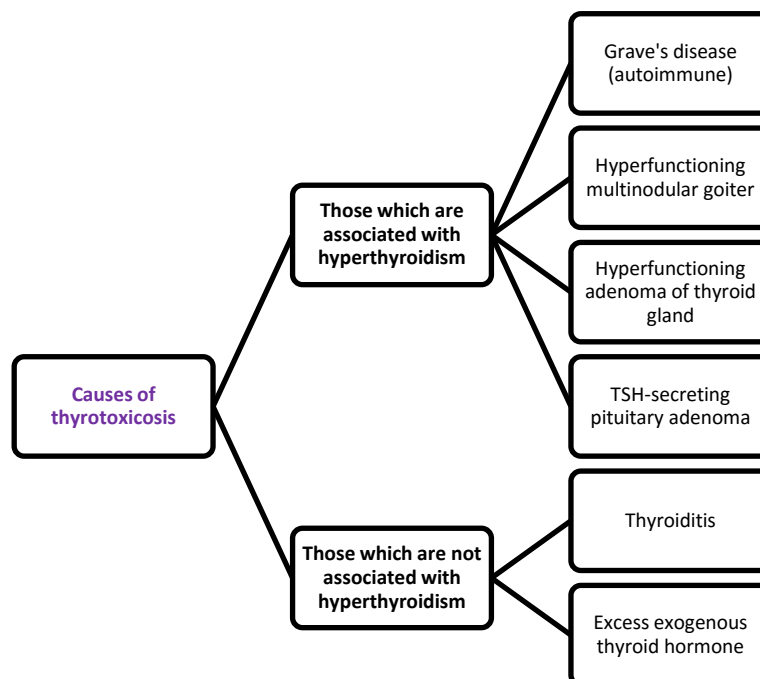




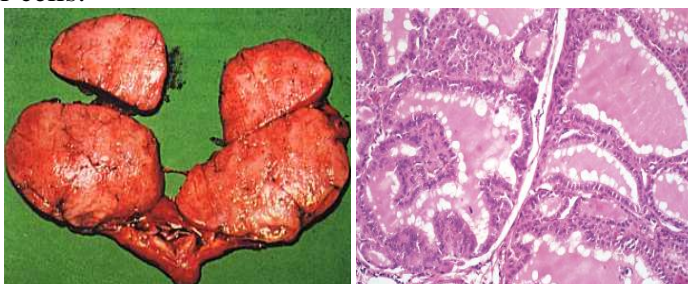
- **Thyrotoxicosis:**

- It is a hypermetabolic state caused by increased production of thyroid hormones (T3 and T4).



- **Grave’s disease:**

- It is an autoimmune disorder affecting mainly females (20-40 years of age).
- It is associated with HLA-D3 inheritance.
- Considered as the most common cause of endogenous hyperthyroidism.
- **Pathogenesis:**
  - ✓ There is a defect in regulatory T-cells.
  - ✓ This will result in expansion of helper T-cells which will produce cytokines that will induce B-cells to differentiate into plasma cells.
  - ✓ Plasma cells will produce the pathogenic Thyroid Stimulating Immunoglobulins (TSIs) which are responsible for the disease.
- **Autoantibodies to TSH-receptor which is found on the surface of thyroid gland:**
  - ✓ TSI (Thyroid Stimulating Immunoglobulin): binding to TSH-receptor and causing elevated production of thyroid hormones (T3, T4). It is more specific for Grave’s disease.
  - ✓ TGI (Thyroid Growth-Stimulating Immunoglobulins): binding to TSH-receptor and causing proliferation of thyroid follicular cells.
  - ✓ TBIIs (TSH-Binding Inhibitor Immunoglobulins): preventing TSH from binding to its receptor.
- **Clinical manifestations of Grave’s disease:**
  - ✓ Goiter (enlargement of thyroid gland). Morphology:
    - ❖ *Gross*: beefy, deep red cut surface with little colloid.
    - ❖ *Histologically*: little colloid with scalloped edges and tall columnar follicular cells.

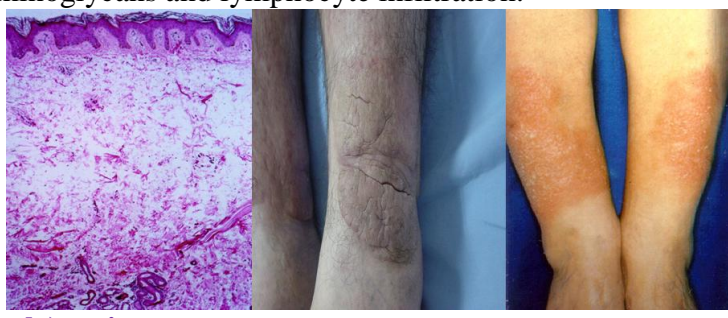




- ✓ Hyperthyroidism ( $\uparrow$  T3, T4).
- ✓ Exophthalmus in 40% of cases (eyeballs protruding outside). The volume of extraocular muscles is increased by:
  - ❖ Infiltration of retro-orbital space by T-cells.
  - ❖ Inflammatory edema and swelling of extraocular muscles.
  - ❖ Accumulation of extracellular matrix components.
  - ❖ Increased number of adipocytes (fatty infiltration).

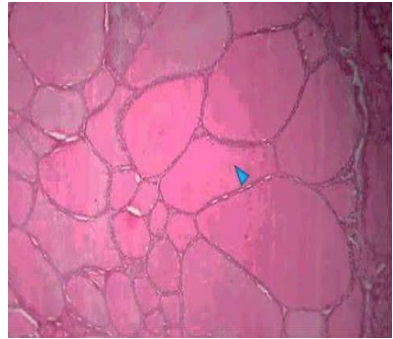


- ✓ Peritibial myxedema (rare): thickening of the dermis of the skin by deposition of glycosaminoglycans and lymphocyte infiltration.



- Diffuse nontoxic (simple) goiter:

- **Goiter means enlargement of the thyroid gland and the most common cause is iodine deficiency**  $\rightarrow$  leads to impaired thyroid hormones synthesis  $\rightarrow$  no negative feedback on the anterior pituitary gland  $\rightarrow$   $\uparrow$  TSH  $\rightarrow$  hypertrophy and hyperplasia of follicles (to overcome the hormone deficiency, ensuring a euthyroid state).
- **In this condition, there is enlargement of the thyroid gland without nodularity (enlarged follicles are filled with colloid).**
- **Morphology:**
  - ✓ Hyperplastic phase: diffusely and symmetrically enlarged.
  - ✓ Crowded columnar cells in follicles (similar to Grave's disease).
  - ✓ Colloid distribution is not uniformed in follicles.
  - ✓ Gross: cut surface is brown, glassy and translucent.
  - ✓ Histologically: follicular epithelium is flattened and cuboidal, colloid is abundant during periods of involution.
- **Clinical course:**
  - ✓ Majority of persons are euthyroid.
  - ✓ Mass effects from the enlarged thyroid gland.
  - ✓ Serum T3 and T4 levels are usually normal.



- Multinodular goiter:

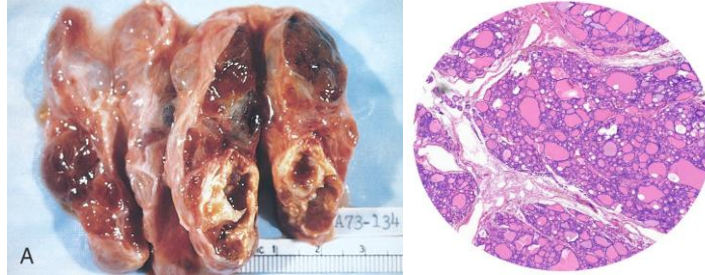
- All long-standing simple goiters convert into multinodular goiters.
- Usually mistaken for neoplastic involvement.
- More common in females and older individuals.



- There are recurrent episodes of hyperplasia and involution leading to irregular enlargement of the thyroid gland. Follicles might rupture leading to hemorrhage, scarring and calcifications.

- **Morphology:**

- ✓ Gross: multilobulated asymmetrically enlarged gland producing pressure on midline structures (trachea and esophagus). Cut surface will show irregular nodules with brown gelatinous colloid. Older lesions will show hemorrhage, fibrosis, calcification and cystic changes.
- ✓ Histologically: colloid rich follicles lined by flattened inactive epithelium.



- **Clinical features:**

- ✓ Mass effect of the enlarged gland (airway obstruction and dysphagia).
- ✓ patient are euthyroid or have subclinical hyperthyroidism.
- ✓ An autonomous nodule may develop producing (toxic multinodular goiter).
- ✓ Incidence of malignancy is low ( $< 5\%$ ).