Endocrine system 2024
Thyroid gland part 1

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Diseases of thyroid gland

Same general rules of all endocrine glands!(refer to lecture 1)

- Mass effect.
- Hyperthyroidism (thyrotoxicosis).
- Hypothyroidism.

- Again, there is no relation between mass effect and level of hormonal production

Thyroid diseases

1. ***Mass effect***: enlargement can be due to: inflammation, neoplasms, autoimmune diseases. (details later)

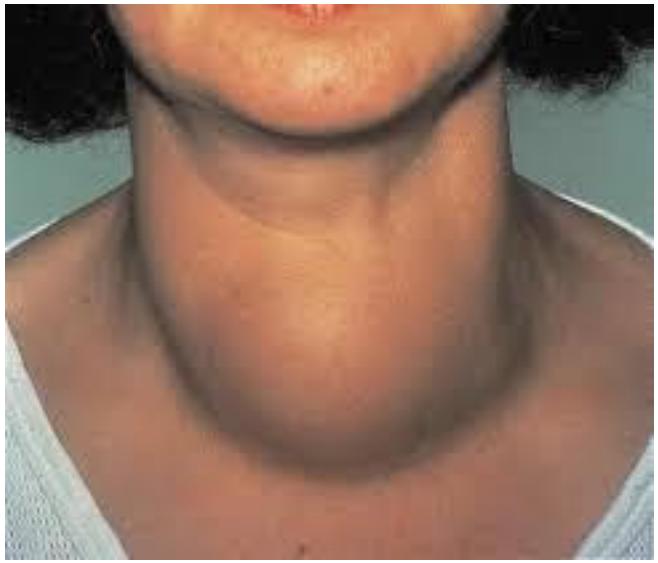
   Thyroid enlargement, due to any cause is called: **goiter.**

AGAIN: enlarged gland doesn't necessarily mean increased hormone production.

2. ***Hyperthyroidism and thyrotoxicosis.***

3. ***Hypothyroidism.***

Goiter: enlarged thyroid.. Regardless of the cause.



Clinical manifestations of hyperthyroidism (thyrotoxicosis)

- Thyroid hormones increase basal metabolic rate, increase appetite, increase breakdown of fat and glucose
- Also increase heart rate, cause hypertension
- Increase body temperature

- SO if these hormones are increased you expect to see a wide range of symptoms.

Clinical manifestations of thyrotoxicosis

a. Constitutional symptoms : warm flushed skin, heat intolerance and excessive sweating ,weight loss despite increased appetite.

b. Malabsorption, and diarrhoea (because of increased intestinal motility)

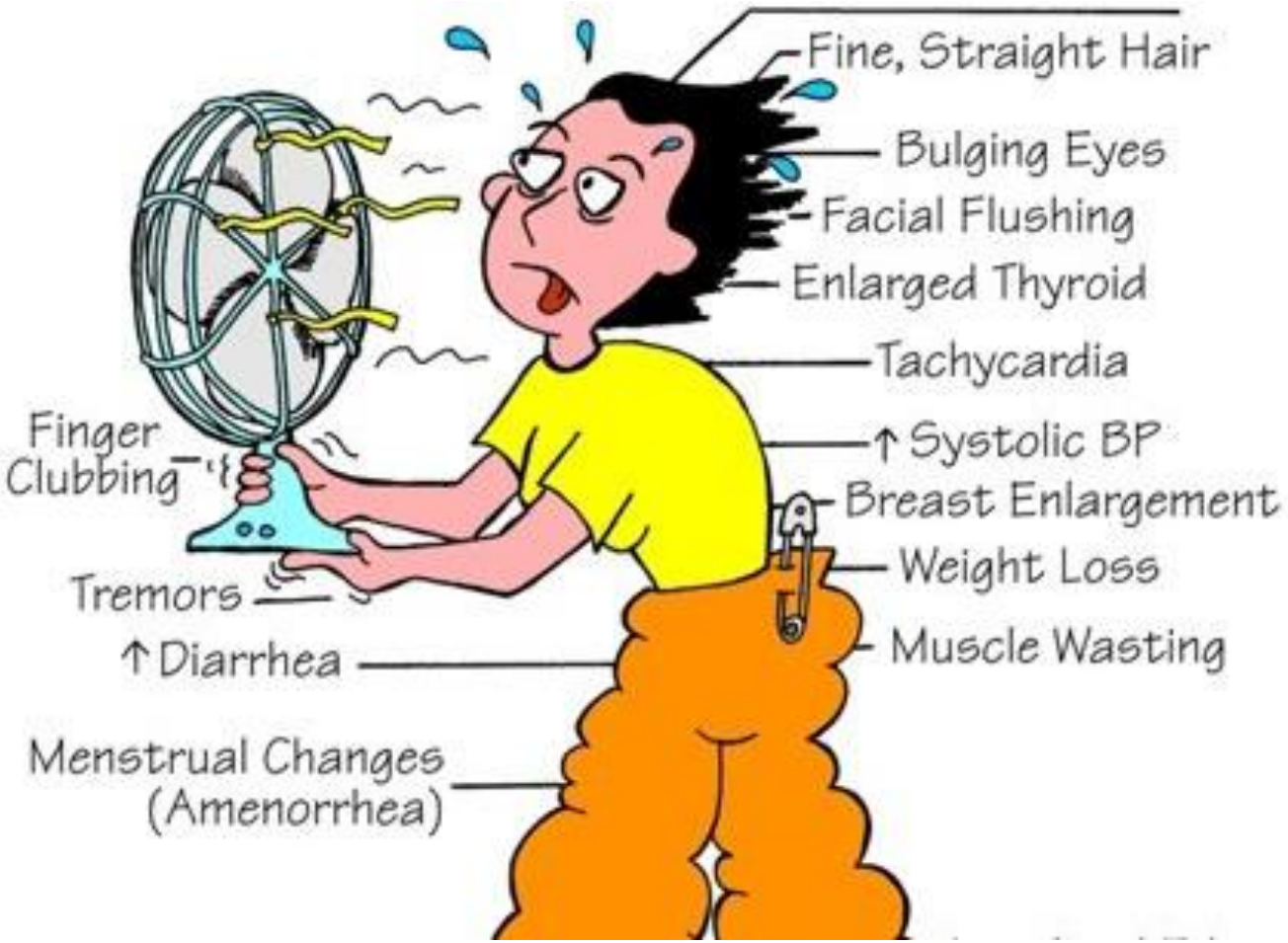
c. Tachycardia and elderly patients may develop heart failure due to aggravation of pre-existing heart disease

d. Nervousness, tremor, and irritability.

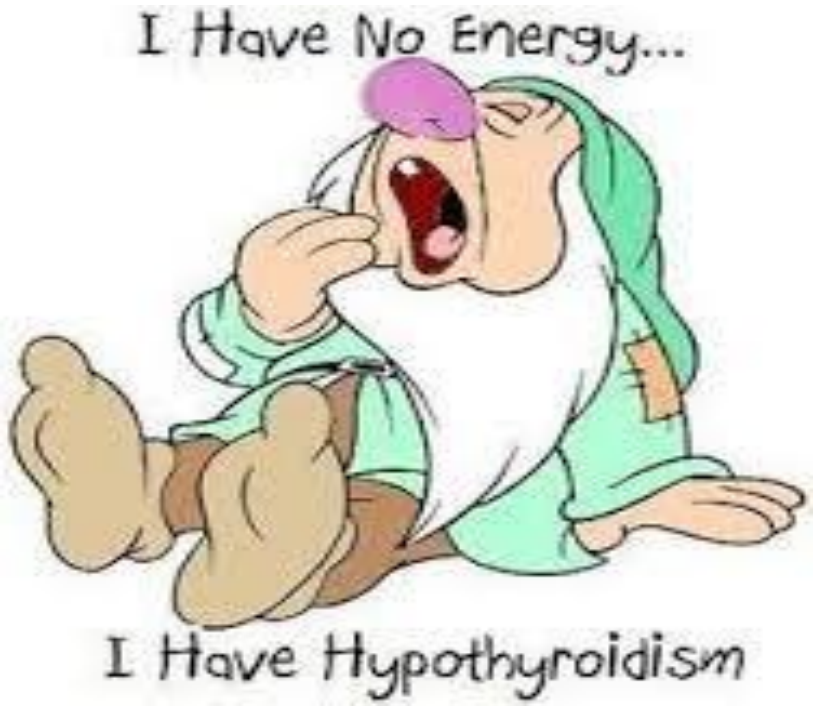
e. A wide, staring gaze and lid lag because of sympathetic overstimulation of the levator palpebrae superioris

f. 50% develop proximal muscle weakness (thyroid myopathy).

hyperthyroidism



hypothyroidism



HYPOTHYROIDISM

Primary causes

a. - Worldwide, the most common cause of hypothyroidism is dietary deficiency of iodine.

b. In most developed countries, autoimmune diseases predominate such as Hashimoto thyroiditis

c. Genetic defects such as *Thyroid dysgenesis or* congenital biosynthetic defect (dyshormogentic goitre).

Secondary causes: Pituitary or hypothalamic disorder.

hypothyroidism

It causes two clinical syndromes.

- **Cretinism**.. Hypothyroidism in infancy and early childhood
- **Myxedema**… hypothyroidism in older children and adults.

- The difference of features of hypothyroidism among these age groups is because thyroid hormones are vital early in life for brain and body development.

Cretinism :*R*efers to hypothyroidism developing in infancy or early childhood

1. Endemic cretinism: in dietary iodine deficiency is endemic, including mountainous areas (the Himalayas)
2. *Sporadic cretinism.* Caused by enzyme defects that interfere with thyroid hormone synthesis

Clinical features of cretinism include:

- Impaired development of skeletal system- short stature,
- Coarse facial features, protruding tongue, umbilical hernia.
- Central nervous system problems , with mental retardation

M*yxedema.* or Gull syndrome :

a. cold intolerance and obesity

b. Generalized apathy and mental sluggishness that in the early stages of disease may mimic depression

c. Broadening and coarsening of facial features

d. Enlargement of the tongue, and deepening of the voice.

e. Bowel motility is decreased, resulting in constipation.

f. Pericardial effusions are common; in later stages, the heart is enlarged, and heart failure may supervene.

g. Mucopolysaccharide-rich edematous fluid accumulates in skin, subcutaneous tissue, and number of visceral sites

Thyroiditis.

- = inflammation of the thyroid gland
- Several types:
- 1. Chronic Lymphocytic (Hashimoto) Thyroiditis
- 2.Subacute Granulomatous (de Quervain) Thyroiditis
- 3. Subacute Lymphocytic Thyroiditis
- 4.Riedel thyroiditis

1.Hashimoto thyroiditis.. Named after a Japanese doctor.

Chronic Lymphocytic (Hashimoto) Thyroiditis

- *Is the most common cause of hypothyroidism in areas of the world where iodine levels are sufficient.*
- 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

***NOTE: ALL THYROID DISEASES ARE MORE IN WOMEN**

- It can occur in children and is a major cause of non-endemic goiter in children

. A significant genetic component is supported by the

a. Concordance of disease in 40% of monozygotic twins,

b. the presence of circulating antithyroid antibodies in 50% of asymptomatic siblings of affected patients .

- ***Clinically*** ,

1. ***Painless*** *thyroid enlargement associated with some degree of hypothyroidism,*
2. - In the usual clinical course, hypothyroidism develops gradually

- Patients with Hashimoto thyroiditis often :

1. Have *other autoimmune diseases*
2. Are at *increased risk for the development of B cell non-Hodgkin lymphomas* within the thyroid gland.

Note:

- The relationship between Hashimoto disease and thyroid epithelial cancers remains controversial, with some morphologic and molecular studies suggesting a predisposition to papillary carcinomas

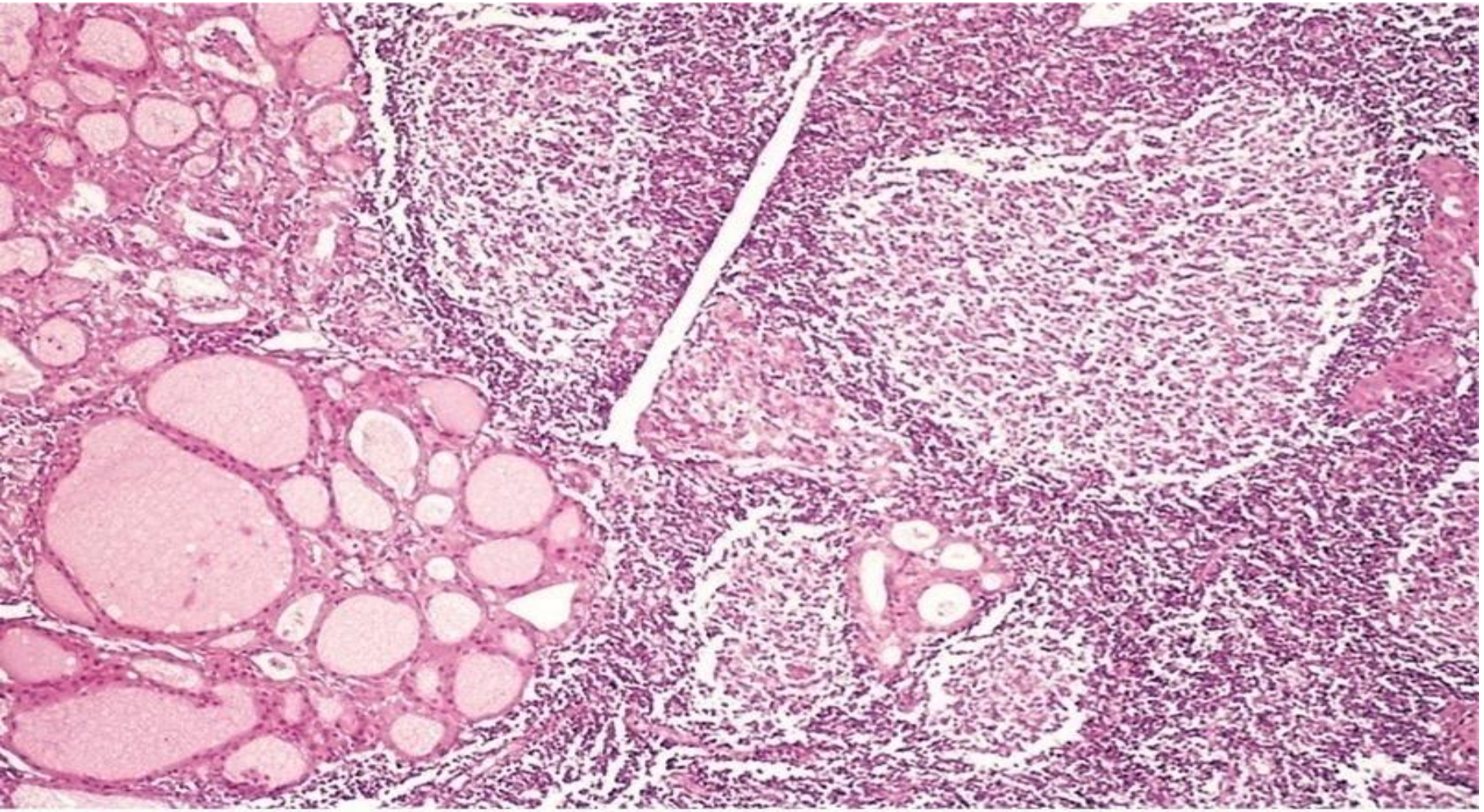
- Gross(macroscopic) features:

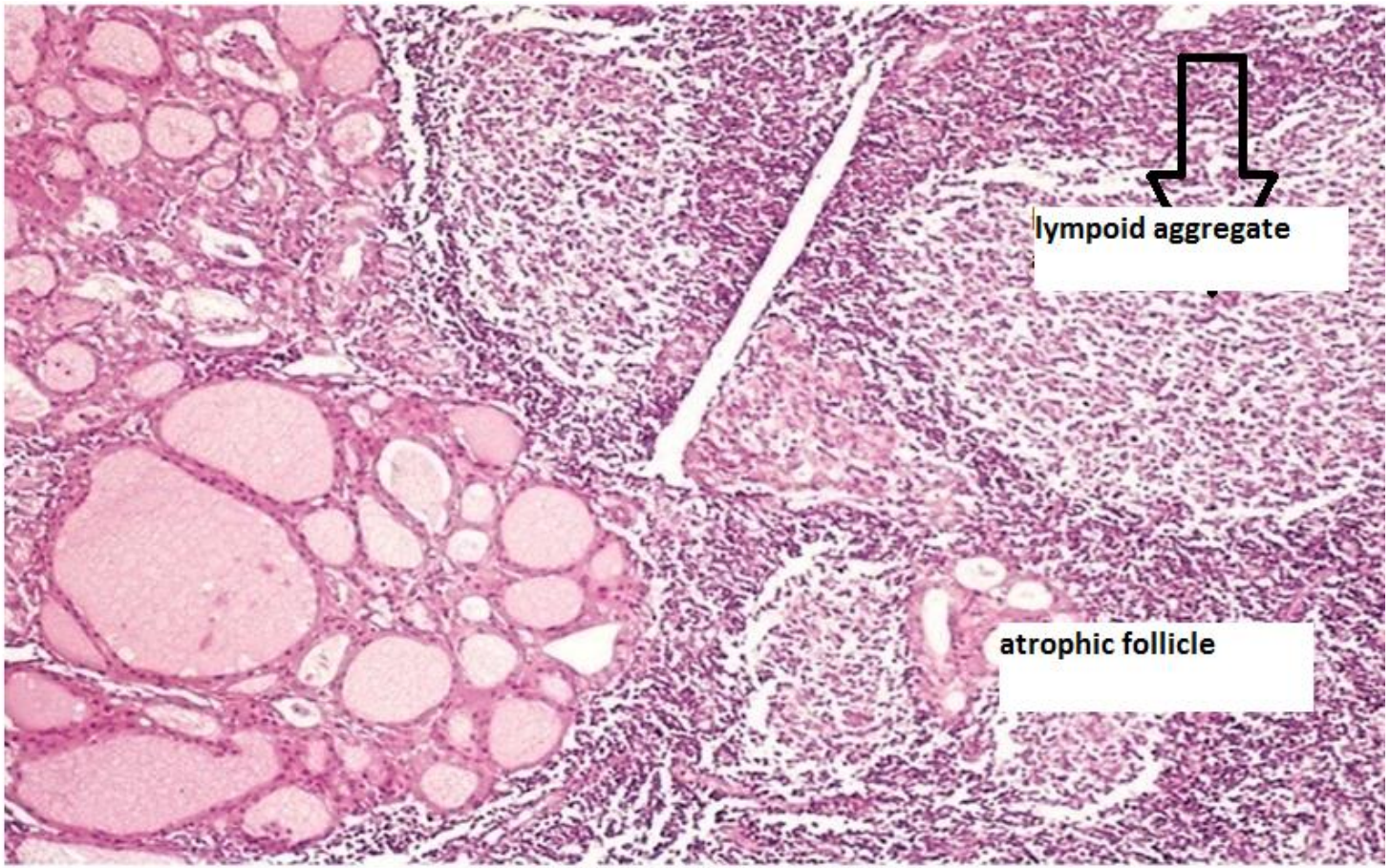
- Diffuse and symmetric enlargement of the thyroid but localized enlargement may be seen in some cases to raise suspicion for neoplasm

Microscopic examination reveals

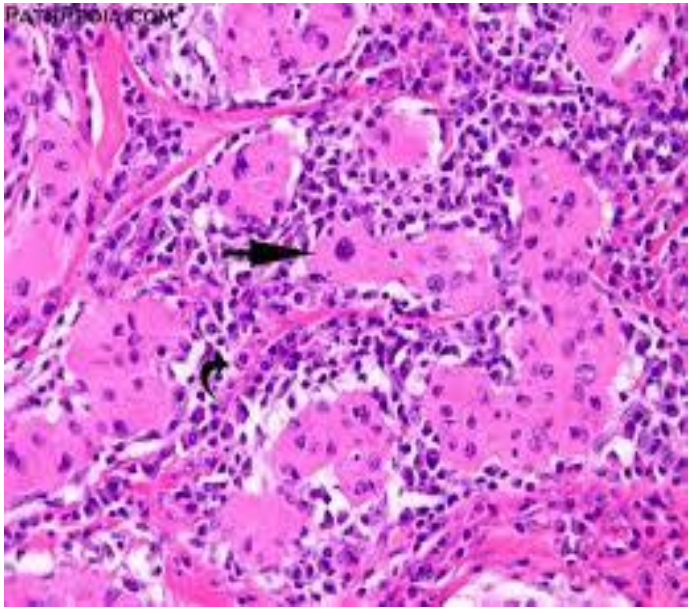
1. Infiltration by small lymphocytes, plasma cells, and well-developed germinal centers
2. The thyroid follicles are atrophic
3. Some follicles are lined by epithelial cells with abundant eosinophilic, cytoplasm, termed Hürthle cells and these Hurthle cells have numerous mitochondria

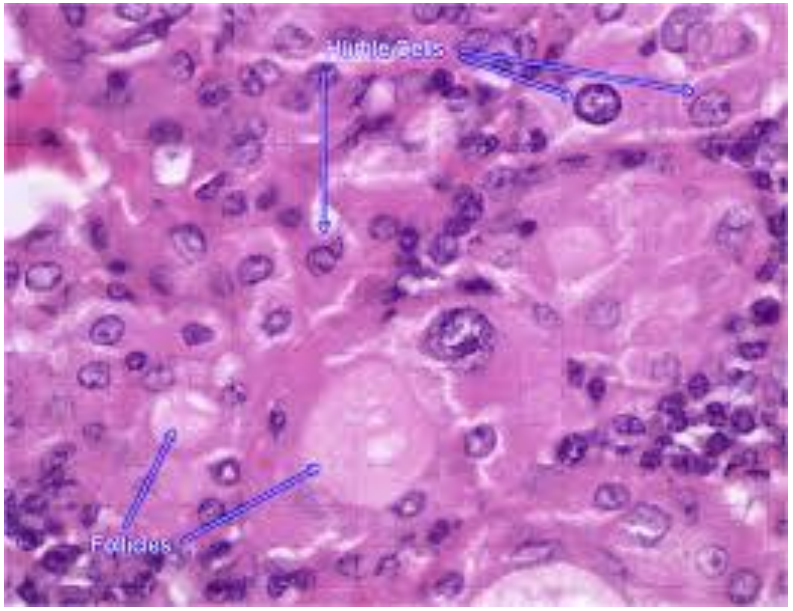
Hashimoto thyroiditis





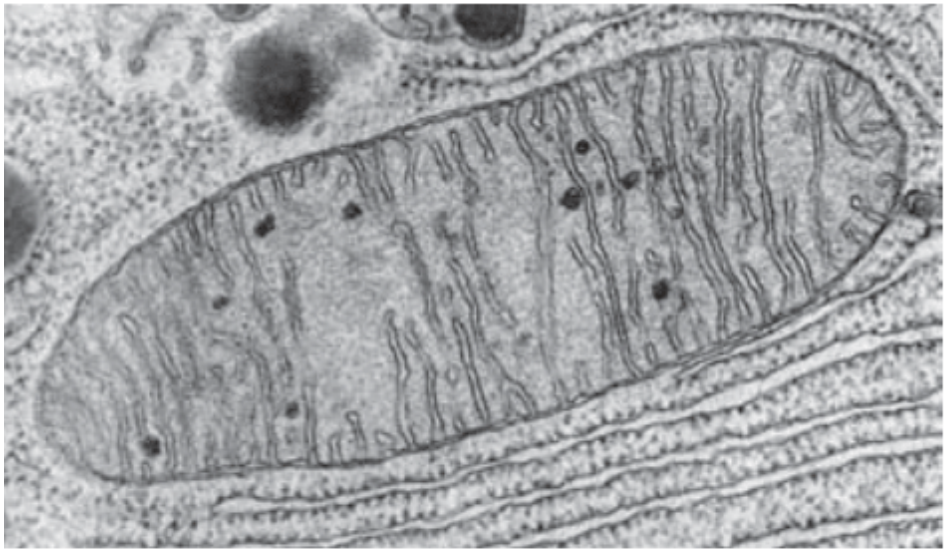
Hurthle cells: large cells with abundant eosinophilic cytoplasm, due to increased mitochondria





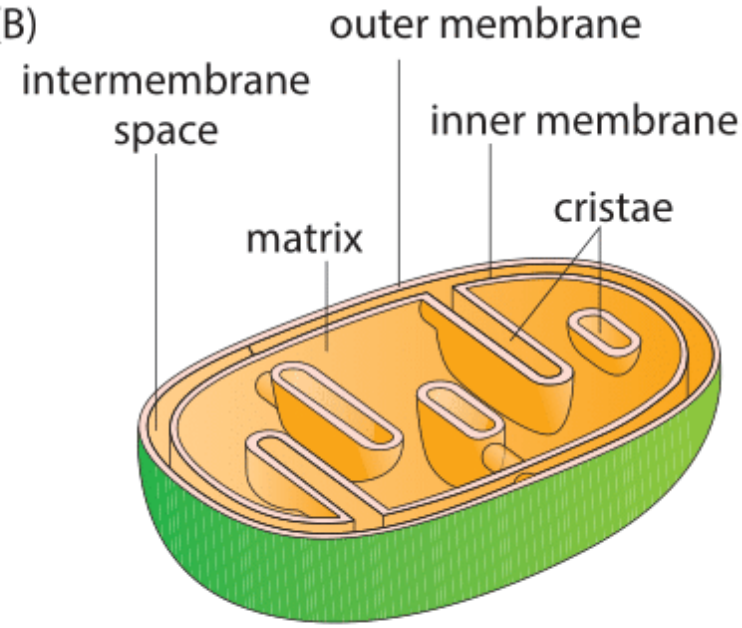
Hurthle cell cytoplasm is full of mitochondria

(A)



0.5 µm

(B)



3-D view of mitochondrion

2. Subacute Granulomatous (de Quervain) Thyroiditis

- Is much less common than Hashimoto disease
- Is most common between the ages of 30 and 50 and,
- More frequently in women than in men.
- Is believed to be caused by a viral infection and a majority of patients have a history of an upper respiratory infection just before the onset of thyroiditis.

Gross- The gland has intact capsule, and may be unilaterally or bilaterally enlarged.

- Clinical Features :

-Acute onset characterized by neck pain (with swallowing)

- Fever, malaise (tiredness), and variable enlargement of the thyroid.

- Transient hyperthyroidism may occur as a result of disruption of follicles and release of excessive hormones.

- The leukocyte count is increased.

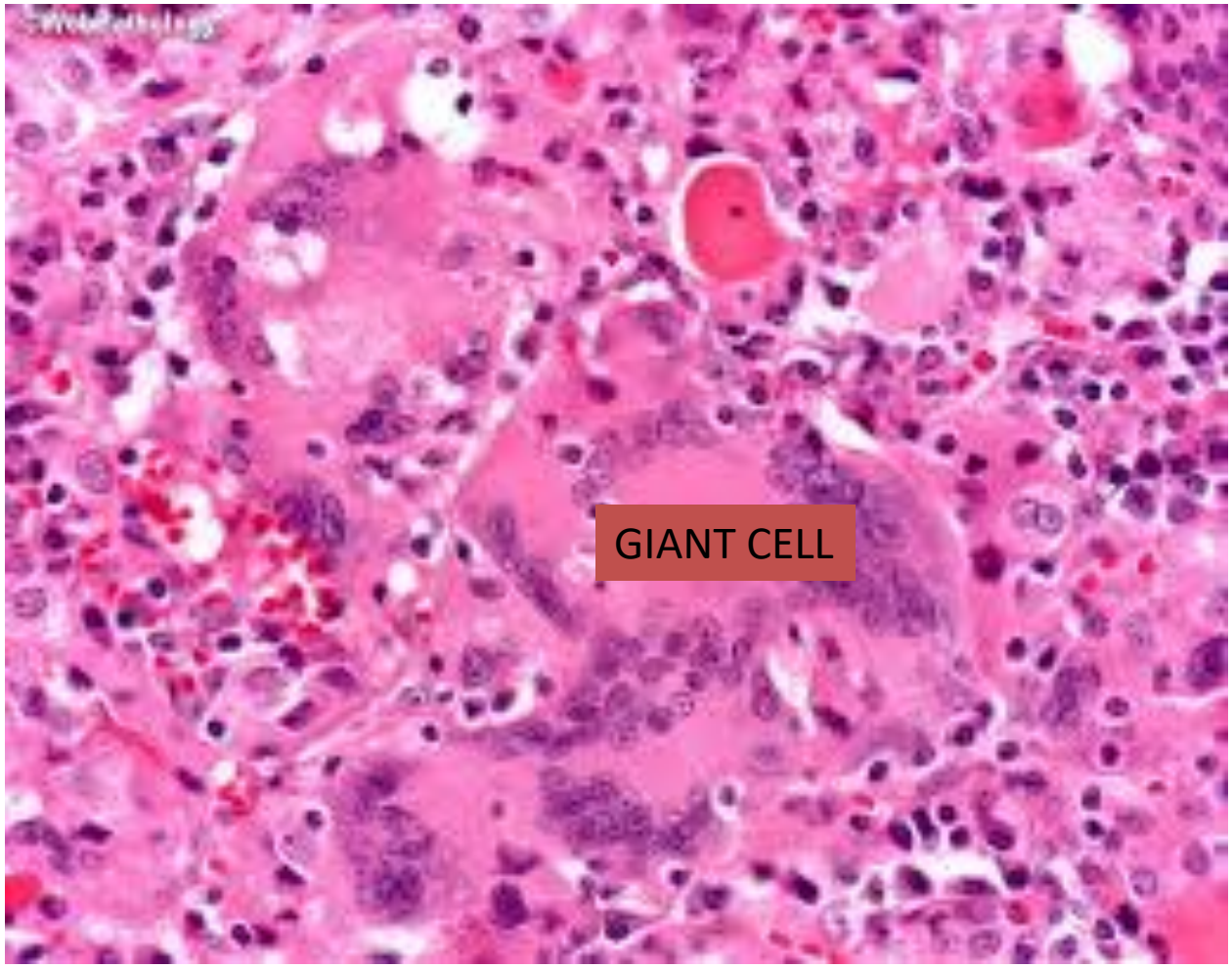
- With progression of disease and gland destruction, a transient hypothyroid phase may ensue.

- The condition typically is self-limited, with most patients returning to a euthyroid state within 6 to 8 weeks

Histologic examination reveals

1. Disruption of thyroid follicles, with extravasation of colloid leading to a neutrophilic infiltrate, which is replaced by lymphocytes, plasma cells, and macrophages.
2. The extravasated colloid provokes a granulomatous reaction with giant cells that contain fragments of colloid.
3. Healing occurs by resolution of inflammation and fibrosis.

Subacute granulomatous thyroiditis



3. Subacute Lymphocytic Thyroiditis :

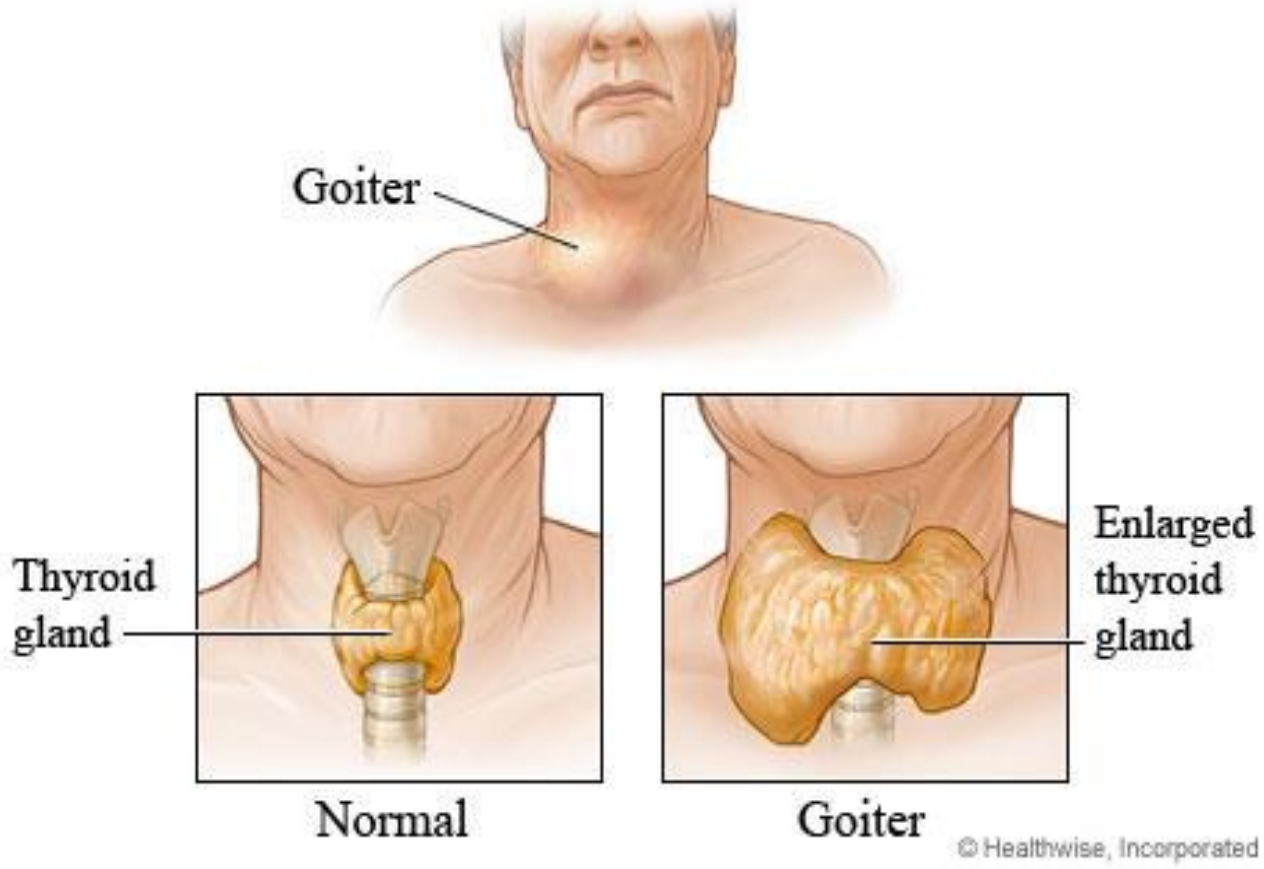
- Also is known as *silent* or *painless* thyroiditis;
- And in a subset of patients the onset of disease follows - pregnancy (*postpartum thyroiditis*).
- Most likely to be autoimmune because circulating antithyroid antibodies are found in a majority of patients
- It mostly affects middle-aged women, who present with a *painless* neck mass or features of thyrotoxicosis

4. Riedel thyroiditis,:

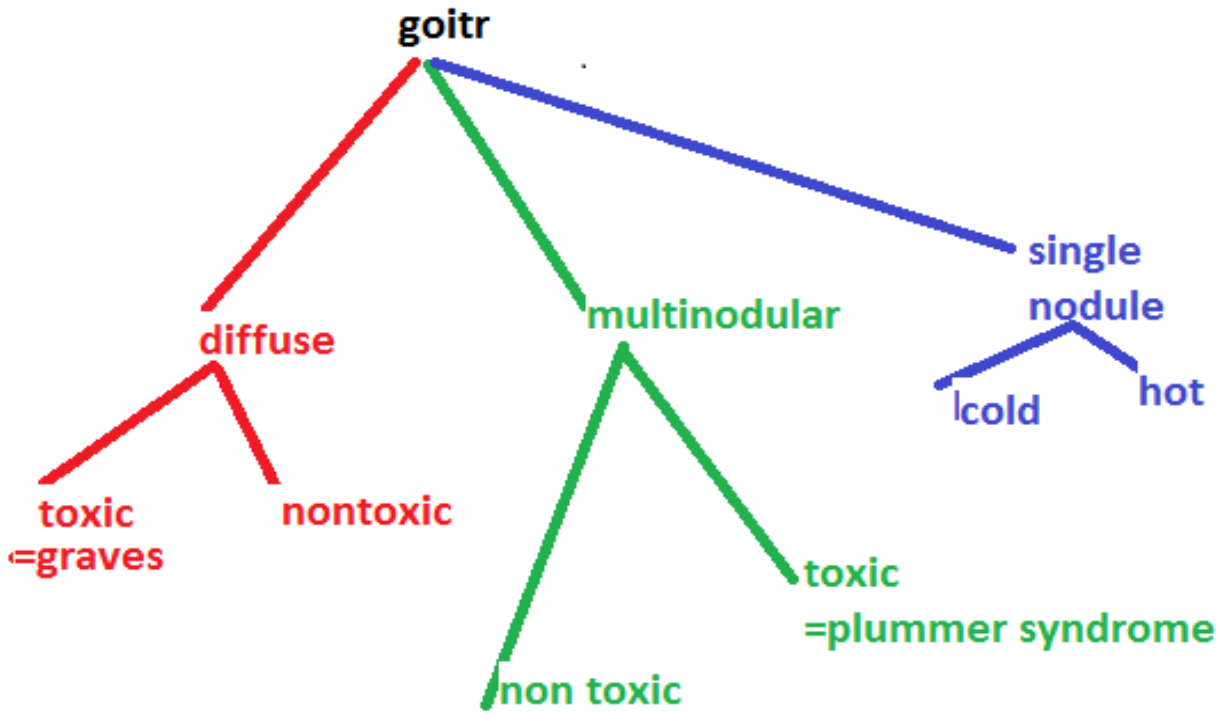
A rare disorder of unknown etiology,

- Characterized by extensive fibrosis involving the thyroid and adjacent structures simulating a thyroid neoplasm
- May be associated with idiopathic fibrosis in other parts of the body, such as the retroperitoneum
- The presence of circulating antithyroid antibodies in most patients suggests an autoimmune etiology

Goiter


Goiter
Thyroid gland
Enlarged thyroid gland
Normal
Goiter
© Healthwise, Incorporated

Goiter


goitr
diffuse
multinodular
single
nodule
toxic
=graves
nontoxic
cold
hot
toxic
=plummer syndrome
non toxic

Graves disease

- Named after an Irish surgeon: Robert Graves.
- Robert Invented the seconds-hand on watches and he used the timing of the pulse using the watch.
- Introduced giving food and liquids to patients with fever instead of withholding nourishment.
- One of the first doctors to introduce bedside learning.

GRAVES DISEASE

The most common cause of endogenous hyperthyroidism with a peak incidence in women between the ages of 20 and 40.

Triad of manifestations:

A. Thyrotoxicosis, All patients

B. Localized, infiltrative dermopathy (pretibial myxedema), minority of cases and involves the skin overlying the shins, and manifests as scaly thickening

C. Infiltrative ophthalmopathy with resultant exophthalmos in 40% of patients

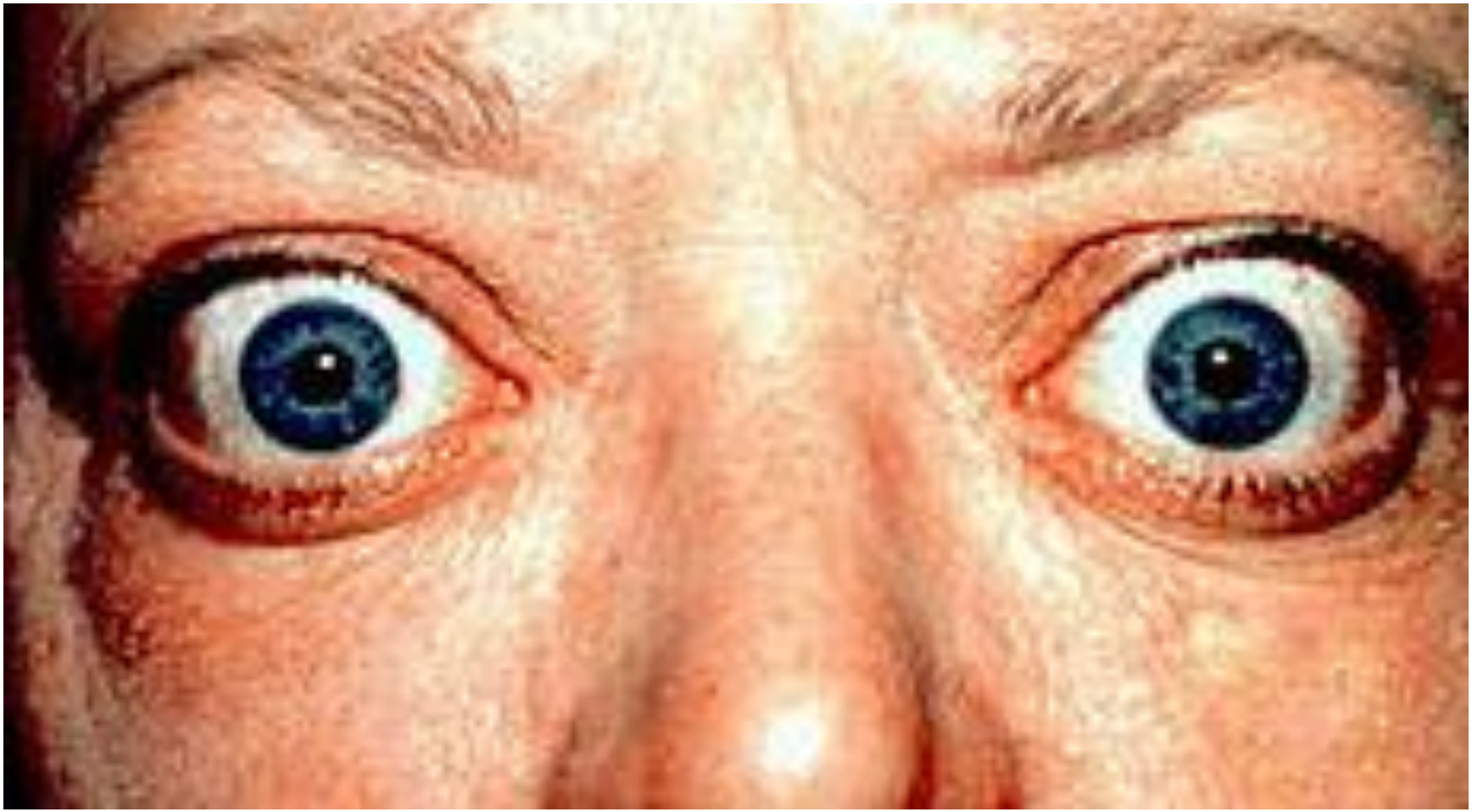
Exophthalmos is the result of increased volume of the retro-orbital connective tissues by

1. Marked infiltration of T cells with inflammatory edema
2. Accumulation of glycosaminoglycans
3. Increased numbers of adipocytes (fatty infiltration).

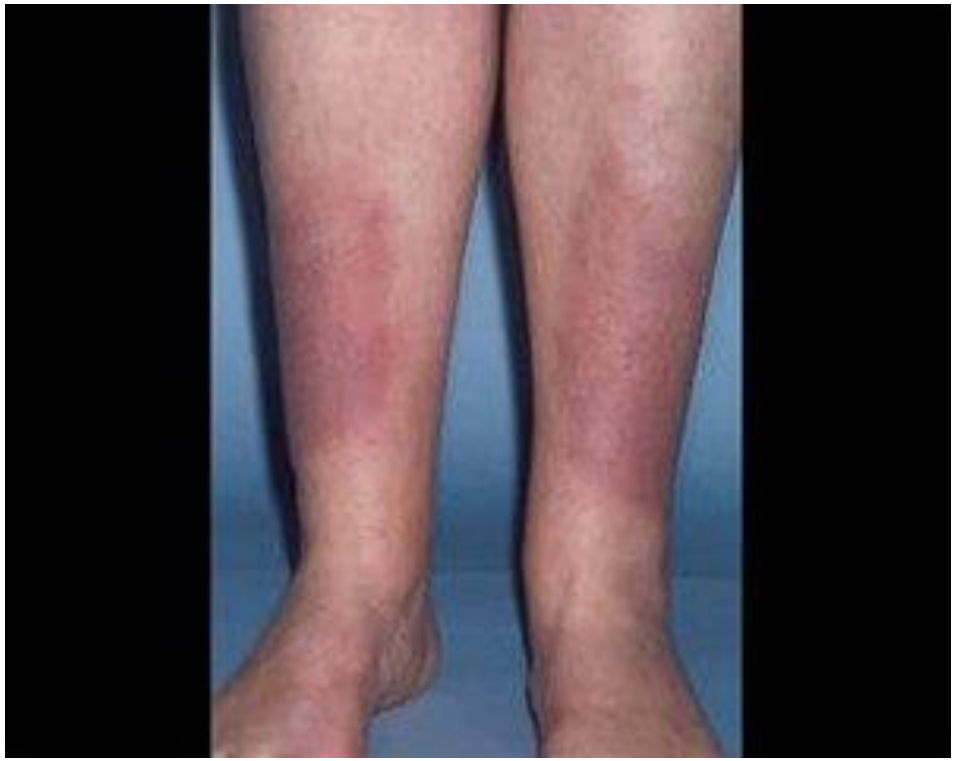
- These changes displace the eyeball forward, potentially interfering with the function of the extraocular muscles

- Exophthalmos may persist after successful treatment of the thyrotoxicosis, and may result in corneal injury.

exophthalmus



Pretibial myxedema



PATHOGENESIS :- Genetic factors are important in the causation of Graves disease, the incidence is increased in relatives of affected patients, and the concordance rate in monozygotic twins is 60%.

- A genetic susceptibility is associated with the presence of HLA-DR3.
- it is characterized by a breakdown in self-tolerance to thyroid autoantigens, and is the production of multiple autoantibodies

Autoantibodies in GRAVES :

1. Thyroid-stimulating immunoglobulin:

- An IgG antibody binds to the TSH receptor and mimics the action of TSH, with resultant increased hormones

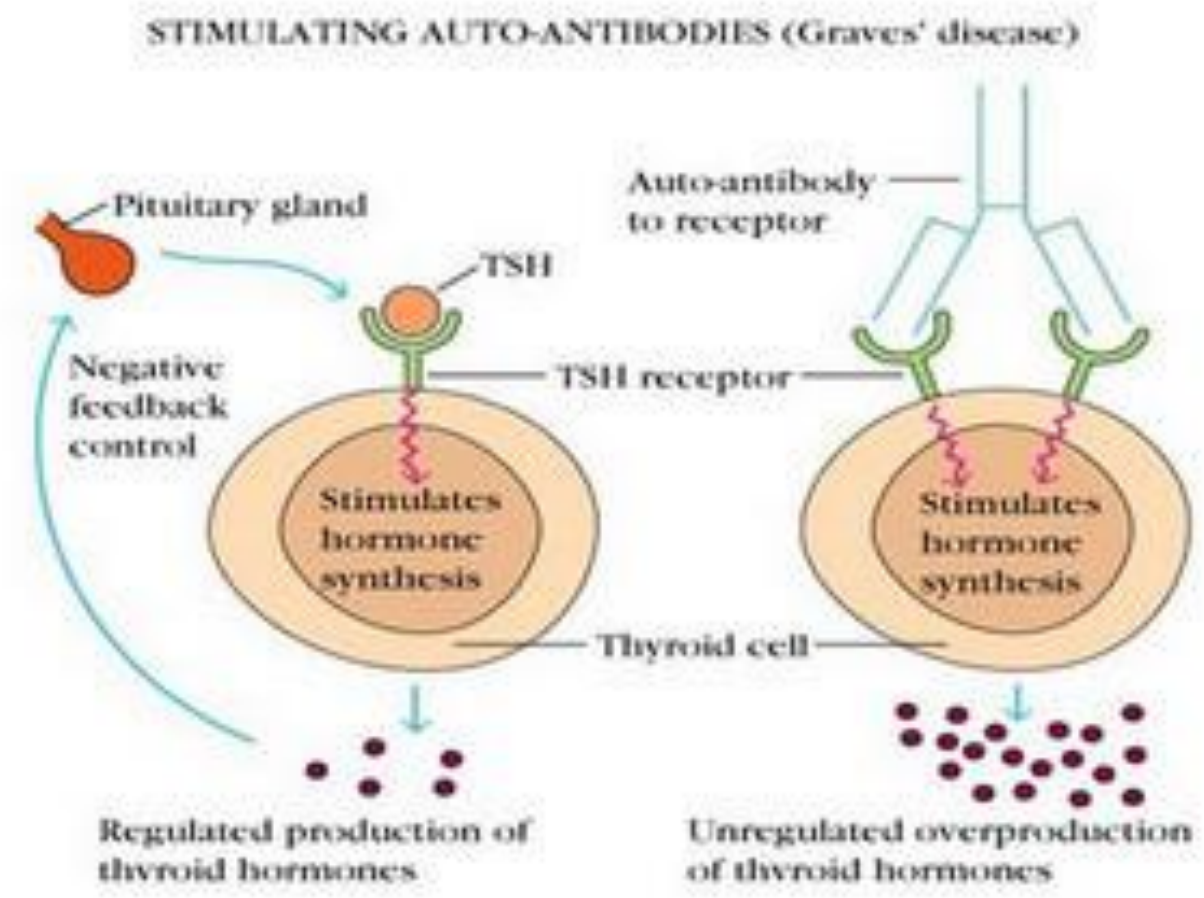
2. Thyroid growth-stimulating immunoglobulins:

- Directed against the TSH receptor, and have been implicated in the proliferation of follicular epithelium

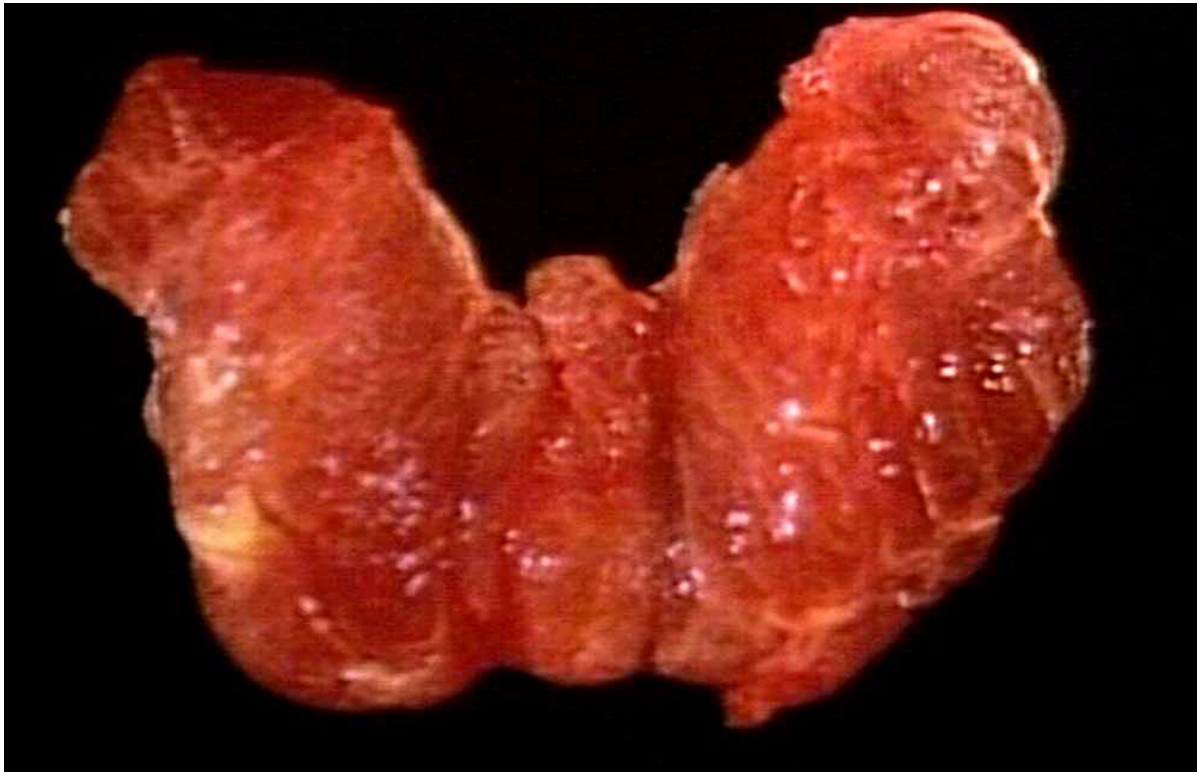
3. TSH-binding inhibitor immunoglobulins:

- Prevent TSH from binding to its receptor on thyroid cells and in so doing may actually inhibit thyroid cell function, a finding explains why some patients with Graves spontaneously develop episodes of hypothyroidism.

Note the autoantibodies in Grave's cause stimulation of hormone synthesis



Gross: Diffuse Symmetrical enlargement of the thyroid gland with intact capsule,



On microscopic examination,

a. The follicular cells in untreated cases are tall and crowded.

b. Lymphoid infiltrates, consisting predominantly of T cells, with few B cells and plasma cells are present throughout the interstitium; with formation of germinal centers.

DIFFUSE AND MULTINODULAR GOITER

Enlargement of the thyroid, or *goiter,* is the most common manifestation of thyroid disease

Mechanism :

- *The goiters reflect impaired synthesis of thyroid hormone* often caused by dietary iodine deficiency and this leads to to a compensatory rise in the serum TSH, which in turn causes hyperplasia of the follicular cells and, ultimately, gross enlargement of the thyroid gland .

Goiters can be endemic or sporadic.

Endemic goiter :Occurs in geographic areas where the soil, water, and food supply contain little iodine.

- The term *endemic* is used when goiters are present in more than 10% of the population in a given region.
- Such conditions are common in mountainous areas of the world, including the Himalayas and the Andes but with increasing availability of iodine supplementation, the frequency and severity of endemic goiter have declined

Sporadic goiter : Less common than endemic goiter.

- more common in females than in males, with a peak incidence in puberty or young adulthood, when there is an increased physiologic demand for T_4.
- It may be caused by several conditions, including the:

a. Ingestion of substances that interfere with thyroid hormone synthesis , such as excessive calcium and vegetables such as cabbage, cauliflower, sprouts, .

b. Hereditary enzymatic defects that interfere with thyroid hormone synthesis *(dyshormonogenetic goiter).*

-In most cases, the cause of sporadic goiter is not apparent.

MORPHOLOGY :

- Initially, the gland is diffusely and symmetrically enlarged (diffuse goiter) but later on it becomes multinodular goiter.

On microscopic examination,

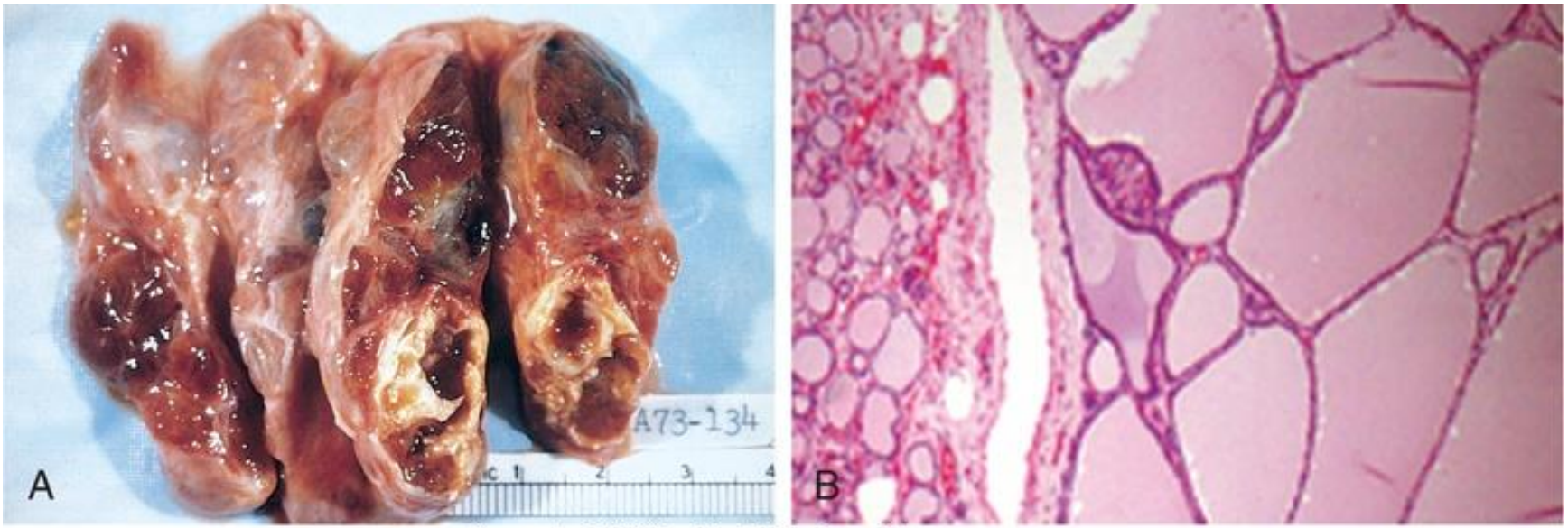
a. The follicular epithelium may be hyperplastic in the early stages of disease or flattened and cuboidal during periods of involution.

b. Colloid is abundant in the latter periods (colloid goiter).

c. With time, recurrent episodes of hyperplasia and involution produce a more irregular enlargement of thee thyroid, termed multinodular goiter and virtually all long-standing diffuse goiters convert into multinodular goiters.

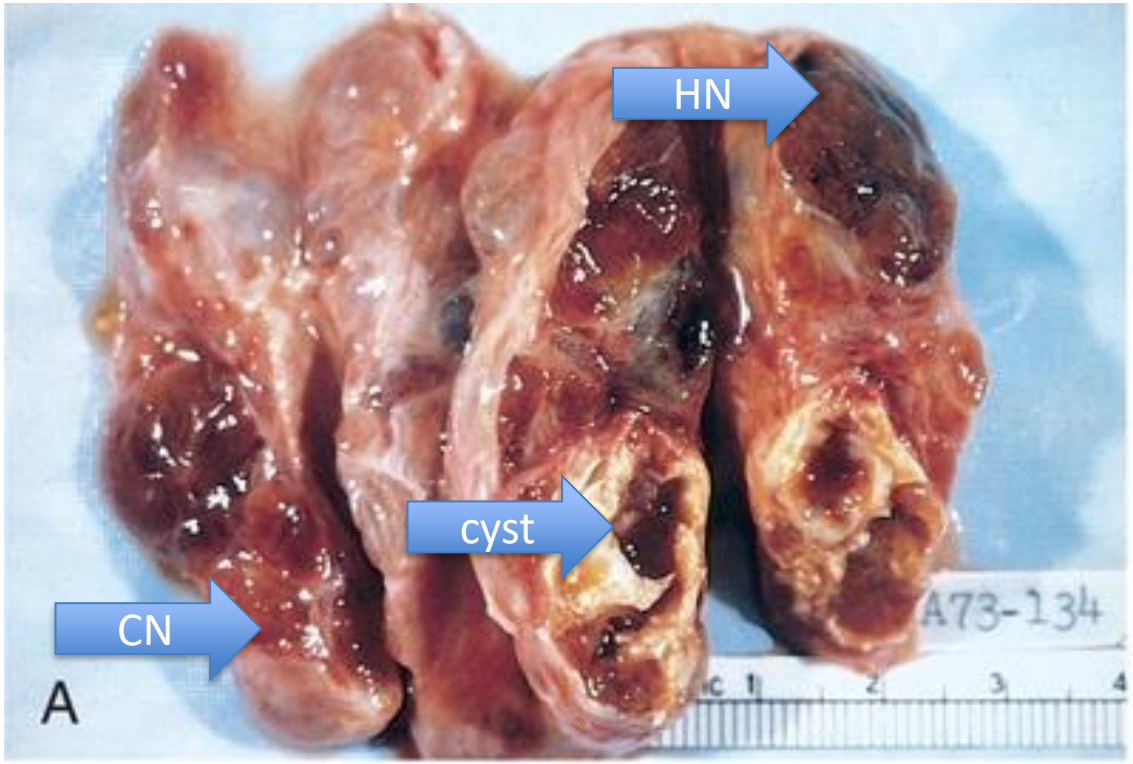
Macroscopic appearance

- Multinodular goiters cause multilobulated, asymmetrically enlarged glands . Old lesions often show fibrosis, hemorrhage, calcification



Kumar et al: Robbins Basic Pathology, 9e.

Multinodular goiter: thyroid shows several nodules, some are hemorrhagic (HN), others contain colloid (CN) and some become cystic.



Note:

- Multinodular goiters typically are hormonally silent (no hyperthyroidism)
- however, 10% of patients can manifest with thyrotoxicosis due to the development of autonomous nodules producing hormone independent of TSH stimulation and this condition, called toxic multinodular goiter or **Plummer syndrome**


Thank you!