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Review Article

A Review on Thyroid Disease

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Abstract

Patients with abnormalities of thyroid gland function or structure come to medical attention for several reasons. They present with symptoms attributable to physiologic effects of increased or decreased plasma concentrations of thyroid hormone (hyperthyroidism or hypothyroidism, respectively). They may also present with symptoms related to localized or generalized enlargement of the gland (diffuse goiter, multinodular goiter, or single thyroid nodule). These changes may result from functional abnormalities or neoplasia, benign or malignant. The following symptoms are typical problems that may eventually be diagnosed as specific thyroid diseases or syndromes. For diagnoses related to hyperthyroidism (thyrotoxicosis), these complaints may include weight loss, anxiety or nervousness, increased sweating, tremulousness, diarrhea, palpitations, muscular weakness, heat intolerance, or history of treatment of an "overactive" thyroid. For diagnoses related to hypothyroidism, typical problems include fatigue, weight gain, depression, lethargy, dry skin, cold intolerance, voice change, change in menses, muscle cramps, or treatment of a thyroid condition. Thyroid enlargement (goiter) may present in the context of hyper- or hypothyroidism. It may also occur in a patient with normal thyroid hormone production (euthyroid patient). Typical complaints related to thyroid enlargement include generalized neck swelling (diffuse goiter), neck mass (uninodular or multinodular goiter), dysphagia, neck pain, or hoarseness. Finally, patients may be referred with no complaints but with "abnormal thyroid function tests" that lead to a search for symptoms and signs of thyroid dysfunction. Thyroid storm refers to an increasingly rare but still highly dangerous form of thyrotoxicosis that, in addition to the other complaints of hyperthyroidism, is marked by extreme temperature elevation and/or change in mental status, ranging from extreme agitation to coma. Hypothyroid crisis refers to advanced thyroid hormone deficiency manifested by hypothermia and obtundation.

Keywords: Thyroid storm, diffuse goiter, overactive, uninodular, neoplasia.

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1. Introduction

Thyroid is among the largest endocrine gland in human, the two hormones produced by thyroid are the most crucial and important hormones interfering in various aspects of metabolism. Tetraidothyronine most is known as thyroxin (T4) and triidothyronine (T3) are the thyroid hormones although T3 is produced outside thyroid gland in peripheral tissues from deiodination of T4. Thyroid produce T4 and T3 internally which is triggered by Thyroid Stimulating Hormone (TSH) itself biosynthesized in pituitary gland as result of Thyrotropin Releasing Hormone (CRH). Thyroid hormones dysfunctions due to variety of disorders related with the thyroid gland are well established, which comprised from many abnormalities in the thyroid gland itself leading into hypothyroidism and hyperthyroidism.

The definition of non-thyroidal syndrome arises from the fact that thyroid hormones within blood circulation is reduced not due to the malfunction of thyroid organ. The apparent clinical manifestation of established hypothyroidism is not as a result of thyroid abnormality, but the suppressed serum levels of T3, T4 are belong to other peripheral and central diseases, which in practice nothing to do with thyroid gland. The non-thyroidal disease accompanied with the clinical manifestations which are occurred not only as result of hypothyroidism with no thyroid origin and is associated syndromes of other vital and key hormonal deficiencies. Starvation and illness are the clinical conditions which suppressing the serum thyroid hormonal concentration. At initial stage of sickness, the T3 concentration reduce slightly, but T3 and also T4 concentration in blood circulation drop further as the disease status getting worse and progressed. Although the serum concentration of T3, T4 are dropped, but this occurs without the increase in the amount of TSH.

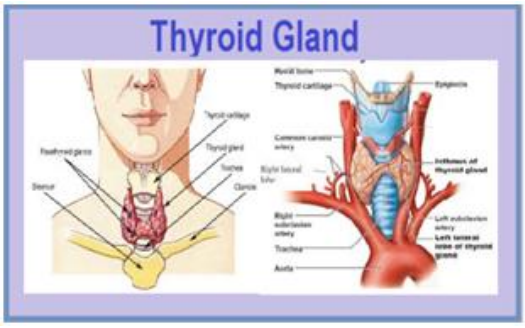

Figure 1

2. Physiology

The thyroid is an endocrine gland. Its location is in the inferior, anterior neck, and it is responsible for the formation and secretion of the thyroid hormones as well as iodine homeostasis within the human body. The thyroid produces approximately 90% inactive thyroid hormone, or thyroxine (T4), and 10% active thyroid hormone, or triiodothyronine (T3). Inactive thyroid hormone is converted peripherally to either activated thyroid hormone or an alternative inactive thyroid hormone. Cardiac output, stroke volume, and resting heart rate increase through positive chronotropic and inotropic effects.

Active thyroid hormone increases myocardial intracellular calcium to increase contraction force and speed. Concomitantly, vasculature in the skin, muscle, and heart dilate, resulting in decreased peripheral vascular resistance while blood volume increases through activation of the renin-angiotensin-aldosterone system.

Basal metabolic rate (BMR), heat production, and oxygen consumption elevate through thyroid hormone activation of mitochondrial uncoupling proteins. Glucose and fatty acid uptake and oxidation also increase, which results in increased thermogenesis and necessitates increased heat dissipation. Heat intolerance in hyperthyroidism is attributable to this increase in thermogenesis. Compensation for increased thermogenesis is also mediated by thyroid hormone through increases in blood flow, sweating, and ventilation.

Resting respiratory rate and minute ventilation undergo stimulation by active thyroid hormone, triiodothyronine (T3), to normalize arterial oxygen concentration in compensation for increased rates of oxidation. T3 also promotes oxygen delivery to the tissues by simulating erythropoietin and hemoglobin production and promoting folate and cobalamin absorption through the gastrointestinal tract.

T3 is responsible for the development of fetal growth centers and linear bone growth, endochondral ossification, and epiphyseal bone center maturation following birth. Additionally, T3 simulates adult bone remodeling anddegradation of mucopolysaccharides and fibronectin in extracellular connective tissue.T3 stimulates the nervous system resulting in increased wakefulness, alertness, and responsiveness to external stimuli.

Clinical Significance

Hypothyroidism can be classified as primary (due to thyroid hormone deficiency), secondary (due to TSH deficiency), tertiary (due to thyrotropin-releasing hormone deficiency), and peripheral (extra- thyroidal; panel). Central hypothyroidism (including both secondary and

tertiary) and peripheral hypothyroidism are rare and account for less than 1% of cases.

Primary hypothyroidism

In iodine-sufficient areas, the most common cause of hypothyroidism is chronic autoimmune thyroiditis (also known as Hashimoto's disease). High concentrations of anti-thyroid antibodies (predominantly thyroid peroxidase antibodies and anti-thyroglobulin antibodies) are present in most patients with autoimmune thyroiditis. Raised concentrations of thyroid peroxidase antibodies are also detected in about 11% of the general population. In patients with subclinical hypothyroidism, thyroid peroxidase antibody measurements help to predict progression to overt diseaslodine is an essential component of thyroid hormone. Iodine deficiency can result in goitre, thyroid nodules, and hypothyroidism. The most severe consequence of iodine deficiency is cretinism (ie, restricted mental and physical development in utero and during childhood). Iodine fortification programmes are one of the safest and cheapest public health interventions for the prevention of cognitive and physical impairment. Despite such efforts, suboptimal iodine status still affects large parts of Africa and Asia, as well as specific subpopulations in several high-income countries—most notably, pregnant women in some areas of Italy, USA, and the UK. In populations that shift from severe to mild iodine deficiency, the prevalence of hypothyroidism decreases; in populations shifting from mild deficiency to optimum or excessive intake of iodine, the prevalence of autoimmune hypothyroidism increases.

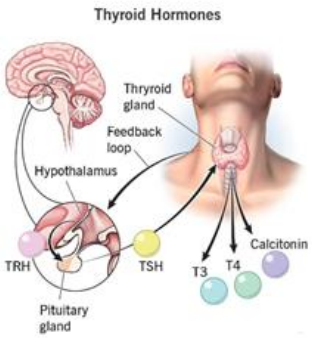

Fig.2

Thyroid hormone also stimulates the peripheral nervous system, resulting in increased peripheral reflexes and gastrointestinal tone, and motility. Thyroid hormone also plays a role in reproductive health and other endocrine organ function. It allows for the regulation of normal reproductive function in both men and women by regulating both the ovulatory cycle and spermatogenesis.

Thyroid hormone also regulates pituitary function; growth hormone production and release are stimulated by thyroid hormone while inhibiting prolactin production and release. Additionally, renal clearance of many substances, including some medications, can be increased due to activated thyroid hormone stimulation of renal blood flow and glomerular filtration rate.

Clinical Significance

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Symptoms

The most common symptoms of hyperthyroidism are feeling anxious or nervous, being unable to tolerate heat, having heart palpitations, feeling tired and losing weight, even if you're eating the same amount of food.

An enlarged thyroid (goitre)

- Breathlessness
- Eye problems
- Increased appetite
- Tremor
- sweating
- changes in bowel habits or menstrual patterns
- Thin skin
- Fine, brittle hair

If hyperthyroidism is lift untreated or is not treated properly, a life threatening complication called thyroid storm (extreme over activity of the thyroid gland) can occur symptoms include:

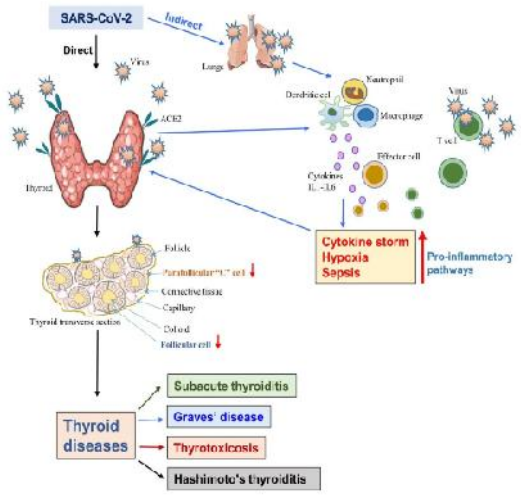
- Confusion
- Coma
- Fever
- High blood pressure
- Irregular heartbeat, which can be fatal Jaundice association with liver enlargement

Pathophysiology

The thyroid is a butterfly-shaped gland located in the front of the neck just above the trachea. It weighs approximately 15 to 20 grams in the adult human. The thyroid produces and releases into the circulation at least two potent hormones, thyroxine (T4) and triiodothyronine (T3), which influence basal metabolic processes and/or enhance oxygen consumption in nearly all body tissues. Thyroid hormones also influence linear growth, brain function including intelligence and memory, neural development,

dentition, and bone development (Larsen, 2003). The thyroid gland produces T4 and T3 utilizing iodide obtained either from dietary sources or from the metabolism of thyroid hormones and other iodinated compounds. About 100 µg of iodide is required on a daily basis to generate sufficient quantities of thyroid hormone.

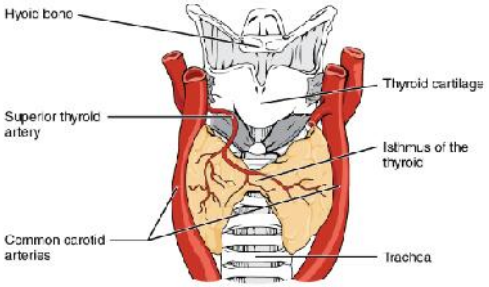
Dietary ingestion of iodide in the United States ranges between 200 and 500 µg/day and varies geographically; ingestion is higher in the western part of the United States than in the eastern states. The specialized thyroid epithelial cells of the thyroid gland are equipped with a Na/I symporter that helps concentrate iodide 30 to 40 times the level in plasma to ensure adequate amounts for theT4 and T3 circulate bound primarily to carrier proteins. T4 binds strongly to thyroxine binding globulin (TBG, ~ 75 percent) and weakly to thyroxine binding prealbumin (TBPA, transthyretin, ~ 20 percent) and albumin (~5 percent). T3 binds tightly to TBG and weakly to albumin, with little binding to TBPA. The geometric mean for serum T4 in normal individuals is approximately 8 µg/dl, while the mean serum T3 level is approximately 130 ng/dl.



Under normal protein binding conditions, all but 0.03 percent of serum T4 and 0.3 percent of serum T3 is protein bound. Only a small amount of unbound (or free) T4 (approximately 2 ng/dl) and T3 (approximately 0.3ng/dl) circulates in a free state, and it is this free concentration that is considered responsible for the biological effects of the thyroid hormones. There are physiologic situations associated with a change in the serum concentration of these thyroid-binding proteins—such as pregnancy, non-thyroidal illness, or ingestion of drugs—that affect the level and/or affinity of these binding proteins. Under these circumstances, the serum concentrations of total T4 and total T3 change in parallel to the changes that occur in the thyroid hormone binding proteins, but the serum concentrations of free T4 and free 3 remain normal and the individual remains euthyroid. In contrast, the serum concentration of free T4 and free T3 are raised in hyperthyroidism and decreased in hypothyroidism

3. Diagnosis

In general, your doctor may test for an underactive thyroid if you are feeling increasingly tired, have dry skin, constipation and weight gain, or have had previous thyroid problems or a goiter. Blood tests Diagnosis of hypothyroidism is based on your symptoms and the results of blood tests that measure the level of TSH and sometimes the level of the thyroid hormone thyroxine. A low level of thyroxine and high level of TSH indicate an underactive thyroid. That's because your pituitary produces more TSH in an effort to stimulate your thyroid gland into producing more thyroid hormone. In addition, TSH tests are used to help diagnose a condition called subclinical hypothyroidism, which usually causes no outward signs or symptoms. In this condition, you have normal blood levels of triiodothyronine and thyroxine, but higher than normal levels of TSH. There are certain factors that can affect blood tests for thyroid problems. One is the blood-thinning medication called heparin. Another is biotin, a vitamin taken as a stand-alone.



Adverse Effect

- Fatigu
- Increased sensitivity to co
- Constipat
- Dry skin
- Weight gain
- Puffy face
- Hoarseness
- Muscle weakness
- Elevated blood cholesterol level
- Muscle aches, tenderness and stiffne
- Pain, stiffness or swelling in your joi
- Heavier than normal or irregular menstrual periods
- Thinning hair
- Slowed heart rate
- Depression
- Impaired memory
- Enlarged thyroid gland (goiter)

Drug Interaction

The thyroid is a gland located in the front of the neck, it produces the hormone tri-iodothyronine (T3) and the pre-

hormone thyroxine (T4), which is subsequently converted in the periphery to the active hormone T3. The thyroid hormones stimulate diverse metabolic activities throughout the body, leading to regulation of the basal metabolic rate.

Iodide absorbed from the diet is an essential element for thyroid hormone production. The iodide ion is transported into the hormone-producing follicular cells, where it is oxidized by the enzyme thyroperoxidase and added to the protein thyroglobulin as part of thyroid hormone synthesis.

A negative feedback loop regulates the levels of thyroid hormones. When circulating T3 and T4 levels drop too low, the hypothalamus increases release of thyrotropin-releasing hormone (TRH), which acts on the anterior pituitary gland to stimulate the release of thyroid stimulating hormone (TSH), causing the thyroid gland to release more T4 and T3. Disruption to this mechanism results in hypothyroidism or hyperthyroidism.

TSH and free T4 levels are used initially to assess if patients have thyroid dysfunction. A TSH value within its standard reference range (0.4–4.5mU/L) excludes most cases of thyroid dysfunction. The normal reference range for free T4 is 9–25pmol/L.

Strategies for managing thyroid disorders aim to alleviate symptoms and restore normal thyroid hormone levels. Thyroid hormones are essential for metabolism, and disordered thyroid function can alter the metabolism of some medications. It is therefore important to consider this effect on medicines, and be aware that this may change when treatment for thyroid dysfunction is started. The potential for medication interactions should also be considered.

This article aims to provide an overview of the common considerations for both physiological and pharmacological interactions encountered during the management of thyroid disorders.

Hypothyroidism refers to any state when thyroid hormone production is inadequate. In the UK, the annual incidence is 1–2% of the general population, with the incidence being six times greater among women. Potential hypothyroidism symptoms include tiredness, cold intolerance, constipation and weight gain.

Prevention

Physicians have long dedicated themselves to the promotion of health and prevention of disease in mankind. Rabi-Ebn-Ahmad Akhvaini, a Persian scholar, defined medicine as a profession that maintains health status, when disturbed by disease and restores health in man, using knowledge and practice . Preventive medicine is, hence, concerned with precluding the appearance of risk factors, delaying the progression to overt disease, and decreasing the impact of illness. By definition, there are 4 distinct types of prevention in different phases of disease. Primordial prevention is the maintenance and promotion of health in the community by averting the appearance of risk factors of a disease. Primary prevention is performed by controlling or reducing risk factors to prevent overt disease in previously healthy individuals.

Secondary prevention is avoiding the progression of latent or mild illness to more advanced stages (presence of physiological abnormality without sign or symptom manifestation). Tertiary prevention is the optimization of medical care and management to improve an already established disease and avoidance of complications and disabilities (presence of sign and symptoms) . Quaternary prevention is a newer concept that refers to actions taken to identify a patient or a population at risk of over-medicalisation to protect them from invasive medical interventions and provide them with care procedures that are ethically acceptable. Approaches to prevention overlap and merge, yet all levels are equally important and complementary. Primordial and primary preventions are related to health of the whole population, while secondary and tertiary preventions are generally focused on people who already have signs of disease.

The terms "prevention" OR "screening" with either of the following keywords, “iodine”, “iodine deficiency”, “thyroid”, “hypothyroidism”, “hyperthyroidism”, “thyroid nodules”, and “thyroid cancer” were used to search Medline for papers published from July 2001 to July 2015. A combination of more general search term usage with additional filtering of articles was applied to include all relevant articles related to the 4 types of prevention in thyroid disease. After reviewing, authors divided the articles into 2 parts: one related to primary and primordial (446 articles) and the other related to secondary and tertiary preventions (2361 articles). We reviewed all abstracts of studies published in both French and English and included those appropriately.

4. Treatment

In general, your doctor may test for an underactive thyroid if you are feeling increasingly tired, have dry skin, constipation and weight gain, or have had previous thyroid problems or a goiter.

Blood tests

Diagnosis of hypothyroidism is based on your symptoms and the results of blood tests that measure the level of TSH and sometimes the level of the thyroid hormone thyroxine. A low level of thyroxine and high level of TSH indicate an underactive thyroid. That's because your pituitary produces more TSH in an effort to stimulate your thyroid gland into producing more thyroid hormone. In addition,

TSH tests are used to help diagnose a condition called subclinical hypothyroidism, which usually causes no outward signs or symptoms. In this condition, you have normal blood levels of triiodothyronine and thyroxine, but higher than normal levels of TSH.

Levothyroxine causes virtually no side effects when used in the appropriate dose and is relatively inexpensive. If you change brands, let your doctor know to ensu There are certain factors that can affect blood tests for thyroid problems. One is the blood-thinning medication called heparin. Another is biotin, a vitamin taken as a stand-alone supplement or as part of a multivitamin. Let your doctor know about any medications or supplements you take before having blood tests done Standard treatment for hypothyroidism involves daily use of the synthetic thyroid hormone levothyroxine (Levo-T, Synthroid, others). This oral medication restores adequate hormone levels, reversing the signs and symptoms of hypothyroidism.

You'll likely start to feel better soon after you start treatment. The medication gradually lowers cholesterol levels elevated by the disease and may reverse any weight gain. Treatment with levothyroxine will likely be lifelong, but because the dosage you need may change, your doctor is likely to check your TSH level every year.

Determining proper dosage may take time
- Increased appetit
- Insomnia
- Heart palpitatior
- Shakiness

If you have coronary artery disease or severe hypothyroidism, your doctor may start treatment with a smaller amount of medication and gradually increase the dosage. Progressive hormone replacement allows your heart to adjust to th re you're still receiving the right dosage.

Also, don't skip doses or stop taking the drug because you're feeling better. If you do, the symptoms of hypothyroidism will gradually return.

Levothyroxine is best taken on an empty stomach at the same time every day. Ideally, you'll take the hormone in the morning and wait an hour before eating or taking other medications. If you take it at bedtime, wait four hours after your last meal or snack.

Anti-thyroid medicine
These medications slowly ease symptoms of hyperthyroidism by preventing the thyroid gland from making too many hormones. Anti-thyroid medications include methimazole and propylthiouracil. Symptoms usually begin to improve within several weeks to months. Treatment with anti-thyroid medicine typically lasts 12 to 18 months. After that, the dose may be slowly decreased or stopped if symptoms go away and if blood test results show that thyroid hormone levels have returned to the standard range. For some people, anti-thyroid medicine puts hyperthyroidism into long-term remission. But other people may find that hyperthyroidism comes back after this treatment.

Although rare, serious liver damage can happen with both anti-thyroid medications. But because propyl thiouracil has caused many more cases of liver damage, it's generally used only when people can't take methimazole. A small number of people who are allergic to these medicines may develop skin rashes, hives, fever or joint pain. They also can raise the risk of infection.

5. Conclusion

The thyroid gland maintains the level of metabolism in the tissues that is optimal for their normal function. Thyroid hormone stimulates the o2 consumption of most of the cells in the body, regulates lipid and carbohydrate metabolism, and is also necessary for normal growth and maturation. The main function of the gland is to synthesize and secrete the thyroid hormones, namely, thyroxine (T4), triiodothyronine (T3) and calcetonine. The thyroid gland plays an important role in the normal metabolic rate and that is why a precise control system is operating to provide the right amounts of thyroid hormones at different conditions, both suprathyroid and autoregulatory mechanisms are involved in this control system. The secretion of thyrotropin (TSH), which is the major modulator of thyroid function, is regulated at the level of the pituitary thyrotroph by the antagonistic effects of thyroid hormones and the TSH releasing hormone (TRH), the former inhibits and the latter stimulates the synthesis and secretion of (TSH). Therefore, excess thyroid hormone leads to decreased secretion of (TSH), and thyroid hormone insufficiency is associated with (TSH) hypersecretion, TSH stimulates all steps of thyroid hormone synthesis and secretion. Ischemic heart disease is defined by world health organization as: myocardial impairment due to imbalance between coronary blood flow and myocardial requirement, caused by changes in the coronary circulation. In the last 20 years, epidemiolgic and experimental studies have provided considerable evidence linking certain risk factors for coronary

More than 80% of the biologically active hormone T3 derives from peripheral conversion of T4 secreted by the thyroid gland. Clinical and experimental evidence has shown that T3 play a major role in modulating heart rate and cardiac contractility as well as arterial peripheral resistance. T3 actions are carried out by binding with specific nuclear receptors that regulate responsive genes encoding for structural and functional cardiac proteins,

direct, extra nuclear, nontranscriptional effects, have also been described. In severe illnesses of non-thyrodial origin including myocardial infarction and chronic heart failure, down regulation of thyroid hormone system and changes in thyroid homeostasis may occur. This condition which has been called “euthyroid sick syndrome” or “Low T3 syndrome”.

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