-123 (^{123}I), is performed in the nuclear medicine department of a hospital or clinic. Radioiodine collects in the thyroid gland before being excreted in the urine. While in the thyroid the radioactive emissions can be detected by a camera, producing a rough image of the shape (a radio dine scan) and tissue activity (a radioiodine uptake) of the thyroid gland.A normal radioiodine scan shows even uptake and activity throughout the gland. Irregularity can reflect an abnormally shaped or abnormally located gland, or it can indicate that a portion of the gland is overactive or underactive, different from the rest.

For example, a nodule that is overactive ("hot") to the point of suppressing the activity of the rest of the gland is usually a thyrotoxic adenoma, a surgically curable form of hyperthyroidism that is hardly ever malignant. In contrast, finding that a substantial section of the thyroid is inactive ("cold") may indicate an area of non-functioning tissue such as thyroid cancer. The amount of radioactivity can be counted as an indicator of the metabolic activity of the gland. A normal quantitation of radioiodine uptake demonstrates that about 8 to 35% of the administered dose can be detected in the thyroid 24 hours later. Overactivity or under activity of the gland as may occur with hypothyroidism or hyperthyroidism is usually reflected in decreased or increased radioiodine uptake. Different patterns may occur with different causes of hypo- or hyperthyroidism.

Biopsy

A medical biopsy refers to the obtaining of a tissue sample for examination under the microscope or other testing, usually to distinguish cancer from noncancerous conditions. Thyroid tissue may be obtained for biopsy by fine needle aspiration or by surgery. Needle aspiration has the advantage of being a brief, safe, outpatient procedure that is safer and less expensive than surgery and does not leave a

visible scar. Needle biopsies became widely used in the 1980s, but it was recognized that accuracy of identification of cancer was good but not perfect. The accuracy of the diagnosis depends on obtaining tissue from all of the suspicious areas of an abnormal thyroid gland. The reliability of needle aspiration is increased when sampling can be guided by ultrasound, and over the last 15 years, this has become the preferred method for thyroid biopsy in North America.

6. Adverse Effects

Many medications can cause side effects. A side effect is an unwanted response to a medication when it is taken in normal doses. Side effects can be mild or severe, temporary or permanent. The side effects listed below are not experienced by everyone who takes this medication. If you are concerned about side effects, discuss the risks and benefits of this medication with your doctor.The following side effects have been reported by at least 1% of people taking this medication. Many of these side effects can be managed, and some may go away on their own over time.

- abdominal cramps
- diarrhea
- headache
- heat intolerance
- sleep difficulties
- sweating
- weight loss

Although most of these side effects listed below don't happen very often, they could lead to serious problems if you do not check with your doctor or seek medical attention.Check with your doctor as soon as possible, if any of the following side effects occur:

- confusion
- dizziness
- fast or irregular heartbeat
- feeling faint
- mood swings
- muscle weakness
- nervousness
- psychosis
- restlessness (extreme)
- tremors

7. Drug Interactions:

If you are taking any of these medications, speak with your doctor or pharmacist. Depending on your specific circumstances, your doctor may want you to:

- stop taking one of the medications,
- change one of the medications to another,
- change how you are taking one or both of the medications, or
- Leave everything as is.

An interaction between two medications does not always mean that you must stop taking one of them. Speak to your doctor about how any drug interactions are being managed or should be managed. Medications other than those listed above may interact with this medication. Tell your doctor or prescriber about all prescription, over-the-counter (non-prescription), and herbal medications you are taking. Also tell them about any supplements you take. Since caffeine, alcohol, the nicotine from cigarettes, or street drugs can affect the action of many medications, you should let your prescriber know if you use them.

Table 2: Interaction between desiccated thyroid

amphetamines	iron supplements
antacids that contain aluminum	ketamine
birth control pills	phenytoin
calcium polystyrene	rifampin
calcium supplements	sodium iodide I 131
carbamazepine	sodium polystyrene
cholestyramine	sympathomeimetic medications
colestipol	theophyllines
diabetes medications	tricyclic antidepressants
digoxin	warfarin
estrogens	

Prevention:

The usual treatment for hypothyroidism is thyroid hormone replacement therapy. With this treatment, synthetic thyroid hormone (e.g., levothyroxine) is taken by mouth to replace the missing thyroid hormone. Treatment is usually life-long.Most people who take thyroid replacement therapy do not experience side effects. However, if too much thyroid hormone is taken, symptoms can include shakiness, heart palpitations, and difficulty sleeping. Women who are pregnant may require an increase in their thyroid replacement by up to 50%. It takes about 4 to 6 weeks for the effect of an initial dose or change in dose to be reflected in laboratory tests. Hyperthyroidism can be treated with iodine (including radioactive iodine), anti-thyroid medications or surgery. Radioactive iodine can destroy parts of the thyroid gland. This may be enough to get hyperthyroidism under control. In at least 80% of cases, one dose of radioactive iodine is able to cure hyperthyroidism. However, if too much of the thyroid is destroyed, the result is hypothyroidism.

Radioactive iodine is used at low enough levels so that no damage is caused to the rest of the body. It isn't given to pregnant women because it may destroy the thyroid gland of the developing fetus.Larger doses of regular iodine, which does not destroy the thyroid gland, help block the release of thyroid hormones. It is used for the emergency treatment of thyroid storm, and to reduce the excess production of thyroid hormones before surgery. Anti-thyroid medications (e.g., methimazole) can bring hyperthyroidism under control within 6 weeks to 3 months. These medications cause a decrease in the production of new thyroid hormones by the thyroid gland. Larger doses will work more quickly, but may cause side effects including skin rashes, nausea, loss of taste sensation, liver cell injury, and, rarely, a decrease of blood cell production in the bone marrow.

8. Treatment

Treatments for thyroid disorders stemming from the over or under production of thyroid hormones rely mainly on medicines and surgery. Treating hyperthyroidism involves suppressing the manufacture of thyroid hormone, while hypothyroidism calls for hormone replacement. Conventional medicine offers extremely effective techniques for lowering, eliminating or supplementing hormone production. Before deciding which treatment is best for you, your doctor will make an evaluation based on your particular thyroid condition as well as your age, general health and medical history.

Treatments for hyperthyroidism

Thyroid hormone production can be suppressed or halted completely in these ways:

- Radioiodine treatment (a form of radiotherapy)
- Anti-thyroid medication
- Surgery

If your doctor decides that radioiodine treatment is best, you will be asked to swallow a tablet or liquid containing radioactive iodine in amounts large enough to damage the cells of your thyroid gland and to limit or destroy their ability to produce hormones.Occasionally more than one treatment is needed to restore normal hormone production. It is not advisable for breastfeeding or pregnant women to use this method of treatment, and women should be advised not to conceive for at least six months after treatment. Men, meanwhile, should not father a child for at least four months after this treatment. Many patients eventually become hypothyroid with this form of treatment, and you will need to have routine thyroid tests for an indefinite period afterwards.If you start using anti-thyroid medications such as propylthiouracil or carbimazole, your hyperthyroid symptoms should begin to disappear in about three to four weeks, as the hormones already in your system run out and the medication starts to impair hormone production by the thyroid gland.There are two ways of using these medications. One is to give very high doses to stop the thyroid gland producing any hormone, and then supplementing with thyroid tablets.

The other is to give a very carefully titrated dose and monitor regularly until the thyroid hormone level eventually comes down to a normal range. Both methods work equally well.Once normal thyroid function is restored the dosage of medication may gradually be reduced. Unfortunately some people relapse on this treatment, and you will need regular blood tests while taking the medicines to monitor your thyroid levels.Side effects are usually quite mild but there is one serious rare complication called agranulocytosis, involving reduced bone marrow production of white blood cells. One sign of this is a sore throat. You should seek medical advice if you develop a sore throat while on anti-thyroid medications so the doctor can do a blood test to check that your white blood cells are fine.Surgery is often recommended for people under 45 years old when their hyperthyroidism is due to toxic adenomas (hot nodules), since these nodules tend to be resistant to radioactive iodide. Surgery is also recommended where medication has failed to control thyroid production or is contraindicated. Once the tissue has been removed surgically, hormone levels typically return to normal within a few weeks. Again, thyroid monitoring is important as some patients become hypothyroid over time.

Treating subacute thyroiditis:

Although subacute thyroiditis can bring on temporary hyperthyroidism, this condition usually does not require medical treatment. Any pain associated with the inflamed thyroid can generally be relieved with paracetamol. If over-the-counter medicines don't help, your doctor may prescribe other anti-inflammatory medication for a short period of time.

Treating hypothyroidism

Hypothyroidism calls for a lifelong regimen of thyroid hormone replacement. No surgical techniques or conventional medicines can boost the thyroid's hormone production once it slows down.Although hormones from animal extracts are available, doctors generally prescribe synthetic forms of thyroid hormone, such as levothyroxine. Side effects are rare, but some people experience nervousness or chest pain while taking these medicines. Usually adjusting the levels of medication will alleviate any unpleasant effects.

Treating thyroid cancer

Thyroid cancer is usually treated by removing surgically either the cancerous tissue or the whole thyroid gland, a procedure known as a thyroidectomy. If the cancer has spread beyond the thyroid, any other affected tissue, such as the lymph glands in the neck, will also be removed. Other forms of therapy may also be used, normally as an adjunct to surgery. These include radioiodine therapy, radiotherapy or chemotherapy, depending on the type of cancer and how much it has spread.

Medical treatment

Levothyroxine is a stereoisomer of thyroxine which is degraded much slower and can be administered once daily in patients with hypothyroidism. Natural thyroid hormone from pigs is also used, especially for people who cannot tolerate the synthetic version. Graves' disease may be treatedwiththe thioamide drugs propylthiouracil, carbimazole ormethimazole, or rarely with Lugol's solution. Hyperthyroidism as well as thyroid tumors may be treated with radioactive iodine.Percutaneous Ethanol Injections, PEI, for therapy of recurrent thyroid cysts and metastatic thyroid cancer lymph nodes is an alternative to the usual surgical method.

Surgery

Thyroid surgery is performed for a variety of reasons. A nodule or lobe of the thyroid is sometimes removed for biopsy or for the presence of an autonomously functioning adenoma causing hyperthyroidism. A large majority of the thyroid may be removed, a subtotal thyroidectomy, to treat the hyperthyroidism of Graves' disease, or to remove goiter that is unsightly or impinges on vital structures.A complete thyroidectomy of the entire thyroid, including associated lymph nodes, is the preferred treatment for thyroid cancer. Removal of the bulk of the thyroid gland usually produces hypothyroidism, unless the person takes thyroid hormone replacement. Consequently, individuals who have undergone a total thyroidectomy are

typically placed on thyroid hormone replacement for the remainder of their lives. Higher than normal doses are often administered to prevent recurrence. If the thyroid gland must be removed surgically, care must be taken to avoid damage to adjacent structures, the parathyroid glands and the recurrent laryngeal nerve. Both are susceptible to accidental removal and/or injury during thyroid surgery. The parathyroid glands produce parathyroid hormone, a hormone needed to maintain adequate amounts of calcium in the blood. Removal results in hypoparathyroidism and a need for supplemental calcium and vitamin D each day. In the event the blood supply to any one of the parathyroid glands is endangered through surgery, the parathyroid gland involved may be re-implanted in surrounding muscle tissue. The recurrent laryngeal nerves provide motor control for all external muscles of the larynx except for the cricothyroid muscle, which also runs along the posterior thyroid. Accidental laceration of either of the two or both recurrent laryngeal nerves may cause paralysis of the vocal cords and their associated muscles, changing the voice quality.

Radioiodine therapy

Large goiters that cause symptoms but do not harbor cancer, after evaluation and biopsy of suspicious nodules, can be treated by an alternative therapy with radioiodine. The iodine uptake can be high in countries with iodine deficiency, but low in iodine sufficient countries. The 1999 release of recombinant human TSH, Thyrogen, in the USA, can boost the uptake to 50-60% allowing the therapy with Iodine 131. The gland shrinks by 50-60% but can cause hypothyroidism and rarely pain syndrome, which arises due to radiation thyroiditis. It is short lived and treated by steroids.

9. Conclusion

Diseases of the thyroid gland are common in primary care medicine and most can be diagnosed and treated satisfactorily by the primary care physician. In some instances thyroid disease may present in patients in a subtle manner and these clinical signs and symptoms are often mistaken for the natural course of ageing especially when they manifest in the elderly. It is for this reason that a correct diagnosis is imperative. Correct diagnosis of thyroid disease enables the clinician to effectively manage the patient and thus vastly improve the patient's quality of life. The importance of the use of correct thyroid function tests are not only required for the diagnosis of the condition but also for the long- term management of the patient. It is a fundamental tool in monitoring patient response to treatment as well as guiding the clinician with regard to dose titration. Discovery Health published evidence-based guidelines in March 2003 in order to educate the clinician with regard to the correct use of thyroid function tests in order to diagnose thyroid disease. There was, however, a significant change in the ordering patterns of laboratory investigations once the article had been published. Tests that were non- specific for the initial diagnosis of suspected thyroid disease were not being requested as frequently as before. Tests that were specific and served to confirm the diagnosis of thyroid disease were requested at an increased frequency.

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