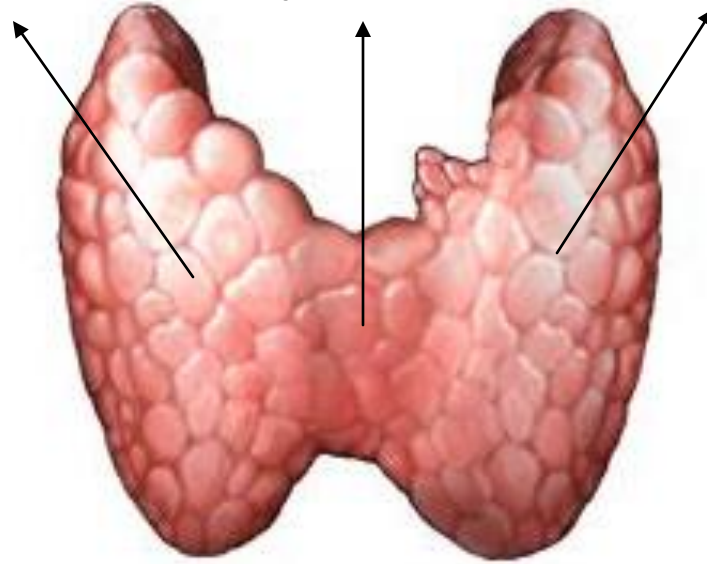


429's Pathology Team represents:

Thyroid pathology 1st part — 2nd edition

(revised with Dr.Hala Kfoury)

-Hypothyroidism -Thyrotoxicosis -Hashimoto Thyroiditis



Then a schedule summarizing both !!

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I. Hypothyroidism

Etiology

- Hypothyroidism is caused by any structural or functional derangement that interferes with the production of adequate levels of thyroid hormone
- Divided into primary and secondary categories, depending on whether it arises from an intrinsic abnormality in the thyroid or results from hypothalamic or pituitary disease

Prevalence increases with age, and it is nearly tenfold more common in women than in men.

Primary

- Postablative: surgery, radioiodine therapy, or external radiation
- Hashimoto thyroiditis*
- Iodine deficiency*
- Congenital biosynthetic defect (dyshormonogenetic goiter)*
- Drugs (lithium, iodides, *p*-aminosalicylic acid)*
- Rare developmental abnormalities of the thyroid (thyroid dysgenesis)

Secondary

- Pituitary or hypothalamic failure (uncommon)

Hashimoto thyroiditis and postablative hypothyroidism account for the vast majority of cases of hypothyroidism, particularly in regions with adequate dietary iodine

Clinical Manifestations

Cretinism

- Hypothyroidism developing in infancy or early childhood
- Results from congenital lack of a thyroid gland (*because of maternal hypothyroidism before fetal thyroid is developed*): **congenital cretinism**
- *Common in areas of the world where dietary iodine deficient*
- *Rarely: may result from inborn errors in metabolism e.g. enzyme deficiencies → interfere with the biosynthesis of normal levels of thyroid hormone: **sporadic cretinism***



Features:

Impaired development of

- skeletal system
- central nervous system

Severe mental retardation

- Brain needs maternal T_4 & T_3
- Severity depends on time at which thyroid deficiency occurs in utero
- Before the development of the fetal thyroid gland → severe
- Later in pregnancy, after the fetal thyroid has developed → normal brain development

Short stature

Coarse facial features

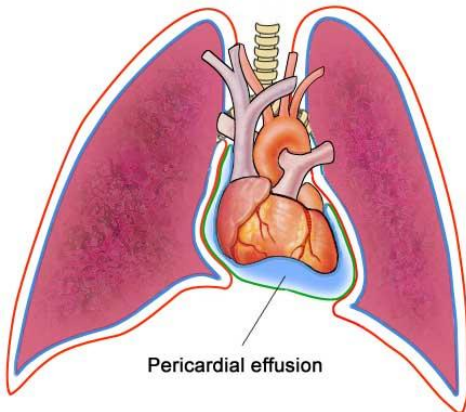
Protruding tongue

Umbilical hernia

Myxedema: in adults & older children

Early: generalized apathy and mental sluggishness; <i>mimic depression</i>	Mucopolysaccharide-rich edema accumulates in skin, subcutaneous tissue, and a number of viscera =
Listlessness (Lacking Energy)	Broadening and coarsening of facial features
Cold intolerance	Enlargement of the tongue
Obesity	Deepening of the voice
Decreased bowel movements → constipation	Pericardial effusions → heart enlargement → heart failure

Edema is non-pitting; result of glycosaminoglycans & hyaluronic acid deposition in tissues



II. Thyrotoxicosis

It is a hypermetabolic state caused by elevated circulating levels of T3 and T4.

[Because it is most commonly a **hyperfunction-ing** of the thyroid gland, it is referred to as **hyperthyroidism**]

Clinical Manifestations

Related to

- 1- Changes in the hypermetabolic state induced by excessive amounts of hormones.
- 2- Over activity of the sympathetic nervous system.

- 1) Soft, warm & flushed skin. 2) Heat intolerance & excessive sweating.
- 2) Hypermotility of GIT , diarrhea .
- 3) Palpitation , Tachycardia.
- 4) Nervousness , Tremors & irritability.
- 5) Proximal muscle weakness (thyroid myopathy)



6) Lid lag , wide staring eyes & exophthalmos (in Graves)

Etiology

What causes hyperthyroidism ?

- **Graves Disease** [When the whole gland produces extra thyroid hormones].
- Functioning adenoma "*Hot nodule*"
[When a single nodule on the gland produces extra thyroid hormones].
- Thyroiditis.
- Drugs "*such as anti-arrhythmic drugs*"
[structurally similar to thyroxine and may cause either under- or over activity of the thyroid].
- Post-partum thyroiditis [during the year after a woman gives birth].
- pituitary adenoma.

Graves Disease: [most common cause of endogenous hyperthyroidism]

An autoimmune disorder in which antibodies may be present in the serum.

[Antibodies to : **TSH receptor**, thyroid peroxidase, and thyroglobulin]

-TSH receptor auto anti-bodies found in a patient's serum :

- **TSI [Thyroid stimulating immunoglobulins]:**
these antibodies act as LATS (Long Acting Thyroid Stimulants), activating the cells in a longer and slower way than the normal thyroid-stimulating hormone (TSH), leading to an elevated production of thyroid hormone.
- **TGI [Thyroid growth immunoglobulins]:**
these antibodies bind directly to the TSH-receptor and have been implicated in the growth of thyroid follicles.
- **TBII [Thyrotropin Binding-Inhibiting Immunoglobulins]:**
these antibodies inhibit the normal union of TSH with its receptor. Some will actually act as if TSH itself is binding to its receptor, thus inducing thyroid function. Other types may not stimulate the thyroid gland, but will prevent TSI and TSH from binding to and stimulating the receptor.

-Incidence & risk factors:

- Women affected more than men.
- Age between 20-40.
- Genetic susceptibility:
 1. presence of **HLA-B8**
 2. Presence of **DR3**
 3. Presence of **CTLA-4** (cytotoxic T-lymphocyte-associated-4 gene)

-Etiology:

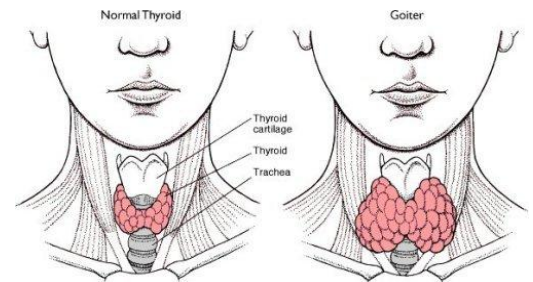
Presence of *anti-TSH receptor* [long-acting thyroid stimulator (LATS)], an IgG antibody that binds to the TSH receptor and mimics the action of TSH, stimulating adenylcyclase increasing the release of thyroid hormones.

-Symptoms & signs:

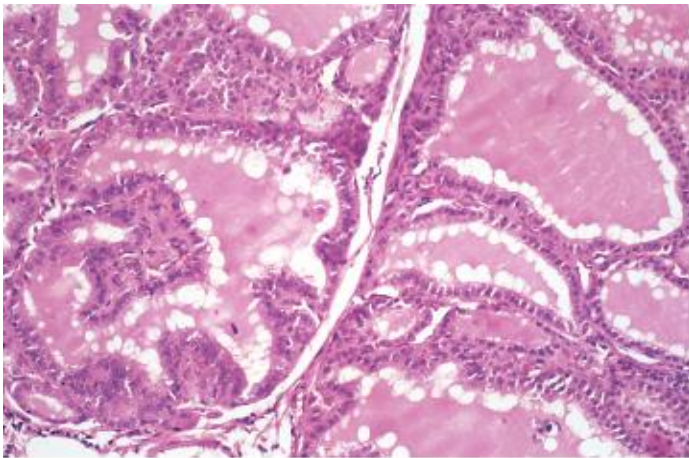
- 1) Hyperthyroidism Due to hyperfunction.
- 2) *Diffuse* enlargement of the thyroid. (It is not LOCALIZED !!!)
- 3) Infiltrative ophthalmopathy with resultant *exophthalmos*.
- 4) Localized, infiltrative dermopathy [*pre-tibial-myxedema*]



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-Histopathology:



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1-cells Lining the follicle :

- Increase in number and size.
- Arranged in a pseudo papillary appearance

2- Scalloped appearance :

- Crescent shaped spaces between the epithelial cell and the margin of the colloid all the way around the circumference.
- Indicative of a hyperactive lining epithelium because the colloid is actively absorbed by the enlarged pseudo papillary projections of the lining epithelium.

-How to Manage ?

- 1-Normalize Thyroid Hormones (Anti-Thyroid Drugs)
- 2-Operation.

Thyroiditis		Chronic Lymphocytic (Hashimoto) Thyroiditis	
Definition	Inflammation of the thyroid gland	Gradual thyroid failure because of autoimmune destruction of the thyroid gland	
Pathogenesis	<ul style="list-style-type: none"> A condition that results in: acute illness with severe thyroid pain <p><u>Example:</u> infectious thyroiditis</p> <ul style="list-style-type: none"> subacute granulomatous thyroiditis. <p>Disorders that causes little inflammation</p> <p>Illness appears primarily as thyroid dysfunction</p> <p><u>Example:</u> subacute lymphocytic [painless] thyroiditis</p> <p>fibrous [Reidel] thyroiditis.</p>	<ul style="list-style-type: none"> Autoimmune disease Immune system reacts against a variety of thyroid antigens Sensitization* of autoreactive CD4+ T-helper cells to thyroid antigens Most common cause of hypothyroidism in areas of the world where iodine levels are sufficient (where iodine is not low). Male : Female predominance; 1:10 	
Morphology		<ul style="list-style-type: none"> Depletion of thyroid epithelial cells (thyrocytes) Thyrocytes are replaced by mononuclear cell infiltration and fibrosis. Abundant eosinophilic, granular cytoplasm, termed Hürthle, or oxyphil, cells 	
Clinically	<p>Clinically significant types of thyroiditis:</p> <ol style="list-style-type: none"> <i>Hashimoto thyroiditis</i> <i>(or chronic lymphocytic thyroiditis)</i> Subacute granulomatous thyroiditis Subacute lymphocytic thyroiditis 	<ul style="list-style-type: none"> A Painless enlargement of the thyroid, usually symmetric and diffuse Some degree of hypothyroidism Hypothyroidism develops gradually In Middle-aged woman 	

*, sensitization /administration of an antigen to induce a primary immune response.

Diseases of The Thyroid Gland

	Hypothyroidism	Thyrotoxicosis (hyperthyroidism)	Graves Disease	Hashimoto disease
Definition	A condition characterized by abnormally low thyroid hormone production.	It is a hypermetabolic state caused by elevated circulating levels of T3 and T4.	Autoimmune disorder in which certain antibodies may be present in the serum	Autoimmune disease in which the immune system reacts against a variety of thyroid antigens.
Causes	Primary: 1- Hashimoto thyroiditis 2- Congenital biosynthetic defect 3- Thyroid dysgenesis 4- Iodine deficiency 5- Drugs / Postablative Secondary: Pituitary or hypothalamic failure	Primary: 1- Graves disease 2- Hyperfunctioning multinodular goiter 3- Hyperfunctioning adenoma Secondary: TSH-secreting pituitary adenoma	Presence of anti-TSH receptor [long-acting thyroid stimulator (LATS)], an IgG antibody that binds to the TSH receptor and mimics the action of TSH	Progressive depletion of thyroid epithelial cells (thyrocytes), replaced by mononuclear cell infiltration and fibrosis.
Histopathology			1-Cells Lining the follicle: -Increase in number and size -Arranged in a pseudo papillary appearance 2-Scalloped appearance: Crescent shaped spaces between the epithelial cell and the margin of the colloid	1- Lymphocyte infiltration with plasma cells 2- The follicular cells will have Hürthle-cell change > cells will stain pink
Clinical presentation	- Cretinism (Impaired development of skeletal system and CNS) - Myxedema (Cold intolerance, constipation, obesity) - Non-pitting edema	Heat intolerance and excessive sweating Hypermotility of GIT, diarrhea Proximal muscle weakness (Thyroid myopathy) Lid lag, wide staring eyes & exophthalmus (in Graves) Palpitation, Tachycardia Nervousness , Tremors & irritability	- Hyperthyroidism. - Diffuse enlargement of the thyroid. - Exophthalmos. - pre-tibial-myxedema	