

PATHOLOGY OF THYROID- II

TYPES OF GOITER

- **Diffuse nontoxic goiter (Simple/Colloid)-**
 - Endemic
 - Sporadic
- **Multinodular goiter**
 - Endemic
 - Sporadic



PATHOGENESIS

Iodine Lack

Goitrogens



Reduced thyroid hormone production



Increased TSH stimulation



Cyclic hyperplasia / involution



Diffuse non-toxic goiter

(non nodular enlargement of the entire gland)



Repeated hyperplasia / involution

Growth of hyperplastic

Fibrosis of involuted areas
areas

Multinodular Goiter

Uneven follicular hyperplasia

Generation of new follicles

Accumulation of colloid

physical stress

rupture of follicles & vessels.

hemorrhages, scarring & calcifications



CLINICAL COURSE OF A GOITER

- Iodine deficiency --> TSH increase
 - Increasing TSH causes hypertrophy of thyroid (**diffuse nontoxic goiter**)
 - Follicles may become autonomous with greater intrinsic growth and functional capability (**multinodular goiter-MNG**)
 - Follicles continue to grow and function despite decreasing TSH ("toxic" MNG)
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DIFFUSE GOITER

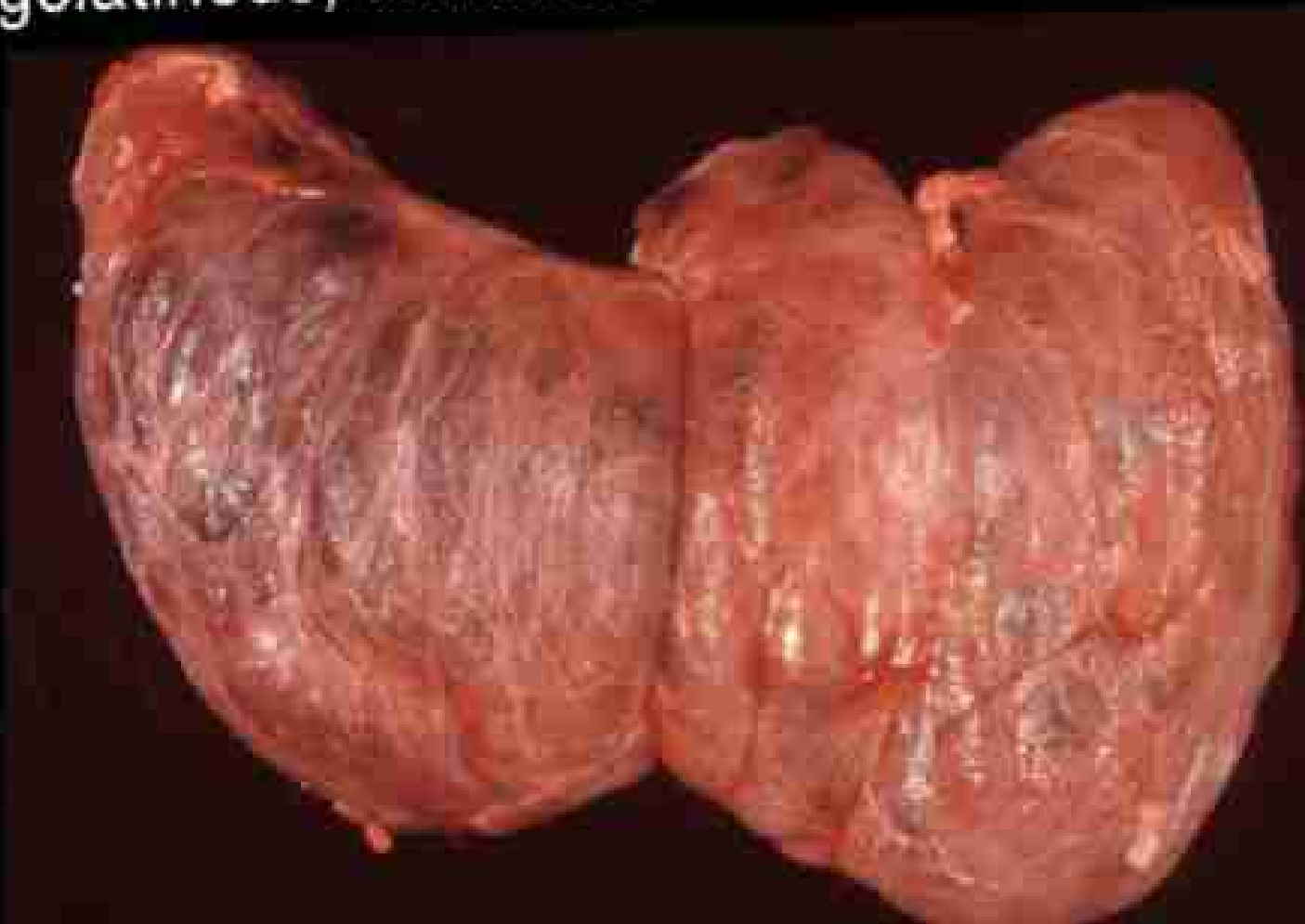


- More common in females
- Appears at puberty/adolescence → regress/MNG



GROSS- DIFFUSE COLLOID GOITER

- Diffusely enlarged, symmetric (100-150 g)
- C/S- gelatinous, translucent brown



MICROSCOPY -DIFFUSE

1. Hyperplastic phase

- Tall columnar follicular epithelium
- Formation of new follicles

2. Phase of colloid involution

- Large follicles distended with colloid & lined by flattened epithelium



MULTINODULAR GOITER

- End stage of long-standing simple goiters
- Tumor like enlargement with nodularity





Traditional mask

Nigeria 16th Century





Clinical presentation

- Cosmetic disfigurement
- Compressive symptoms- dysphagia & choking
- Most are euthyroid
- 10% cases- thyrotoxicosis – “Toxic MNG”- Plummer's disease.
- No ophthalmopathy/dermopathy



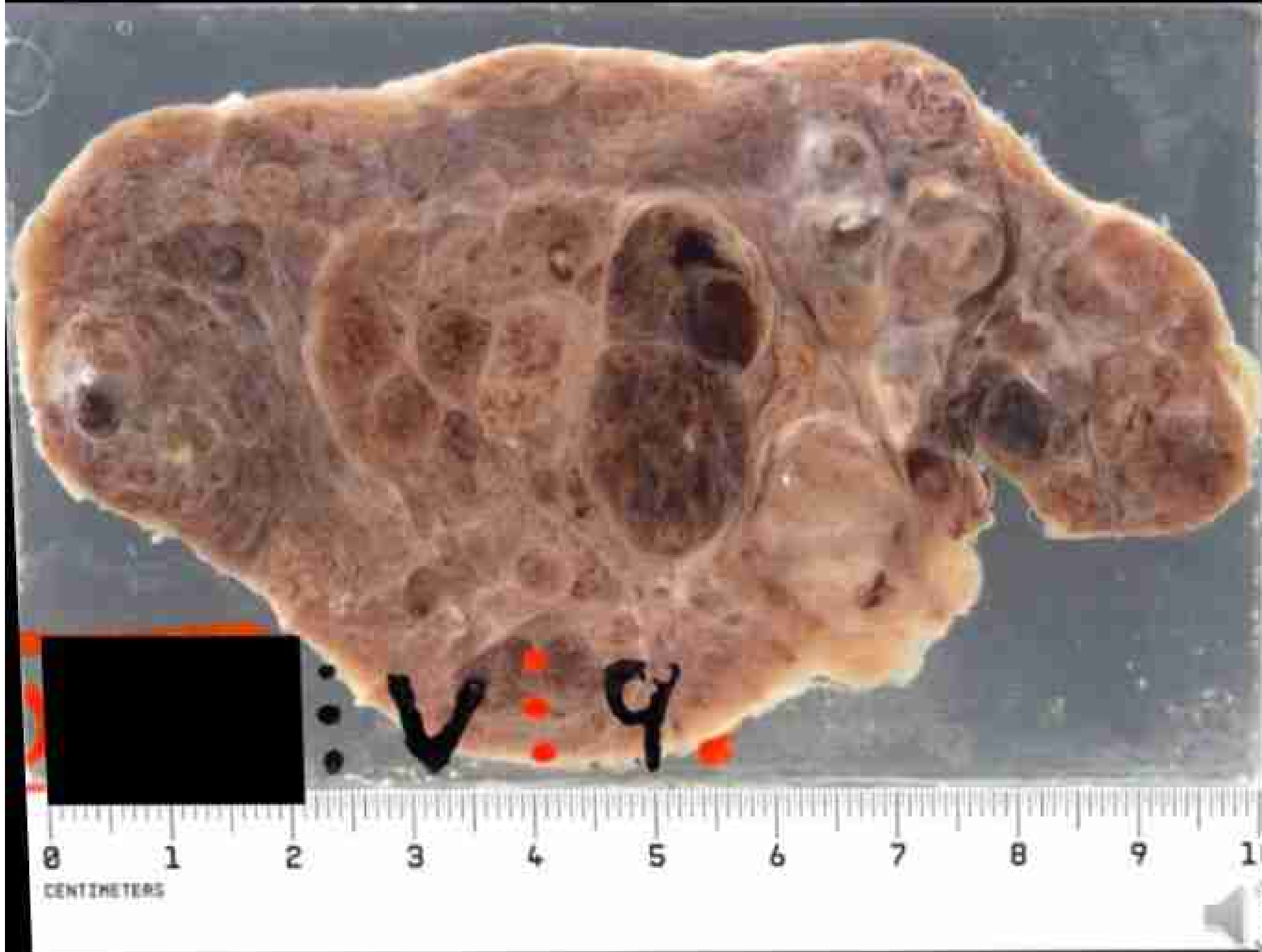
GROSS- MNG

- Asymmetric & extreme enlargement
- 5 cardinal features
 - Nodularity with poor encapsulation (varying sized nodules)
 - Fibrous scarring
 - Hemorrhage,
 - Cystic degeneration
 - Focal calcification





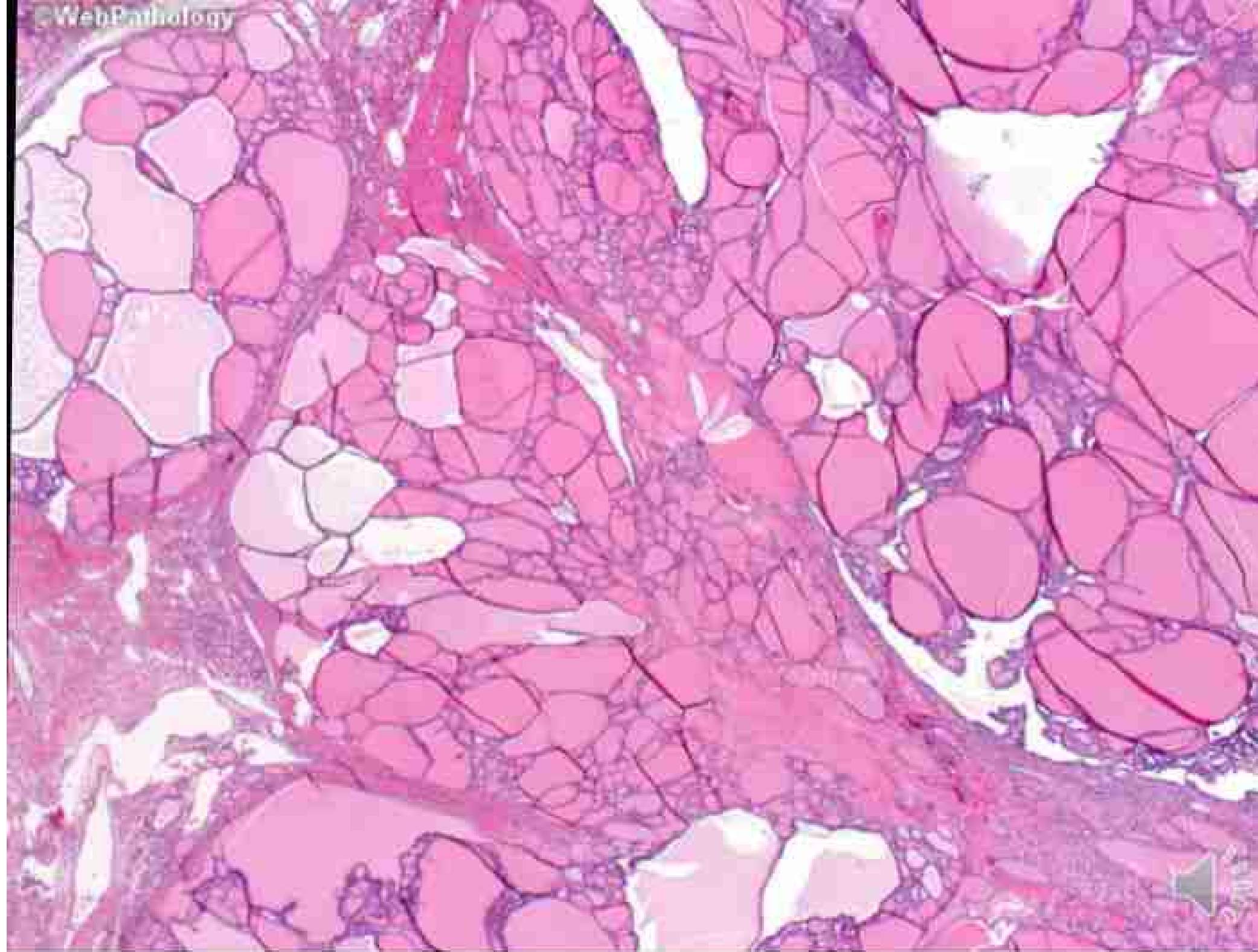






MICROSCOPY

- Partial / incomplete encapsulation of nodules
- Small / large follicles lined by flat epithelium





variably sized and shaped follicles

the follicles are distended with colloid

MICROSCOPY CONTD...

- Partial / incomplete encapsulation of nodules
- Small / large follicles lined by flat epithelium
- Degenerative changes-
 - Hemorrhage, hemosiderin-laden macrophages, cholesterol crystals
 - Fibrosis, scarring with foci of calcification
 - Cystic change

TREATMENT INTERVENTIONS

- Population Level

- Salt Iodization

- Individual Level

- Iodized water

- Iodine oil (oral)

- Iodine injections

LIFE
SAVING
DOT



HYPERTHYROIDISM

HYPERTHYROIDISM

Thyrotoxicosis – hypermetabolic state - elevated circulating levels of free T3 & T4

- **Associated with hyperfunction** (hyperthyroidism) – MC cause (Grave's disease)
- **Not associated with hyperfunction**
 - Excessive release of preformed thyroid hormone (e.g., thyroiditis)
 - Extra thyroidal source (drugs- thyroxine, struma ovarii)

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HYPERTHYROIDISM -CLINICAL FEATURES

- Hypermetabolic state
- Sympathetic overactivity

Raised BMR

- Heat intolerance- warm, moist skin
- Weight loss** despite increased appetite

Cardiovascular system - Earliest

- Tachycardia** , palpitations , atrial fibrillation





HOW TO DIAGNOSE HYPERTHYROIDISM...

- To establish diagnosis of thyrotoxicosis
 - TSH levels (screening) – decreased
 - Free T4 and/ or T3 levels - increased
- To determine etiology : RAUI
 - diffusely increased uptake (*Graves disease*),
 - increased uptake in a solitary nodule (*toxic adenoma*)
 - decreased uptake (*thyroiditis*).





GRAVES DISEASE

Diffuse toxic goiter / Basedow disease /
Primary hyperplasia / Exophthalmic goiter

GRAVES DISEASE

Most common cause of endogenous hyperthyroidism.



Robert Graves(1835)-
characterized by “violent and long continued palpitations in females” associated with enlargement of the thyroid gland.



EPIDEMIOLOGY

- Typically a disease of **adult women**
- Peak incidence : 20 – 40yrs of age
- $F > M$

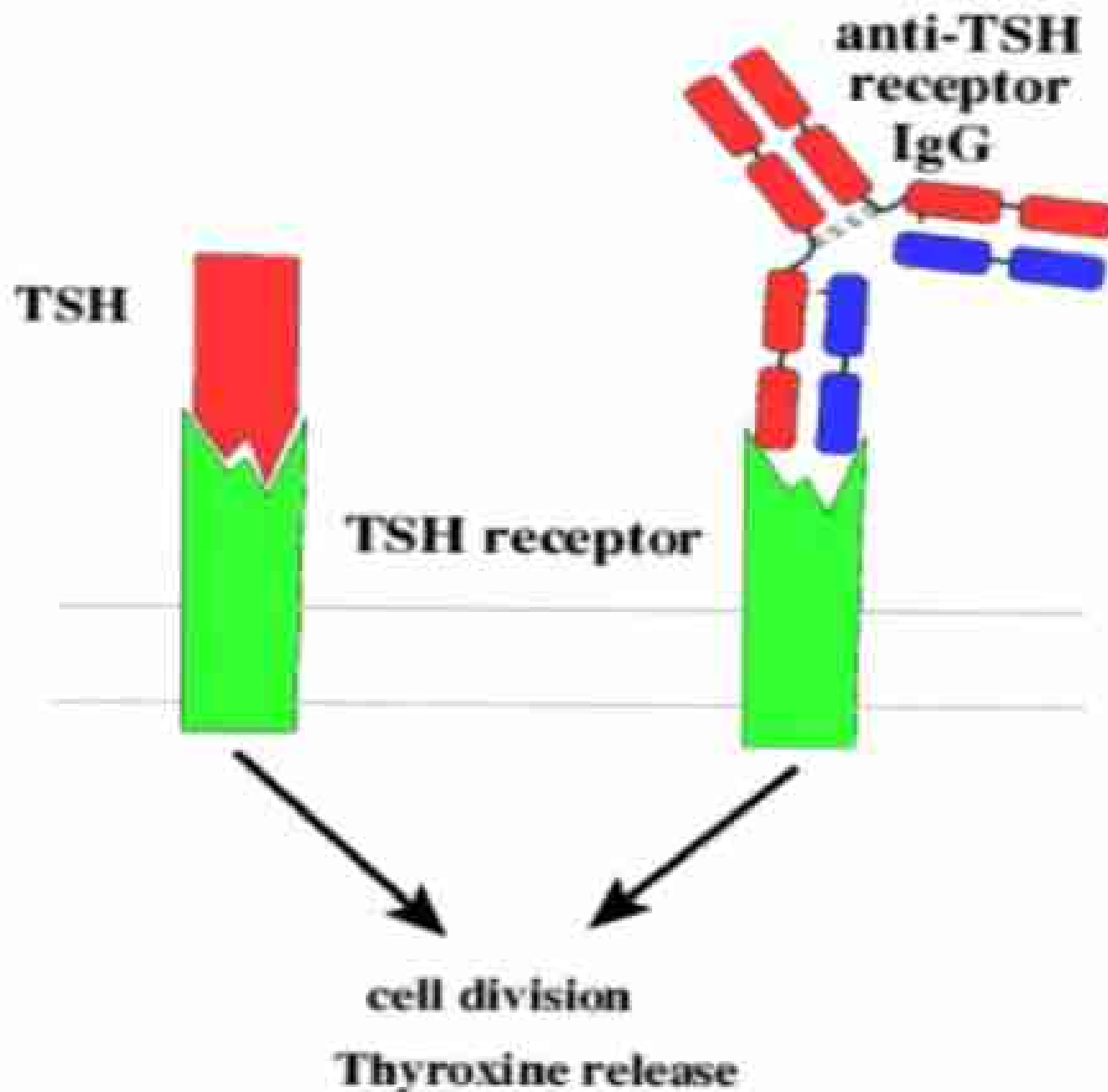
CLINICAL TRIAD

- **Hyperthyroidism** associated with **diffuse enlargement** of the gland
- **Infiltrative ophthalmopathy** --> **exophthalmos**
- **Localized, infiltrative dermopathy** --> **pretibial myxedema**



PATHOGENESIS

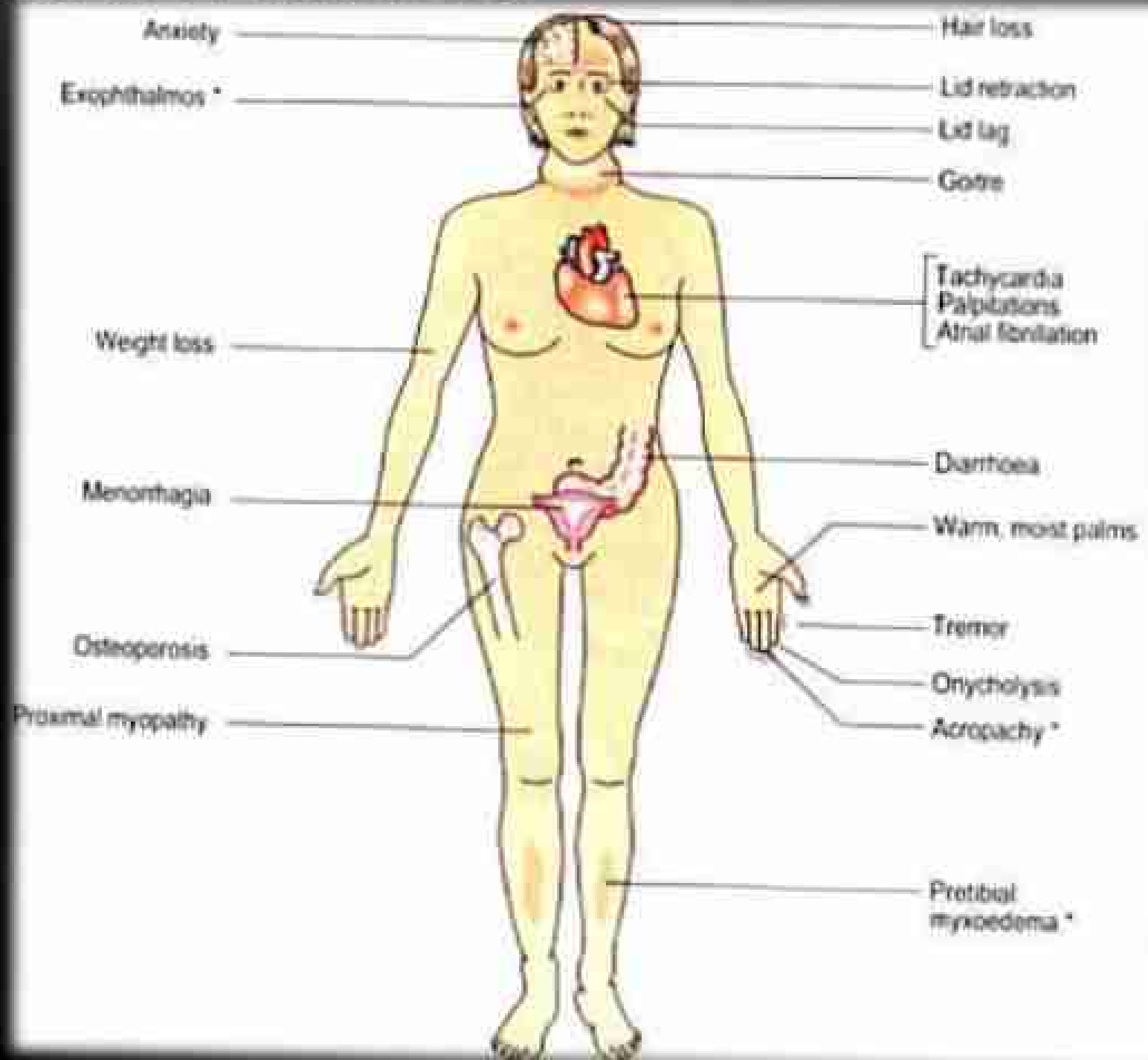
- Autoimmune disorder
- Auto antibodies against
 - TSH receptor - **Thyroid Stimulating Ig (TSI)** - Most common & specific
 - Thyroid peroxisomes
 - Thyroglobulin



TSI + TSH receptor --> mimics its actions --> increasing the release of thyroid hormones.

- Aberrant expression of TSH receptor on orbital & pretibial fibroblasts --> extra thyroidal changes
- Associated with other autoimmune diseases
- Familial; strong HLA association (HLA -DR3)

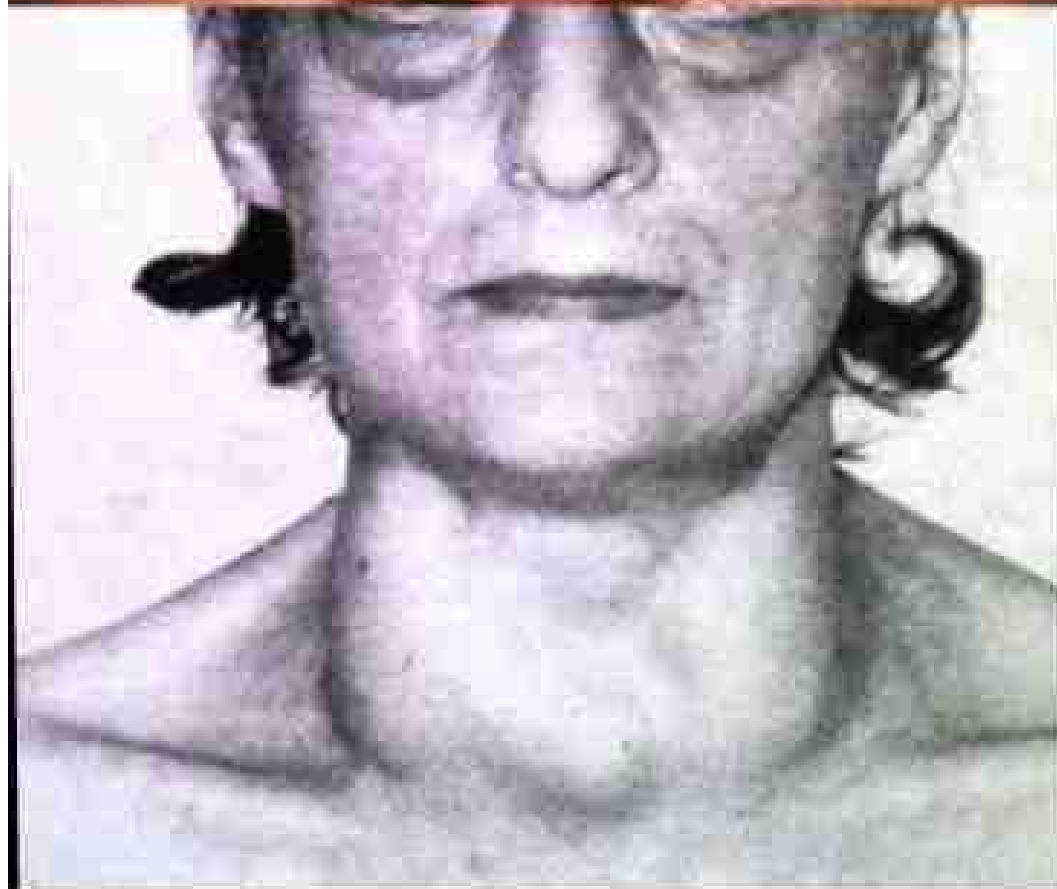
CLINICAL FEATURES





EXTRA THYROIDAL CHANGES

- Retro orbital connective tissue + extra ocular muscles + pretibial skin
 - Marked infiltration mononuclear cells (T cells)
 - Inflammation with edema and swelling
 - Accumulation of extracellular matrix components
 - Fatty infiltration



DIAGNOSIS

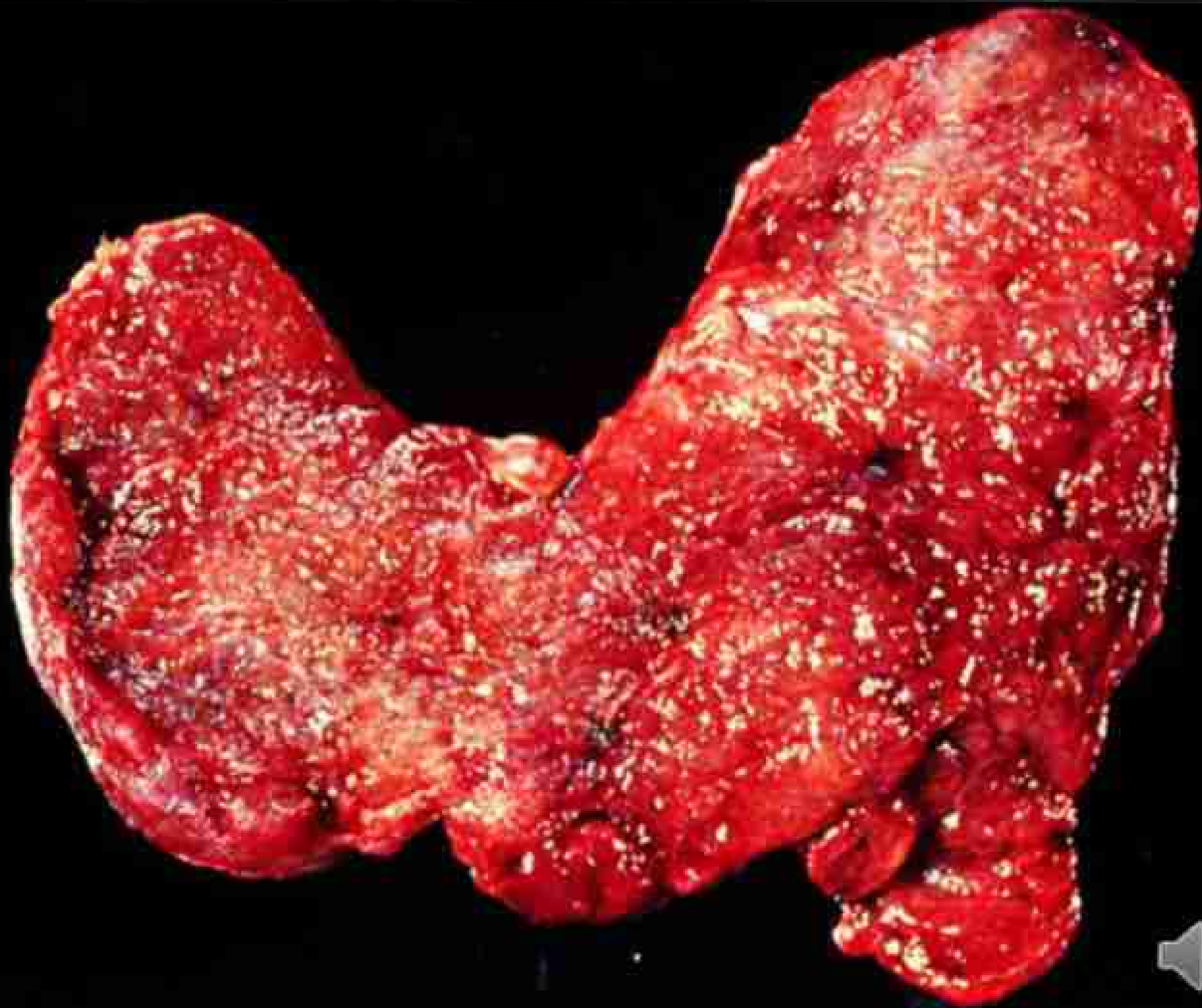
- Serum TSH levels— decreased - Most useful single screening test
- Free T4 & T3 levels -- increased
- RAIU— diffuse increased uptake
- USG - increased vascularity ('thyroid bruit')

MORPHOLOGY

Granuloma :

- Diffuse, symmetrically enlarged
- Smooth surface
- C/S- Red meaty appearance (beefy deep red)

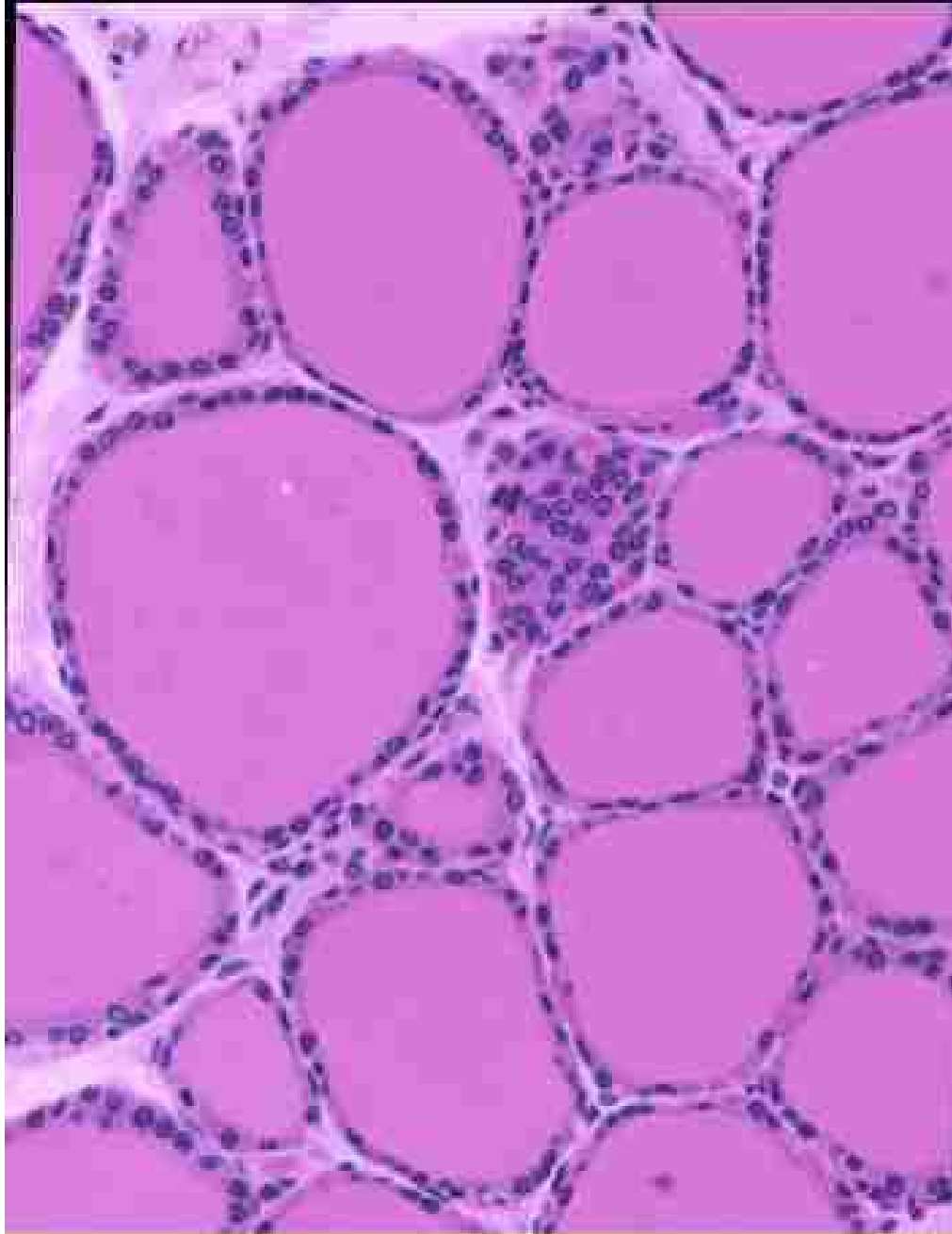




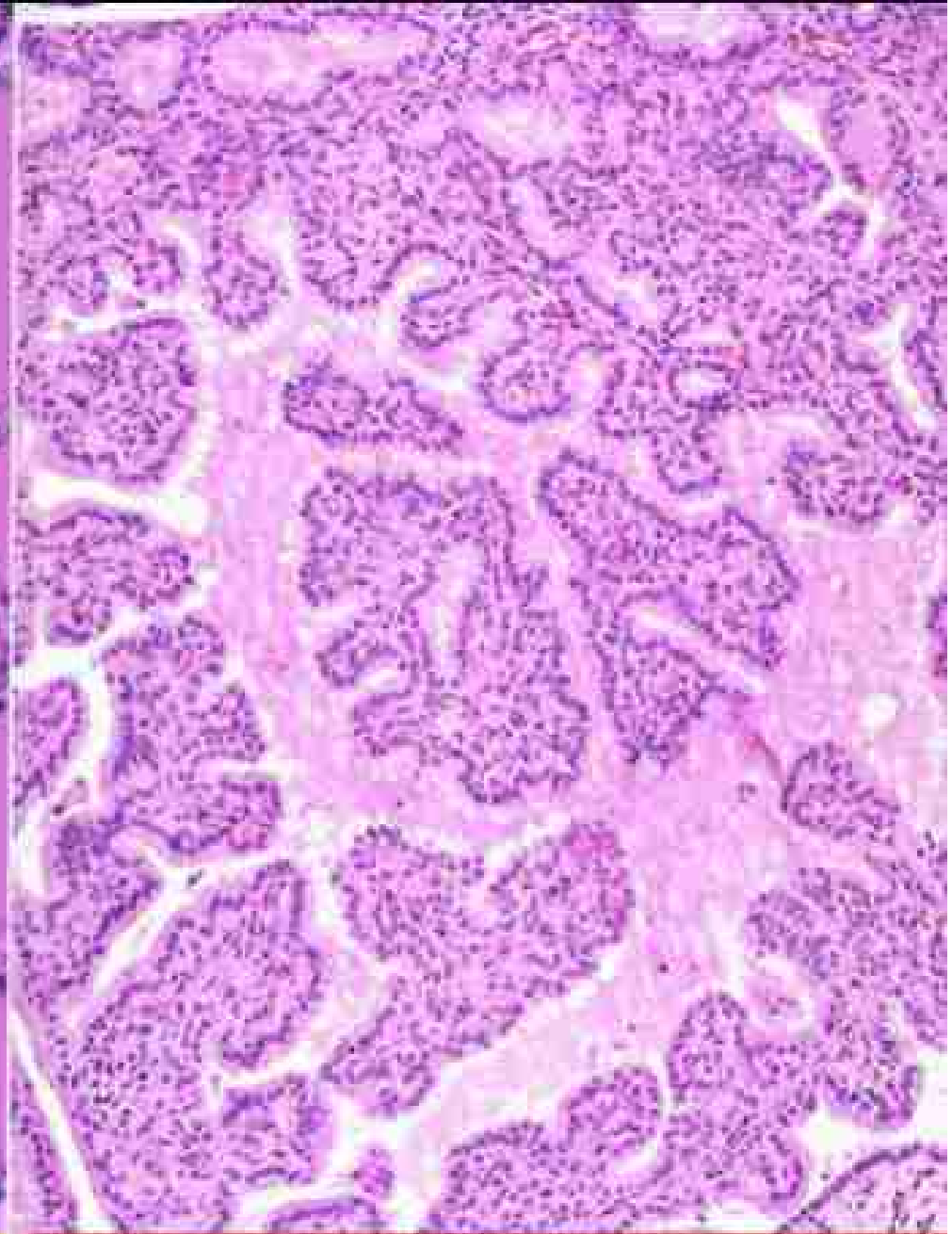
Microscopy

- Diffuse hyperplasia & hypertrophy
- Follicular epithelium- tall & columnar
- Pale & foamy colloid with scalloped margins
- Lymphoid infiltrates (T cells) with germinal centers

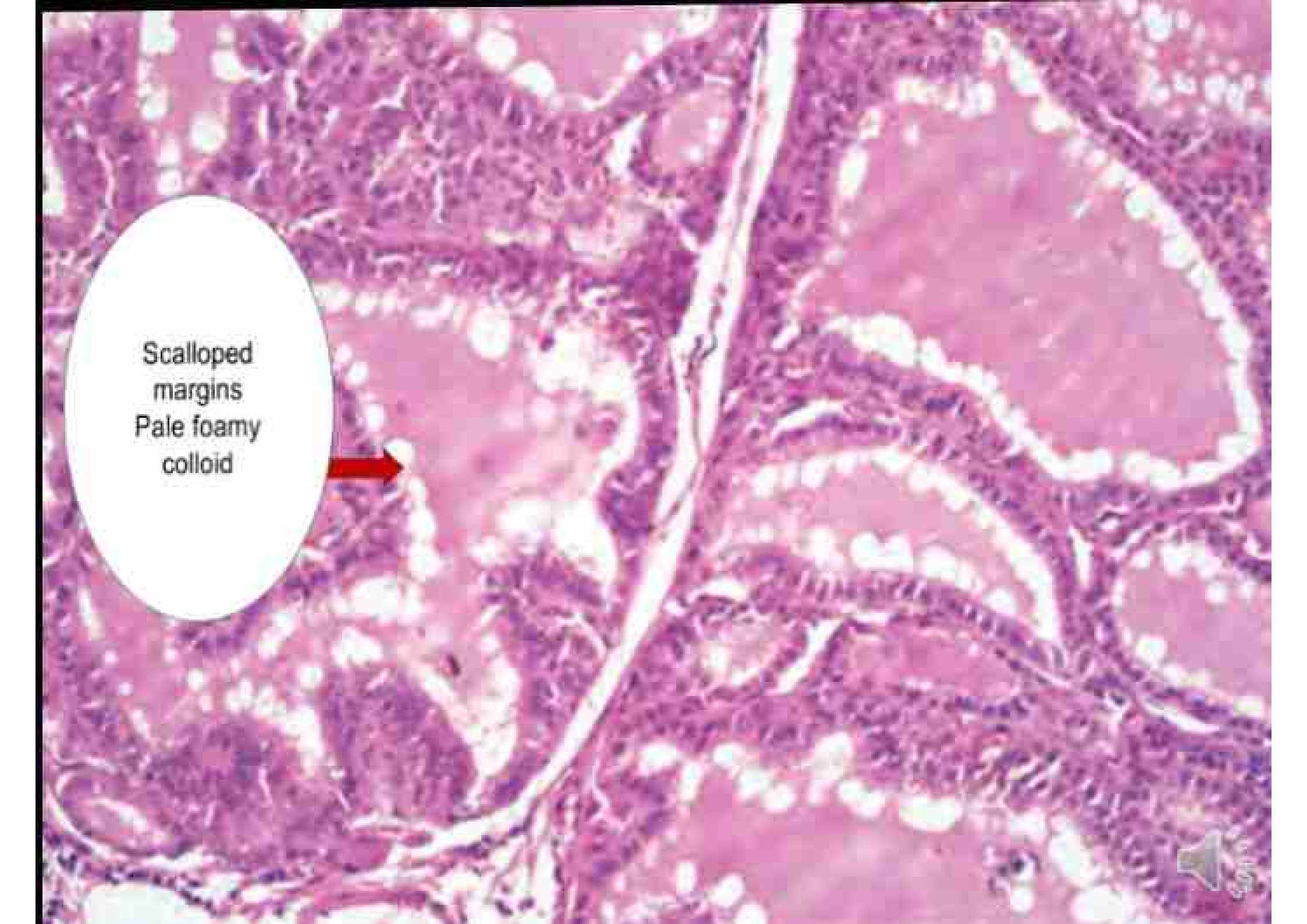




NORMAL - acini lined by flattened epithelium



Papillary hyperplasia



This histological slide shows thyroid tissue with several follicles. A callout box on the left contains the text 'Scalloped margins', 'Pale foamy colloid', and 'Pale foamy colloid'. A red arrow points from the box to a follicle that exhibits these features. The follicles are lined by a simple cuboidal epithelium, and the colloid is pale and foamy. The overall architecture is typical of thyroid tissue.

Scalloped
margins
Pale foamy
colloid
Pale foamy
colloid

TREATMENT

- Symptomatic treatment by β -blockers
- Decreasing thyroid hormone synthesis-
 - Propylthiouracil (PTU)
 - Radioiodine ablation
- Thyroidectomy (only with compressive symptoms)





TRY TO ANSWER

A 2-year-old child is brought to the family physician because of failure to thrive. Physical examination shows that the child is short and has coarse facial features, a protruding tongue, and an umbilical hernia. As the child matures, profound mental retardation becomes apparent. A deficiency of which of the following hormones is most likely to explain these findings?

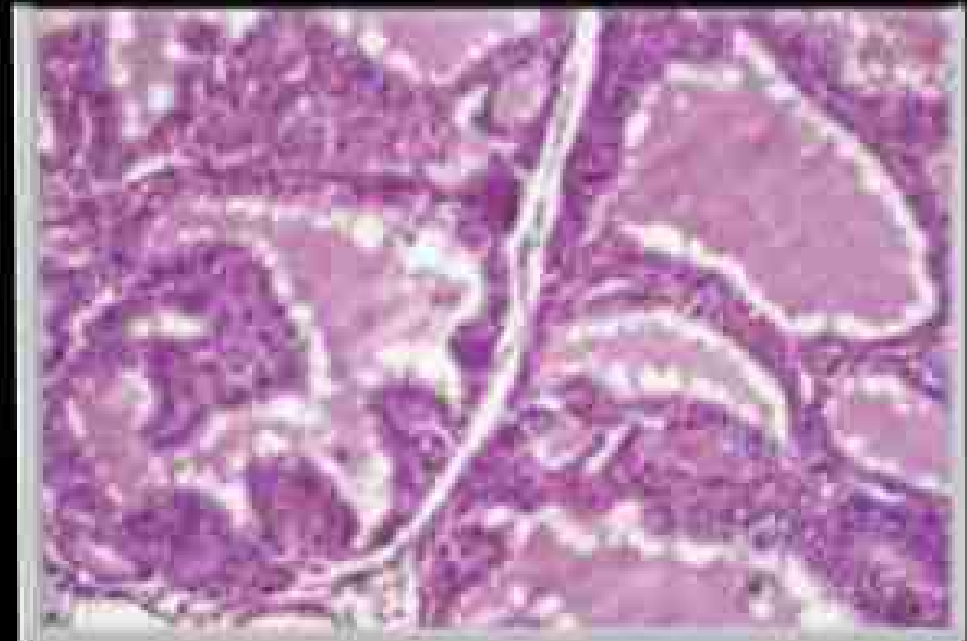
- ☐ (A) Cortisol
- ☐ (B) Norepinephrine
- ☐ (C) Somatostatin
- ☐ (D) Thyroxine (T4)
- ☐ (E) Insulin

2. A 40-year-old man sees his physician because of weight loss, increased appetite, and double vision. On physical examination, his temperature is 37.7°C, pulse is 106/min, respirations are 15/min, and blood pressure is 140/80 mm Hg. A fine tremor is observed in his outstretched hands. He has bilateral proptosis and corneal ulceration. Laboratory findings include a serum TSH level of 0.1 μ U/mL. A radioiodine scan indicates increased diffuse uptake throughout the thyroid. He receives propylthiouracil therapy, and his condition improves. Which of the following best describes the microscopic appearance of the patient's thyroid gland?

- ☐ (A) Destruction of follicles, lymphoid aggregates, and Hürthle cell metaplasia
- ☒ (B) Papillary projections in thyroid follicles and lymphoid aggregates in the stroma
- ☐ (C) Follicular destruction with inflammatory infiltrates containing giant cells
- ☐ (D) Nodules with nests of cells separated by hyaline stroma that stains with Congo red
- ☐ (E) Enlarged thyroid follicles lined by flattened epithelial cells

3. A 22-year-old woman has experienced increasing fatigue and a 7-kg weight loss without dieting over the past 4 months. She also has experienced increasing anxiety and nervousness with no apparent changes in her job or home life. She now has diarrhea. Physical examination shows a diffusely enlarged thyroid gland. Her temperature is 37.6°C, pulse is 103/min, respirations are 17/min, and blood pressure is 135/75 mm Hg. A radionuclide scan of the thyroid shows a diffuse increase in uptake. The figure shows the representative microscopic appearance of the thyroid gland at high power. What is most likely to produce these findings?

- ☐ (A) Antibodies against TSH receptor
- ☐ (B) Dietary deficiency of iodine
- ☐ (C) Mutation in the *RET* proto-oncogene
- ☐ (D) Maternal deficiency in T4
- ☐ (E) Irradiation of the neck



ASSIGNMENTS

1. Write the causes, clinical features and investigations in Hypothyroidism and hyperthyroidism??
2. Write the etiopathogenesis, gross, microscopy and clinical features of goiter?
3. Write short note on the pathogenesis, gross, microscopy and clinical features of Graves disease?
4. Myxedema is seen in
5. Pretibial myxedema is seen in