THYROID PATHOLOGY

LEC.2

Thyroid Pathology

Notes on normal anatomy & histology of thyroid gland

1. Thyroid gland consists of two lobes which are connected by the isthmus.

2. Develop by envagination of pharyngeal epithelium that descends to its normal position in the anterior neck.

3. Divided into lobules of 20-40 follicles, each with a single layer of cuboidal to low columnar epithelium, filled with thyroglobulin that is secreted by follicular cells as colloid.

4. Thyroid gland secrets T4 mainly & less quantity of T3, this secretion in under the control of TSH of pituitary gland & TRH of hypothalamus.

5. Interfollicular stroma contains C cells, formerly called Para follicular cells, derived from neural crest; they secrete calcitonin, which lowers serum calcium by promoting bone absorption of calcium and inhibiting bone resorption by osteoclasts.

6. Parathyroid glands are either within the thyroid stroma or just behind the thyroid gland.

Pathology of thyroid gland. including:

I. Hyperthyroidism.

II. Hypothyroidism.

III. Mass lesions of thyroid gland.

Hyperthyroidism & thyrotoxicosis.

Hyperthyroidism is a hyper function of thyroid gland (elevated levels of free T4& T3). This condition is either associated with Thyrotoxicosis or not.

Thyrotoxicosis is a hypermetabolic state caused by elevated levels of free T3 & T4. This elevated level of hormones is either from hyper functioning thyroid gland or from extra thyroid sources.

Causes of thyrotoxicosis

I. *Associated with hyperthyroidism either.*

(A) Primary. (Diseases of thyroid gland)

1. Graves disease.

2. Hyper functioning (toxic) multi nodular goiter.

3. Hyper functioning (toxic) adenoma.

(B) Secondary (Extra thyroid diseases).

TSH secreting pituitary adenoma

II. *Not associated with hyperthyroidism*.

1. Subacute granulomatous thyroiditis. (Painful)
2. Subacute lymphocytic thyroiditis. (Painless)
3. Struma ovarii (ectopic thyroid tissue within ovarian teratoma).
4. Factitious thyrotoxicosis. (Exogenous thyroid hormones intake).

Thus, strictly speaking, hyperthyroidism is only the most common category of thyrotoxicosis .

Clinical features:

Clinical features of thyrotoxicosis are due to excess thyroid hormone as well as those related to over activity of the sympathetic nervous system.

These symptoms include:

1. Constitutional symptoms. Like soft, warm, flushed skin. Heat intolerance & excessive sweating are common. Weight loss despite increased appetite is due to sympathetic overactitivity.
2. Systematic symptoms.

a. GIT symptoms. Include malabsorption syndrome, diarrhea,hypremotility.

b. **Cardiac symptoms**. palpitation & tachycardia, congestive heart failure in elderly patients.

c. **Neuromuscular symptoms.** Tremor, nervousness & irritability, 50% develop muscle weakness.

d. **Ocular manifestations**. Exophthalmos (wide staring gaze) and lid lag.

e. **Thyroid storm**. It is a medical emergency characterized by abrupt onset of severe hyperthyroidism. This condition occurs most commonly in patient with Grave's disease. Significant number of patients dies because of cardiac arrhythmias.

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

1. **Measurement of serum TSH concentration**.

The most useful single screening test for hyperthyroidism.

In primary hyperthyroidism (due to thyroid diseases), TSH levels are decreased even at the earliest stages, While in secondary hyperthyroidism (due to extra thyroid diseases like in diseases of pituitary or hypothalamus), TSH levels are either normal or high.

2. **Measurement of free T4.** In primary hyperthyroidism is usually increased.

Grave's disease: (**Autoimmune hyperthyroidism**)

Most common cause of hyperthyroidism.

It is characterized **by a triad of manifestations**:

1. **Thyrotoxicosis:** Caused by hyper functional, diffuse enlarged thyroid.
2. **Ophthalmopathy**: exophthalmos in 40% of cases.
3. **Pretibial myxedema**: A localized, infiltrative dermopathy.

- About 85% of cases are occurred in young female between 20 – 40 years.
- An increased incidence of Grave's disease occurs among family members (associated with HLA-DR3).

Pathogenesis of Grave's disease:

Grave's disease is an autoimmune disease explanation:

I. Presence of variety of autoantibodies in the serum of patient with grave's disease; (TSH receptor is the target for these autoantibodies).

Types of autoantibodies are:

1. Thyroid stimulating immunoglobulins (TSI) which lead to increased release of thyroid hormones.
2. Thyroid growth- stimulating immunoglobulins (TGI) which lead to proliferation of thyroid follicular epithelium.

3. TSH binding inhibitor immunoglobulins (TBIIs) prevent TSH from binding normally to its receptor on thyroid epithelial cells.

In such doing, some forms of TBIIs mimic the action of TSH, resulting in stimulation of thyroid epithelial cells activity, while other forms may actually inhibit thyroid cell function.

Thus it is not unusual to find the coexistence of stimulating & inhibiting immunoglobulins in the sera of the same patient.

It is likely that autoantibodies are also play role in the development of ophthalmopathy

II. Presence of many CD4+ helper T cells within the thyroid. These cells are thought to trigger the B cells to produce autoantibodies.

MORPHOLOGY OF GRAVE'S DISEASE:

Gross

Thyroid gland is diffusely enlarged, soft & its capsule is intact

MIC There is diffuse hypertrophy & hyperplasia of thyroid follicular cells, which result in followings.

1. Follicular cells are crowded & become tall, columnar.
2. This crowding result in formation of papillae.
3. The colloid within the lumen of follicles is pale, with scalloped margins.

4. Lymphoid infiltrates, consisting mainly of T cells, with fewer B cells & mature plasma cells; germinal centers are common.

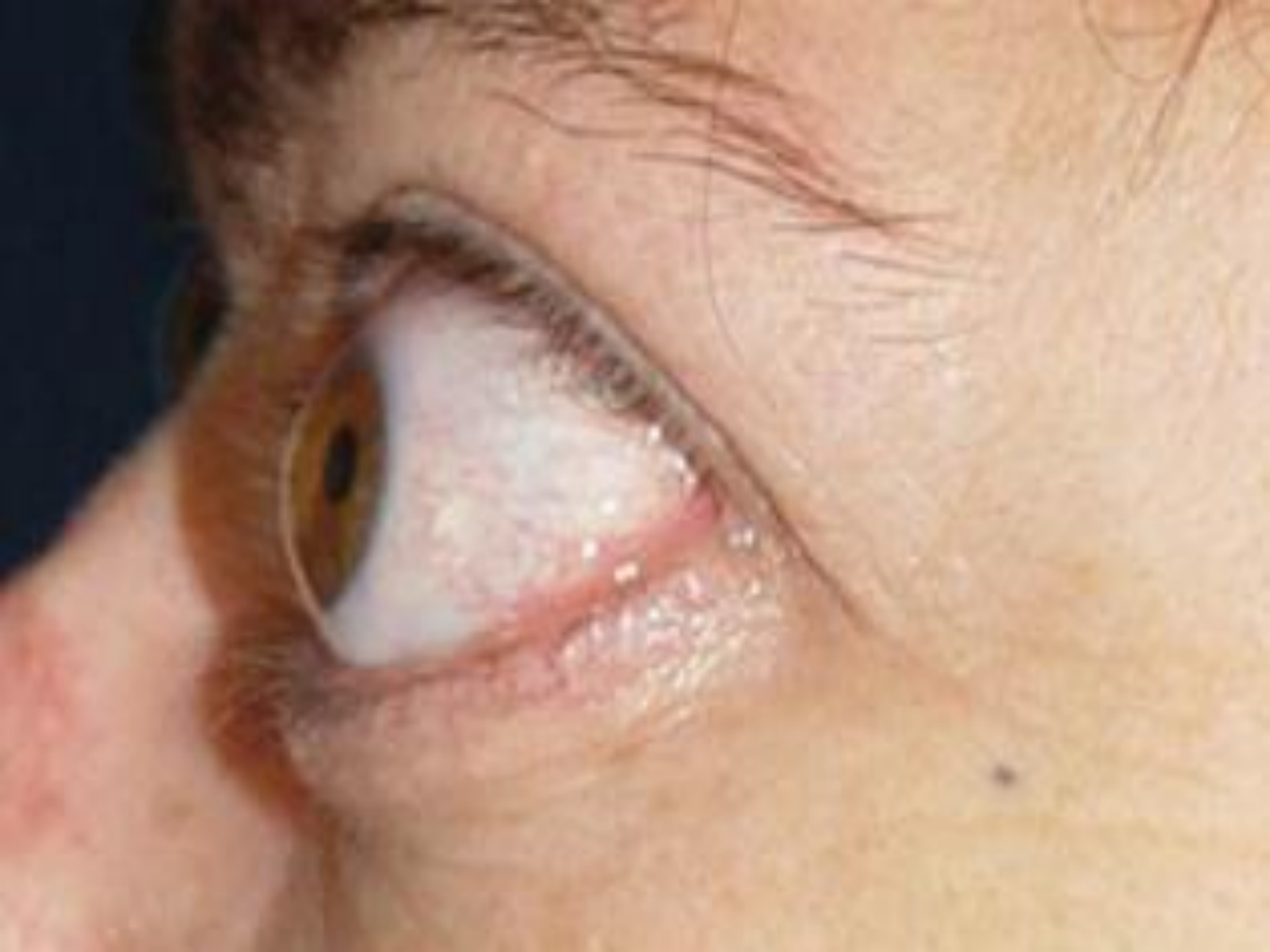
5. Extra thyroidal changes.

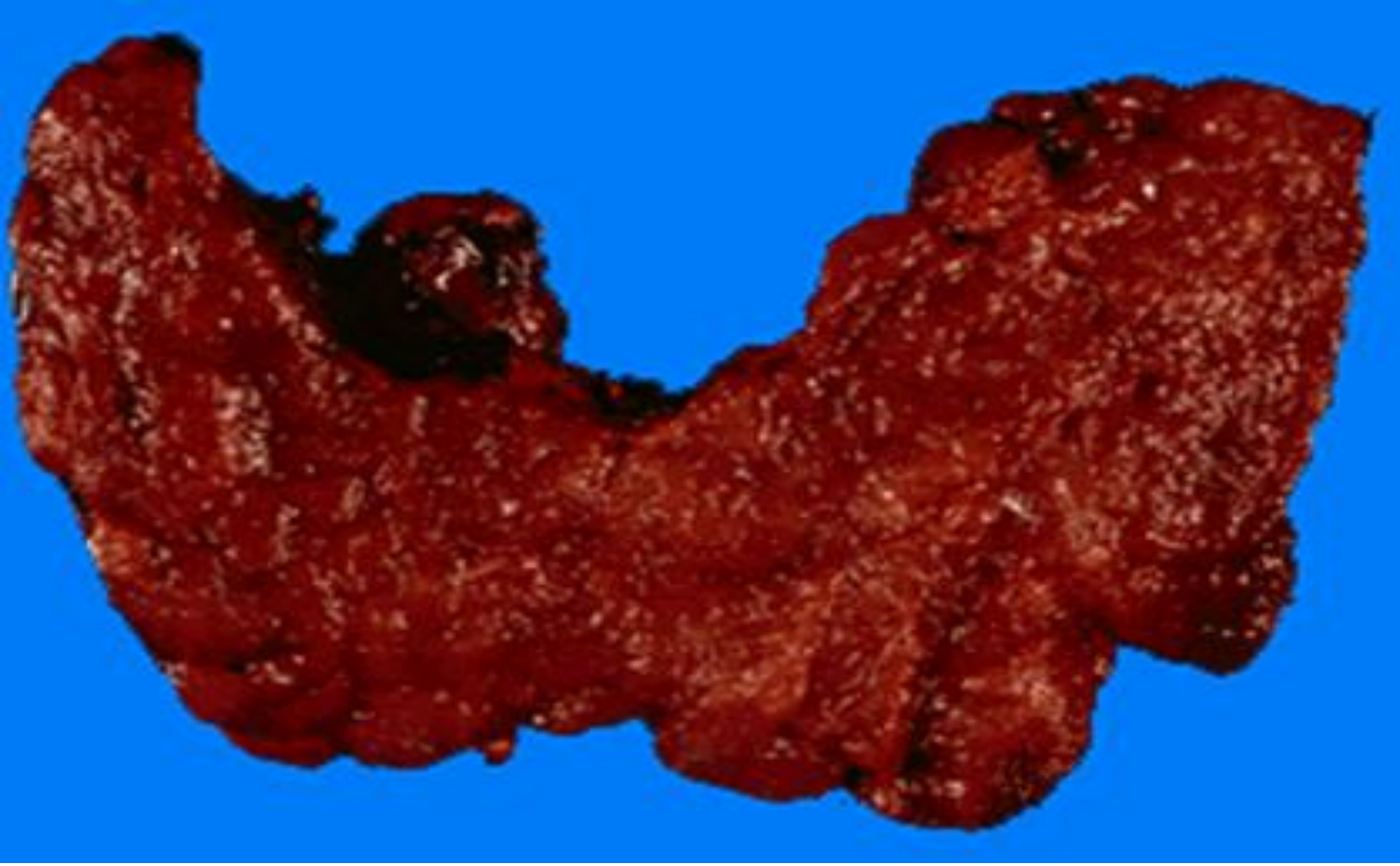
In ophthalmopathy: the tissues of orbit are edematous, due to the presence of (hydrophilic glycosaminoglycan's, infiltration by lymphocytes mostly T cells, & fibrosis of orbital muscles).

Dermatopathy is characterized by thickening of the dermis (deposition of glycosaminoglycan's & lymphocyte infiltration).

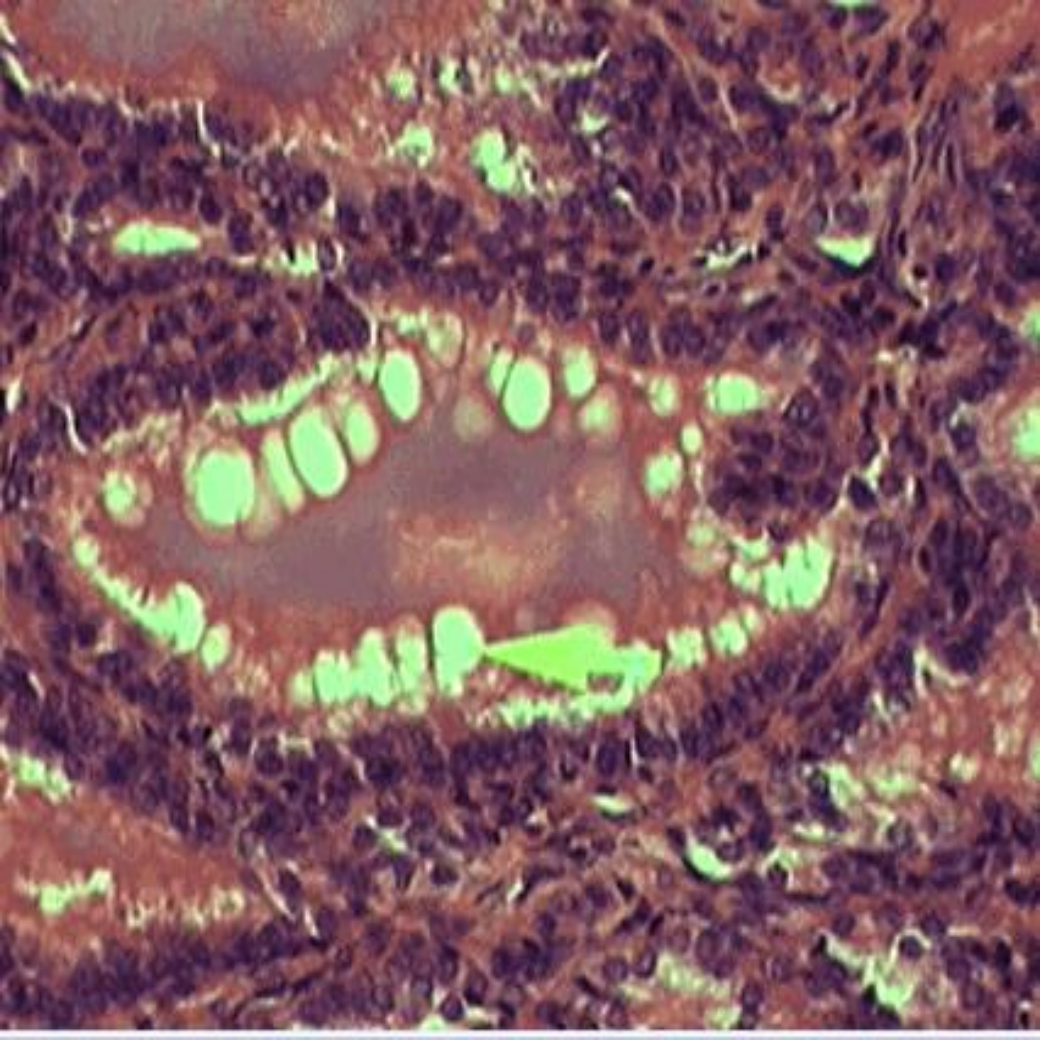
An overlapping between Grave's disease & Hashimoto's disease (autoimmune hypothyroidism) features may occur.

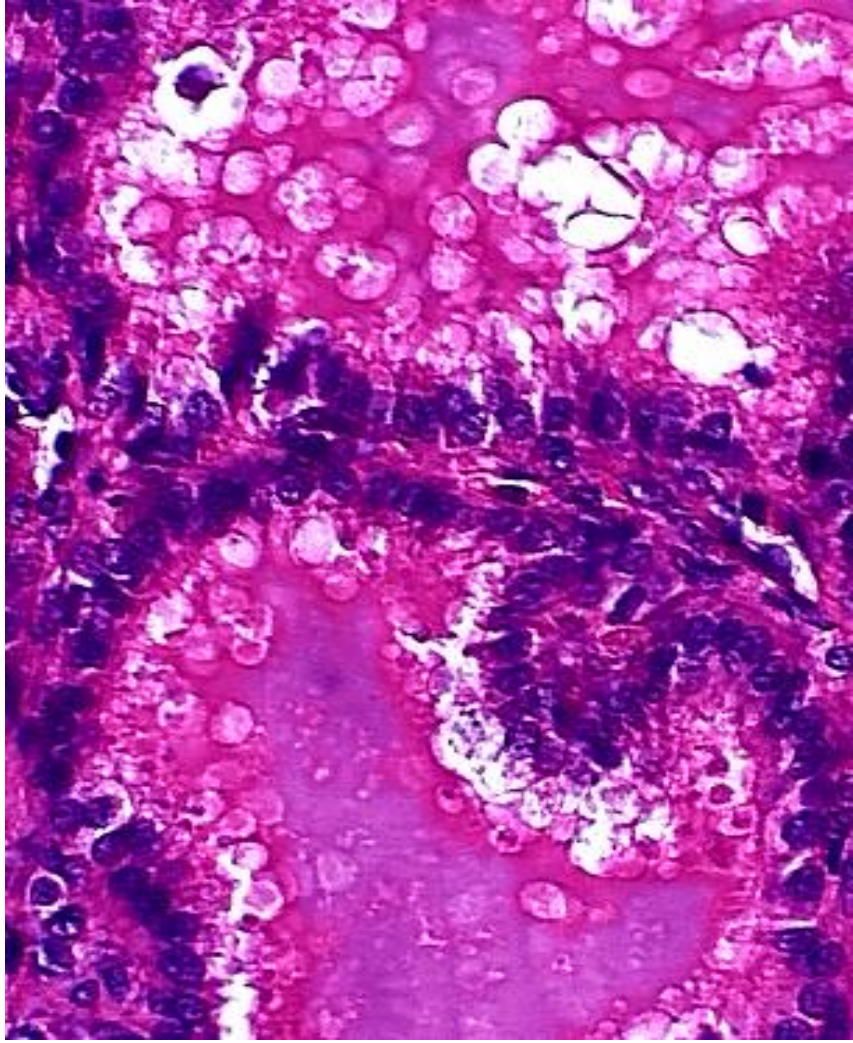
In both disorders (Grave's & Hashimoto's diseases) the frequency of other autoimmune diseases such as systemic lupus erythematosus, pernicious anemia, types I diabetes mellitus & Addison's disease is increased.





Grave’s disease





Microscopic features of Grave’s disease

Hypothyroidism:

Caused by any structural or functional derangement that interferes with the production of adequate levels of thyroid hormones.

This disorder is sometimes divided into primary & secondary categories according to sites of defect in production of thyroid hormones.

Causes of hypothyroidism:

I. primary hypothyroidism (defect in the thyroid gland).

1. Post surgery or post radiotherapy on thyroid gland.
2. Primary idiopathic hypothyroidism.
3. Hashimoto's thyroiditis.*
4. Iodine deficiency.*
5. Congenital biosynthesis defect (dyshormonogenetic goiter).*

II. Secondary hypothyroidism. (extra thyroidal causes).

Pituitary or hypothalamic failure. (Uncommon)

Clinical features:

The clinical manifestations of hypothyroidism are include **Cretinism & Myxedema**.

Cretinism.

It is refers to hypothyroidism develop in infancy & early childhood.

Causes of cretinism.

1. Dietary iodine deficiency (endemic).
2. Inborn errors of metabolism. This is most likely due to enzymatic deficiencies that interfere with synthesis of thyroid hormones.

Clinical features of Cretinism Include

1. Impaired development of the skeletal system & central nervous system, with secondary mental retardation & short stature.
2. Protruding tongue & umbilical hernia.

The severity of mental retardation in cretinism appears to be directly influenced by maternal thyroid hormones, including T3 &T4 that cross the placenta & are critical to fetal brain development.

If there is maternal thyroid deficiency before the development of fetal thyroid gland, mental retardation is severe.

In contrast, reduction in maternal thyroid hormones later in pregnancy, after the fetal thyroid has developed, allows normal brain development.

Myxedema

It is a state of hypothyroidism occurs in older children & adults.

The clinical manifestations of myxedema include:

1. Generalized apathy & mental sluggishness that in the early stages of disease mimic depression.
2. Cold intolerance & often obese.

3. Mucopolysaccharid rich edema accumulate in skin, subcutaneous tissue & a number of visceral sites with resultant broadening & coarsening of facial features, enlargement of tongue & deepening of the voice.

4. Bowel motility is decreased resulting in constipation.

5. In the later stages the heart is enlarged & heart failure may supervene.

Lab. Data.

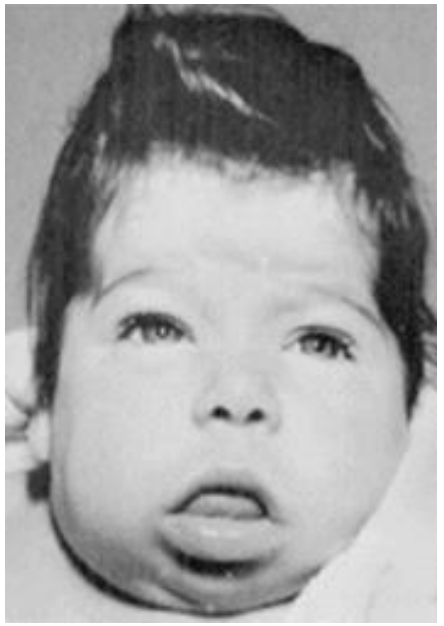
1. Measurement of the serum TSH level is the most sensitive screening test for hypothyroidism: (is increased in primary hypothyroidism due to loss of inhibitory mechanisms of T4 & T3 on pituitary & hypothalamus).

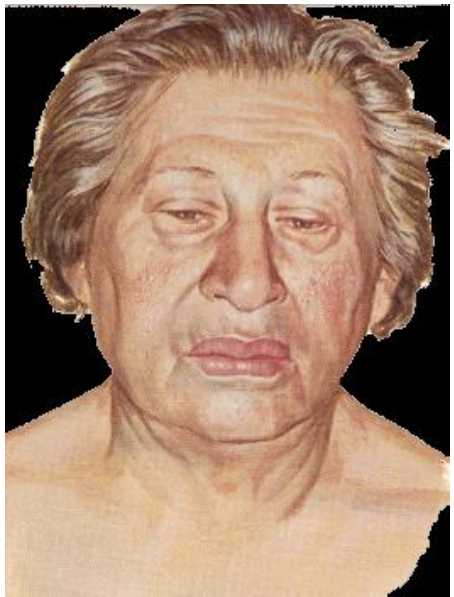
The level of TSH is not increased in secondary hypothyroidism).

2. T4 levels are decreased in both primary & secondary hypothyroidism

HYPO-THYROIDISM

- **Cretinism**
  - Severe retardation
  - CNS/Musc-skel
  - Short stature
  - Protruding tongue
  - Umbilical hernia
  - Maternal iodine defic.
- **Myxedema (coma)**
  - Sluggishness
  - Cool skin





Thank you