

Endocrine system

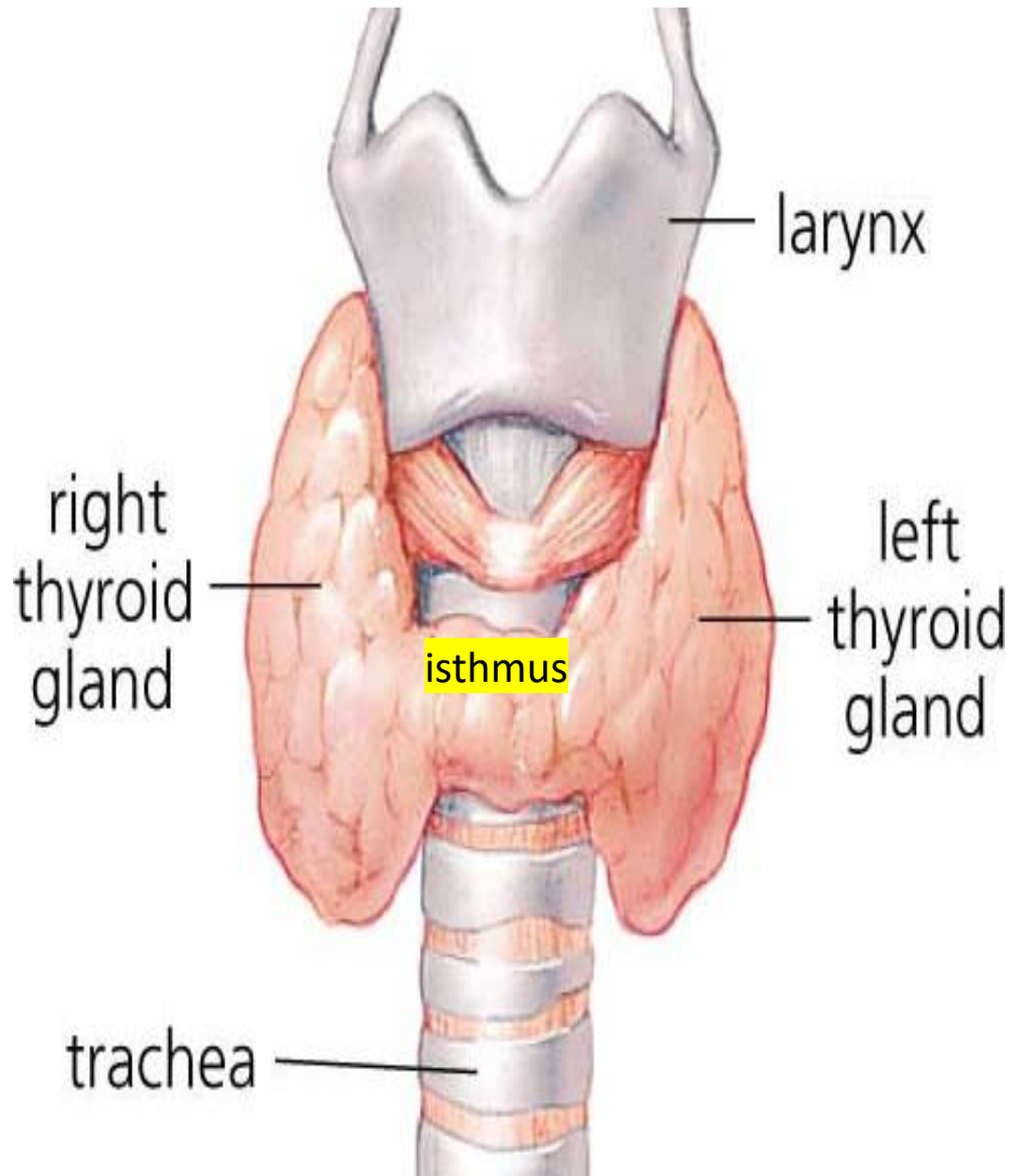
Thyroid gland part 1

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Thyroid gland

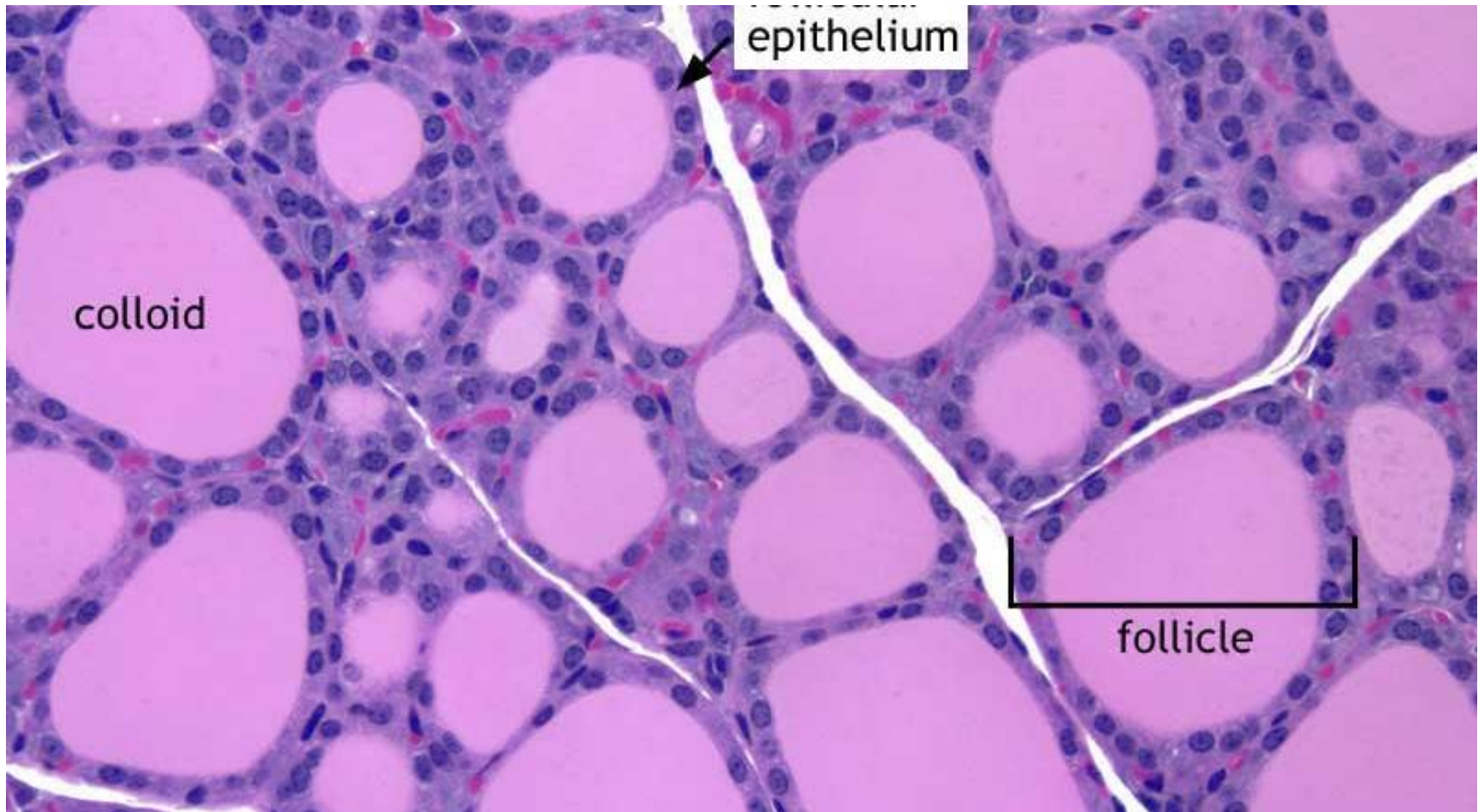
- The thyroid gland consists of two lobes (right and left) that are connected by the isthmus.
- The right and left lobes are pear shaped with the apex directed upwards.
- The thyroid is attached to the larynx; it moves upwards during swallowing. So if you see a neck mass ask the patient to swallow, if the mass moves upwards, then it is from the thyroid.



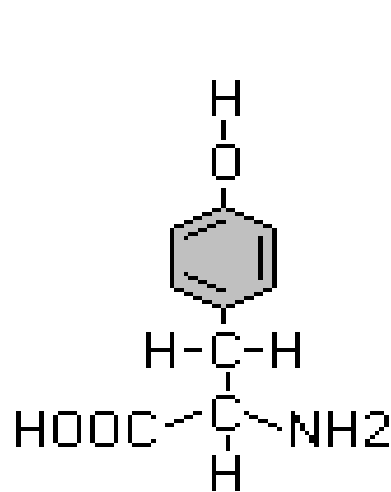
Thyroid gland histology

- The thyroid gland is composed of follicles lined by follicular epithelial cells which are cuboidal to low columnar.
- The follicles contain **colloid** which is composed of **thyroglobulin** which is the iodinated **precursor** protein of thyroid hormones.

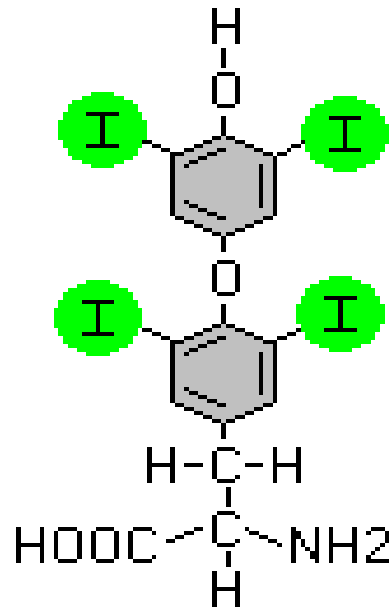
Histology



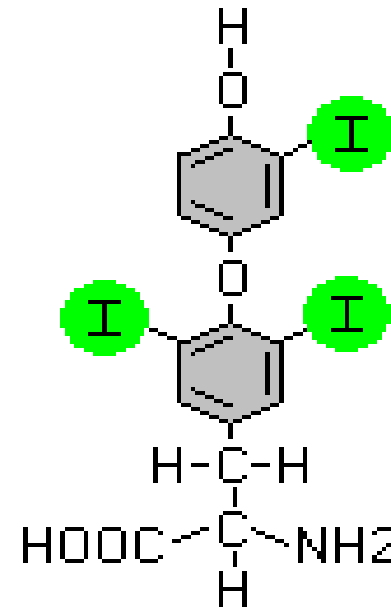
Thyroid hormones



Tyrosine



Thyroxine (T₄)



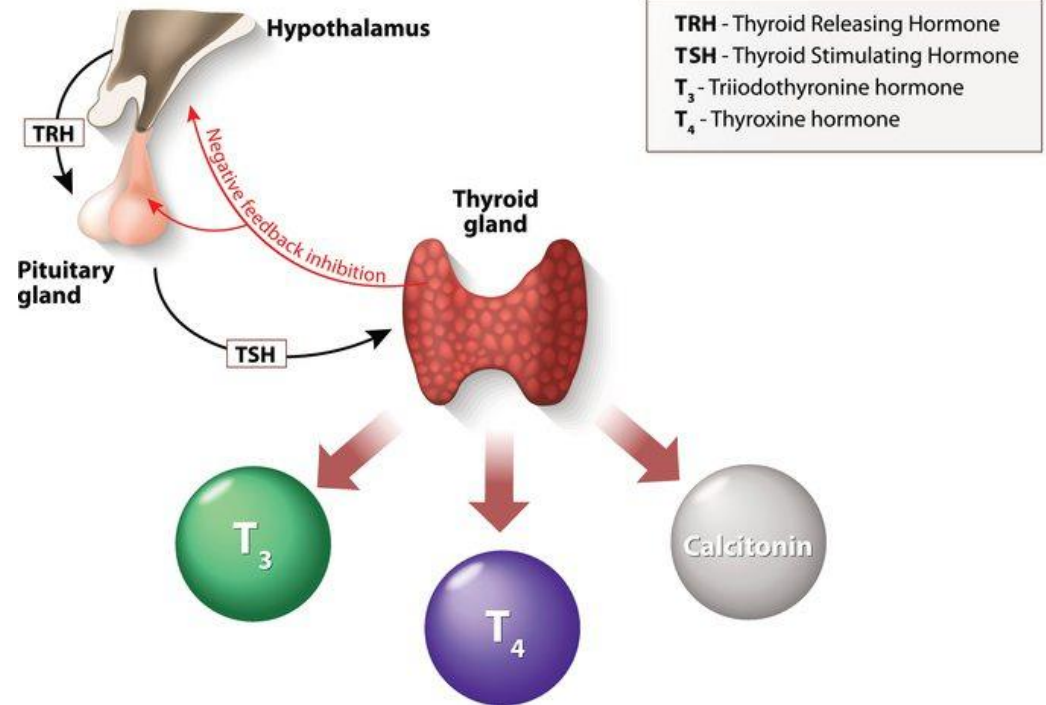
Triiodothyronine (T₃)

Note that thyroid hormones are derived from tyrosine. The main two are T₃ and T₄. Note relation to iodide atom (T₃: 3 iodine atoms and T₄ ; 4 atoms)

Note that the thyroid gland also secretes calcitonin, from C cells= parafollicular cells.



THYROID HORMONES



Diseases of thyroid gland

Same general rules of all endocrine glands!

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

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

2. ***Hyperthyroidism***
3. ***Hypothyroidism***.

Goiter: enlarged thyroid.. Regardless of the cause.



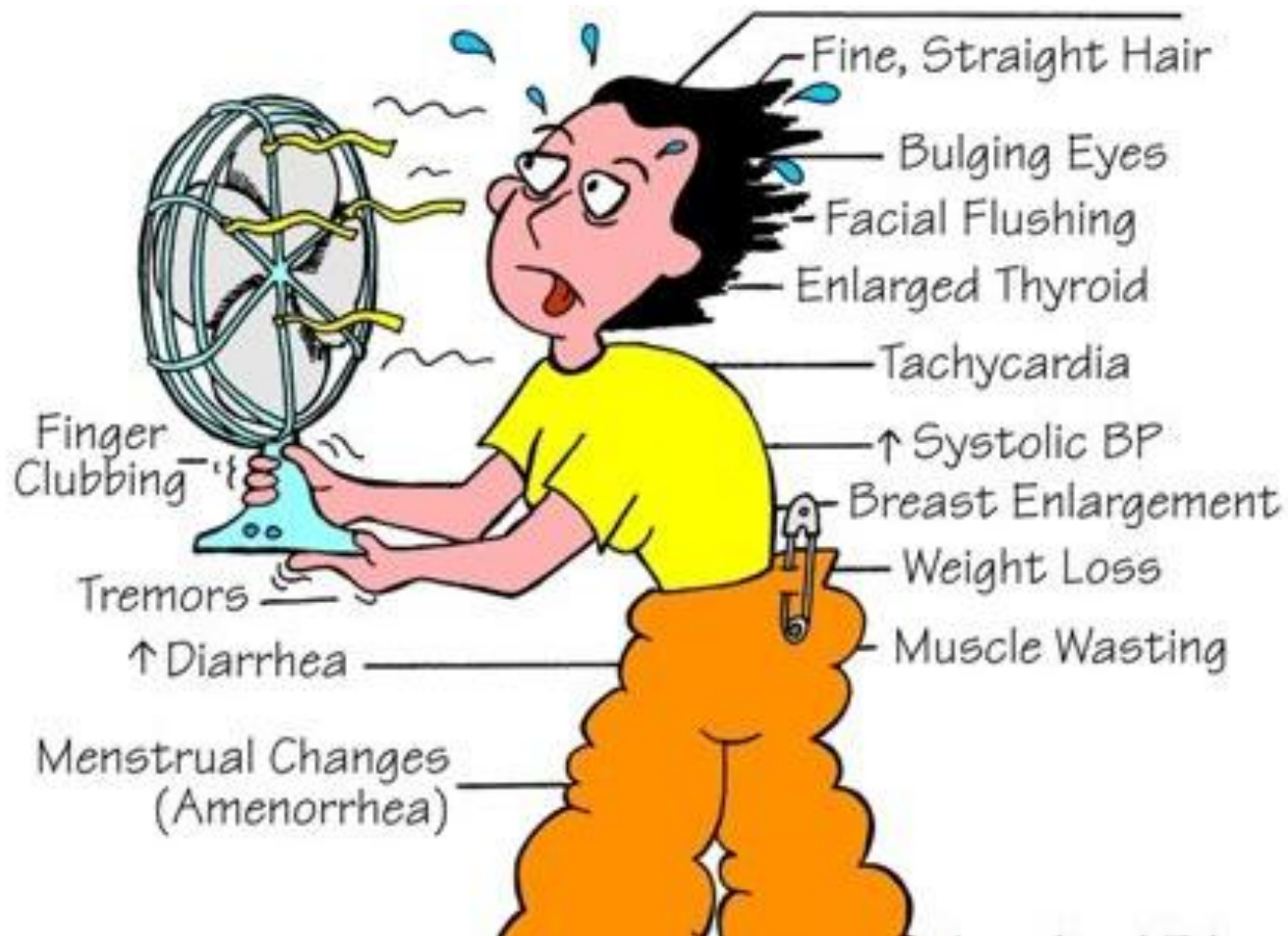
Clinical manifestations of hyperthyroidism (thyrotoxicosis)

- Thyroid hormones increase basal metabolic rate, increase appetite, increase breakdown of fat and glucose
- Also increase heart rate and cause hypertension
- Increase body temperature
- SO if these hormones are increased you expect to see a wide range of symptoms.

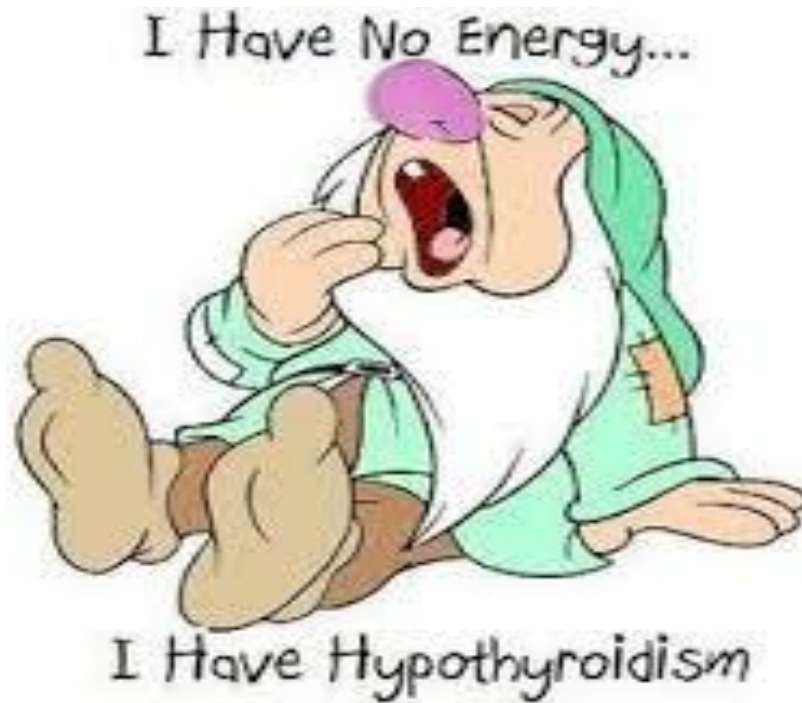
Clinical manifestations of thyrotoxicosis

- 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
- 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 (dyshormogenic 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 :Refers to hypothyroidism developing in infancy or early childhood

1. Endemic cretinism: 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:

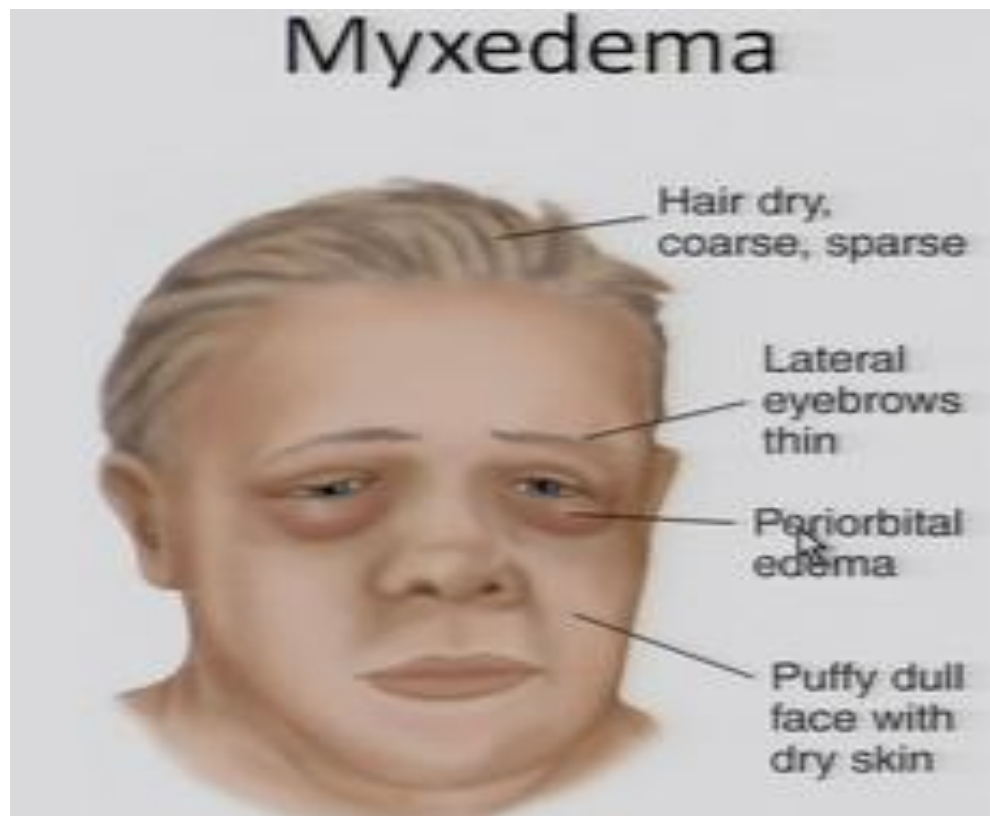
- Impaired development of skeletal system- short stature,
- Coarse facial features, protruding tongue
- Central nervous system problems , with mental retardation



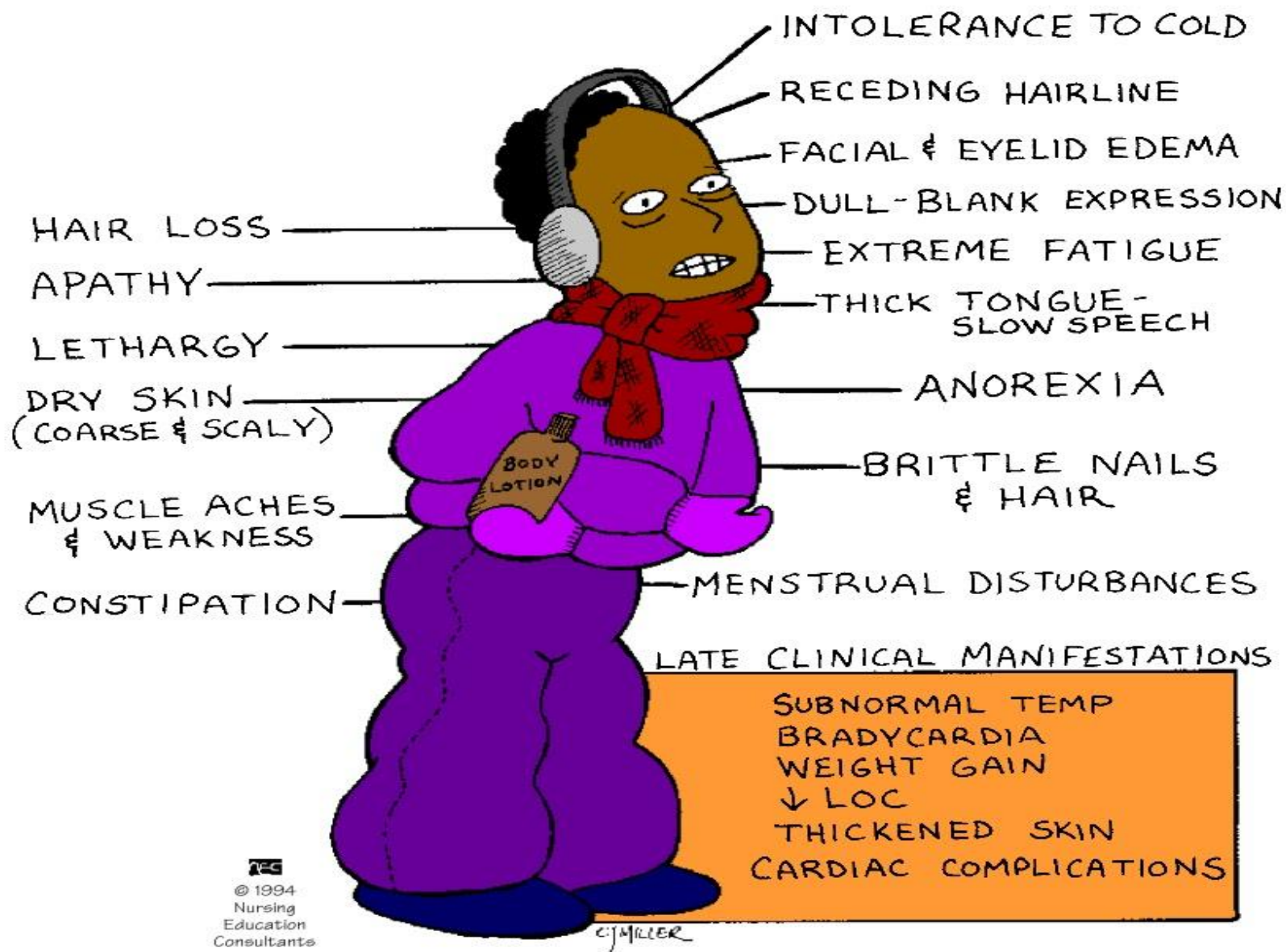
Myxedema, or Gull syndrome :

- 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

Myxedema



HYPOTHYROIDISM



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

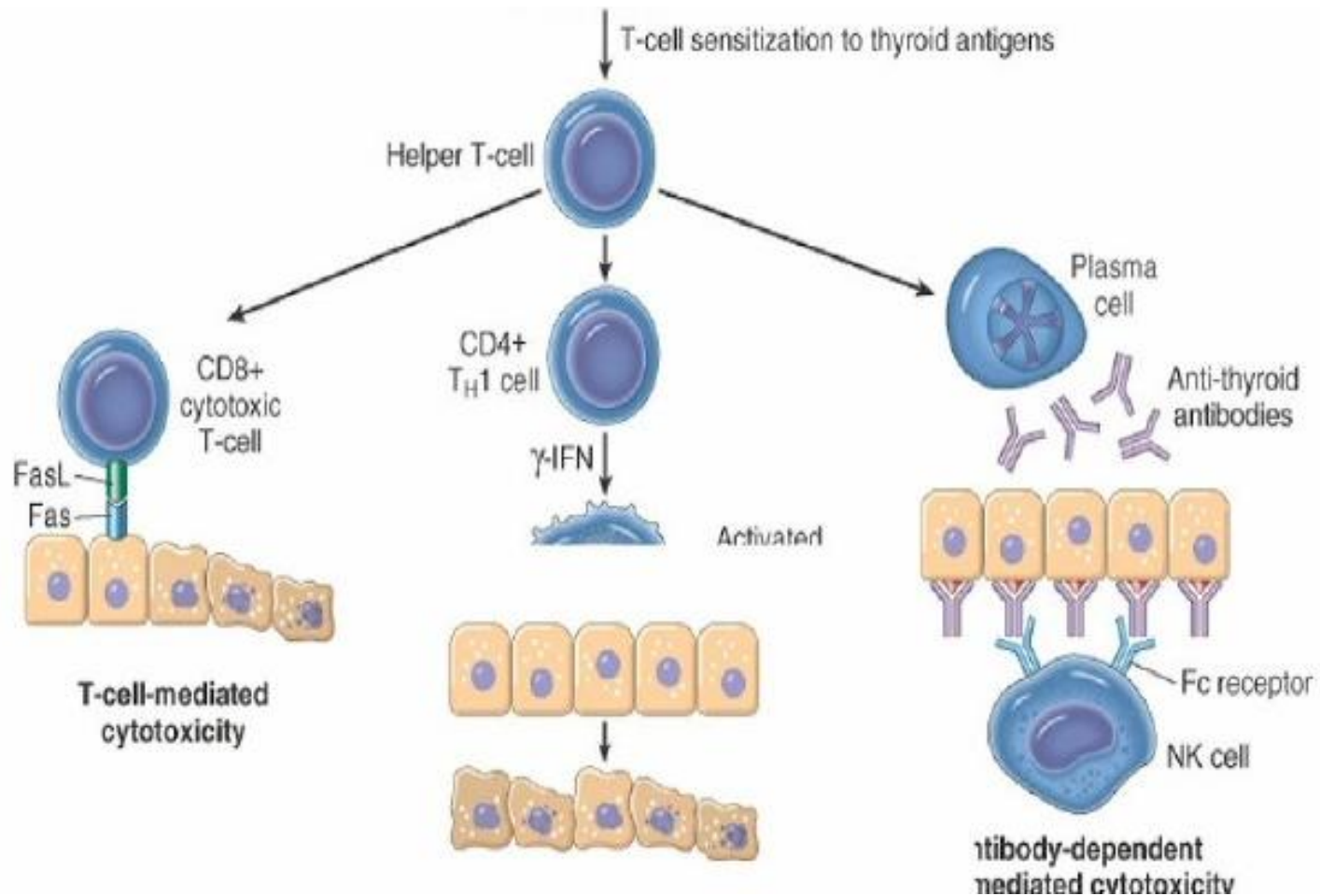
PATHOGENESIS of Hashimoto thyroiditis :-

Caused by breakdown in self-tolerance to thyroid antigens

- Circulating **autoantibodies** against thyroid antigens are present in the vast majority of patients
- Multiple immunologic mechanisms may contribute to thyroid damage.

- I. **Cytokine-mediated cell death**: Excessive T cell activation leads to the production of inflammatory cytokines such as IFN- γ in the thyroid with resultant recruitment and activation of macrophages and damage to follicles .
- II. Binding of anti-thyroid antibodies (antithyroglobulin, and antithyroid peroxidase antibodies), followed by **antibody-dependent cell-mediated cytotoxicity**
- III. **T cell mediated cytotoxicity.**

HASHIMOTO



▪

HASHIMOTO

- A significant genetic component is supported by the
 - a. Concordance of disease in 40% of monozygotic twins,
 - b. the presence of circulating anti-thyroid 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; however, it *may be preceded by transient thyrotoxicosis* due to disruption of thyroid follicles ,and secondary release of thyroid hormones (*hashitoxicosis*).

SO: at the beginning of the disease the destruction by autoimmune antibodies might cause increased release of thyroid hormones from the destructed follicles but later there is so much destruction and no new colloid is formed, resulting in hypothyroidism

- 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:

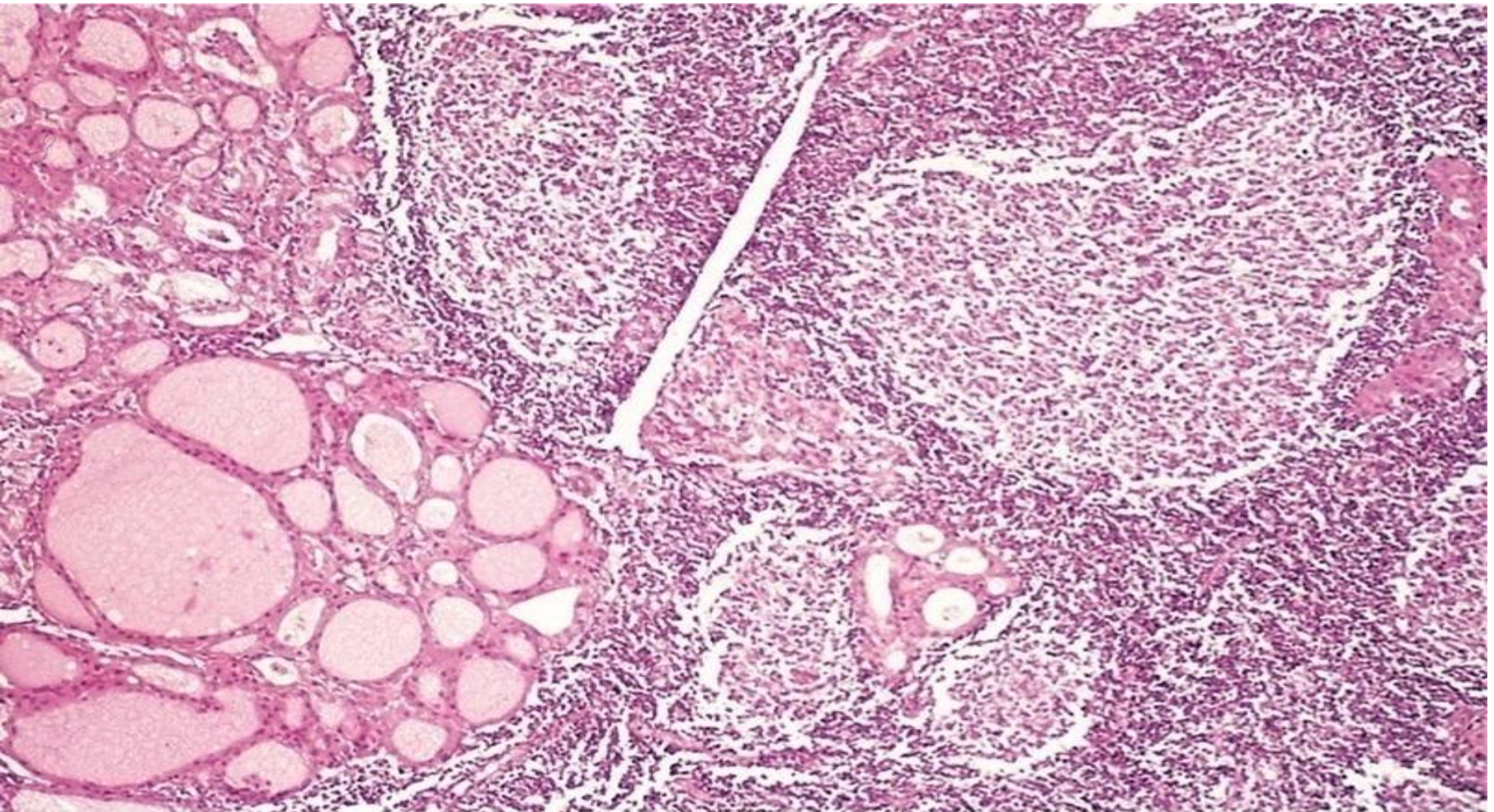
- The relationship between Hashimoto disease and thyroid epithelial cancers remains controversial, with some morphologic and molecular *studies suggesting a predisposition to papillary carcinomas*

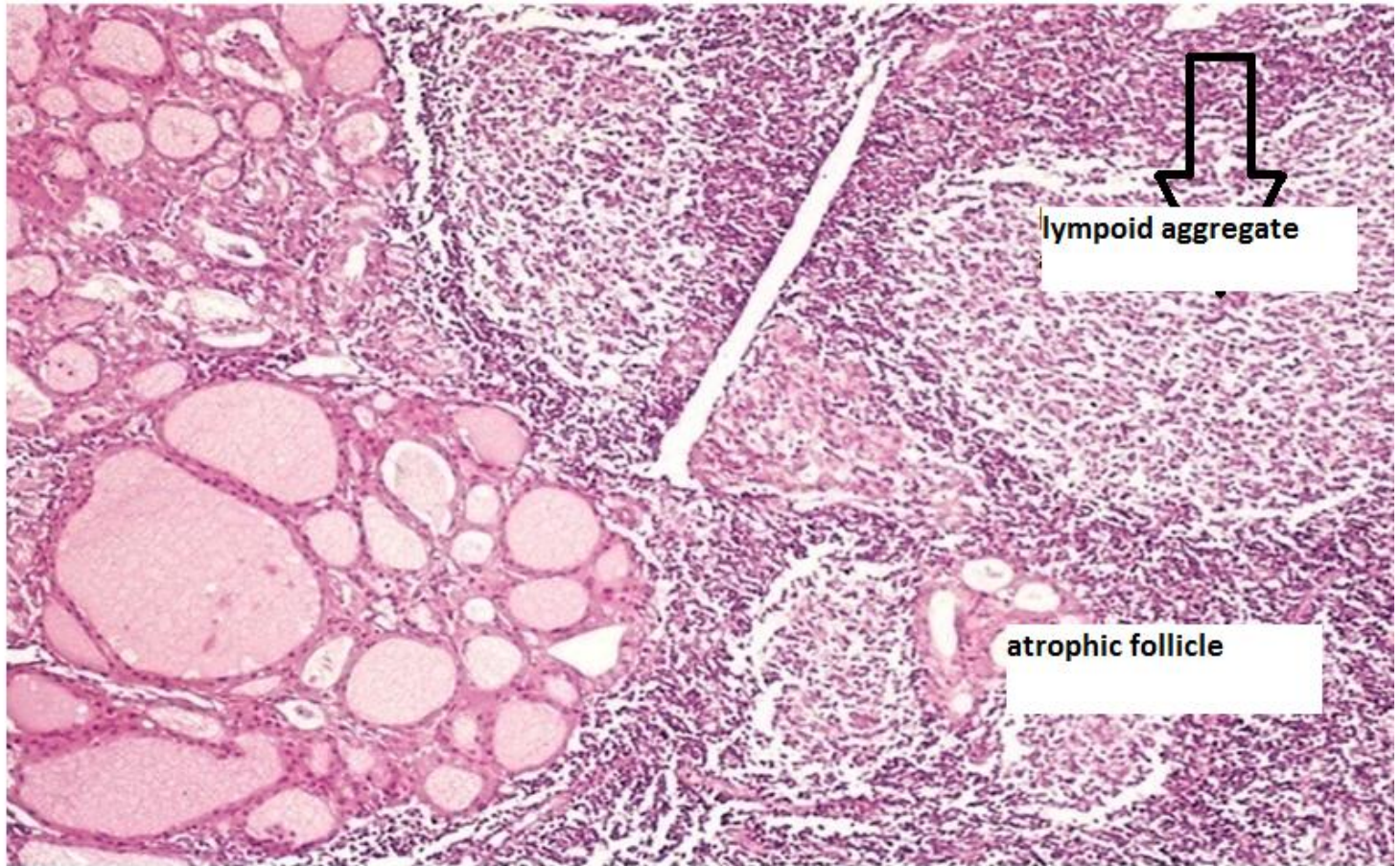
- Gross(macroscopic) features:
 - **Diffuse** and **symmetric** enlargement of the thyroid but localized enlargement may be seen in some cases to raise suspicion for neoplasm

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

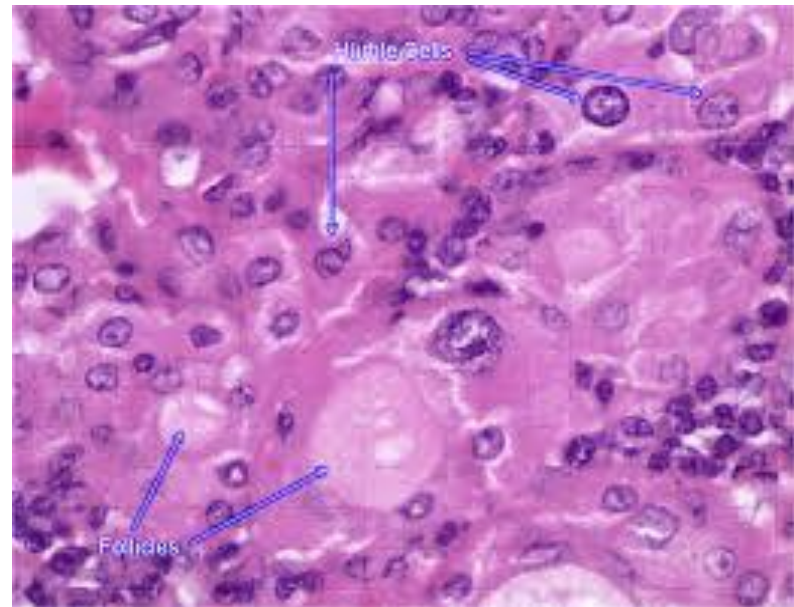
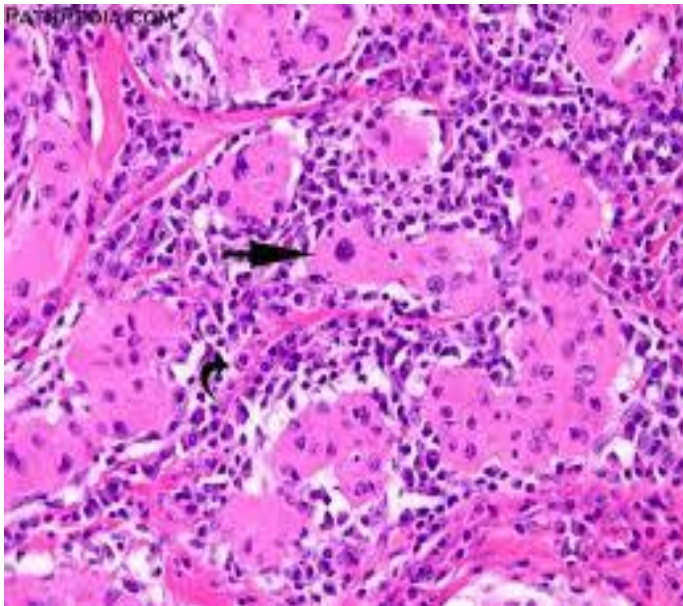




lymphoid aggregate

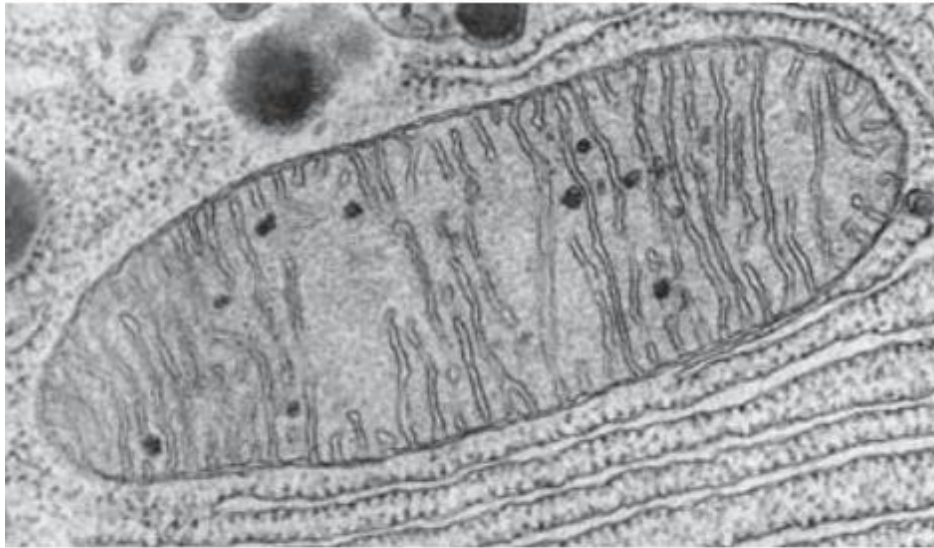
atrophic follicle

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



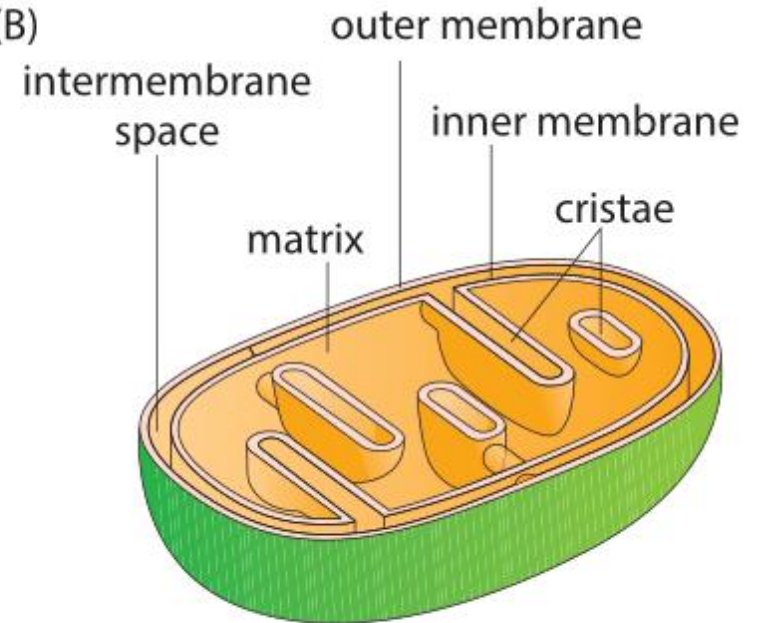
Hurthle cell cytoplasm is full of mitochondria

(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
- 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.

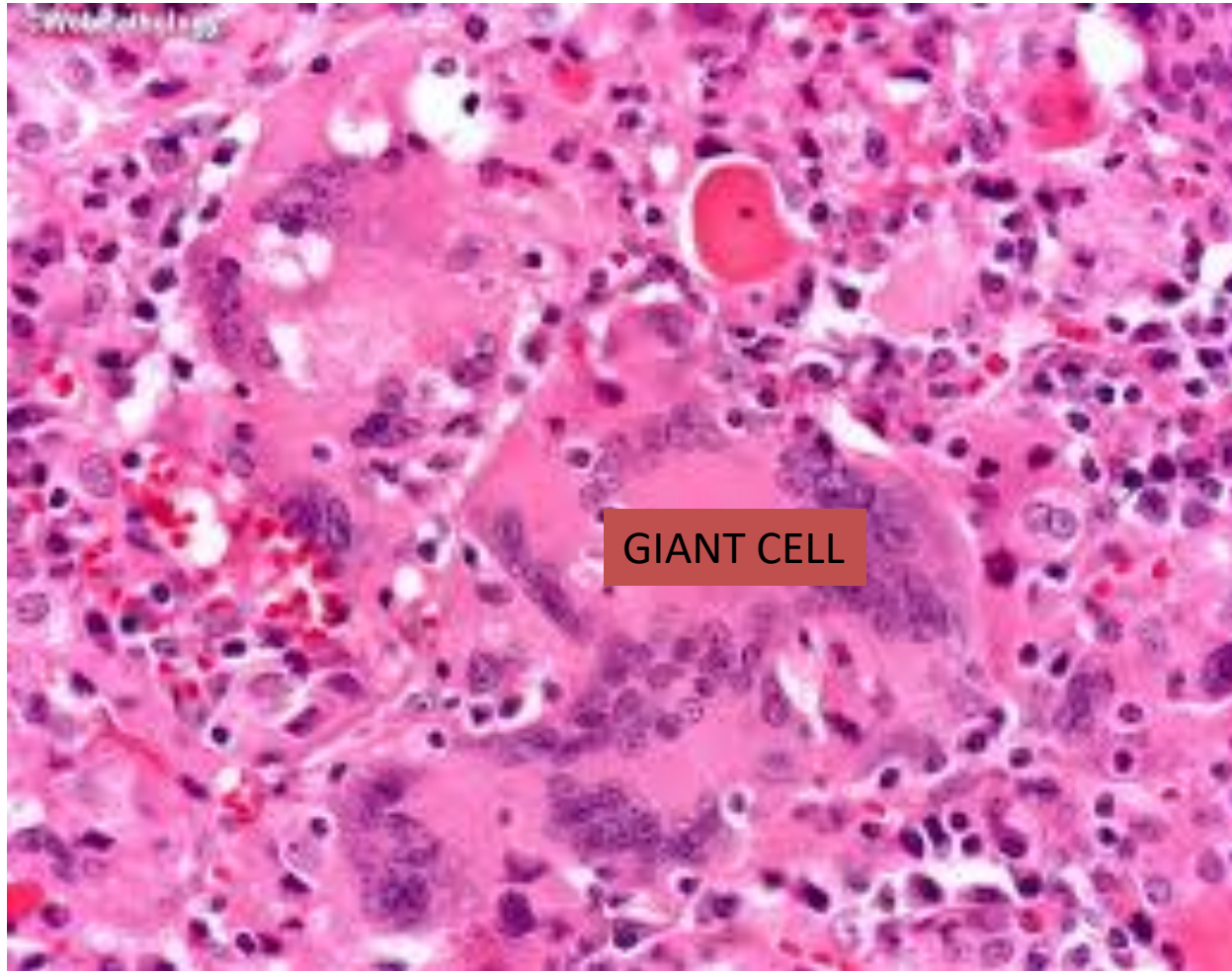
- Clinical Features :

- 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

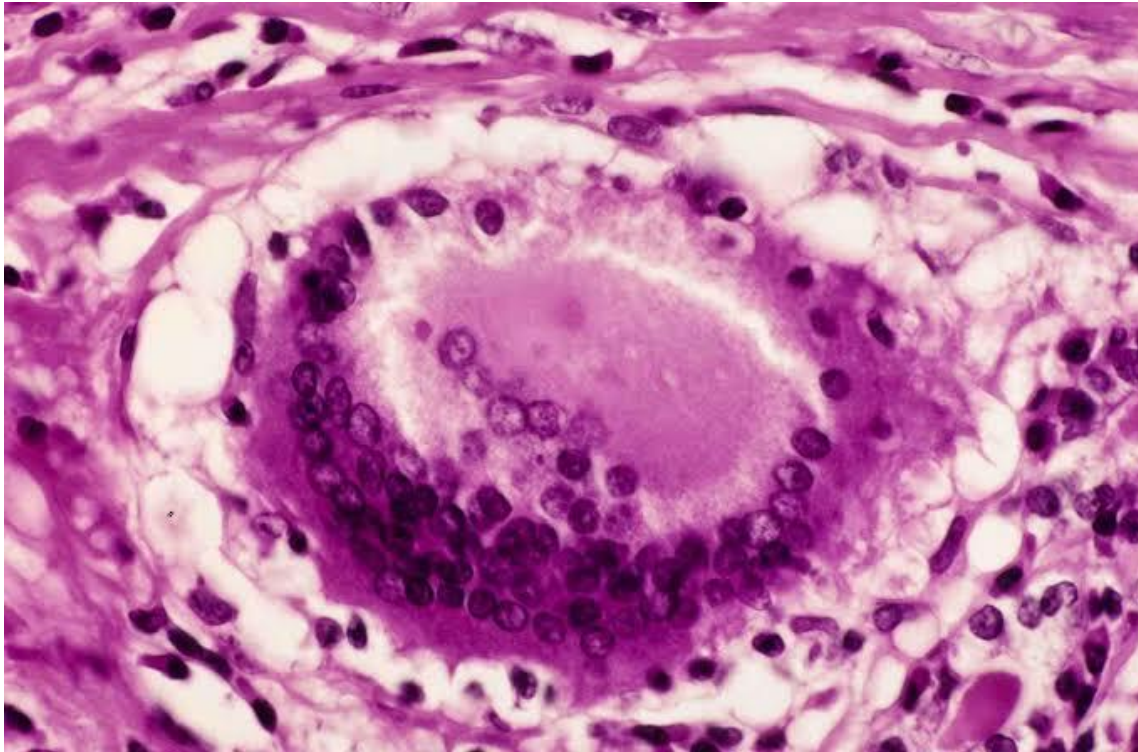
Histologic examination reveals

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



Giant cell in subacute granulomatous thyroiditis



3. Subacute Lymphocytic Thyroiditis :

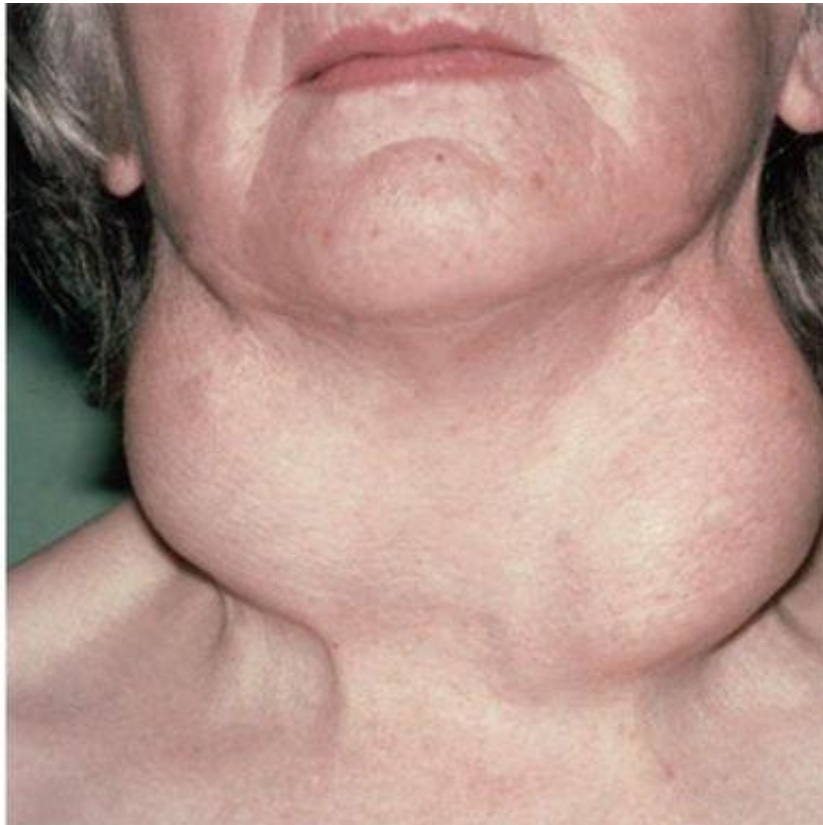
- Also is known as *silent or painless* thyroiditis;
- And in a subset of patients the onset of disease follows - pregnancy (*postpartum thyroiditis*).
- Most likely to be *autoimmune* because circulating antithyroid antibodies are found in a majority of patients
- It mostly affects middle-aged women,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

4. Riedel thyroiditis,:

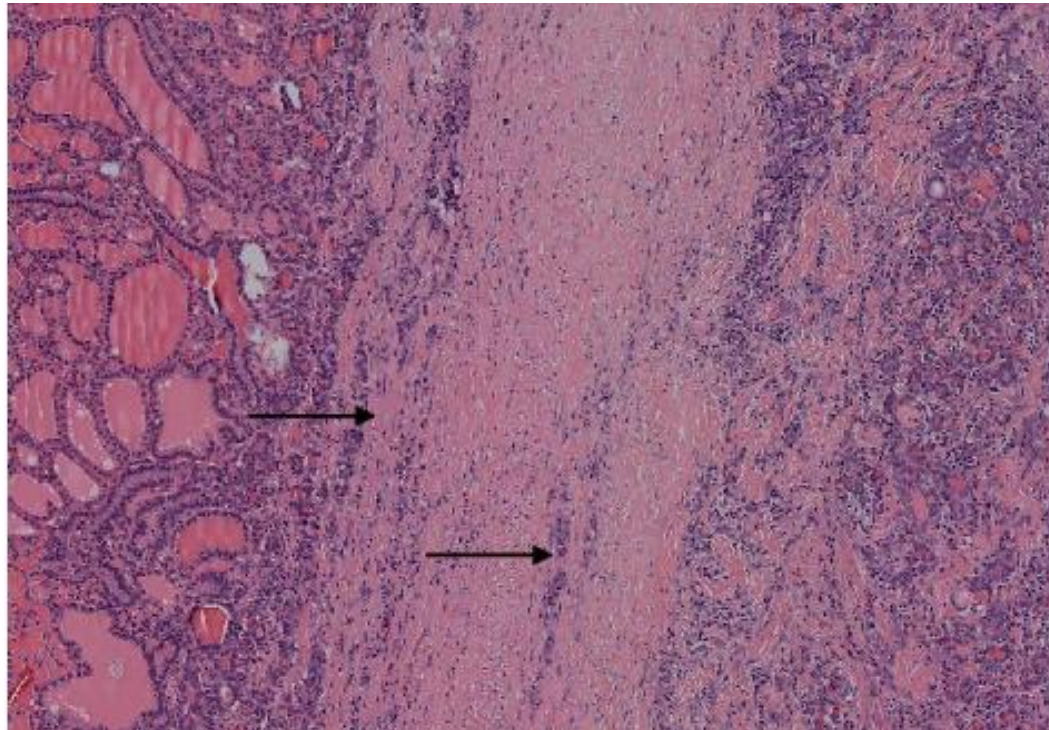
A rare disorder of unknown etiology,

- 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

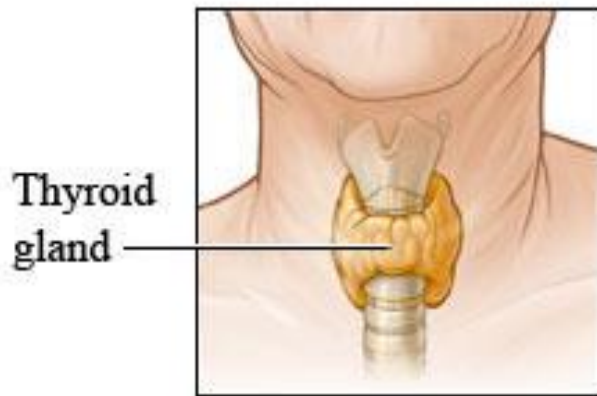
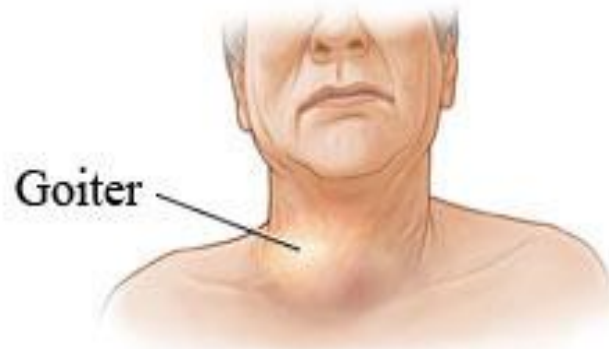
RIEDEL'S
Thyroiditis



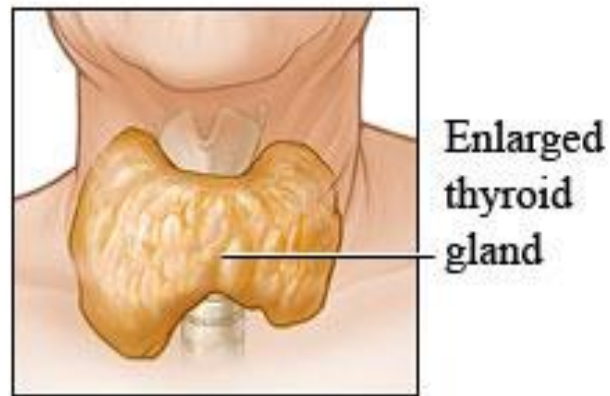
Riedel thyroiditis: fibrosis



Goiter

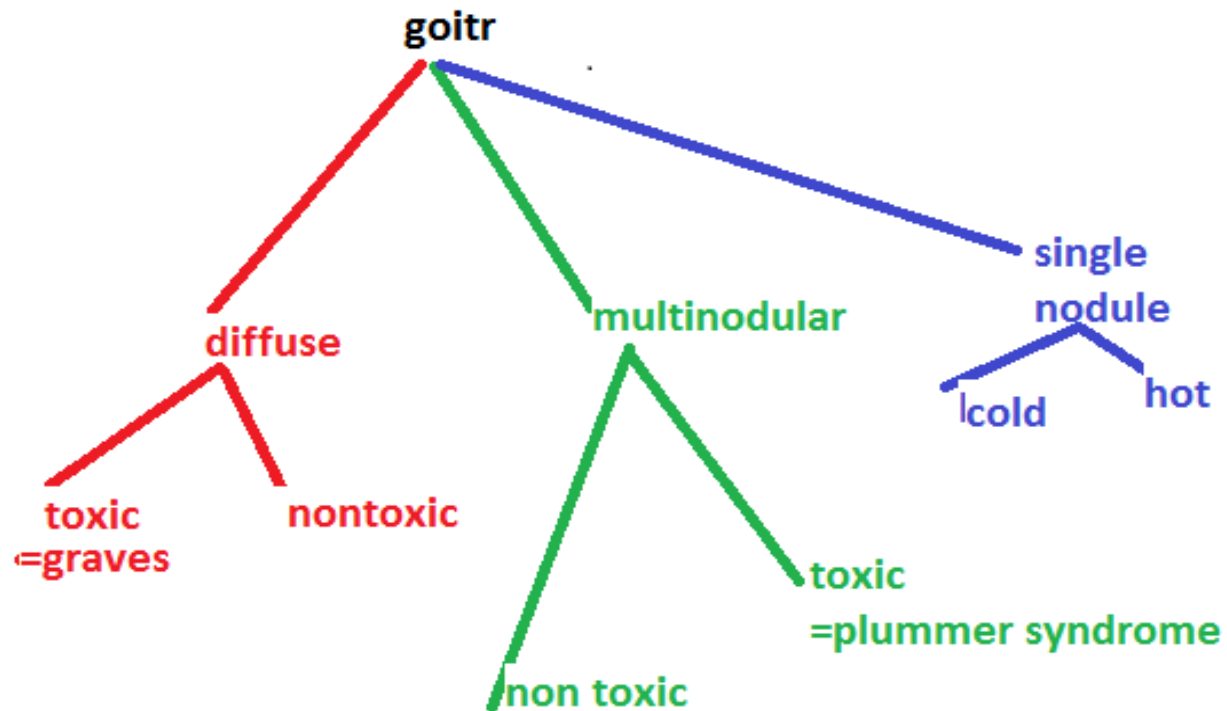


Normal



Goiter

Goiter



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

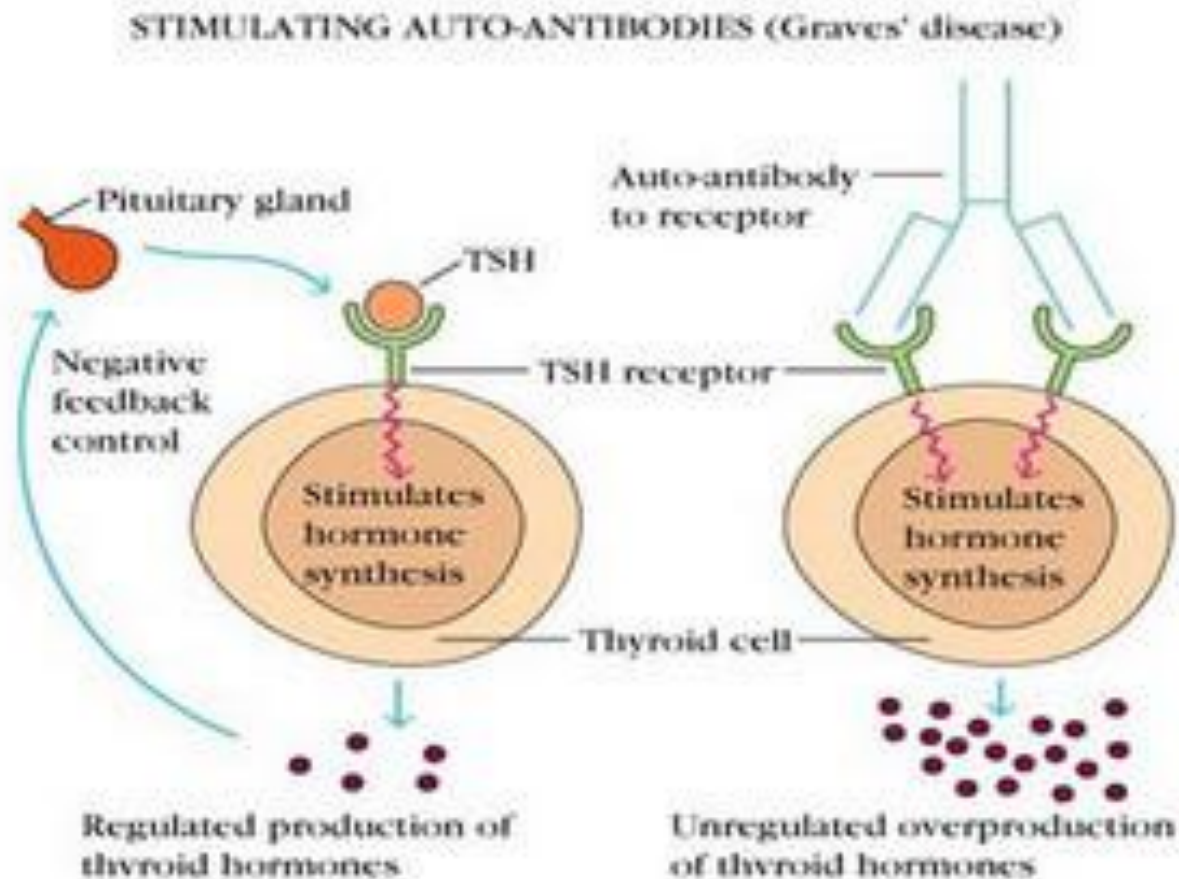
2. Thyroid growth-stimulating immunoglobulins:

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

3. TSH-binding inhibitor immunoglobulins:

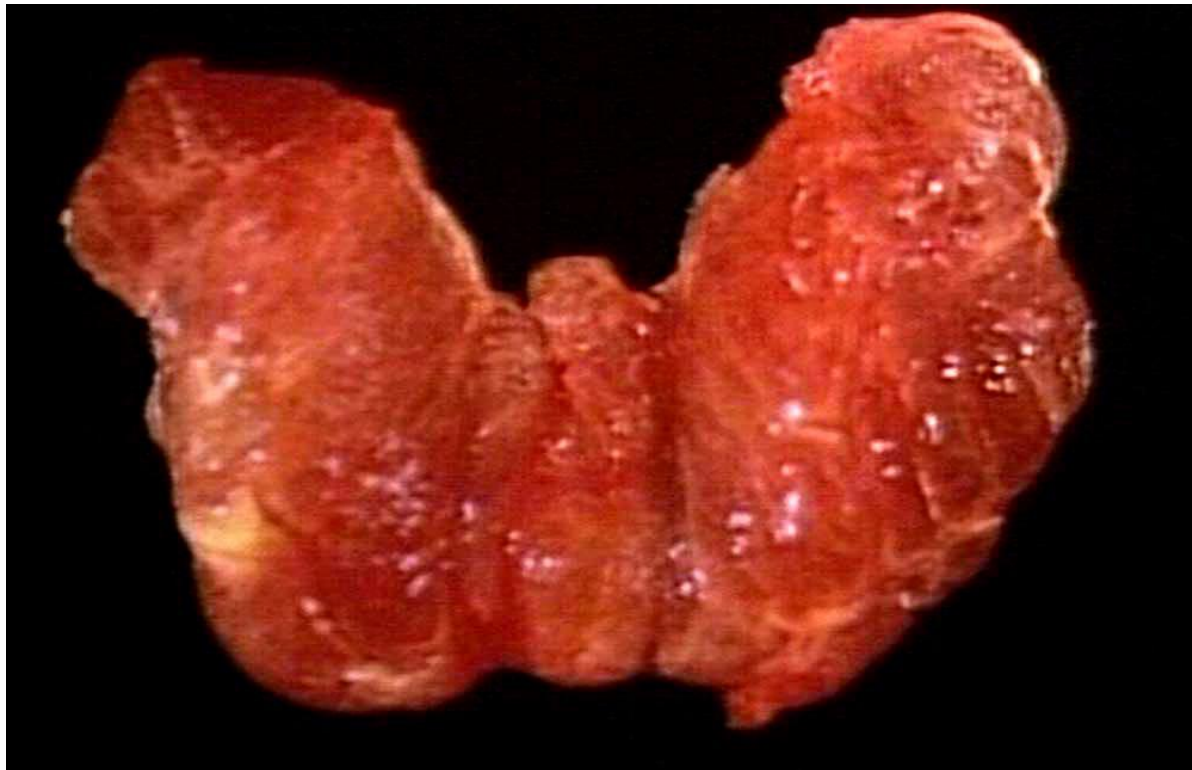
- Prevent TSH from binding to its receptor on thyroid cells and in so doing may actually inhibit thyroid cell function, a finding explains why some patients with Graves spontaneously develop episodes of hypothyroidism.

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



Note: The coexistence of stimulating *and* inhibiting immunoglobulins in the serum of the same patient may explain why some patients with Graves disease spontaneously develop episodes of hypothyroidism

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.



Thank you!

