جامعة الملك سعود
King Saud University

PATHOLOGY
TEAM 437

Revised By
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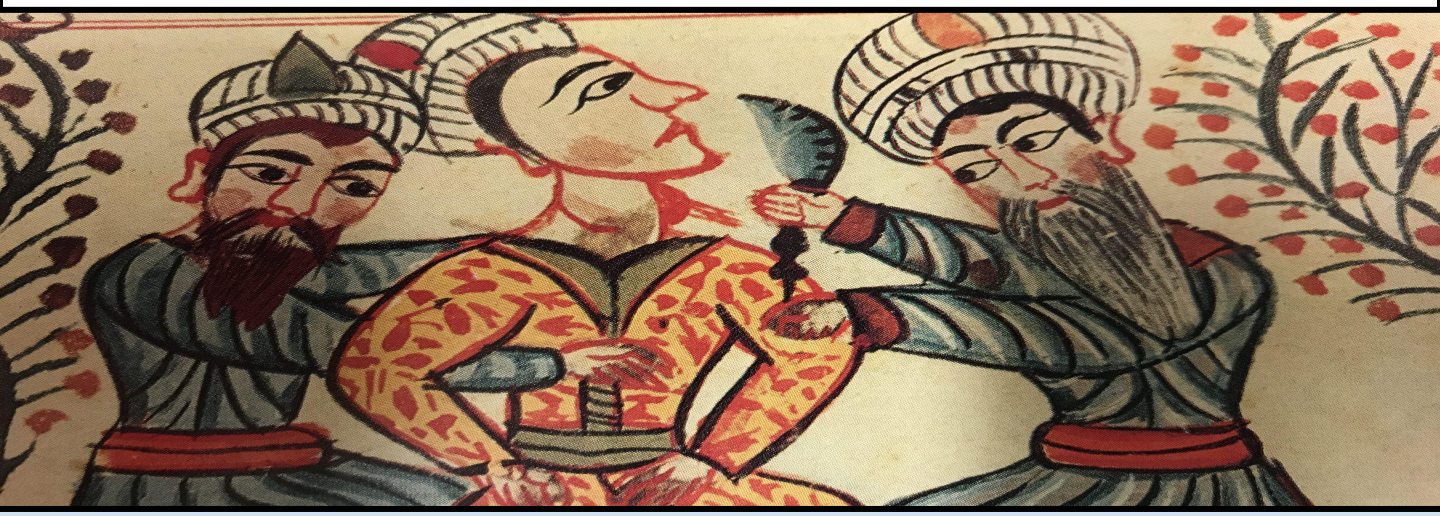
MED437
KING SAUD UNIVERSITY

واعلموا أن مهمتكم ليست ورقة تنالونها.....
إنما مهمتكم أمة تحيونها.....

Hypo, Hyperthyroidism and Hashimoto's Thyroiditis



أبو القاسم خلف بن عباس الزهراوي 936 م(324هـ), عالِم في العلوم الشرعية وطبيب أندلسي مسلم,أشهر جراح مسلم في العصور الوسطى الزهراوي أجرى عملية استئصال الغدة الدرقية. وهي عملية لم يجرؤ أي جراح على إجرائها إلا في القرن التاسع عشر بعده بتسعة قرون وقد بين هذه العملية بقوله: هذا الورم الذي يسمى فيلة الحلقوم يكون ورما عظيما على لون البدن وهو في النساء كثير وهو على نوعين إما أن يكون طبيعيا وإما أن يكون عرضيا, فأما الطبيعي فلا حيلة فيه وأما العرضي فيكون على ضربين أحدهما شبيه بالسلع الشحمية والضرب الآخر شبيه بالورم الذي يكون من تعقد الشريان وفي شقه خطر فلا ينبغي أن تعرض لها بالحديد البتة إلا ما كان منها صغيرا أن سبرتها وفتشتها بالمدس فألفيتها تشبه السلعة الشحمية ولم تكن متعلقة بشيء من العر وق فشقها كما تشق على السلع وتخرجها بما يحويها من الكيس إن كانت فى كيس وإلا فاستقص جميعها ثم عالج الموضع بما ينبغي من العلاج

الشكر موصول لجميع من عمل على هذه المحاضرة:

القادة: فايز غياث الدرسوني — شيرين العكيلي

الأعضاء:

حسن العريني	Golden member	نورة القاضي	Golden member
عبدالرحمن آل الشيخ		مشاعل القحطاني	
منصور العبرة		بتول الرحيمي	Golden member
عبدالعزيز الضرغام		رناد الفرم	
محمد الأصقه			
عبدالجبار اليماني			
محمد سعيد القحطاني			

Color index:
-Text
-important
-Notes
-Extra

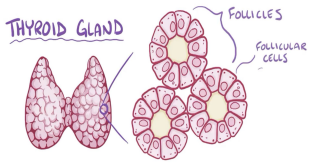
Objectives:

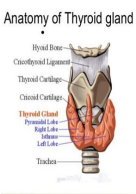
- Know the ways in which thyroid disorders present.
- Know the major causes and manifestations of hypo,hyperthyroidism and thyroiditis .
- Know the causes of the thyroid endemic goiter and its pathology.

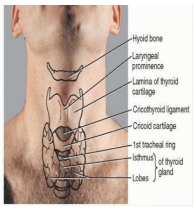
Thyroid anatomy:

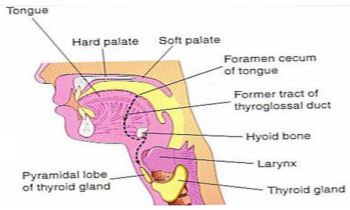
The thyroid gland consists of two bulky lateral lobes connected by a relatively thin isthmus, usually located below and anterior to the larynx.

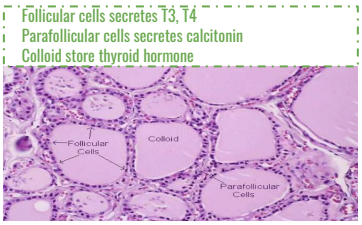
The thyroid gland develops embryologically from an invagination of the developing pharyngeal epithelium that descends from the foramen cecum at the base of the tongue to its normal position in the anterior neck

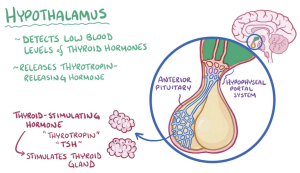












Thyroid Diseases

Clinical recognition of diseases of the thyroid is important, because most are amenable to medical or surgical management. Diseases include:

Excessive release of thyroid hormones (hyperthyroidism)	Mass lesions	Thyroid hormone deficiency (hypothyroidism)

Excessive release of thyroid hormones (hyperthyroidism).

What is thyrotoxicosis ?

Thyrotoxicosis is a hypermetabolic state due to **elevated circulating levels of free T3 and T4** whatever the source is, most of the time it's due to thyroid but it could be due to drugs (exogenous) or inflammation (thyroiditis)

Because it is caused most commonly by **hyperfunction** of the thyroid gland, thyrotoxicosis often is referred to as hyperthyroidism.

In certain conditions, however, the oversupply either is related to excessive release of pre-formed thyroid hormone (e.g., in thyroiditis) or comes from an extrathyroidal source, rather than a hyperfunctioning gland.

What are the most common causes of thyrotoxicosis ?

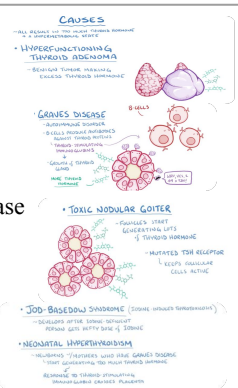
The three most common causes of thyrotoxicosis:
Primary:
• Diffuse hyperplasia of the thyroid associated with Graves' disease (accounts for 85% of cases)
• Hyperfunctional multinodular goiter not all goiter is hyperfunctional
• Hyperfunctional adenoma of the thyroid not all adenoma are functional

Other causes

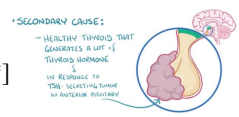
ASSOCIATED WITH HYPERTHYROIDISM

Primary:

1. Diffuse toxic hyperplasia (Graves disease)
2. Hyperfunctioning ("toxic") multinodular goiter
3. Hyperfunctioning ("toxic") adenoma
4. Iodine-induced hyperthyroidism
5. Neonatal thyrotoxicosis associated with maternal Graves disease



Secondary:
TSH-secreting pituitary adenoma (rare)[*]



NOT ASSOCIATED WITH HYPERTHYROIDISM

1. Granulomatous (de Quervain) thyroiditis (painful)
2. Subacute lymphocytic thyroiditis (painless)
3. Struma ovarii (ovarian teratoma with ectopic thyroid)
4. Factitious thyrotoxicosis (exogenous thyroxine intake)

Diagnosis of hyperthyroidism

•The diagnosis of hyperthyroidism is based on clinical features and laboratory data.

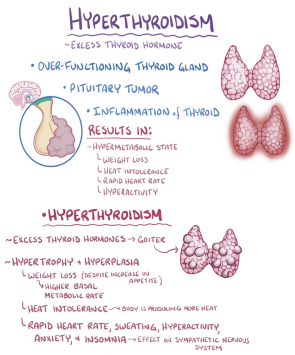
•The measurement of serum TSH is the most useful single screening test for hyperthyroidism.

•Free thyroid hormone assays.T4 is more important than T3

•Measurement of radioactive iodine uptake by the thyroid gland

Clinical manifestation of thyrotoxicosis

Hypermetabolic state induced by excessive amounts of thyroid hormone ,over activity of the sympathetic nervous system:



Constitutional symptoms (weight loss, fever, sweating…)

Gastrointestinal diarrhea

Cardiac palpitation, tachycardia

Neuromuscular proximal muscle weakness

Ocular lid lag, exophthalmos (only in case of graves)

Thyroid storm (medical emergency) occurs when there's acute onset of severe hyperthyroidism. May cause death because of an arrhythmia due to elevated levels of catecholamines

Apathetic hyperthyroidism (**imp**) occurs in older adults who have **diabetes,** symptoms of thyrotoxicosis will be blunted. Only detected when you do lab work.

Thyroid hormone deficiency (hypothyroidism).

What is hypothyroidism?

•Hypothyroidism is caused by any structural or functional derangement that interferes with the production of adequate levels of thyroid hormone

•Worldwide, the most common cause of hypothyroidism is dietary deficiency of iodine, while in most developed nations, autoimmune causes predominate

causes of hypothyroidism

PRIMARY

•Developmental (thyroid dysgenesis: PAX8, FOXE1, TSH receptor mutations)

•Thyroid hormone resistance syndrome (THRB mutations) (rare)

•Postablative

- Surgery, radioiodine therapy, or external irradiation

•Autoimmune hypothyroidism

- Hashimoto thyroiditis[*]

•Iodine deficiency [*]

•Drugs (lithium, iodides, p-aminosalicylic acid)[*]

•Congenital biosynthetic defect (dyshormonogenetic goiter)[*] (rare)

•Genetic defects in thyroid development

SECONDARY (CENTRAL)

•Pituitary failure (rare)

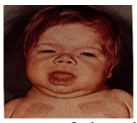
•Hypothalamic failure (rare)

Clinical manifestations of hypothyroidism

Cretinism:

refers to hypothyroidism developing in **infancy or early childhood**: Endemic cretinism, sporadic cretinism

Cretinism may come as an MCQ case, know the symptoms



Clinical features of cretinism include impaired development of the skeletal system and central nervous system, with severe mental retardation, short stature, coarse facial features, a protruding tongue, and umbilical hernia.

In early pregnancy it's more severe because the brain isn't developed yet

Myxedema:

Hypothyroidism developing in **older children and adults** results in a condition known as **myxedema**

Manifestations of myxedema include:

1-generalized apathy and mental sluggishness that in the early stages of disease may mimic depression.

2-Cold intolerance, obesity. The skin is cold and pale

3-Broadening and coarsening of facial features (matrix substances)

4-enlargement of the tongue, and deepening of the voice.

5-Constipation.

6-Pericardial effusions are common. In later stages, the heart is enlarged, and heart failure may supervene.

Laboratory evaluation

•Measurement of serum TSH is the most sensitive screening test for this disorder

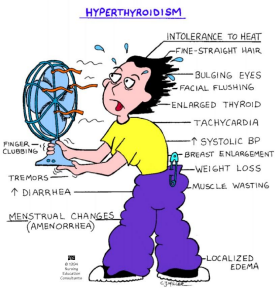
•The serum TSH is increased in primary hypothyroidism

•Serum T4 is decreased in patients with hypothyroidism of any origin.

Summary (made by us from the slides)

Hyperthyroidism

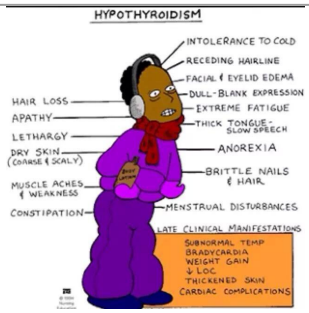
Excessive release of thyroid hormones (hyperthyroidism).
Thyrotoxicosis:Hypermetabolic state induced by excessive amounts of thyroid hormone ,over activity of the sympathetic nervous system
(Fever ,weight loss sweating ,diarrhea,arrhythmia,heat intolerance ,apathetic hyperthyroidism)
most common causes of thyrotoxicosis :
Diffuse hyperplasia of the thyroid associated with Graves disease
Hyperfunctional multinodular goiter
Hyperfunctional adenoma of the thyroid
Diagnosis:clinical and lab,serum TSH for screening ,free thyroid essay,Radioactive iodine



Extra

Hypothyroidism

Hypothyroidism is caused by any structural or functional derangement that interferes with the production of adequate levels of thyroid hormone
-autoimmune (hashimoto thyroiditis)most common in rich countries
-Iodine deficiency most common in poorer countries
Cretinism: infant hypothyroidism could be endemic or sporadic
Myxedema: If patient is older young ,adult
Myxedema:generalized apathy,mental sluggishness,mimic depression,obesity, cold intolerance ,tongue enlargement ,voice deepening ,constipation,pericardial effusion,heart enlargement and failure
LAB:measure TSH,TSH increases in primary hypothyroidism ,Serum T4 is decreased in patients with hypothyroidism of any origin.



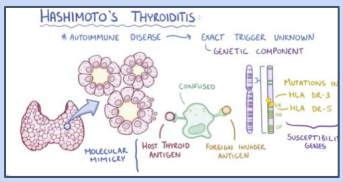
Extra

Thyroiditis

Clinically significant types of thyroiditis:
1-Hashimoto thyroiditis (or chronic lymphocytic thyroiditis)
2- Subacute (granulomatous) thyroiditis, (de Quervain).
3- Subacute lymphocytic thyroiditis.

Chronic Lymphocytic (Hashimoto) Thyroiditis

Overview



•Hashimoto thyroiditis is the most common cause of hypothyroidism in areas of the world where iodine levels are sufficient. Most common cause worldwide is iodine deficiency.
•It is characterized by gradual thyroid failure secondary to autoimmune destruction of the thyroid gland.
•It is most prevalent between the ages of 45 and 65 years and is more common in women than in men, with female predominance in a ratio of 10:1 to 20:1.

Pathogenesis
Picture "A"

•Hashimoto thyroiditis is caused by a breakdown in **self-tolerance** to thyroid autoantigens. Thus, circulating autoantibodies against thyroid antigens are present in the vast majority of patients. (Mediated by **T-Cells**)
It could be direct damage by CD8 cytotoxic T-cell. Or indirect by CD4 helper T-cell secretes IFN-gamma to activate macrophages and damage the cells. Or by antibodies.

Description

•A significant genetic component. It could affect more than member in the family
•Increased susceptibility to Hashimoto thyroiditis is associated with polymorphisms in multiple immune regulation–associated genes, the most significant of which is the linkage to **cytotoxic T lymphocyte– associated antigen-4** gene (**CTLA4**)

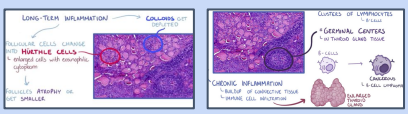
Clinical Features

•Painless enlargement of the thyroid, usually associated with some degree of hypothyroidism
•It may be preceded by transient thyrotoxicosis caused by disruption of thyroid follicles, with secondary release of thyroid hormones (hashitoxicosis). Early sign
•As hypothyroidism supervenes, **T4 and T3 levels progressively fall**, accompanied by a **compensatory increase in TSH**. Due to **chronic** lymphocytic infiltration
•Patients with Hashimoto thyroiditis often have other autoimmune diseases and are at increased risk for the development of B cell non-Hodgkin lymphomas.

Morphology
Gross

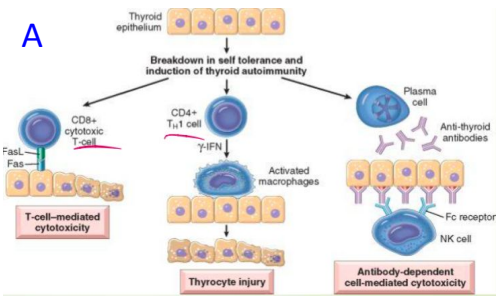
•Diffuse and symmetrical enlargement.
•The cut surface is **pale and gray-tan** in appearance, and the tissue is firm and somewhat friable. Picture "B"

Morphology
Microscopy

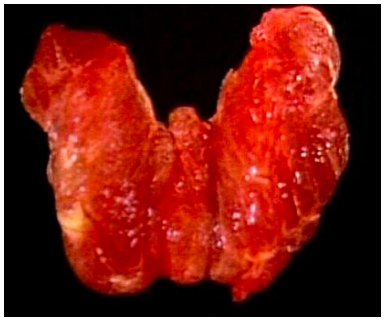


•Infiltration of the parenchyma by a **mononuclear inflammatory infiltrate** containing small **lymphocytes**, **plasma cells**, and well-developed **germinal centers.** Collection of B cells surrounded by T cells
•The thyroid follicles are atrophic and are lined in many areas by epithelial cells distinguished by the presence of abundant eosinophilic, granular cytoplasm, termed **Hürthle,** or **oxyphil cells.** a metaplastic response in which normal basophilic cells turn into eosinophilic cells full of mitochondria, but don't function.
• Interstitial connective tissue is increased and may be abundant. Less commonly, the thyroid is small and atrophic as a result of more extensive fibrosis **(fibrosing variant)**
•Unlike in Reidel thyroiditis, the fibrosis does not extend beyond the capsule of the gland.
In Reidel thyroiditis, fibrosis occurs go adjacent tissues as well.

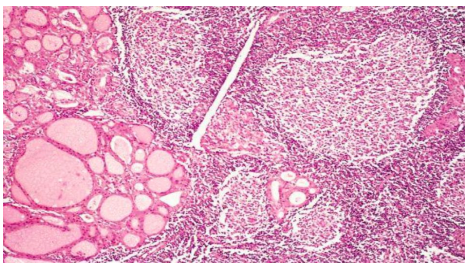
A



B



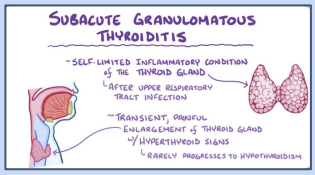
Morphology here inflammation on the right follicles on the left



Subacute Granulomatous (de Quervain) Thyroiditis

Painful (tender) thyroid, acute process, self limiting

Overview

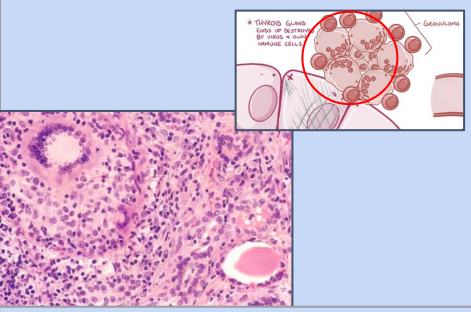


- Subacute thyroiditis is believed to be caused by a viral infection or an inflammatory process triggered by viral infections.
- most common between 30 and 50 years of age and, like other forms of thyroiditis, occurs more frequently in women than in men.
- A majority of patients have a history of an upper respiratory infection just before the onset of thyroiditis.
- The onset of this form of thyroiditis often is acute, characterized by pain in the neck (particularly with swallowing), fever, malaise, and variable enlargement of the thyroid.

Progression of the inflammation.

- Transient hyperthyroidism may occur, as in other cases of thyroiditis, as a result of disruption of thyroid follicles.
- The **leukocyte** count and **erythrocyte sedimentation rates** (ESR) are increased.
- With progression of disease and gland destruction, a transient hypothyroid phase may ensue.
- The condition typically is self-limited, with most patients returning to a euthyroid state within 6 to 8 weeks.
- Biopsy type? Fine Needle Aspiration (FNA)

Morphology



- The gland is firm, with an intact capsule, and may be unilaterally or bilaterally enlarged.
- Histologic examination reveals disruption of thyroid follicles, with extravasation of colloid[1] leading to a polymorphonuclear (neutrophils) infiltrate because it is acute., which is replaced over time by lymphocytes, plasma cells, and macrophages.
- The extravasated colloid provokes an exuberant granulomatous reaction with giant cells[2]
- Healing occurs by resolution of inflammation and fibrosis.

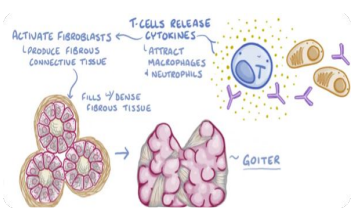
1: when colloid leaves the lumen, it's considered as a foreigner attracting macrophages.
2: composed of epithelioid macrophages (histiocytes).

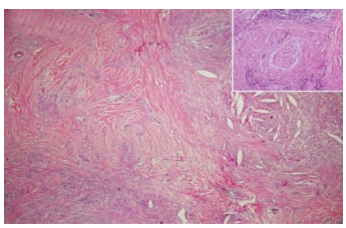
Subacute Lymphocytic Thyroiditis (only in female slides)

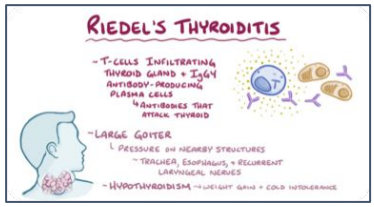
- In a subset of patients the onset of disease follows pregnancy (postpartum thyroiditis). This disease is most likely to be autoimmune in etiology.
- Painless neck mass or features of thyroid hormone excess.
- The histologic features consist of lymphocytic infiltration and hyperplastic germinal centers within the thyroid parenchyma.

Riedel thyroiditis

- Rare disorder of unknown etiology, is characterized by extensive fibrosis (important) involving the thyroid and contiguous neck structures.
- Clinical evaluation demonstrates a hard and fixed thyroid mass, simulating a thyroid neoplasm.
  -Dr note (this disease is very invasive and mimic Malignancy)







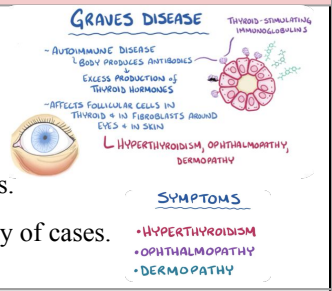
Graves disease

Graves disease is the most common cause of endogenous hyperthyroidism. It is characterized by a triad of manifestations:

1-Thyrotoxicosis, caused by a diffusely enlarged, hyperfunctional thyroid, is present in all cases.

2-An infiltrative ophthalmopathy with resultant exophthalmos is noted in as many as 40% of patients.

3-A localized, infiltrative dermopathy (sometimes designated pretibial myxedema) is seen in a minority of cases.



Epidemiology

-Graves disease has a peak incidence between the ages of 20 and 40, with women being affected up to seven times more commonly than men.
-Genetic factors are important in the causation of Graves' disease
Graves disease is associated with the presence of certain human leukocyte antigen (HLA) haplotypes, specifically HLA-DR3, and polymorphisms in genes whose products regulate T-cell responses, including the inhibitory T Cell receptor CTLA-4 .

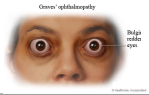
Pathogenesis

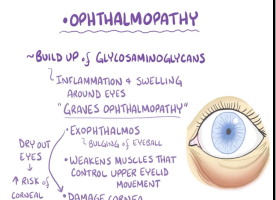
•**Graves disease is characterized** by a breakdown in self-tolerance to thyroid autoantigens, of which the most important is the TSH receptor.The result is the production of multiple autoantibodies, including:
1-Thyroid-stimulating immunoglobulin most common cause : An IgG antibody that binds to the TSH receptor and mimics the action of TSH, relatively specific for Graves disease.
2- Thyroid growth-stimulating immunoglobulins: Also directed against the TSH receptor.
3- TSH-binding inhibitor immunoglobulins: These anti-TSH receptor antibodies prevent TSH from binding to its receptor on thyroid epithelial cells and in so doing may actually **inhibit** thyroid cell function.

The coexistence of stimulating and inhibiting immunoglobulins in the serum of the same patient is not unusual—a finding that may explain why some patients with Graves disease spontaneously develop episodes of hypothyroidism. Graves' disease patients have mainly hyperthyroidism but sometimes they get episodes of hypothyroidism because of inhibiting antibodies

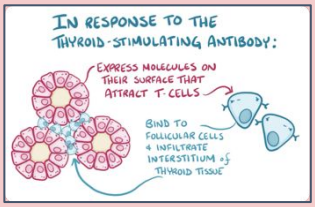
-In **Graves ophthalmopathy**, a result of several causes

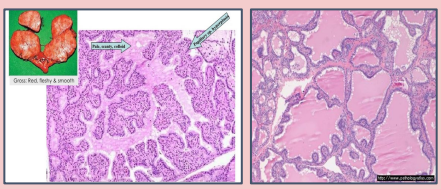
(1) marked infiltration of the retroorbital space by mononuclear cells
(2) inflammatory edema and swelling of extraocular muscles
(3) accumulation of extracellular matrix components
(4) increased numbers of adipocytes





Morphology





•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 (imp. it tells you that there's no invasion outside the thyroid)

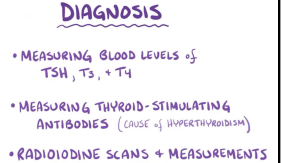
•On microscopic examination, the follicular epithelial cells in untreated cases are tall, columnar, and more crowded than usual. This crowding often results in the formation of small papillae. Such papillae lack fibrovascular cores, **in contrast with those of papillary carcinoma.**
•The colloid within the follicular lumen is pale, with scalloped margins."vacuolated".

•Lymphoid infiltrates, are present throughout the interstitium; germinal centers are common. Notice that it has germinal centers as in hashimoto, but the difference is that hashimoto has Hurthle cells "characteristic feature"

•The dermopathy, if present, is characterized by thickening of the dermis, as a result of deposition of glycosaminoglycans and lymphocyte infiltration.

Diagnosis

•Laboratory findings in Graves disease include elevated serum free T4 and T3 and depressed serum TSH.
•Because of ongoing stimulation of the thyroid follicles by TSIs, radioactive iodine uptake is increased, and radioiodine scans show a diffuse uptake of iodine



DIFFUSE AND MULTINODULAR GOITER

What is Goiter ?

Goiter: Enlargement of the thyroid, is the most common manifestation of thyroid disease.

- They reflect impaired synthesis of thyroid hormone, most often caused by dietary iodine deficiency
- Impairment of thyroid hormone synthesis leads to a compensatory rise in the serum TSH, causes hypertrophy and hyperplasia of thyroid follicular cells and, ultimately, gross enlargement of the thyroid gland.
- The compensatory increase in functional mass of the gland is enough to overcome the hormone deficiency, ensuring a euthyroid metabolic state in the vast majority of affected persons.
- If the underlying disorder is sufficiently the compensatory responses may be inadequate to overcome the impairment in hormone synthesis, resulting in goitrous hypothyroidism
- Goiters can be endemic or sporadic.

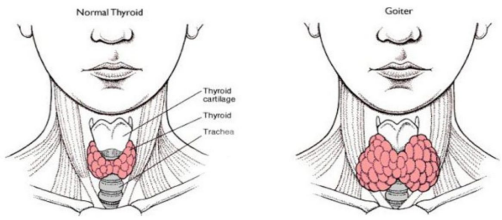
Types of Goiter

- Diffuse, symmetric enlargement of the gland **(diffuse goiter)**: The follicles are lined by crowded columnar cells, which may pile up and form projections
- Colloid-rich gland **(colloid goiter)**
- All long-standing diffuse goiters convert into **multinodular goiters.**
- Multinodular goiters typically are hormonally silent, although a minority (approximately 10% over 10 years) can manifest with thyrotoxicosis secondary to the development of autonomous nodules that produce thyroid hormone independent of TSH stimulation. This condition, known as toxic multinodular goiter or Plummer syndrome1, hyperfunctional toxic multinodular in which one of the nodule secretes the thyroid hormone independent from TSH and TRH.

1: في الاختبارات يحبون ذي الأشياء

Goiter can arise in the following settings:

1-Endemic goiter due to iodine deficiency
2-ingestion of certain food e.g. cabbage
3-Rare inherited defect in thyroid hormone synthesis
4-Drug induced



Multinodular goiter

-**Multinodular goiters** are multilobulated, asymmetrically enlarged glands, which may attain 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.

Clinical features

-The dominant clinical features of goiter are those caused by the mass effects of the enlarged gland.
-In addition to the obvious cosmetic problem of a large neck mass, goiters also may cause airway obstruction, dysphagia, and compression of large vessels in the neck
-A hyperfunctioning (toxic) nodule may develop within a long-standing goiter, resulting in hyperthyroidism.
-The incidence of malignancy in long-standing multinodular goiters is low (less than 5%) but not zero, and concern for malignancy arises with goiters that demonstrate sudden changes in size or associated symptoms (e.g., hoarseness) due to invasion of the laryngeal nerve, which is a scary sign.

Summary (made by us from the slides)

Hyperthyroidism

Excessive release of thyroid hormones (hyperthyroidism).
Thyrotoxicosis:Hypermetabolic state induced by excessive amounts of thyroid hormone ,over activity of the sympathetic nervous system
(Fever ,weight loss sweating ,diarrhea,arrhythmia,heat intolerance ,apathetic hyperthyroidism)

most common causes of thyrotoxicosis :
Diffuse hyperplasia of the thyroid associated with Graves disease
Hyperfunctional multinodular goiter
Hyperfunctional adenoma of the thyroid
Diagnosis:clinical and lab,serum TSH for screening ,free thyroid essay,Radioactive iodine

Hypothyroidism

Hypothyroidism is caused by any structural or functional derangement that interferes with the production of adequate levels of thyroid hormone

-autoimmune (hashimoto thyroiditis)most common in rich countries

-Iodine deficiency most common in poorer countries

Cretinism :infant hypothyroidism could be emdimic or sporadic

- If patient is older young ,adult:myxedema

Myxedema:generalized apathy,mental sluggishness,mimic depression,obesity, cold intolerance ,tongue enlargement ,voice deepening ,constipation,pericardial effusion,heart enlargement and failure
LAB:measure TSH,TSH increases in primary hypothyroidism ,Serum T4 is decreased in patients with hypothyroidism of any origin.

Thyroiditis:

1-Hashimoto thyroiditis

(or chronic lymphocytic thyroiditis). Most common cause if iodine is sufficient,autoimmune destruction of thyroid,self tolerance breaks down leads In circulating autoantibodies against thyroid T-cell mediated,
Has a genetic component (CTLA4)
Clinically:Painless enlargement,hashitoxicosis ,Fall in T4 and T3 and increase TSH
Risk of B cell non hodgkin lymphoma
Grossly :diffuse symmetrical enlargement,gray tan appearance friable
Microscopy :mononuclear inflammatory infiltrate within the parenchyma ,lymphocytes plasma cells, germinal centers,atrophy of the thyroid follicles ,Hurthle oxyphils,granular cytoplasm,and abundant eosinophils,fibrosing variant
Does not extend beyond the capsule (not like reidel thyroiditis)

2- Subacute (granulomatous) thyroiditis, (de Quervain).

-caused by viral infection (URTI),acute ,neck pain with swallowing
-transient hypothyroidism May occurs ,thyroid follicular distribution ,after that distribution we will not have thyroid gland any more so eventually we will have hypothyroidism
-High ESR and leukocytosis,self limited condition,Biopsy:FNA
Capsule is intact ,bilateral or unilateral enlargement
-microscopy:extravasated colloid leads in infiltration by polymorph,granuloma fibrosis when heald

3-Riedel thyroiditis

Rare,unknown cause,extensive fibrosis ,malignant like Mass effect,thyroid neoplasm stimulations
extend beyond the capsule

Graves disease

Graves disease is the most common cause of endogenous hyperthyroidism. It is characterized by a triad of manifestations:1-exophthalmos 2-dermopathy

3-hyperthyroidism

women more than man 20-40

Pathogenesis:self tolerance breaks down,multiple autoantibodies production ,IgG AB binds to TSHR,mimic action of TSH

-In Graves ophthalmopathy, a result of several causes

(1) marked infiltration of the retroorbital space by mononuclear cells
(2) inflammatory edema and swelling of extraocular muscles
(3) accumulation of extracellular matrix components
(4) increased numbers of adipocytes

-morphology:thyroid enlargment (hypertrophy +hyperplasia),intact capsules,in microscopy:tall, columnar, and more crowded than usual. This crowding often results in the formation of small papillae. Such papillae lack fibrovascular cores, in contrast with those of papillary carcinoma.,germinal center and lymphoid infiltrate
Laboratory findings in Graves disease include elevated
serum free T4 and T3 and depressed serum TSH.
Radioactive iodine uptake is increase because of TSI

DIFFUSE AND MULTINODULAR GOITER

Enlargement of the thyroid, is the most common manifestation of thyroid disease.impaired synthesis of thyroid,caused by dietary iodine deficiency leads to rise serum TSH,Types:Endemic and sporadic

Goiter either diffuse or colloid ,diffuse progress into multinodular

Goiter can arise in the following settings: 1-Endemic goiter due to iodine deficiency 2-ingestion of certain food e.g. cabbage 3-Rare inherited defect in thyroid hormone synthesis 4-Drug induced
Multinodular goiters :multilobulated, asymmetrically enlarged , may attain massive size.
mass effects of the enlarged gland can lead to different signs and symptoms (large neck mass, goiters also may cause airway obstruction, dysphagia, and compression of large vessels in the neck)

microscopic :-
-colloid-rich follicles lined by flattened, inactive epithelium
-areas of follicular epithelial hypertrophy and hyperplasia.
-low risk of malignancy
-toxic nodules may developed

Summary: pathoma

THYROID GLAND

I. THYROGLOSSAL DUCT CYST

A. Cystic dilation of thyroglossal duct remnant
1. Thyroid develops at the base of tongue and then travels along the thyroglossal duct to the anterior neck.
2. Thyroglossal duct normally involutes; a persistent duct, however, may undergo cystic dilation.
B. Presents as an anterior neck mass

II. LINGUAL THYROID

A. Persistence of thyroid tissue at the base of tongue
B. Presents as a base of tongue mass

HYPERTHYROIDISM

I. BASIC PRINCIPLES

A. Increased level of circulating thyroid hormone
1. Increases basal metabolic rate (due to increased synthesis of Na•-K• ATPase)
2. Increases sympathetic nervous system activity (due to increased expression of B1-adrenergic receptors)
B. Clinical features include
1. Weight loss despite increased appetite
2. Heat intolerance and sweating
3. Tachycardia with increased cardiac output
4. Arrhythmia (e.g., atrial fibrillation), especially in the elderly
5. Tremor, anxiety, insomnia, and heightened emotions
6. Staring gaze with lid lag
7. Diarrhea with malabsorption
8. Oligomenorrhea
9. Bone resorption with hypercalcemia (risk for osteoporosis)
10. Decreased muscle mass with weakness
11. Hypocholesterolemia
12. Hyperglycemia (due to gluconeogenesis and glycogenolysis)

II. GRAVES DISEASE

A. Autoantibody (IgG) that stimulates TSH receptor (type II hypersensitivity)
B. Leads to increased synthesis and release of thyroid hormone
I. Most common cause of hyperthyroidism
2. Classically occurs in women of childbearing age (20-40 years)
C. Clinical features include
I. Hyperthyroidism 2. Diffuse goiter-Constant TSH stimulation leads to thyroid hyperplasia and Hypertrophy (Fig. 15.1 A).
3. Exophthalmos and pretibial myxedema

Summary: pathoma

i. Fibroblasts behind the orbit and overlying the shin express the TSH receptor.
ii. TSH activation results in glycosaminoglycan (chondroitin sulfate and hyaluronic acid) buildup, inflammation, fibrosis, and edema leading to exophthalmos and pretibial myxedema.

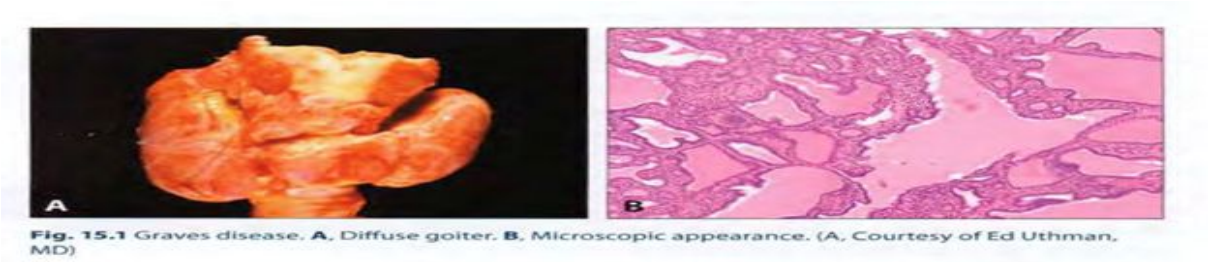


Fig. 15.1 Graves disease. **A**, Diffuse goiter. **B**, Microscopic appearance. (A, Courtesy of Ed Uthman, MD)

D. Irregular follicles with scalloped colloid and chronic inflammation are seen on histology
E. Laboratory findings include
1. Increase total and free T4, decrease TSH (free T J downregulates TRH receptors in the anterior pituitary to decrease TSH release)
2. Hypocholesterolemia
3. Increased serum glucose
F. Treatment involves B-blockers, thioamide, and radioiodine ablation.
G. Thyroid storm is a potentially fatal complication.
1. Due to elevated catecholamines and massive hormone excess, usually in response to stress (e.g., surgery or childbirth)
2. Presents as arrhythmia, hyperthermia, and vomiting with hypovolemic shock
3. Treatment is propylthiouracil (PTU), beta blockers, and steroids.
i. PTU inhibits peroxidase-mediated oxidation, organification, and coupling steps of thyroid hormone synthesis, as well as peripheral conversion ofT4 to Tl.

III. MULTINODULAR GOITER

A. Enlarged thyroid gland with multiple nodules
B. Due to relative iodine deficiency
C. Usually nontoxic (euthyroid)
D. Rarely, regions become TSH-independent leading to T4 release and hyperthyroidism ('Toxic goiter').

HYPOTHYROIDISM

1. CRETINISM

A. Hypothyroidism in neonates and infants
B. Characterized by mental retardation, short stature with skeletal abnormalities, coarse facial features, enlarged tongue, and umbilical hernia
I. Thyroid hormone is required for normal brain and skeletal development.
C. Causes include maternal hypothyroidism during early pregnancy, thyroid agenesis, dyshormonogenetic goiter, and iodine deficiency.
1. Dyshormonogenetic goiter is due to a congenital defect in thyroid hormone production; most commonly involves thyroid peroxidase

Summary: pathoma

II. MYXEDEMA

A. Hypothyroidism in older children or adults
B. Clinical features are based on decreased basal metabolic rate and decreased sympathetic nervous system activity.
1. Myxedema-accumulation of glycosaminoglycans in the skin and soft tissue; results in a deepening of voice and large tongue
2. Weight gain despite normal appetite
3. Slowing of mental activity
4. Muscle weakness
5. Cold intolerance with decreased sweating
6. Bradycardia with decreased cardiac output, leading to shortness of breath and Fatigue
7. Oligomenorrhea
8. Hypercholesterolemia
9. Constipation
C. Most common causes are iodine deficiency and Hashimoto thyroiditis; other causes include drugs (e.g., lithium) and surgical removal or radioablation of the thyroid.

THYROIDITIS

1. HASHIMOTO THYROIDITIS

A. Autoimmune destruction of the thyroid gland; associated with HLA-DRS
1. Most common cause of hypothyroidism in regions where iodine levels are adequate
B. Clinical features
I. Initially may present as hyperthyroidism (due to follicle damage)
2. Progresses to hypothyroidism;.decreased T and increased TSH
3. Antithyroglobulin and antithyroid peroxidase antibodies are often present {sign of thyroid damage).
C. Chronic inflammation with germinal centers and Hurthle cells (eosinophilic metaplasia of cells that line follicles) is seen on histology
D. Increased risk for B-cell (marginal zone) lymphoma; presents as an enlarging thyroid gland late in disease course

II. SUBACUTE GRANULOMATOUS (DE QUERVAIN) THYROIDITIS

A. Granulomatous thyroiditis that follows a viral infection
B. Presents as a tender thyroid with transient hyperthyroidism
C. Self-limited; rarely (15% of cases) may progress to hypothyroidism

III. REIDEL FIBROSING THYROIDITIS

A. Chronic inflammation with extensive fibrosis of the thyroid gland
B. Presents as hypothyroidism with a 'hard as wood,' nontender thyroid gland
C. Fibrosis may extend to involve local structures (e.g., airway).
I. Clinically mimics anaplastic carcinoma, but patients are younger {40s), and malignant cells are absent

Questions

Q1 : A 60-year-old woolen has been feeling tired and sluggish for more than a year. Her thyroid gland is not palpable on physical examination. She has a decreased serum level of T4. but her serum TSH concentration is greatly increased. Which of the following factors is important in the pathogenesis of this condition?
(A) irradiation to the neck during childhood.
(B) Anti-microsomal and anti-thyroglobulin antibodies .
(C) Prolonged iodine deficiency .
(D) Mutations in the RET protooncogene .
Answer : B

Q2 : Subacute granulomatous thyroiditis patients progress to an euthyroid state in 6-8 weeks. What does that mean?
(A) The patient is in a fulminant stage.
(B) The condition is self-limiting.
(C) Sky-high elevation of Thyroid hormones.
(D) No thyroid hormone at all.
Answer : B

Q3 : Plummer syndrome refer to which of the following?
(A) Autonomous thyroxine releasing nodules Independent of TSH.
(B) Colloid rich glands.
(C) Diffuse, symmetric enlargement of the gland.
(D) Silent Multinodular goiter.
Answer : A

Q4 : Exophthalmos with weak extraocular muscle movement occurs in a 20-year-old female and her identical twin sister. Their conditions develop within 3 years of each other, what is the most closely related laboratory finding?
(A) Decreased serum free T4 level .
(B) decreased serum calcium level .
(C) Decreased serum TSH level .
(D) Increased serum cortisol level.
Answer : C

Q5 :A 45-year-old female has a feeling of fullness in her neck but no other complaints. Physical examination confirms diffuse enlargement of the thyroid gland without any apparent masses, this enlargement & painless for more than a year. test for thyroid function reveal a normal free thyroxine (free Ts) and a slightly increased level of TSBA. The most likely cause for these findings is ?
(A) Toxic multinodular goiter .
(B) papillary carcinoma .
(C) subacute granulomatous thyroiditis.
(D) Diffuse nontoxic goiter.
Answer : D

Q6: A 2-year-old child has had failure to thrive. The child is short, with coarse facial features, a protruding tongue, and an umbilical hernia. Profound mental retardation is apparent as the child matures. These findings are best explained by a lack of ?
(A) Cortisol .
(B) Norepinephrine .
(C) Somatostatin .
(D) Thyroxine .
Answer : D

Q7 : A 22-year-old female presents with a 7-kg weight loss without dieting over the last 4 months, She has experienced increasing anxiety and nervousness without apparent changes in her job or home life. Physical examination reveals a diffusely enlarged thyroid gland. Radioiodine uptake shows a diffuse increase in uptake. The microscopic appearance of the lesion leading to these findings is shown here at high power. This lesion is most likely caused by:
(A) Antibodies against TSH receptor .
(B) Dietary deficiency of iodine
(C) Maternal deficiency in T4 .
(D) Irradiation to the neck .
Answer : A

Q8:Which one of the followings usually follows viral infection?
A. Florid lymphocytic
B. Idiopathic fibrosis
C. Riedel thyroiditis
D. Subacute granulomatous
Answer: D

Q9: A 2 year old boy was brought to pediatric surgeon because of large umbilical hernia. Clinical examination showed protruding tongue and unusual short stature. What is the diagnosis?
A. Acromegaly
B. Chronic lymphocytic thyroiditis
C. Cretinism
D. Hyperthyroidism
Answer: C

Q10: A 26 lady went to an endocrinologist because of a large and slightly nodular thyroid gland, fine needle aspiration (FNA) has showed small and large lymphocytosis, plasma cells and hurthle cells. What is the most likely diagnosis?
A. Hashimoto thyroiditis
B. Atypical follicular adenoma
C. Grave's disease
D. Granulomatous thyroiditis
Answer: A

Q11: Which of the following histopathological features expected to be seen in endemic goiter?
A. Chronic inflammation with little colloid and scattered giant cells
B. Flattened thyroid epithelium lining with large amounts of colloid
C. Columnar epithelial cells with scalloped colloid appearance
D. Fibrotic thyroid with mild inflammation
Answer: B

Q12: A 39 years old woman came with heat intolerance, palpitation. Laboratory tests showed elevated T3. The patient underwent a thyroidectomy. What are the possible histopathological features?
A. Hürthle cells
B. cytoplasmic inclusion
C. bifid nuclei (coffee bean like)
D. lymphocytosis
Answer: D

Q13: What is the most common etiology of the endemic colloid goiter?
A. Iodine deficiency
B. Radioactive iodine
C. Drug-induced
D. Inherited defect in thyroid hormone synthesis
Answer: A

Questions

14Q : Which of the following tests should be done first when assessing the functional status of the thyroid gland?
(A) A total T4 level .
(B) Total triiodothyruninc T3 level .
(C) Thyroid-stimulating hormone (TSH) level .
(D) Fine-needle aspiration .
Answer : C

15Q:A 68-year-old male has end-stage. renal disease as a consequence of dominant polycystic kidney disease (DPKD). He has undergone hemodialysis three time, per week for the past 6 years. Which of the following endocrine lesions is the most likely complication of his chronic renal failure?
(A) Multinodular goiter .
(B) Islet cell hyperplasia .
(C) Adrenal atrophy .
(D) Parathyroid hyperplasia .
Answer : D

16Q:Which of the following is true about Hashimoto's Thyroiditis?
(A)Painful enlargement.
(B) Always preceded by transient thyrotoxicosis.
(C) Decrease in TSH.
(D) Associated with other autoimmune diseases .
Answer : D

Q17 : 55 female patient suffering from diffuse thyroid enlargement, investigation shows circulating thyroid antibodies, fine needle aspiration to biopsy the thyroid will show which ONE of the following under the microscope:
A. Diffuse fibrosis and destruction of follicular cells
B. Plasmolymphatic infiltration and hurtle cells
C. Hyperplasia of thyroid due to thyroid adenoma
D. Tall columnar cells with Congo red stain
Answer: B

Q18: A 28 year old woman complained from enlarged thyroid gland associated with unexplained tremor and excessive sweating. A thyroidectomy was performed and showed thyroid follicle with prominent infolding which are lined by cuboidal to columnar cells with vacuolated colloid in the lumen. What is the most likely diagnosis?
A. Hashimoto's thyroiditis
B. Papillary carcinoma
C. Nodular colloid goiter
D. Thyrotoxicosis
Answer: D

Q19: A 38 year old woman was referred to the endocrinologist because of diffuse thyroid enlargement. Thyroid function tests were consistent with hypothyroidism. Biopsy showed numerous mature lymphocytes, plasma cells and benign thyroid follicles showing Hurthle cell change. Which of the following is the most likely etiology for the patient's disease?
A. Dietary deficiency of Iodine.
B. Autoimmune destruction of thyroid follicles.
C. Idiopathic hypothyroidism.
D. Neoplastic proliferation of B lymphocyte.
Answer: B