



“Review on Thyroid Disorders”

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Abstract:

India has an estimated 42 million people suffering from thyroidal disorders. One of the largest endocrine glands in the body, the thyroid gland is crucial to the growth, development, and metabolism of the human body. By continuously releasing a regular amount of thyroid hormones into the bloodstream, it also assists in the regulation of numerous other activities. Hyperthyroidism is due to over and Hypothyroidism is due to under secretion of thyroid hormones. Hyperthyroidism may cause because of diffused hyperplasia of the thyroid associated with Graves' disease, the ingestion of excess exogenous thyroid hormones, overactive multi nodular goiter and overactive adenoma of thyroid. Hypothyroidism usually develops from iodine deficiency. Hypothyroidism developed from chronic lymphocytic the thyroiditis, is known as Hashimoto's disease. It can also developed from decreased TSH level. Iodine as an integral part of thyroid hormones plays major role in both hypo and hyperthyroidism. Availability of iodine to thyroid gland is mainly from foods and water and if these sources are deficient in iodine, then problems like hypothyroidism, cretinism and other iodine deficiency disorders can develop. The prevalence of hyperthyroidism/ thyrotoxicosis and hypothyroidism vary in different countries. Hyperthyroidism prevalence was higher in females than males. Similarly, the prevalence of hypothyroidism and sub clinical hypothyroidism was higher in females than males.

Key words: Goitre, Hyperthyroidism, Hypothyroidism, Iodine deficiency, Thyroid disorders, Thyroid hormones, Thyroid Stimulating Hormone (TSH), Thyroxine(T4), Tri-iodothyronine (T3)

1.Introduction:

Today thyroid disorders are more common among the population. 42 million people are suffering from thyroidal illness or disorders. It is most common disorder of endocrine system. Thyroid gland is located in neck in front of trachea and below the larynx also called as Adam's apple at 5th ,6th ,7th cervical and 1st thoracic vertebrae and is of butterfly shaped. Morphology of thyroid gland includes 2inch of size which consist of 2 lobes, one of each side of trachea (also called windpipe). This lobes are connected by small bridge of thyroid tissue called isthmus. This gland weighs about 18-25 gms.

Function of this gland is to produce, store and release thyroid hormones (TH) in body. This thyroid hormone plays vital role in controlling a broad range of physiological functions in body. This includes metabolism, temperature / heat/ energy homeostasis, cellular growth and development. Women's are more prone to the thyroidal disorders than men as hormonal imbalances are greater in them or due to the condition like PCOS. People with diabetes mellitus are also majorly prone to thyroidal disorders as TH plays important role in glucose metabolism. Thyroid hormones are involved in stimulating erythropoiesis and also in increasing erythrocyte 2,3-diphosphglycerate concentration which can helps in enhancing delivery of oxygen to the tissues. That is why sometimes decreased in thyroid hormone concentration can lead to anemia which may be normocytic, hypochromic, microcytic or macrocytic.

There are mainly two types of thyroid hormones i.e., Triiodothyronine (T3) and Tetraiodothyronine (T4). Tetraiodothyronine is also called as Thyroxine. T3 is 5 times more potent than T4 and acts faster. Based on fluctuation between the levels of thyroid hormones and thyroid Stimulating hormone two main types of thyroid disorders are there. These are Hypothyroidism and Hyperthyroidism. One of the popular endocrine diseases i.e., primary hypothyroidism is

caused by decreased in level of thyroid hormone due to alteration in thyroid gland function while increased in level of thyroid hormone can lead to hyperthyroidism (also known as thyrotoxicosis) that will be results in increased metabolism. It is followed by suppressed TSH levels (to undetectable levels).

Hypothyroidism is further classified into primary hypothyroidism and secondary hypothyroidism. Primary hypothyroidism is causes due to decreased in secretion of thyroid hormones i.e., T3 and T4 from cells of thyroid gland and increased in levels of serum TSH. It is autoimmune disorder. Secondary hypothyroidism is occurs due to inadequate thyrotropin releasing hormone (TRH) produced by hypothalamus order there is insufficient TSH levels produced by pituitary gland and consequently decreased in synthesis and secretion of thyroid hormones.

Hyperthyroidism is excessive concentration or overproduction of thyroid hormones by thyroidal tissue cells. This may be due to increased in released of presynthesized thyroid hormones, an endogenous or exogenous extra source of thyroid hormone. [1, 26,27]

2.Hyperthyroidism:

Hyperthyroidism is a disorder that occurs when thyroid gland makes more thyroid hormone than the body needs. Hyperthyroidism often called as overactive thyroid and sometimes hyperthyreosis, is a condition in which thyroid gland produces and secretes excessive amounts of the free (not protein bound circulating in the blood) thyroid hormones-triiodothyronine (T3) and/or thyroxine or tetraiodothyronine (T4). Thyroid hormones circulate throughout the body in bloodstream and act on virtually every tissue and cell in the body. Hyperthyroidism causes many of the body's functions to speed up. [6,7]

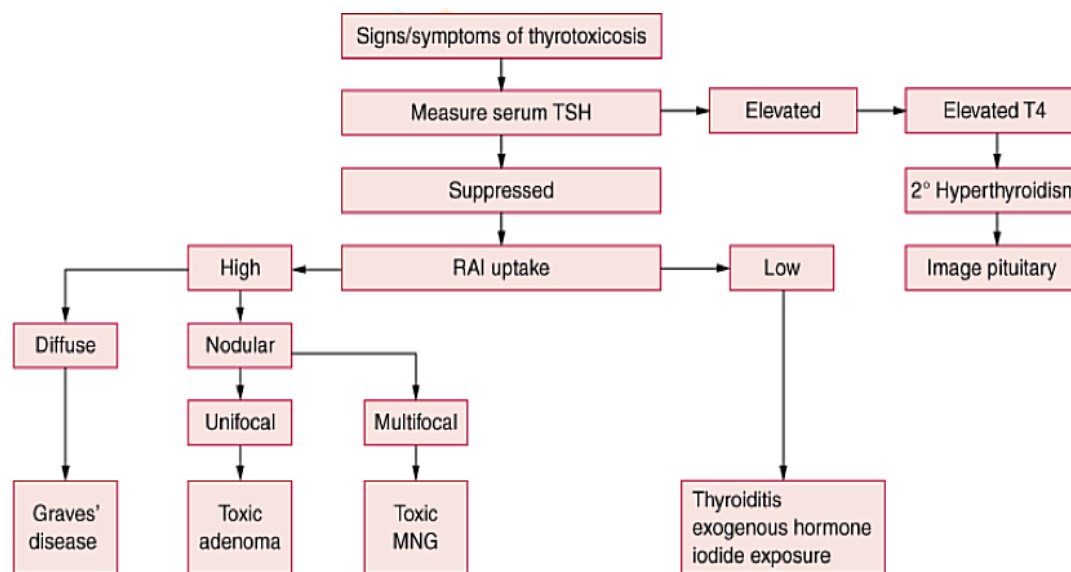


Fig1. Diagnostic algorithm for thyrotoxicosis. MNG = multinodular goiter; RAI = radioactive iodine; TSH = thyroid-stimulating hormone.

(Source: <https://www.accessmedicinetwork.com/amp/posts/49195-hyperthyroidism>)

Symptoms: -

- Fatigue or muscle weakness
- Heat intolerance
- Bulging eyes
- Irregular menstrual periods in girls
- Rapid and irregular heartbeat
- Frequent bowel movements or diarrhea
- weight loss
- Mood swings
- Goiter (enlarged thyroid that may cause the neck to look swollen and can interfere with normal breathing and swallowing) [6,7]

Causes:

Table 1. Causes of Hyperthyroidism [4,7]

Etiological classification	Pathological Mechanism
Graves' disease	Thyroid stimulating hormone receptor-stimulating antibody {TSH-R [Stim] Ab}
Toxic multinodular goiter	Autonomous hyperfunction
Follicular adenoma	Autonomous hyperfunction
Pituitary adenoma	TSH hypersecretion (rare)
Pituitary insensitivity	Resistance to TH
Hypothalamic disease	Excess TRH production

A sudden squirt in the patients suffering from severe hyperthyroidism termed 'thyroid storm' or 'thyroid crisis may occur who have undergone through subtotal thyroidectomy before adequate control of hyperthyroid state, or in a hyperthyroid patient under acute stress, trauma, and with severe infection. Signs and symptoms may include high grade fever, tachycardia, cardiac arrhythmias and coma and may die of congestive heart failure or hyperpyrexia.

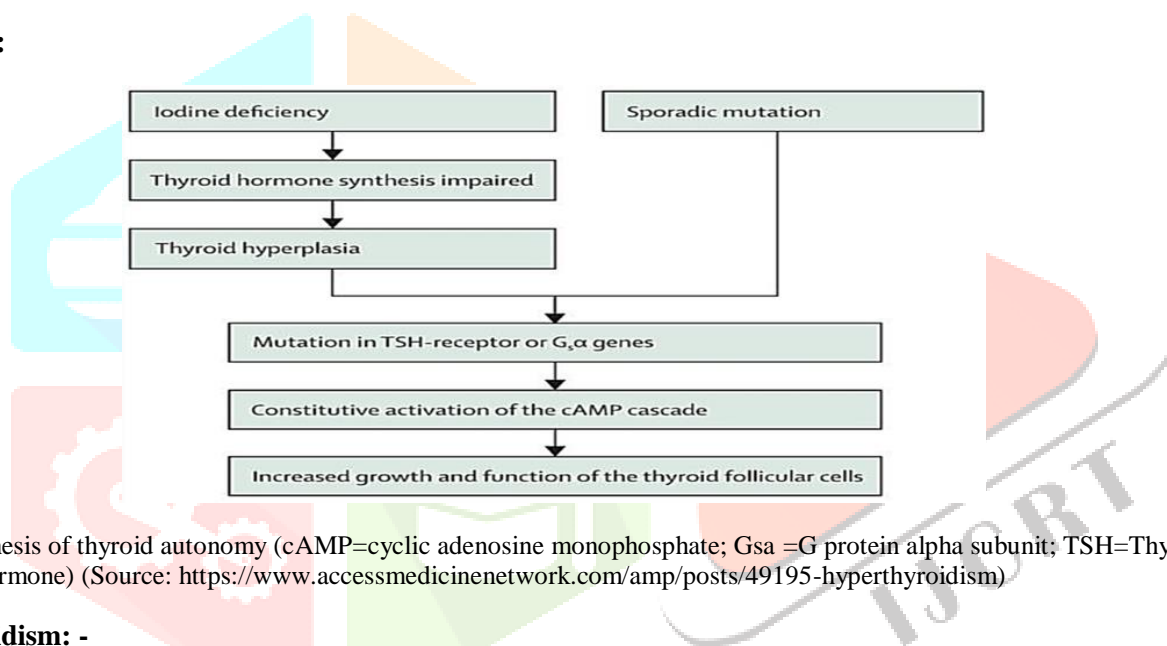
Pathogenesis:

Fig 2. Pathogenesis of thyroid autonomy (cAMP=cyclic adenosine monophosphate; Gsa =G protein alpha subunit; TSH=Thyroid Stimulating Hormone) (Source: <https://www.accessmedicinenetwork.com/amp/posts/49195-hyperthyroidism>)

3.Hypothyroidism: -

Hypothyroidism is one of the most common forms of thyroid dysfunction. It is defined as failure of the thyroid gland to produce sufficient thyroid hormone to meet the metabolic demands of the body. It may be congenital or acquired, primary or secondary, chronic or transient. It refers to a state that results in a deficiency of thyroid hormones, including hypothalamic or pituitary disease and generalized tissue resistant to thyroid hormone, and disorders that affects the thyroid gland directly.

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.

Congenital Hypothyroidism (CH) is a condition due to thyroid hormone deficiency present at the birth.[3,8,9]

Signs and symptoms:

- Fatigue
- Intolerance to cold
- Poor memory and concentration

- Weight gain with poor appetite
- Shortness of breath
- Hoarseness in voice
- In female heavy menstrual periods (and later light periods)
- Poor heating
- Dry coarse skin
- Swelling of limbs [6,8,9]

Causes:

Table 2. Causes of Hypothyroidism

(Source: <https://www.nature.com/articles/s41572-022-00357-7/tables/1>)

Group	Mechanism
1.Primary Hypothyroidism	
Chronic autoimmune thyroiditis (Hashimoto thyroiditis)	Failure of T cell-mediated inflammatory response, cytokine release, infiltration of the thyroid by lymphocytes and development of fibrotic tissue in the thyroid
Disturbed iodine metabolism	Iodine deficiency leads to decreased thyroid hormone production
Irradiation or thyroidectomy	Ablation of thyroid cells
Genetic disease	Loss of function, pathogenetic variant
Infection and/or inflammation	Thyroid cell destruction
Industrial and environmental agents	Interference in various steps of intrathyroidal metabolism
2)Central hypothyroidism (hypothalamic or pituitary)	Pituitary or hypothalamic lesions and/or damage, Heterogeneous mechanisms leading to altered secretion of TSH by thyrotrophs or bioactivity of TSH, involving both hypothalamic and pituitary structures, usually combined with other pituitary hormone deficiencies, including surgery, head trauma, neoplastic lesions, apoplexy, pituitary necrosis, (partial) empty sella, infiltrative lesions or irradiations
3)Congenital Hypothyroidis	congenital genetic mutations rarely cause isolated central hypothyroidism but are more often part of combined pituitary hormone deficiencies and the most common defective genes are PROP1 and POU1F1 [9]

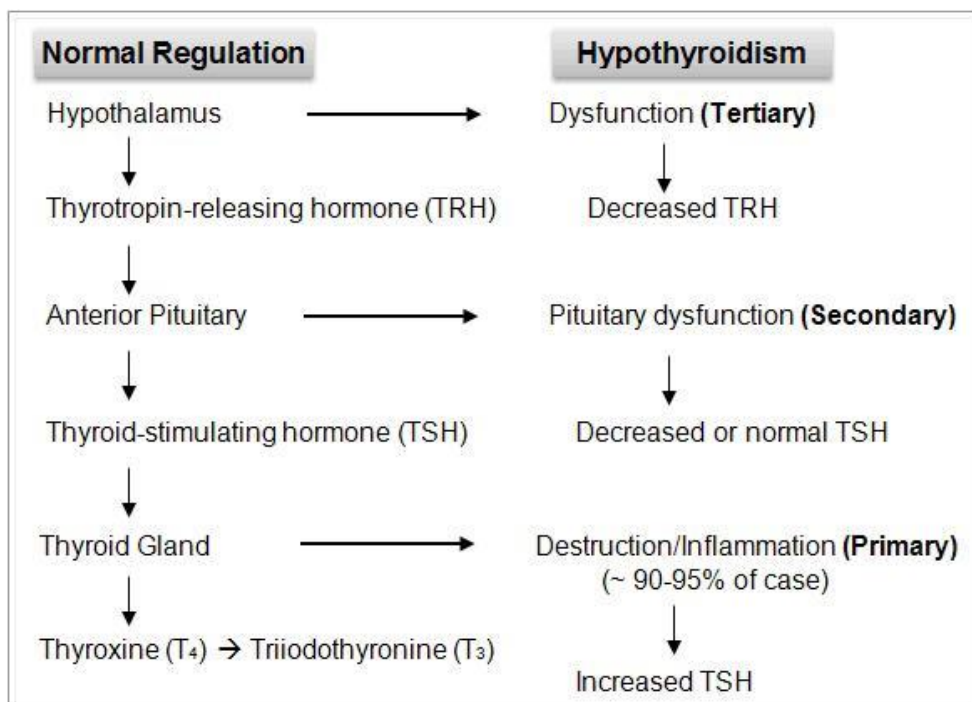
Pathogenesis:-

Fig 3. Pathogenesis of Hypothyroidism

(Source: <https://images.app.goo.gl/JqUh38yzsK4nNeC2A>)**4.Cretinism:**

Cretinism is a situation of major physical and mental retardation due to iodine deficiency, and specifically due to decrease in level of thyroid hormones during early pregnancy. This condition is irreversible, even after treatment with thyroid hormones or iodine soon after birth, but can be corrected if treatment with iodine starts prior to or early in gestation.[10]

Iodine inadequacy has been accepted as the most frequent cause, after starvation, of preventable mental defects which affects hundreds of million people to different levels. Adequate iodine nutrition is important for the prevention of brain damage that could be irreversible by birth, and is only preventable when administered very early in gestation.[11]

The word 'Cretin' is derived from the French, meaning Christ-like because these children are so mentally retarded that they are incapable of committing sins.[3]

Etiopathogenesis:

The causes of congenital hypothyroidism are as follows:

- i. Developmental anomalies e.g., thyroid agenesis and ectopic thyroid.
- ii. Genetic defect in thyroid hormone synthesis e.g., failure in iodine trapping, oxidation, iodination, coupling and thyroglobulin production.
- iii. Foetal exposure to iodides and antithyroid drugs.
- iv. Endemic cretinism in areas with endemic goitre due to dietary deficiency of iodine (sporadic cretinism, on the other hand, is because of developmental anomalies and genetic problems in thyroid hormone synthesis described above).[3]

Signs and symptoms: -

The clinical manifestations usually become evident within a few weeks to months of birth.

- Slow to thrive
- Dry scaly skin

- Hoarse cry
- Bradycardia

As the child ages, clinical picture of fully developed cretinism emerges characterised by:

- Impaired skeletal growth
- Consequent dwarfism
- Round face
- Narrow forehead
- Widely set eyes
- Flat and broad nose [10,11]

Characteristic laboratory findings include a rise in TSH level and fall in T3 and T4 levels.

5. Myxoedema: -

The adult-onset severe hypothyroidism causes Myxedema. The term myxoedema indicates non-pitting oedema due to agglomeration of hydrophilic mucopolysaccharides in the ground substance of dermis and other tissues. Myxedema is a state indicated by thickening and swelling of the skin caused by inadequate production of thyroid hormones by the thyroid gland. [3,25]

Etiopathogenesis: -

Out of the several following causes of myxoedema the first two are the most common causes:

1. Removal of the thyroid by surgery or radiation.
2. Autoimmune (lymphocytic) thyroiditis (termed primary idiopathic myxoedema).
3. Endemic or sporadic goitre.
4. Hypothalamic pituitary lesions.
5. Thyroid cancer.
6. Prolonged administration of antithyroid drugs.
7. Mild developmental anomalies and dysmorphogenesis. [3]

Signs and symptoms:

Myxedema is normally part of a major group of symptoms linked with hypothyroidism

- Brittle hair or fingernails
- Constipation
- Decreased sweating
- Depression
- Dry or pale skin
- Fatigue
- Malaise or lethargy
- Musculoskeletal pain
- Sensitivity to cold
- Thickening of the skin
- Weakness (loss of strength)
- Weight gain
- Less concentration
- Puffiness of face

The laboratory diagnosis in Myxoedema is done by decrease serum T3 and T4 levels and gradedly increased TSH levels as in the case of cretinism but cases with suprathyroid lesions (hypothalamic-pituitary disease) have low TSH levels.

Myxoedema coma is a rare and extreme complication of hypothyroidism with multiple organ abnormalities associated with altered sensorium, it can be fatal. [25]

6.Chronic Lymphocytic (Hashimoto's) Thyroiditis: -

Hashimoto thyroiditis is an autoimmune disease in which by cell and antibody-mediated immune processes there is destruction of thyroid cells and in developed countries is the most common cause of hypothyroidism. In contrast to this worldwide, an inadequate dietary intake of iodine is most common cause of hypothyroidism. This disease is also known known with name chronic autoimmune or chronic lymphocytic thyroiditis. The pathology of the disease involves the formation of antithyroid antibodies attacking the thyroid tissue which causes progressive fibrosis. The diagnosis may take time until later in the disease process and is often challenging. The increased levels of thyroid-stimulating hormone (TSH) and decrease levels of free thyroxine (fT4), coupled with elevated antithyroid peroxidase (TPO) antibodies are the most common laboratory findings. However, earlier on in the course of the disease, patients may exhibit peroxidase symptoms, and laboratory findings of hyperthyroidism or normal values. Possible intermittent destruction of the thyroid gland cells is responsible for this.

Women are more often affected. The female-to-male ratio is at least 10:1. Between the ages of 30 to 50 years most women are diagnosed [17]

Signs and symptoms: -

- Symptoms of Hypothyroidism
- Round puffy face, slow speech, hoarseness in voice
- Hypokinesia
- Periorbital edema
- Mental clouding, depression
- Bradycardia
- Cold, dry, thick skin
- Enlargement of thyroid gland [18]

Causes:

1. Other autoimmune disease association: Hashimoto's disease has been found in association with other autoimmune diseases such as Graves' disease, SLE, rheumatoid arthritis, pernicious anaemia and Type 1 diabetes mellitus, like in other autoimmune diseases.
2. Immune destruction of thyroid cells: The sequence of immune phenomena is initial activation of CD4+ T helper cells. These cells then induce infiltration of CD8+ T cytotoxic cells in the thyroid parenchyma as well as activate B cells to form autoantibodies, which bring about immune destruction of thyroid parenchyma.
3. Detection of autoantibodies: The following autoantibodies against different thyroid cell antigens are detectable in the sera of most patients with Hashimoto's thyroiditis:
 - i. Microsomal autoantibodies of thyroid (against the microsomes of the follicular cells).
 - ii. Thyroglobulin autoantibodies.
 - iii. TSH receptor autoantibodies.
 - iv. Less constantly found are thyroid hormones themselves, thyroid autoantibodies against follicular cell membranes and colloid component other than thyroglobulin.
4. Inhibitory TSH-receptor antibodies: TSH-receptor antibody seen on the surface of thyroid cells in Hashimoto's thyroiditis is inhibitory to TSH, producing hypothyroidism. Graves' disease is present with same antibody where it causes hyperthyroidism. It observes that TSH-receptor antibody can act both to suppress or stimulate the thyroid cells to generate hypo- or hyperthyroidism respectively. Thus, alternate episodes of hypo- or hyperthyroidism may observed in these patients.
5. Genetic basis: The disease has higher incidence in first degree relatives of affected patients. Hashimoto's thyroiditis is seen more often with HLA-DR3 and HLA-DR5 subtypes.[3]

Pathogenesis:

Hashimoto thyroiditis is an autoimmune complaint caused by an vulnerable response to thyroid autoantigens. Circulating autoantibodies against thyroid antigens are present in the vast maturity of cases. The vulnerable response leads to progressive reduction of thyroid epithelial cells associated with lymphocytic infiltrates and fibrosis. The inciting events leading to the autoimmune response haven't been completely illustrated, but multiple immunologic mechanisms that may contribute to thyroid cell damage have been linked, including the following

- CD8 cytotoxic T- cell – intermediated payoff of thyroid epithelial cells.

- Cytokine- intermediated cell death. T- cell activation leads to the product of seditious cytokines similar as interferon- γ in the thyroid gland, with attendant reclamation and activation of macrophages and damage to follicles.
- List of anti-thyroid antibodies (anti-thyroglobulin, and anti-thyroid peroxidase antibodies), followed by antibody-dependent cell – intermediated cytotoxicity. [2]

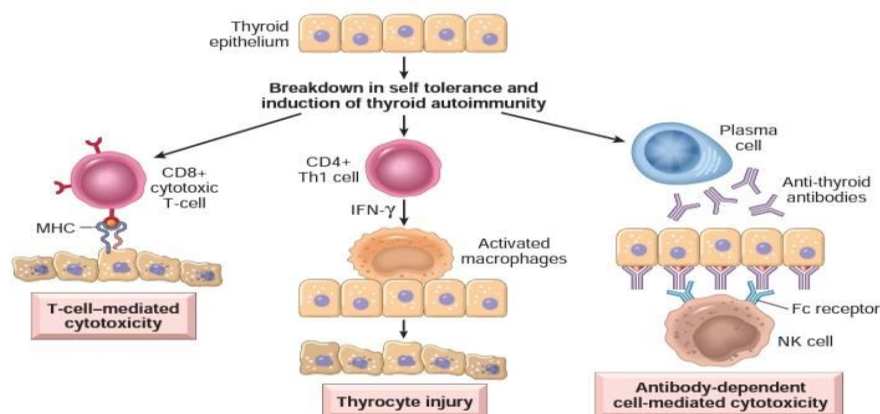


Fig 4. Pathogenesis of Hashimoto's Thyroiditis (Source: <https://images.app.goo.gl/xxrFFamw9YnF67fz5>)

7.Graves disease:

Graves' Disease (GD) is the most common cause of hyperthyroidism worldwide. It was first described by German physician Carl Adolf Von Basdow. It is an autoimmune disorder characterized by presence of TSH receptor autoantibody. These autoantibodies stimulate TSH receptors on thyroid cells and cause hyper-trophy and hyperplasia resulting thyroid gland enlargement. TSHR autoantibodies also cause increased synthesis and secretion of thyroid hormones. GD is primarily disease of thyroid gland but affects multi organ system i.e., heart, liver, muscle, eye and skin. Graves' ophthalmopathy and pretibial myxedema are extrathyroidal manifestations of GD which results from action of TSHR autoantibodies on TSHR present on fibroblast, adipocyte and T cells in extrathyroidal tissue.[20]

In the typical case of Graves' disease, the thyroid gland is enlarged (usually symmetrically) due to diffuse hypertrophy and hyperplasia of thyroid follicular epithelial cells. The gland is usually smooth and soft, and its capsule is intact. On microscopic examination, the follicular epithelial cells in untreated cases are tall, columnar, and more crowded than usual. This crowding often results in the formation of small papillae, which project into the follicular lumen. Such papillae lack fibrovascular cores, in contrast with those of papillary carcinoma. The colloid within the follicular lumen is pale, with scalloped margins. Lymphoid infiltrates, consisting predominantly of T cells, with fewer B cells and mature plasma cells, are present throughout the interstitium; germinal centers are common.

Changes in extrathyroidal tissues include generalized lymphoid hyperplasia. In individuals with ophthalmopathy, the tissues of the orbit are edematous because of the presence of hydrophilic glycosaminoglycans. In addition, there is infiltration by lymphocytes, mostly T cells. Orbital muscles initially are edematous but may undergo fibrosis late in the course of the disease. The dermatopathy, if present, is characterized by thickening of the dermis, as a result of deposition of glycosaminoglycans and lymphocyte infiltration. [2,19]

Signs_and_symptoms: -

- Menstrual disturbances in women (oligomenorrhea or amenorrhea)
- Neck fullness
- Physical signs of hyperthyroidism
- Extrathyroidal physical signs
- Ophthalmopathy
- Proptosis (exophthalmos)
- Double vision (extraocular-muscle dysfunction)
- Periorbital edema, chemosis, scleral injection
- Exposure keratitis
- Optic neuropathy

- Localized dermatopathy
- Acropachy [19,21]

Causes:

Graves' disease is an autoimmune disease and, as already stated, there are many immunologic similarities between this condition and Hashimoto's thyroiditis. These are as follows:

1. Genetic factor association: - Like in Hashimoto's thyroiditis. Graves' disease too has genetic predisposition. A familial occurrence has been observed. Susceptibility to develop Graves' disease has been found associated with HLA-DR3 (Hashimoto's thyroiditis has both HLA-DR3 and HLA-DR5 association, page 804), CTLA-4 and PTPN22 (a T-cell regulatory gene).
2. Autoimmune disease associations:-. Graves' disease may be found in association with other organ-specific autoimmune diseases. Hashimoto's thyroiditis and Graves' disease are frequently present in the same families and the two diseases may coexist in the same patient.
3. Other factors:- Besides these two factors, Graves' disease has higher prevalence in women (7 to 10 times), and association with emotional stress and smoking.
4. Autoantibodies: - Autoantibodies against thyroid antigens are detectable in the serum of these patients too but their sites of action are different from that of Hashimoto's thyroiditis. In Graves' disease, TSH-receptor autoantigen is the main antigen against which autoantibodies are directed.[3]

Pathogenesis:

The serum of more than 90% of patients with Graves disease contains TSH-R[stim] antibody, directed against the TSH receptor site in the thyroid follicular epithelial membrane. This antibody, formerly called long-acting thyroid stimulator (LATS), is now also called thyroid-stimulating immunoglobulin (TSI). When it binds to the cell membrane TSH receptors, TSH-R [stim] Ab (TSI) stimulates hormone synthesis and secretion in somewhat the same way as TSH. Although serum levels of TSH-R [stim] Ab (TSI) correlate poorly with disease severity, its presence can be helpful diagnostically and perhaps prognostically. After discontinuing antithyroid drug treatment, about 30–50% of patients with Graves hyperthyroidism relapse. There seems to be a greatly increased recurrence risk if the TSH-R [stim] Ab (TSI) is still found in plasma at the time of discontinuing antithyroid drug treatment, so this test can perhaps be used to predict likely relapse.

The genesis of TSH-R [stim] Ab (TSI) in patients with Graves' disease is uncertain. However, Graves' disease is familial. A genetic contribution to the development of Graves' disease is suggested by the finding of much higher concordance rates in monozygotic same-sex twin pairs (0.35) than in dizygotic pairs (0.03). In Caucasians, it is associated with the HLA-B8 and HLA-DR3 histocompatibility antigens; in Asians, with HLA-Bw46 and HLA-B5; and in blacks, with HLA-B17. Furthermore, patients with Graves' disease frequently suffer from other autoimmune disorders. The precipitating cause of this antibody production is unknown, but an immune response against a viral antigen that shares homology with TSH-R may be responsible. Another theory of the pathogenesis of Graves' disease is a defect of suppressor T lymphocytes allows helper T lymphocytes to stimulate B lymphocytes to secrete antibodies directed against follicular cell membrane antigens, including TSH-R. [4]

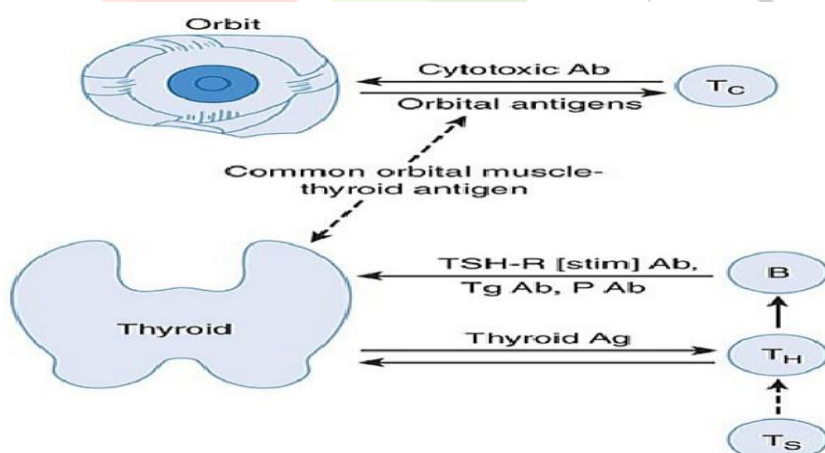


Fig 5. Proposed pathogenesis of Graves' disease. A defect in suppressor T lymphocytes (Ts) allows helper T lymphocytes (TH) to stimulate B lymphocytes (B) to synthesize thyroid autoantibodies. The thyroid receptor–stimulating antibody (TSH-R [stim] Ab or TSI) is the driving force for thyrotoxicosis. Inflammation of the orbital muscles may be due to the sensitization of cytotoxic T lymphocytes (Tc) or to the sensitization of killer cells to a common antigen, the TSH-R, found in both orbital fibroblasts and thyroid follicular cells.

What triggers this immunologic cascade is not known. (Ag, antigen; P Ab, peroxidase or microsomal antibody; Tg Ab, thyroglobulin antibody.) (Source: <https://images.app.goo.gl/bJon2S1EZZTg8GTQ6>)

8.Goiters:

Goiter means enlargement of the thyroid gland and is a general term that conveys the information that the volume of the thyroid gland is larger than normal. Goiter can be associated with euthyroidism, hypothyroidism, or hyperthyroidism. It is larger in males as opposed to females.

Two morphologic forms of goitre are distinguished:

- Diffuse goitre (simple nontoxic goitre or colloid goitre).
- Nodular goitre (multinodular goitre or adenomatous goitre).[24]

Early in its developments induced hypertrophy and hyperplasia of thyroid follicular cells usually result in diffuse, symmetric enlargement of the gland (diffuse goiter). The follicles are lined by crowded columnar cells, which may pile up and form projections similar to those seen in Graves disease. If dietary Iodine subsequently increases, or if the demands for thyroid hormone decrease, the follicular epithelium involutes to form an enlarged, colloid-rich gland (colloid goiter). The cut surface of the thyroid in such cases usually is brown, glassy-appearing, and translucent. On microscopic examination, the follicular epithelium may be hyperplastic in the early stages of disease or flattened and cuboidal during periods of involution. Colloid is abundant during the latter periods.

With time, recurrent episodes of hyperplasia and involution combine to produce a more irregular enlargement of the thyroid, termed multinodular goiter. Virtually all long-standing diffuse goiters convert into multinodular goiters. Multinodular goiters are multilobulate, asymmetrically enlarged glands that may attain a massive size. On cut surface, irregular nodules containing variable amounts of brown, gelatinous colloid are evident. Older lesions often show areas of fibrosis, hemorrhage, calcification, and cystic change. The microscopic appearance includes colloid-rich follicles lined by flattened, inactive epithelium and areas of follicular epithelial hypertrophy and hyperplasia, accompanied by the regressive changes just noted. [2,24]

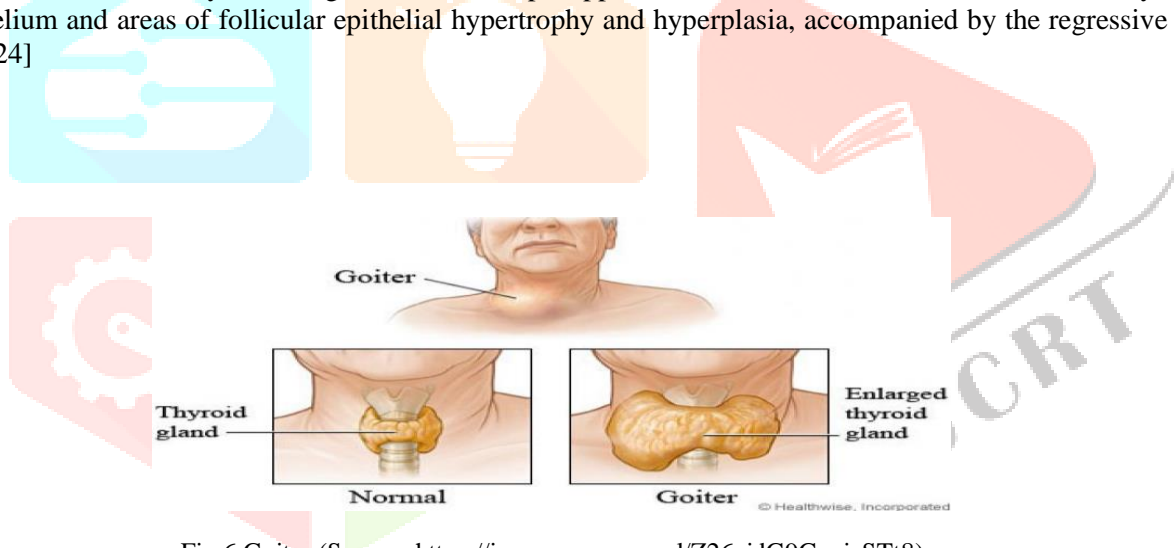


Fig.6 Goiter (Source: <https://images.app.goo.gl/Z26zjdG9GvejaSTt8>)

Pathogenesis:-

The pathogenetic mechanisms of both forms of goitre can be considered together since nodular goitre is generally regarded as the end-stage of long-standing simple goitre. The fundamental defect is deficient production of thyroid hormones due to various etiologic factors described below, but most common is dietary lack of iodine. Deficient thyroid hormone production causes excessive TSH stimulation which leads to hyperplasia of follicular epithelium as well as formation of new thyroid follicles. Cyclical hyperplastic stage followed by involution stage completes the picture of simple goitre. Repeated and prolonged changes of hyperplasia result in continued growth of thyroid tissue while involuted areas undergo fibrosis, thus completing the picture of nodular goitre. [3,24]

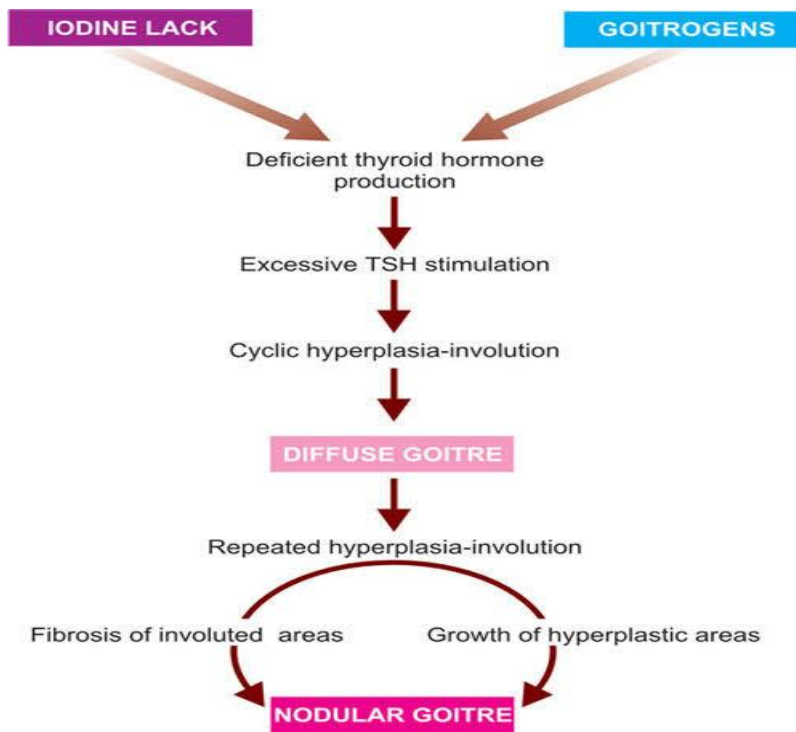


Fig 11. Pathogenesis of Goiter

(Source: <https://images.app.goo.gl/45z9LyxJ6fbr2srA8>)

Goiters can be endemic or sporadic.

- Endemic goiter occurs in geographic areas where the diet contains little iodine. The designation endemic is used when goiters are present in more than 10% of the population in a given region. Such conditions are particularly common in mountainous areas of the world, including the Himalayas and the Andes. With increased availability of dietary iodine supplementation, the frequency and severity of endemic goiter have declined significantly.
- Sporadic goiter occurs less frequently than endemic goitre. The condition is more common in females than in males, with a peak incidence in puberty or young adulthood, when there is an increased physiologic demand for T4. Sporadic goiter may be caused by several conditions, including the excessive ingestion of substances that interfere with thyroid hormone synthesis, such as calcium and vegetables belonging to the Brassicaceae (also called Cruciferae) family (e.g., cabbage, cauliflower, brussels sprouts, turnips). In other instances, goiter may result from inherited enzymatic defects that interfere with thyroid hormone synthesised (dysmorphonogenetic goitre). In most cases, however, the cause of sporadic goitre is not apparent.[2]

Conclusions:

Thyroid dysfunction is common, especially in elderly people. Most people found to have thyroid dysfunction in surveys have subclinical thyroid dysfunction, in particular subclinical hypothyroidism. Among people with subclinical thyroid dysfunction, most have very small increases or decreases in serum TSH concentrations. When asked, some of these people with subclinical thyroid dysfunction have symptoms that are compatible with, though not specific for, thyroid dysfunction or have another indication for testing for thyroid dysfunction. Some people have biochemical or physiological abnormalities that are ameliorated by thyroid hormone therapy, in the case of people with subclinical hypothyroidism, or antithyroid therapy, in the case of subclinical hyperthyroidism. Among people with thyroid dysfunction, therapy may have beneficial effects on intermediate outcomes, such as reduction in serum lipid concentrations and improvement of myocardial contractility. However, appropriate therapy has not been proven to alter long-term morbidity or mortality in people with subclinical thyroid dysfunction. Similarly, while it is accepted that treatment will benefit patients with biochemically overt thyroid dysfunction who present with significant symptoms or complications, the lack of well designed studies makes it difficult to determine whether treatment would provide significant net benefit in persons who have biochemically defined overt thyroid dysfunction but little evidence of illness; the potential for harms is similar but potential for benefit is less. These uncertainties contribute to the difficulty in assessing the value of a screening program for thyroid dysfunction.

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