



Pathology

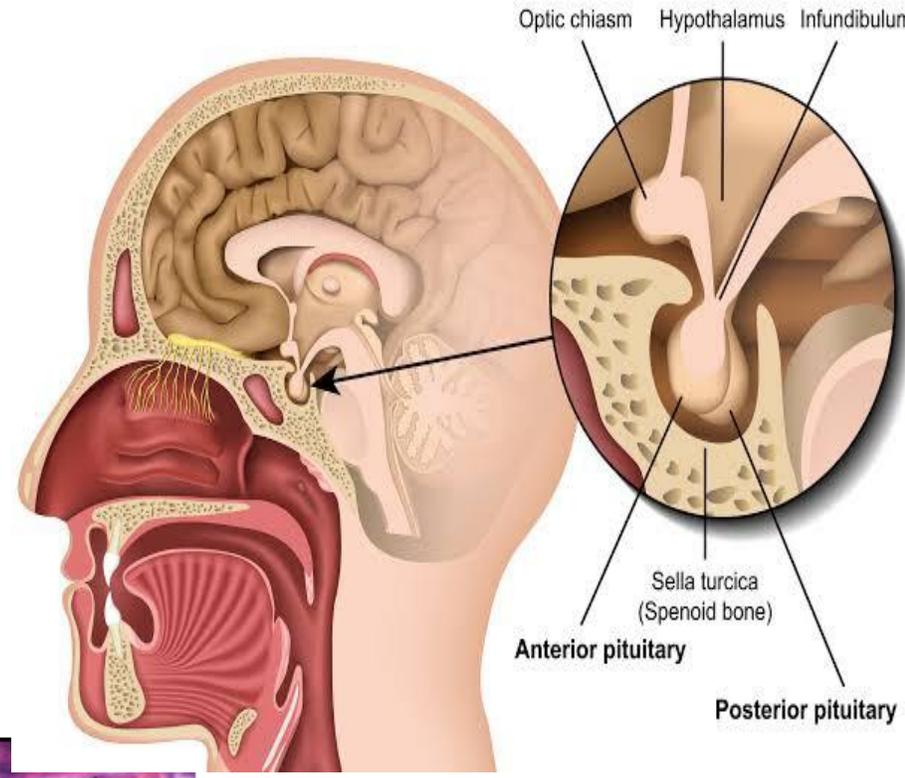
Pituitary , Adrenal and Pancreas

Pituitary gland

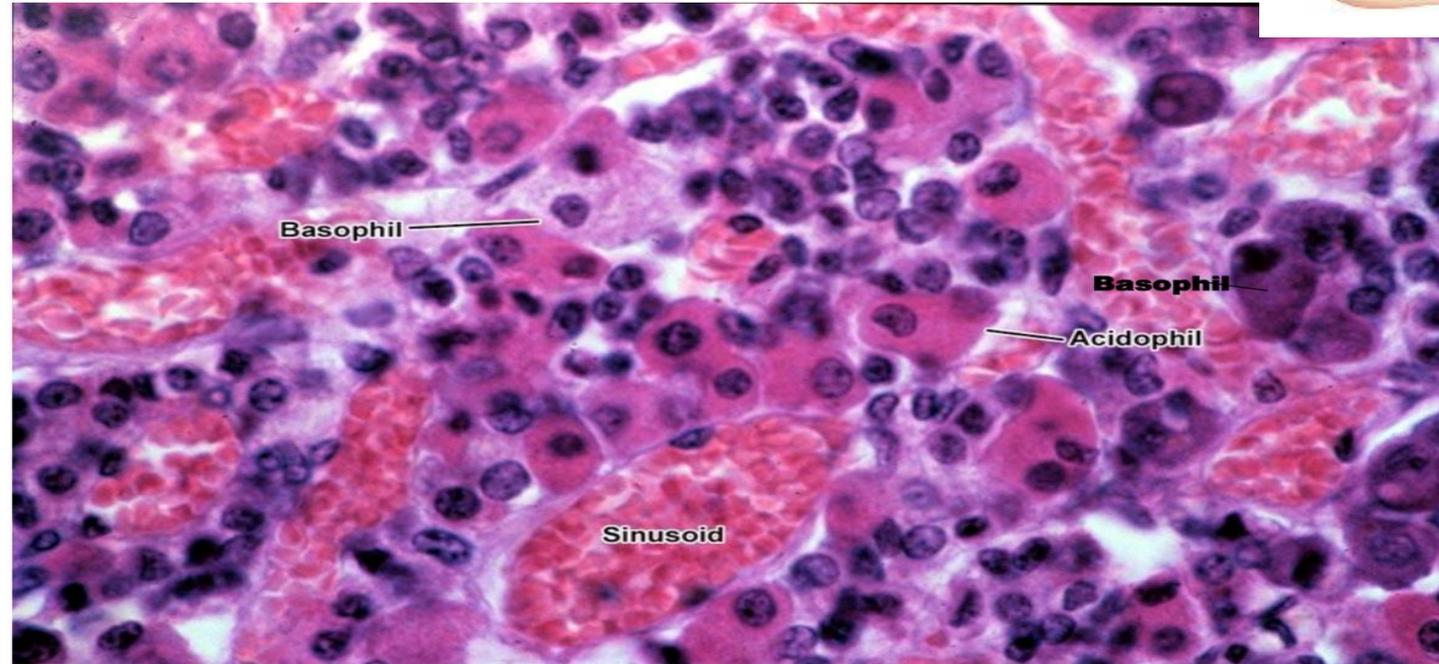
“Master endocrine gland”.

➤ **Parts:**

1. Adenohypophysis (Anterior pituitary).
2. Neurohypophysis (Posterior pituitary).



Anterior pituitary (H&E stain)



Disorders of the anterior pituitary

1-Hyperpituitary syndromes:

Caused by: -Hyperplasia,

-Functioning adenomas of anterior pituitary is the most cause, may produce Prolactin, Growth Hormone, and ACTH

-Carcinoma (rare).

2-Hypopituitarism

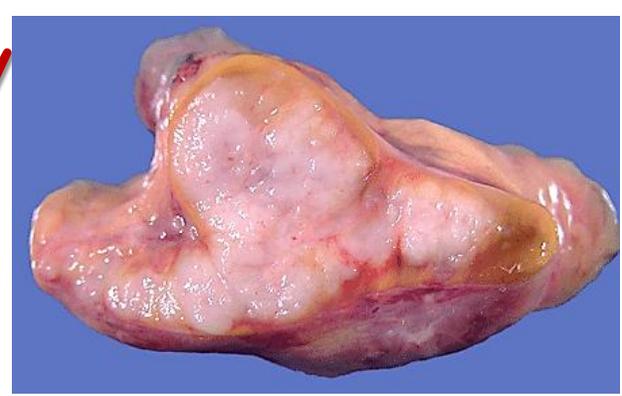
(1) Congenital anomalies (agenesis-Aplasia-hypoplasia).

(2) Sheehan's syndrome which is Post-partum Pituitary Necrosis; Coagulative necrosis, followed by fibrosis.

(3) Destruction of the pituitary by a pituitary adenoma, surgery, radiation or trauma ,metastatic tumors.

Tumors of the anterior pituitary

Pituitary Adenoma

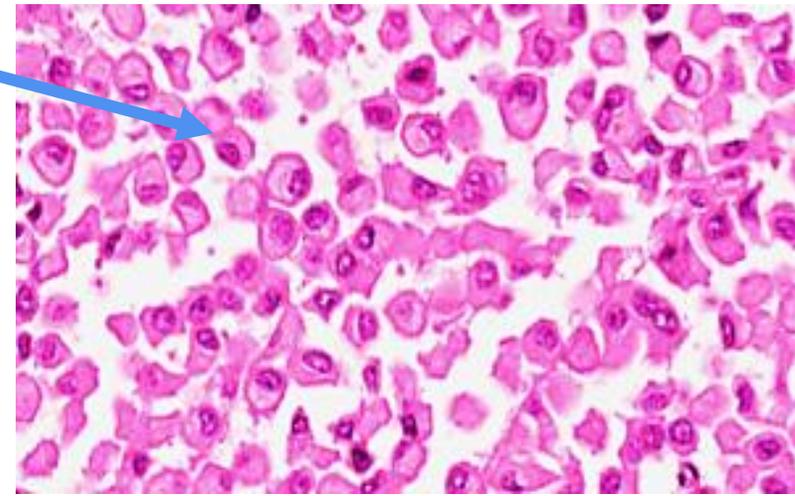
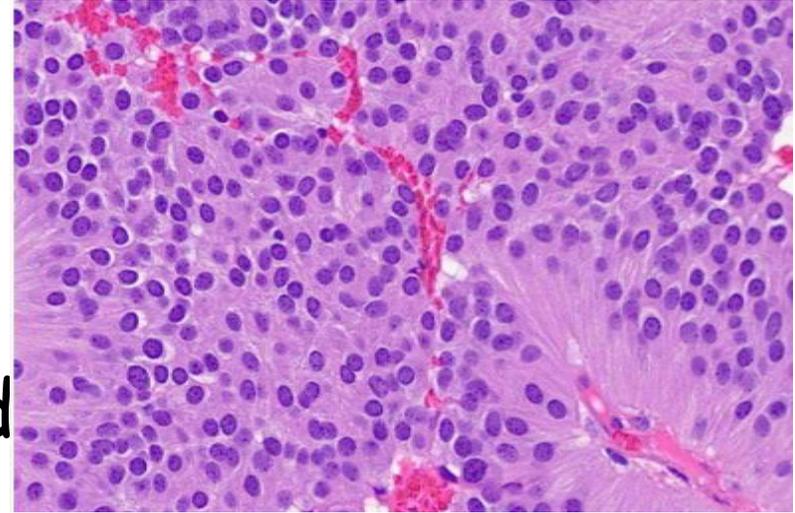


NE Adenomas appear as a lobulated mass covered by a thin, attenuated shiny capsule.

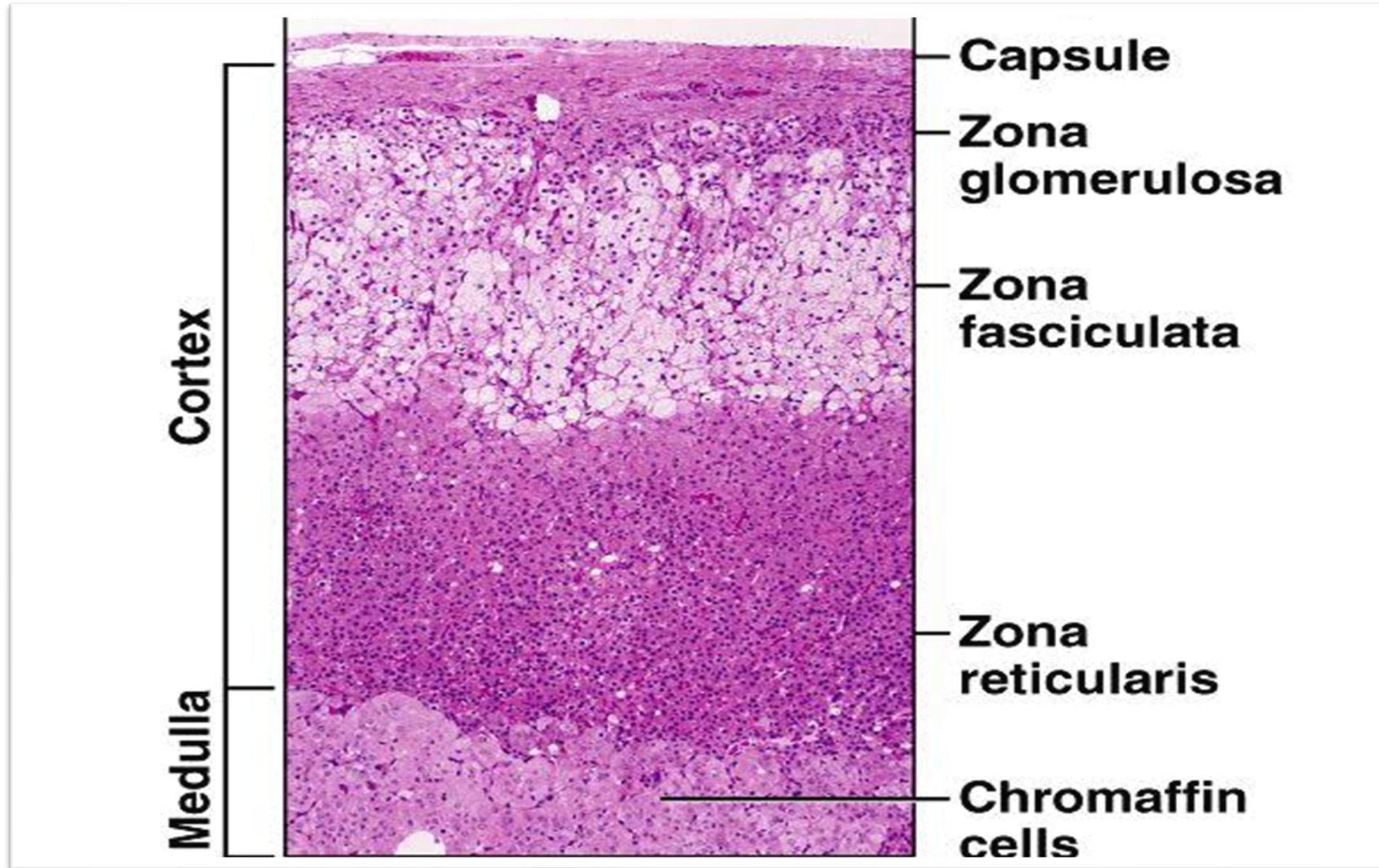
ME

Tumors have a uniform in appearance with fibrovascular stroma; cells classified as acidophilic, basophilic or chromophobic based on content of hormone secretory cells.

- Crooke hyaline change is characterized by large cells with a glassy hyaline appearance (due to accumulation of keratin filaments).



Adrenal gland histology



Diseases of supra-renal gland

1. **Cortical hyperfunction:** due to Hyperplasia, adenoma or carcinoma of the adrenal cortex.

Effects:

1. **Conn's disease:** aldosterone hypersecretion.
2. **Cushing syndrome:** glucocorticoides hypersecretion
3. **Adrenogenital syndrome:** androgen hypersecretion.

Diseases of supra-renal gland

2. Cortical hypofunction

A. Acute adrenal insufficiency leads to shock and death

Waterhouse-Friederichsen Syndrome: Acute Hypofunction occurs in association with overwhelming bacteremia (usually Meningiococcus).

B. Chronic adrenal insufficiency leads to Addison's disease

Causes: 1-Idiopathic Atrophy (60-75%)

2- an autoimmune disease

3-Tuberculosis

4-Amyloidosis

5-Metastatic Carcinoma[lung]

Tumors of suprarenal gland

Primary

Cortex

- *Cortical Adenoma
- *Cortical carcinoma

Medulla

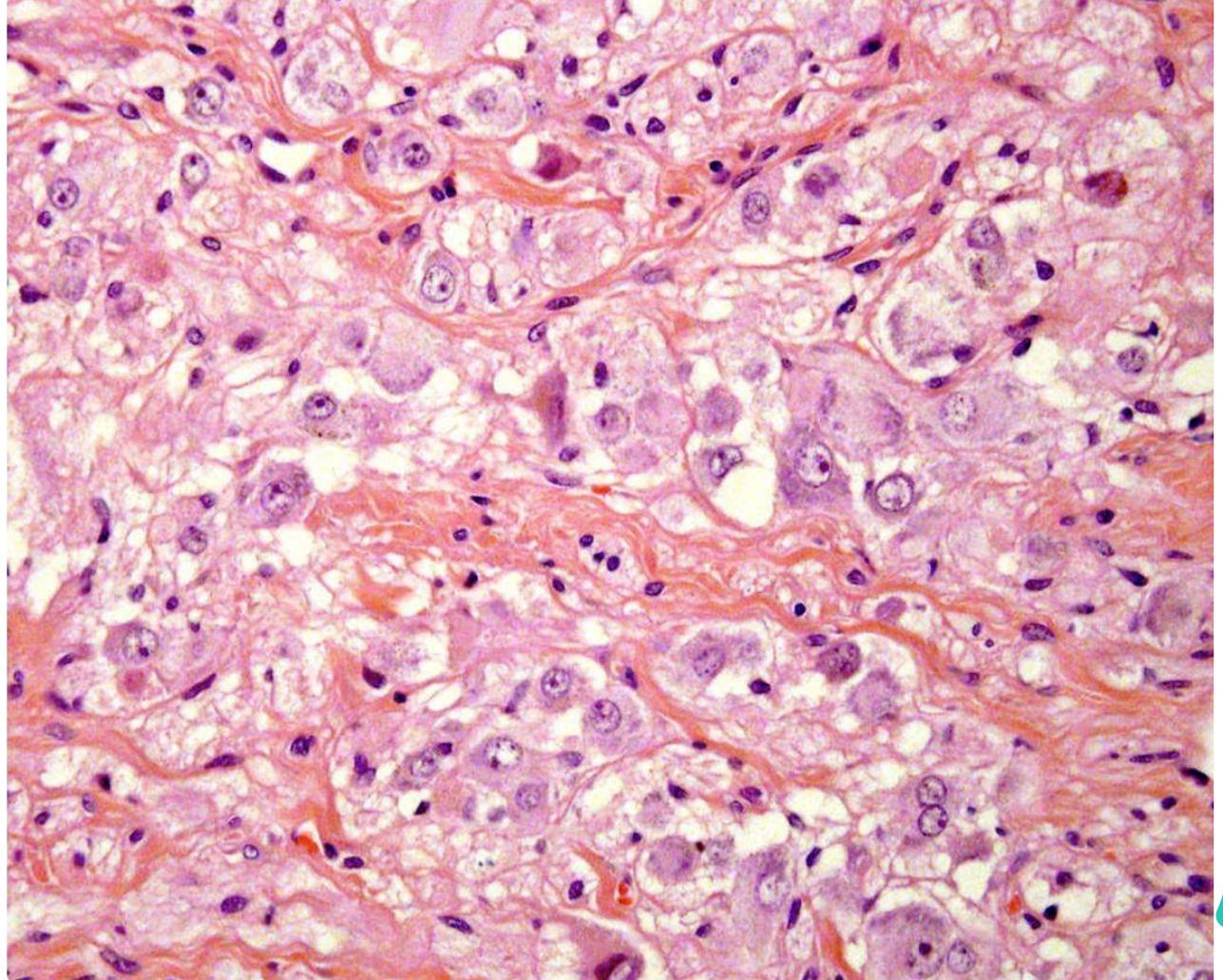
- *Ganglioneuroma
- *Pheochromocytoma
- *Neuroblastoma

Secondary

- *lung
- *breast
- *melanomas

Ganglioneuroma

Benign tumor composed of ganglion cells and nerve fibers (schwanian stroma)



Neuroblastoma

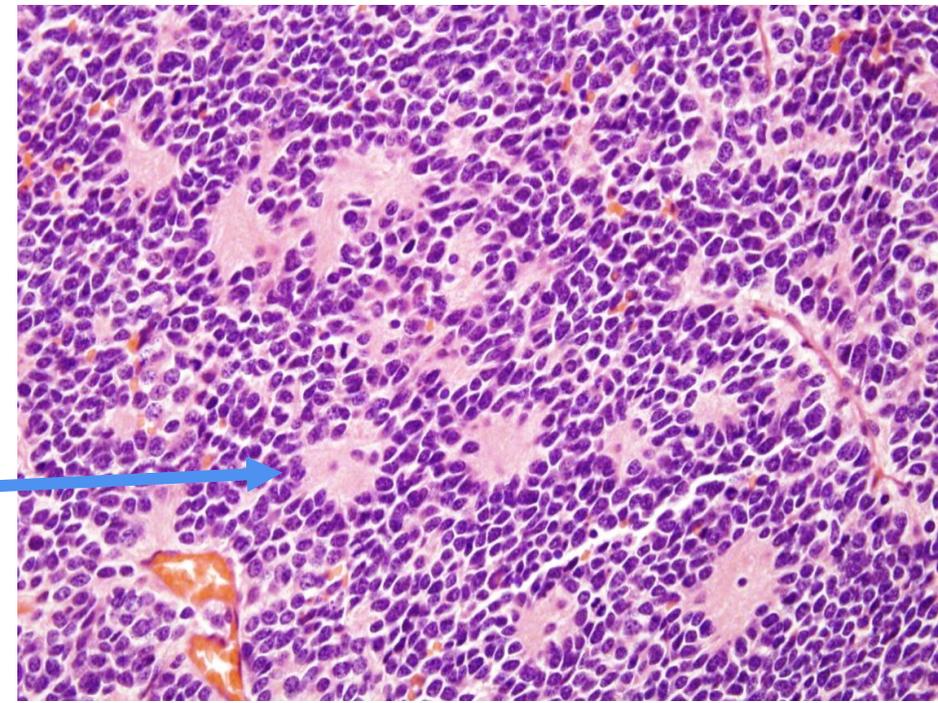
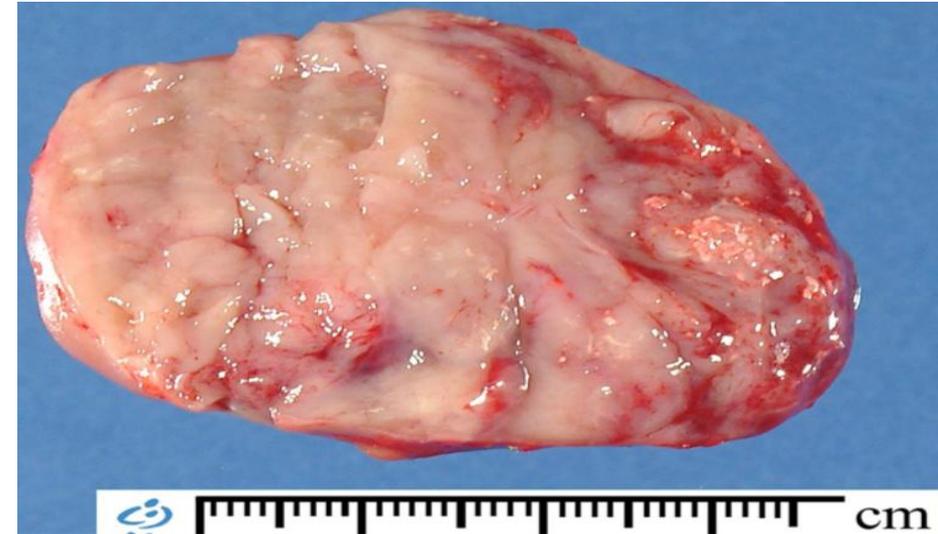
Highly malignant tumor of **children** under the age of 4 years.

N/E:

Large, soft mass with yellow areas of necrosis and red areas of hemorrhage.

M/E:

The tumor consists of small blue malignant round cells with dark nuclei "neuroblasts" arranged in sheets or in rosettes.



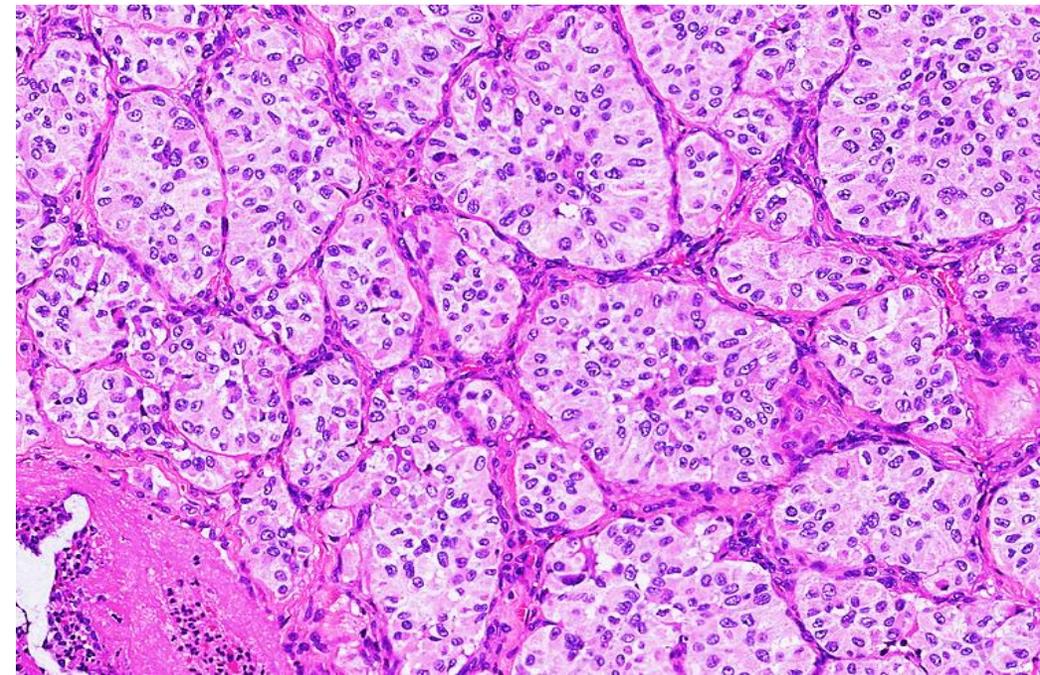
Pheochromocytoma

Paraganglioma of the adrenal medulla composed of chromaffin cells that produce catecholamines.

ME: Nested, trabecular or solid arrangement.

Cells: large, polygonal, uniform or extensively vacuolated.

Cytoplasm: abundant fine, granular red-purple cytoplasm.



Diseases of Endocrine Pancreas

Diabetes Mellitus (DM)

- A group of metabolic disorders characterized by hyperglycemia caused by defects in insulin secretion, insulin action, or both.
- DM causes secondary damage in multiple organ systems, especially the **blood vessels, kidneys, eyes, and nerves.**

Clinically:

A. Classic triad of symptoms: Polyuria + polydipsia + polyphagia

B. Elevated plasma glucose level confirmed by:

- Fasting plasma glucose >126 mg/dL.
- Random plasma glucose ≥ 200 mg/dL (in a patient with classic clinical signs or in repeated measures).
- Glycated hemoglobin (HbA1C) level $\geq 6.5\%$.

Diseases of Endocrine Pancreas

Diabetes Mellitus (DM)

Types:

I. Type 1 DM:

Etiopathogenesis:

- 1) Autoimmune disease due to production of autoantibodies against β cell antigens.
- 2) β cell destruction.
- 3) Absolute insulin deficiency.
- 4) Associated with:
 - Specific class I, MHC genes (HLA-DR 3,4).
 - Environmental factors: as mumps, rubella, and coxsackie B virus infections.

Diseases of Endocrine Pancreas

Diabetes Mellitus (DM)

Types:

II Type 2 DM:

Etiopathogenesis:

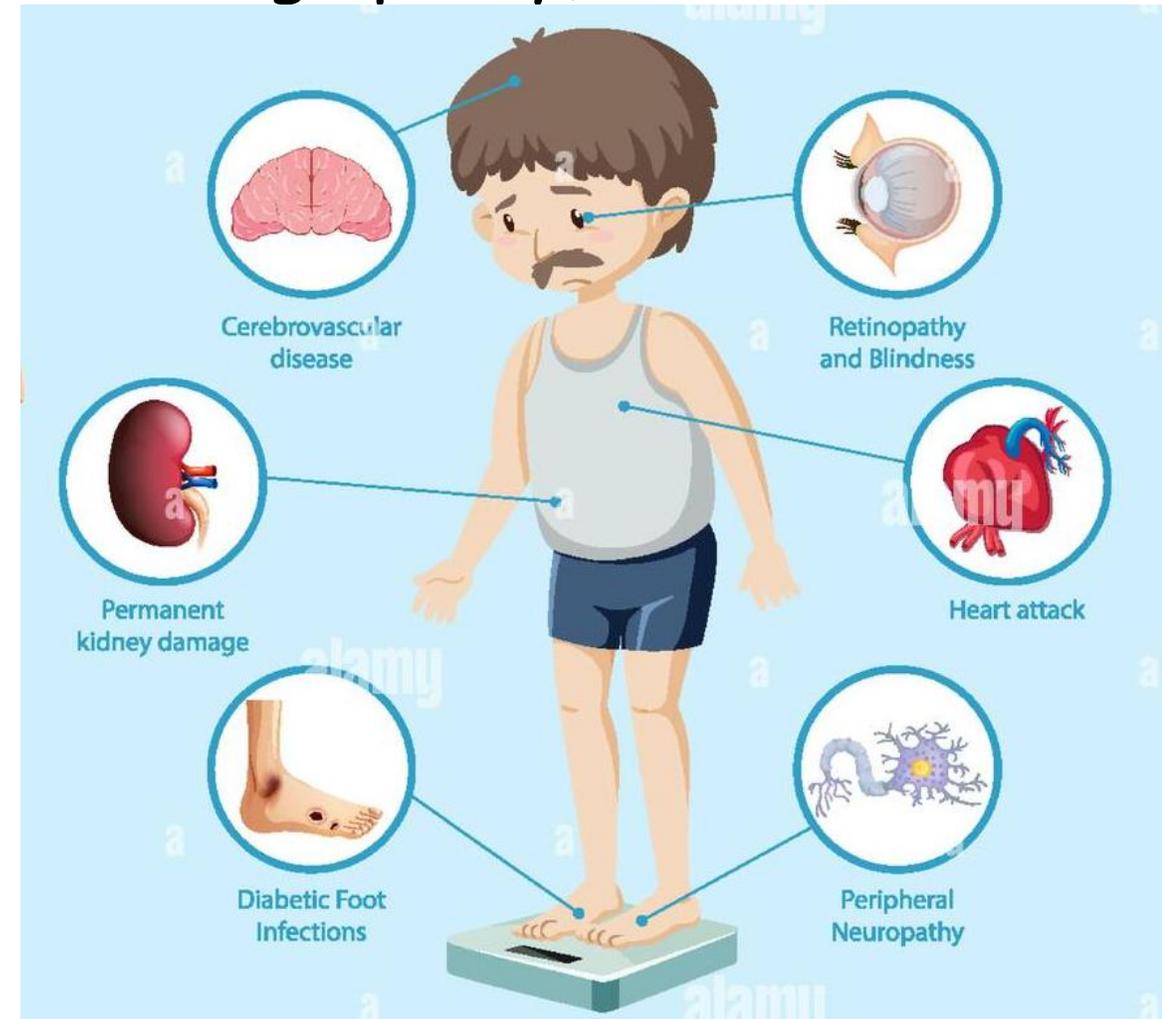
1. **Insulin resistance*** (failure of target tissues to respond normally to insulin) associated with obesity.
2. **Beta cell dysfunction***: B cells compensate for insulin resistance by hypersecretion, followed by β cell failure, and diabetes.

Diseases of Endocrine Pancreas

Diabetes Mellitus (DM)

Complications

1. Diabetic Macrovascular Disease (Macroangiopathy)
2. Diabetic Microangiopathy:
 - a. Diabetic nephropathy.
 - b. Ocular complications.
 - c. Diabetic neuropathy.
3. Increased liability to infections.
4. Impaired wound healing.
5. Diabetic foot
6. Diabetic coma.



Diseases of Endocrine Pancreas

Diabetes Mellitus (DM)

1. Diabetic Macrovascular Disease (Macroangiopathy)

- Its hallmark is accelerated atherosclerosis (greater severity and earlier age at onset).
- Affect the aorta and large- and medium-sized arteries.

Outcomes:

1. **Myocardial infarction** (coronary atherosclerosis), is the **most common cause of death** in diabetics.
2. **Cerebral ischemia and infarction.**
3. **Peripheral vascular diseases:** intermittent claudications and gangrene of the lower extremities.
4. **Renal artery atherosclerosis.**

Diseases of Endocrine Pancreas

Diabetes Mellitus (DM)

2. Diabetic Microangiopathy

- Its hallmark is **diffuse thickening of basement membranes.**

Affects:

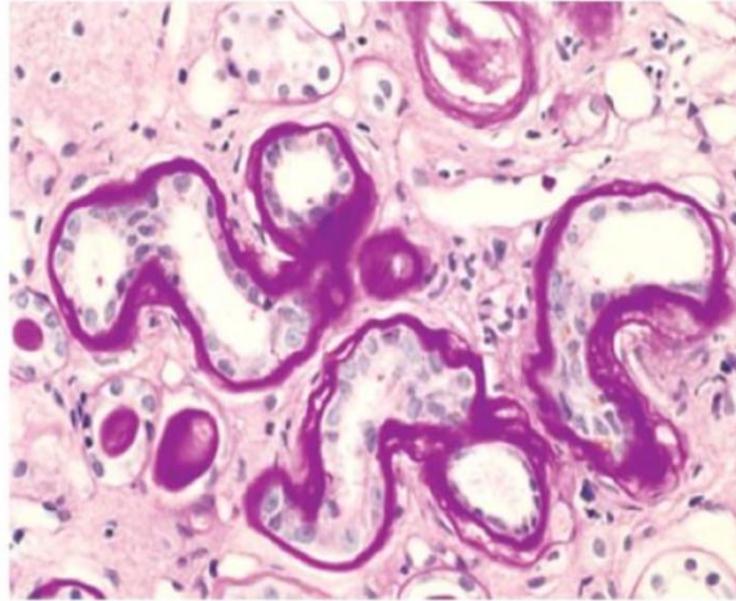
- **Capillaries** of the skin, skeletal muscle, retina, renal glomeruli, and renal medulla.
- **Non-vascular structures:** renal tubules, Bowman capsule, nerves.
- **Outcomes** development of:
 - .a. Diabetic nephropathy.
 - .b. Diabetic retinopathy and ocular complications.
 - .c. Diabetic neuropathy.

**Necrotizing
papillitis**

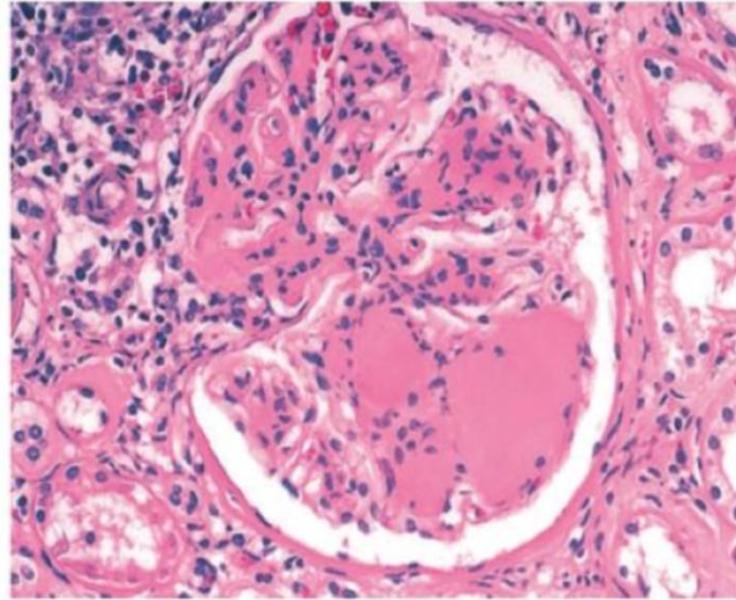


Pyelonephritis

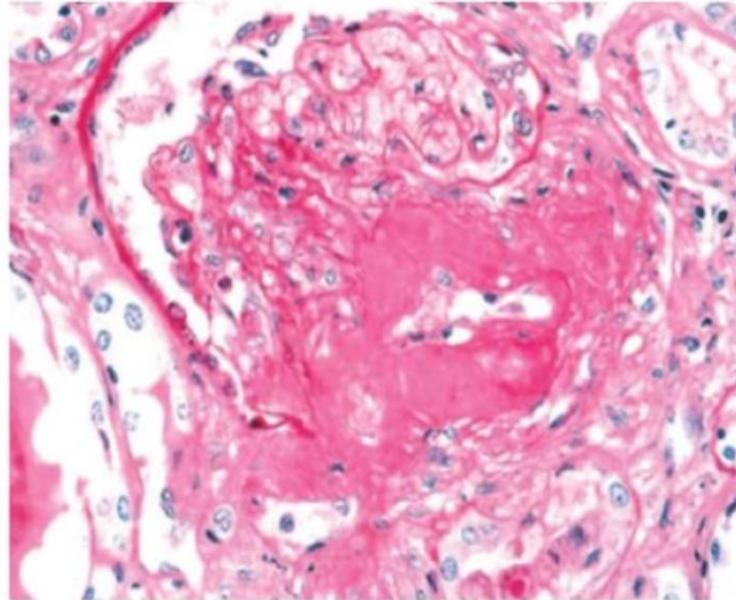
Thickening of tubular basement membranes



Nodular glomerulosclerosis



Severe renal hyaline arteriosclerosis



Nephrosclerosis in long-standing DM



Diseases of Endocrine Pancreas

Diabetes Mellitus (DM)

Other complications:

A. Increased liability to infections: due to hyperglycemia + defects in leukocyte functions and cytokine production.

- Skin, respiratory and urinary tract infections.
- Tuberculosis, fungal infections and AIDS.

B. Impaired wound healing (sensory loss, poor circulation and immune response, infection).

C. Diabetic foot: ulceration, infection, gangrene due to *neuropathy
*poor circulation and increased liability to infection

D. Diabetic coma:

- Diabetic ketoacidosis (common in type 1DM).
- Hypoglycaemic coma.

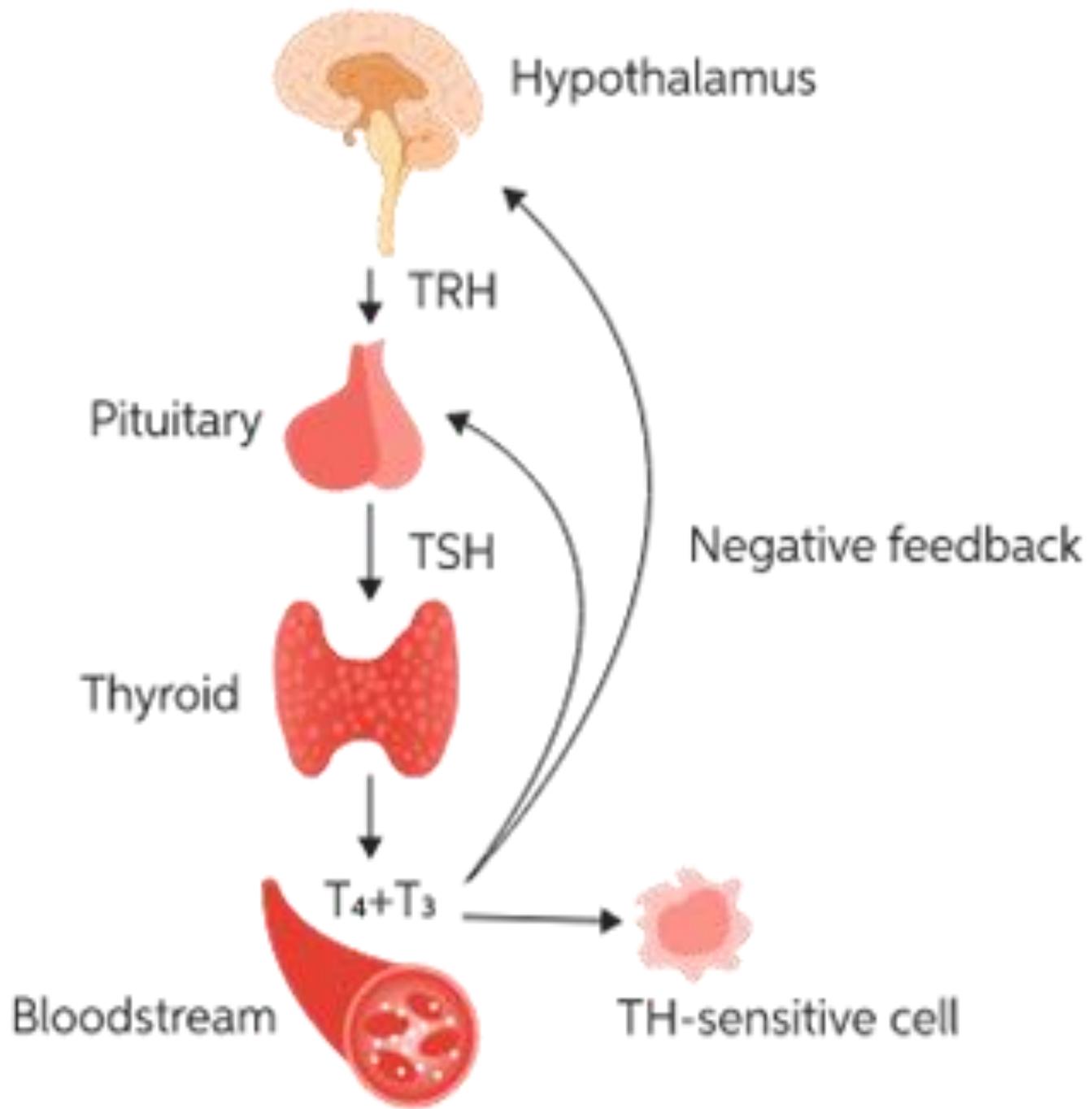
Type 1 Versus Type 2 Diabetes Mellitus

Features	T ₁ DM	T ₂ DM
Age	<ul style="list-style-type: none"> Childhood and adolescence 	<ul style="list-style-type: none"> Usually in adulthood (40y)
Incidence	<ul style="list-style-type: none"> 5% to 10% of cases 	<ul style="list-style-type: none"> 90% of cases
Weight/ass. diseases	<ul style="list-style-type: none"> Normal or weight loss 	<ul style="list-style-type: none"> Obesity and metabolic syndrome
Risk of coma	<ul style="list-style-type: none"> Diabetic ketoacidosis 	<ul style="list-style-type: none"> Non-ketotic hyperosmolar coma
Beta cell mass	<ul style="list-style-type: none"> Depletion 	<ul style="list-style-type: none"> Mild depletion
Insulin level	<ul style="list-style-type: none"> Reduced 	<ul style="list-style-type: none"> Increased (early); normal or moderate decrease (late)
Islet autoantibodies	<ul style="list-style-type: none"> Present 	<ul style="list-style-type: none"> Absent
Etiology	<ul style="list-style-type: none"> Autoimmune destruction and loss of β cells due to failure of self-tolerance 	<ul style="list-style-type: none"> Insulin resistance β cell dysfunction
Genetic linkage	<ul style="list-style-type: none"> MHC class I and II genes; HLADR3, 4 	<ul style="list-style-type: none"> Diabetogenic and obesity-related genes
Pathology (islets of Langerhans)	<ul style="list-style-type: none"> Insulinitis Decreased number and size of islets 	<ul style="list-style-type: none"> Normal islets at early stage Amyloid deposition in islets (late)



Pathology

Non-neoplastic thyroid diseases



Hyperthyroidism

Primary

- Graves disease
- Toxic multinodular goiter
- Toxic follicular thyroid adenoma

Secondary

TSH-secreting pituitary adenoma

Hypothyroidism

Primary

- Iodine deficiency
- Hashimoto thyroiditis
- Postablative
- Genetic defects in thyroid development
- Thyroid hormone resistance

Secondary

Pituitary failure.

Thyroiditis

Types:

- Acute / infectious thyroiditis
- Autoimmune thyroiditis (Hashimoto thyroiditis).
- Riedel thyroiditis
- Subacute granulomatous thyroiditis

Acute Infectious Thyroiditis

Risk factors:

- Malnourished infant, debilitated elderly, immunosuppression, trauma

Etiology:

- Often *Streptococcus haemolyticus*, *Streptococcus pneumoniae*, *Staphylococcus aureus*
- Via blood or direct seeding from upper respiratory infections, causes sudden onset of pain and glandular enlargement

Acute Infectious Thyroiditis

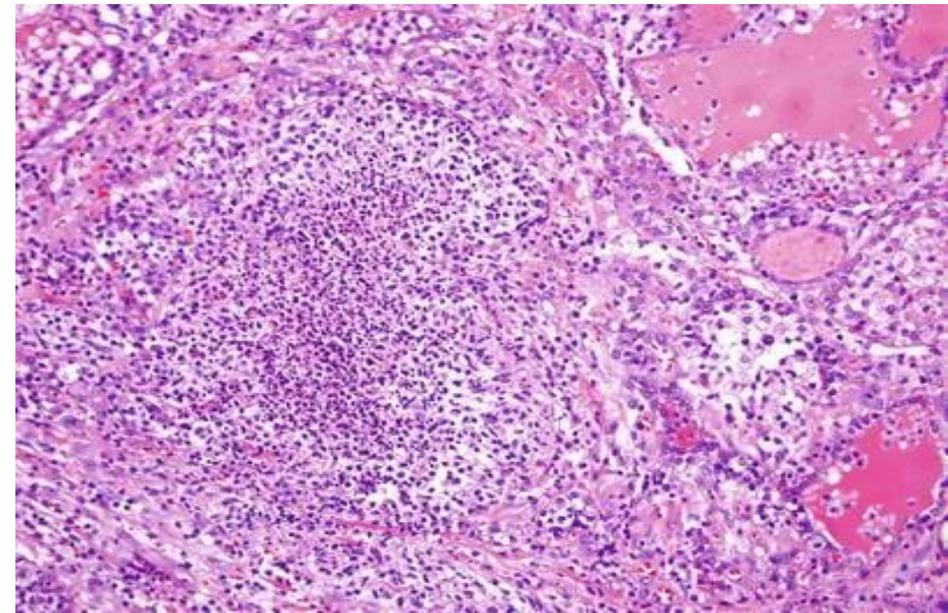
Gross description

- Normal or slightly enlarged thyroid gland
- May have suppurative areas



Microscopic description

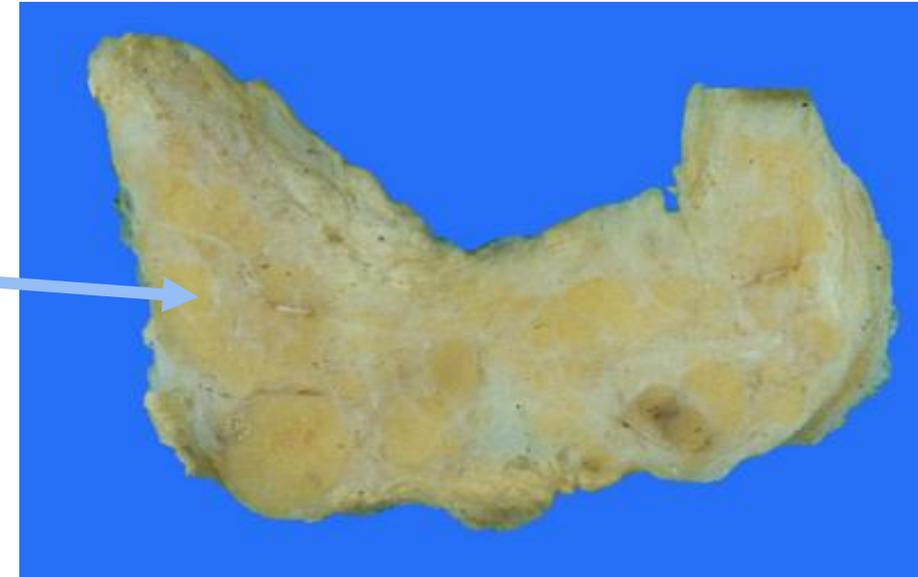
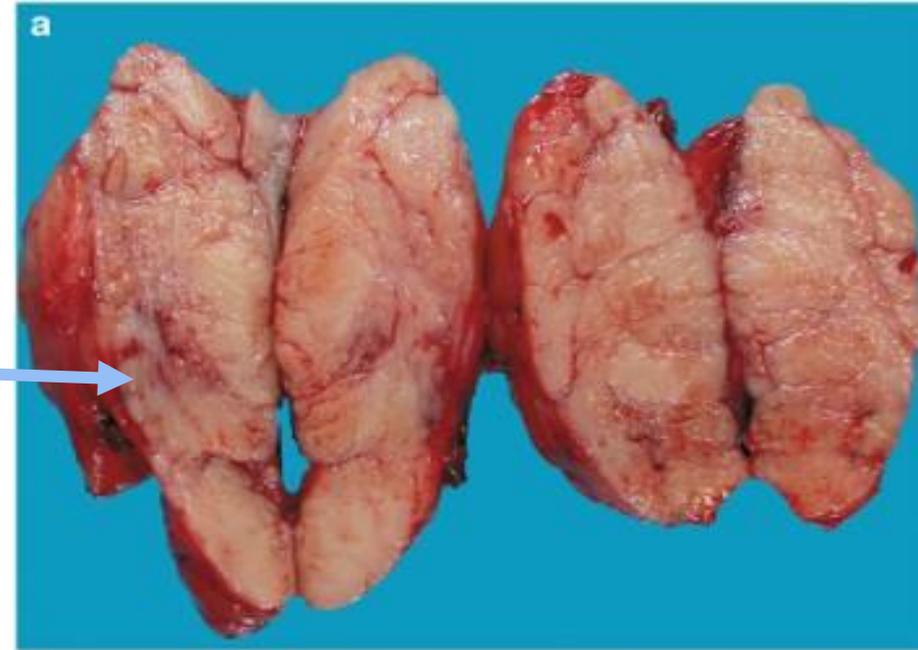
- Neutrophils, possibly microabscesses and tissue necrosis
- Fungi are associated with necrosis, acute inflammation and granulomas



Hashimoto Thyroiditis

Gross

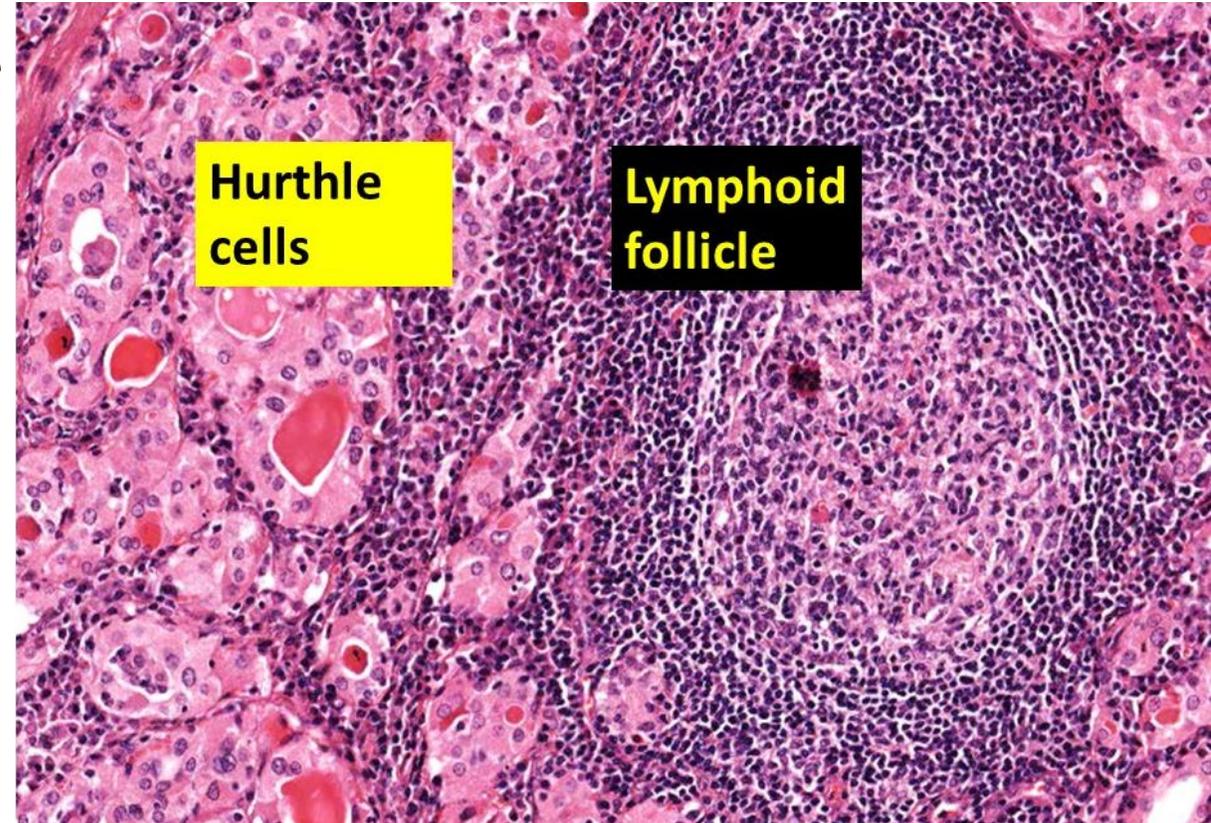
- 1- **Early**... There is symmetrical diffuse enlargement of the thyroid gland with vague nodularity
- The affected areas are pale (gray or yellow) and firm
- They lack the glistening appearance of colloid
- 2- **Late**... The gland becomes symmetrically atrophic



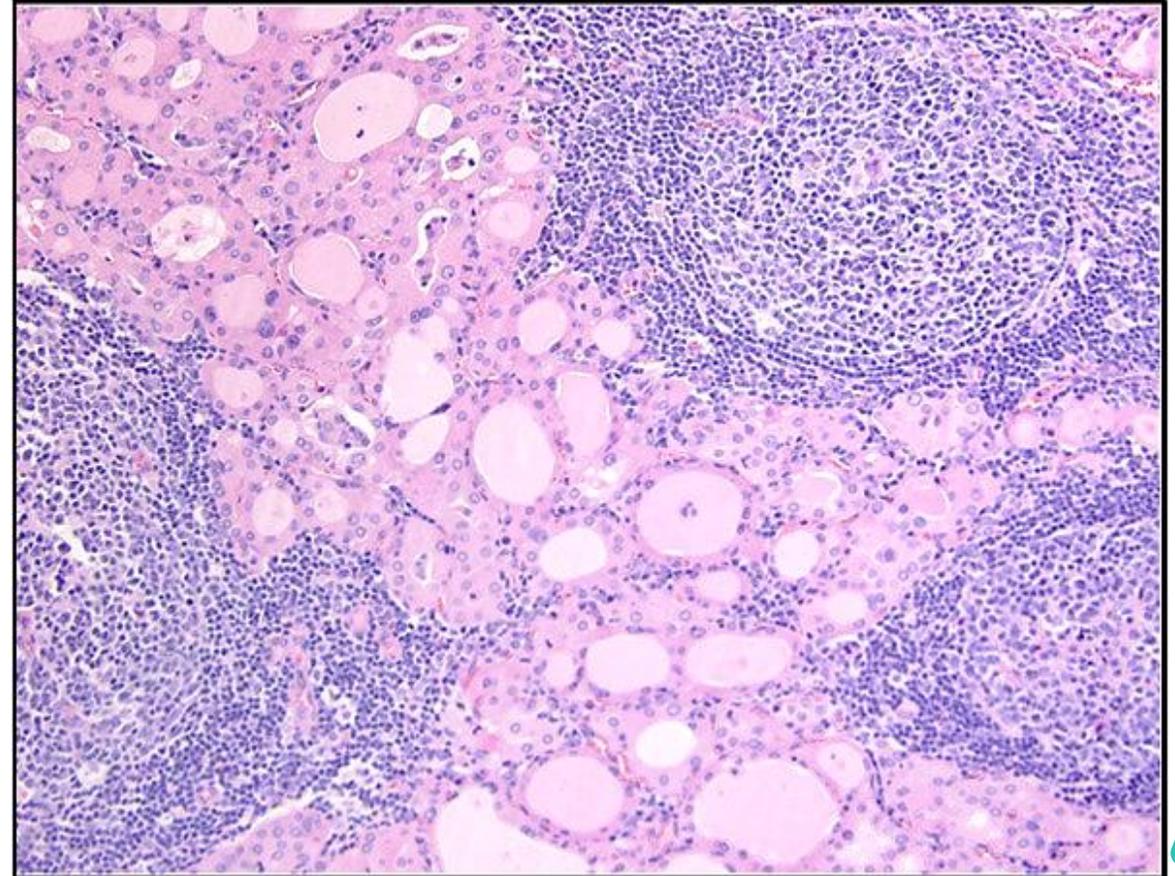
Hashimoto Thyroiditis

Microscope:

- Follicles are atrophied. Follicles are lined by large cubical cells with eosinophilic granular cytoplasm (**Hurthle cells**).
- -Inflammatory cells (lymphocytes, plasma cells, macrophages).
- -Reactive lymphoid follicles.



Hashimoto Thyroiditis



Riedel Thyroiditis

- -Rare of chronic disease of unknown cause.
- Riedel thyroiditis may be part of multifocal idiopathic fibrosclerosis.

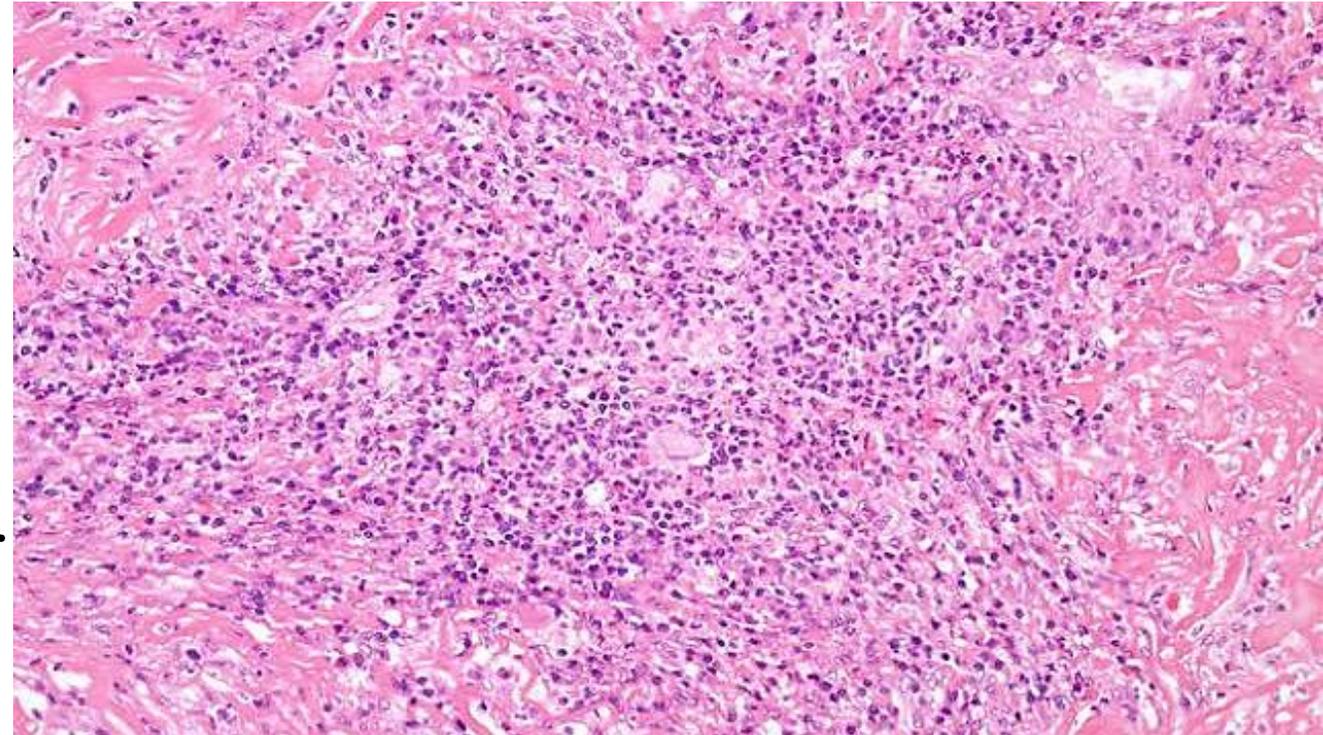
Gross:

- The gland is **stony hard** and greyish white
- Adherent to the surrounding structures



Riedel Thyroiditis

- **Microscopic:**
 - Follicles are atrophied
 - Excess fibrous tissue may extend outside the gland
 - Lymphocytic infiltrate
- **Complications:**
 - Compression manifestations: dysphagia, dyspnea, recurrent laryngeal nerve paralysis.



Subacute Granulomatous Thyroiditis

- A self-limited disorder in which patients present with a **tender** thyroid.
- Etiology is not known but clinical features of preceding respiratory infection suggest a possible viral etiology.

Gross:

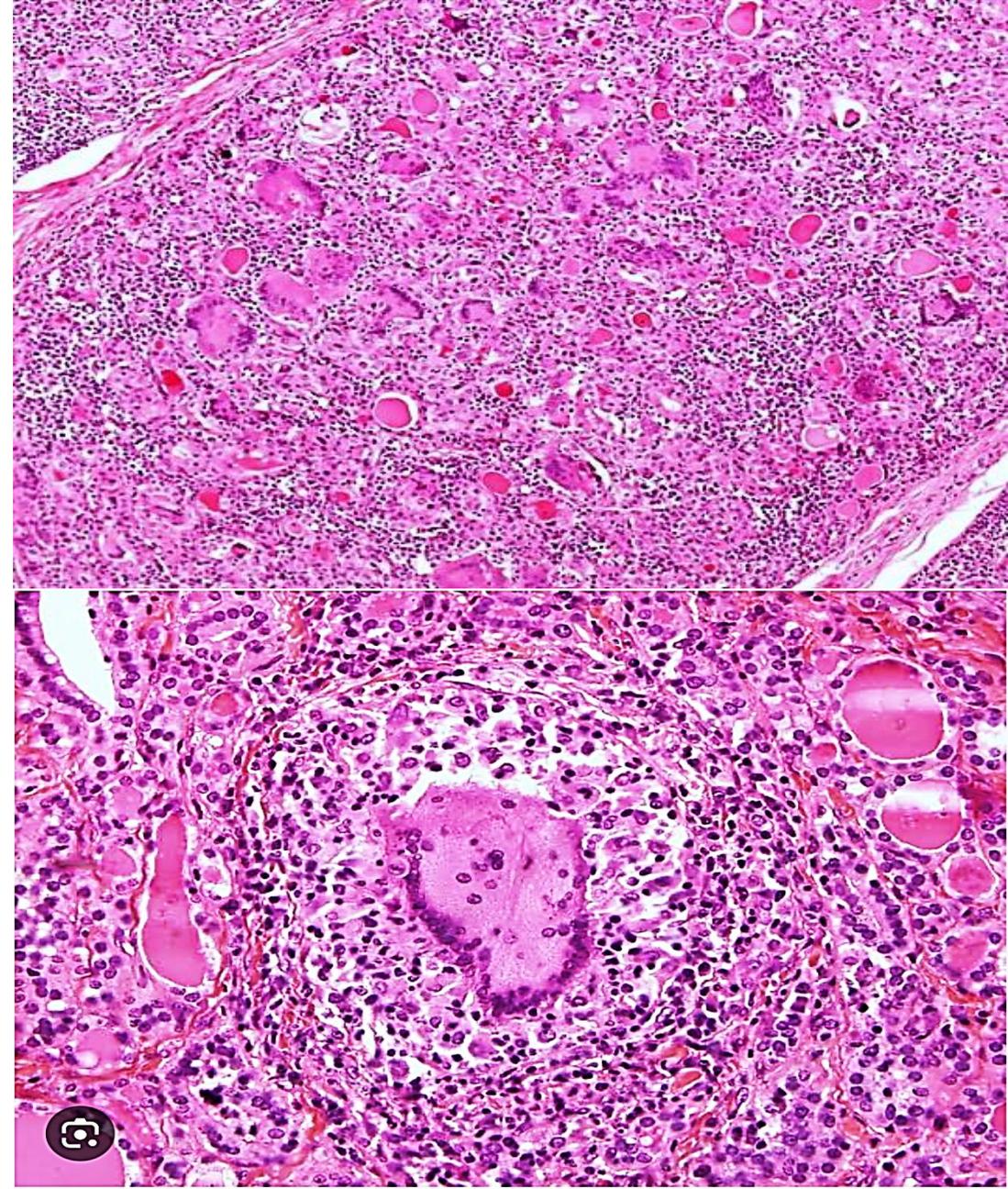
- Moderate enlargement of the gland which is often focal and asymmetrical.
- The cut surface of the involved area is firm and greyish white.



Subacute Granulomatous Thyroiditis

Microscope:

- Early, Acute inflammatory destruction of the thyroid follicles.
- Late, Granulomas consist of central colloid material surrounded by histiocytes and scattered multinucleated giant cells.
- Advanced cases, Fibrosis.



Graves Disease

- **Autoimmune** disease, more common in females.
- Due to auto-antibodies. Most common is **TSI** (thyroid stimulating immunoglobulin).
- Stimulate **TSH receptors** leading to diffuse hyperplasia and hyperfunctioning thyroid follicles with excess thyroid hormone secretion



Graves Disease

Gross

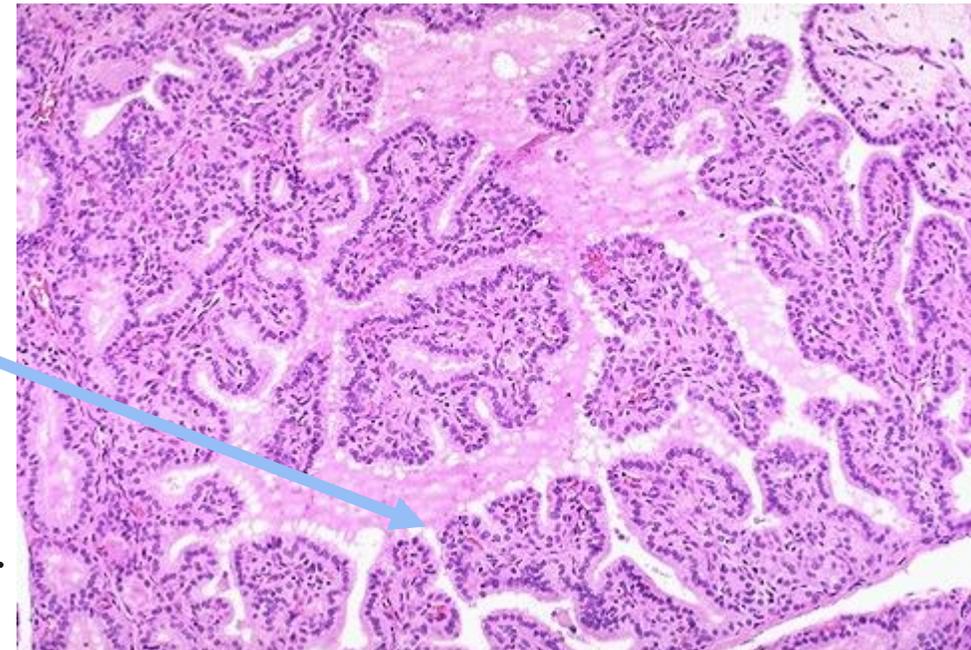
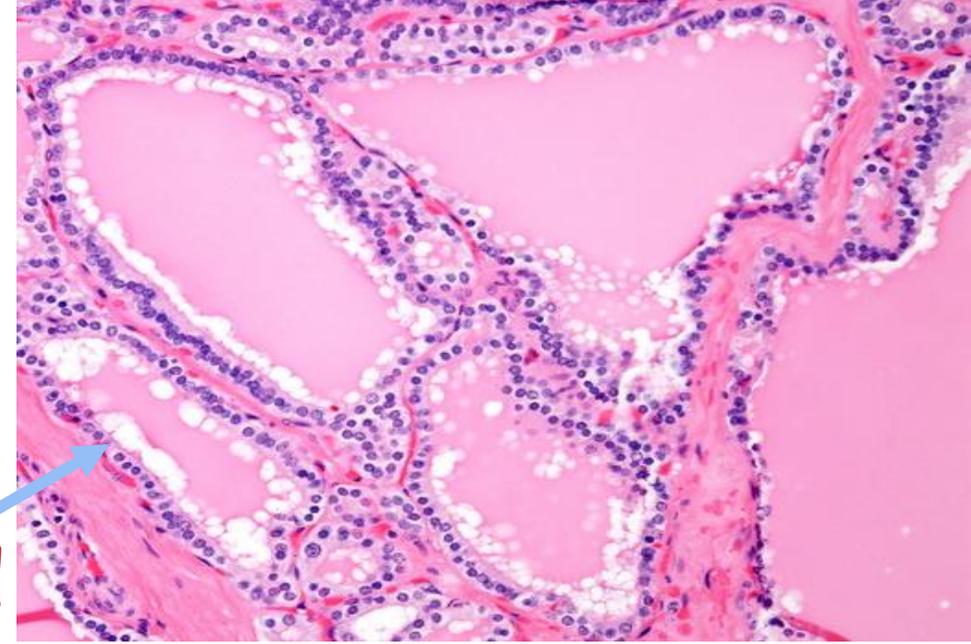
- The thyroid gland is symmetrically enlarged.
- The gland appears **fleshy**.
- Cut surface is firm and dark red.
- Loss of the normal translucence of stored colloid.



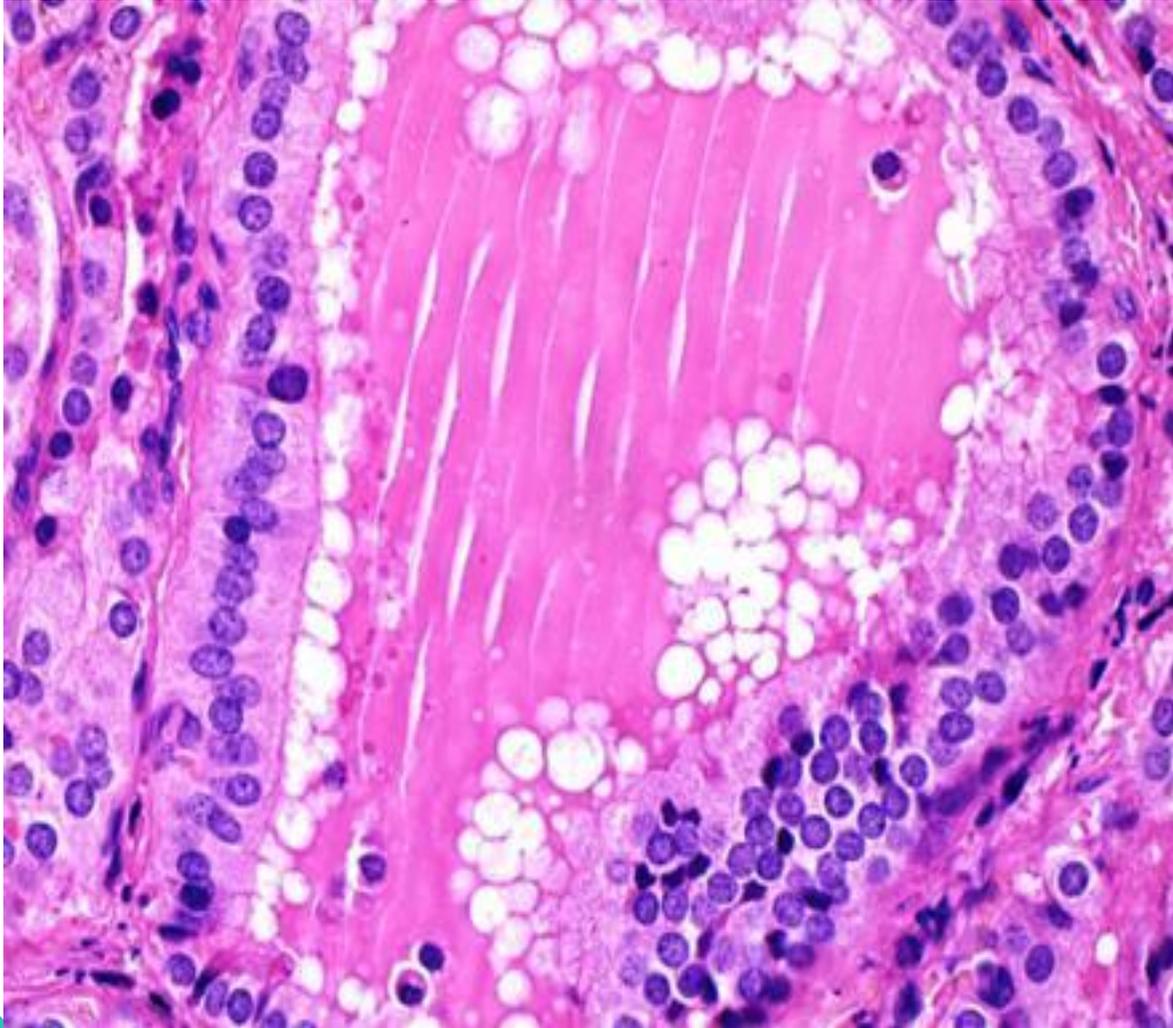
Graves Disease

Microscopic

- the gland is diffusely **Hyperplastic** and highly vascular.
- The follicles are lined by tall columnar cells.
- The colloid is depleted and **scalloped** (moth-eaten) at the periphery.
- Hyperplastic **papillae** that project into the lumen
- of the follicles.
- Lymphocytes and plasma cells **infiltrate** the interstitial tissue and may form reactive lymphoid follicles.



Graves Disease



Goiter

- **Goiter:** Non inflammatory, non neoplastic enlargement of the thyroid gland
- **Goitrogen:** agents that suppress thyroid hormone synthesis, and so elevating TSH levels and leads to hyperplastic changes of thyroid (goitrous enlargement) as cabbage and cauliflower.
- **Classification**
 - Simple (non toxic)
 - Diffuse
 - Multinodular
 - Toxic (associated hyperthyroidism)

Diffuse Simple (Nontoxic) Goiter

- Diffusely involves the thyroid gland without producing nodularity.
- Common in females.

Causes

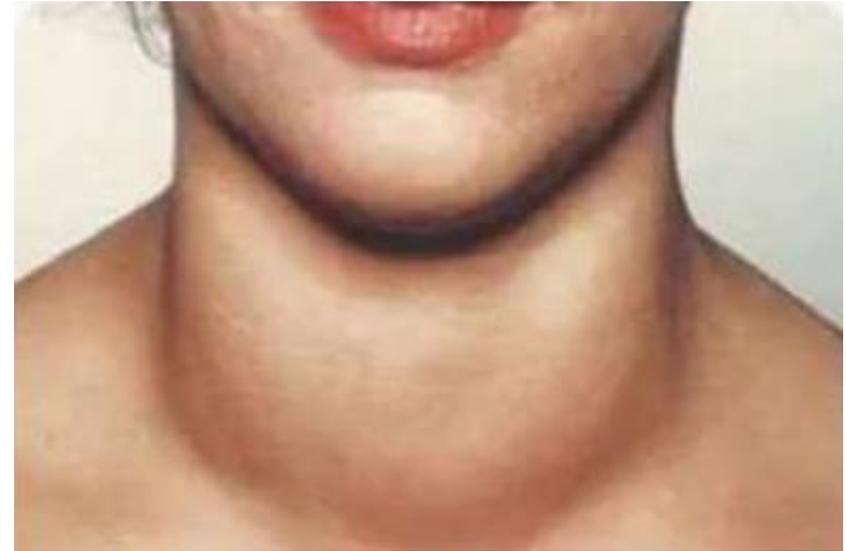
- Physiologic Goiter: Usually seen at times of increased physiological demands as puberty, pregnancy.
- The disease occurs in two forms:
 - Endemic form occurs in geographic areas where the soil, water, and food supply contain low levels of iodine
 - Sporadic form.

Diffuse Simple (Nontoxic) Goiter

- Diffusely involves the thyroid gland the gland has two phases:

1-Hyperplastic stage: there is diffuse and symmetric enlargement of the thyroid gland. There is hypertrophy and hyperplasia of the follicular epithelium with scant colloid.

2-Colloid involution stage: if iodine correction and decreased demand to thyroid hormones occur after a short period of hyperplasia, there is colloid accumulation and atrophy (involution) of follicular epithelium. Most patients are clinically euthyroid.



Simple Multinodular (Nontoxic) Goiter

- Repeated cycles of stimulation and involution of a diffuse goiter lead to rupture of some follicles followed by fibrosis, hemorrhage, scarring, and sometimes calcification.
- This produces an irregular enlargement of the thyroid gland (variable nodularity and scarring).



Simple Multinodular (Nontoxic) Goiter

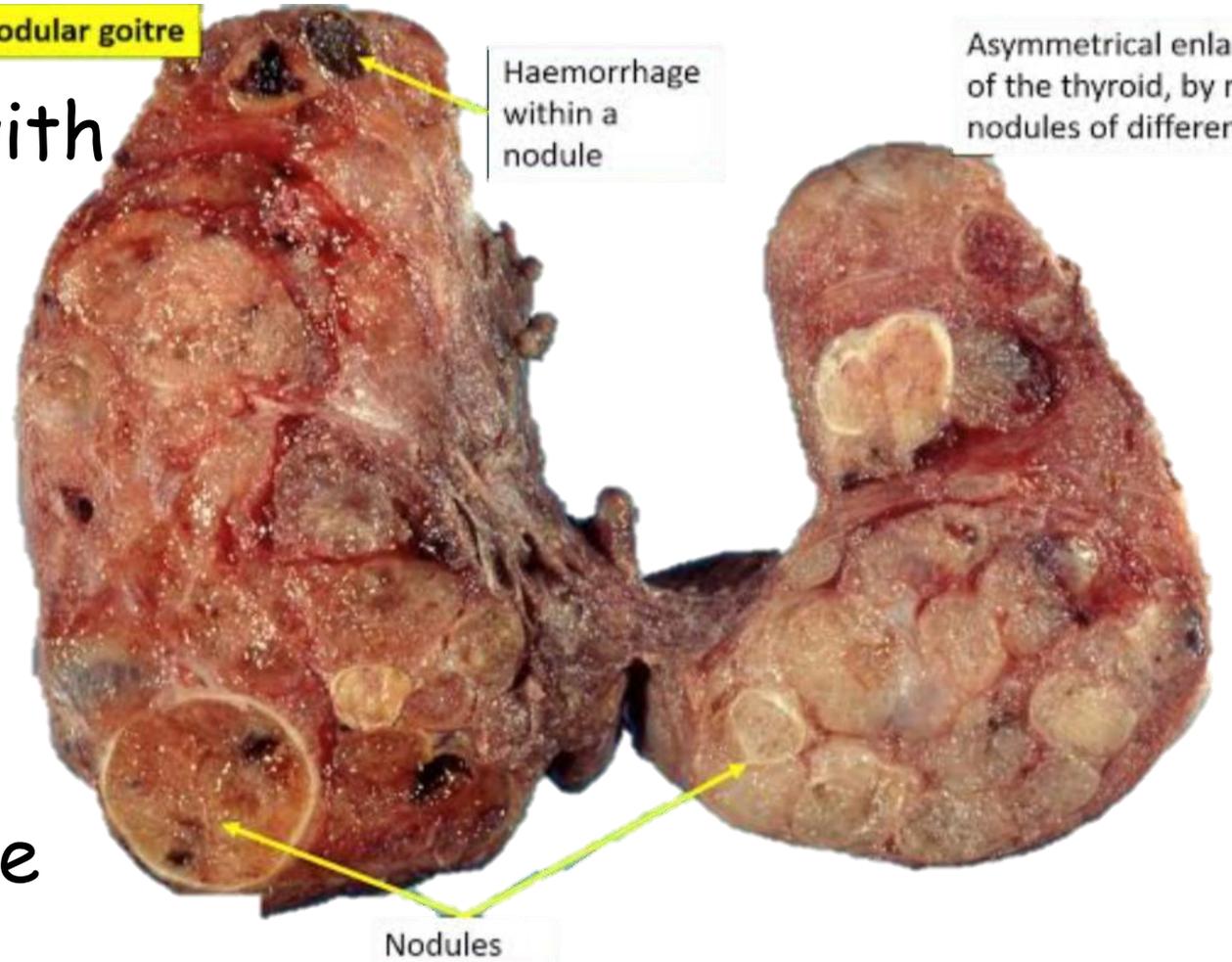
Gross

- The thyroid gland is asymmetrically enlarged with nodular surface.
- The cut surface shows numerous irregular nodules contain glistening colloid.
- Fibrosis, calcification, hemorrhage & cystic degeneration may be present.

- Multinodular goitre

Haemorrhage
within a
nodule

Asymmetrical enlargement
of the thyroid, by multiple
nodules of different sizes

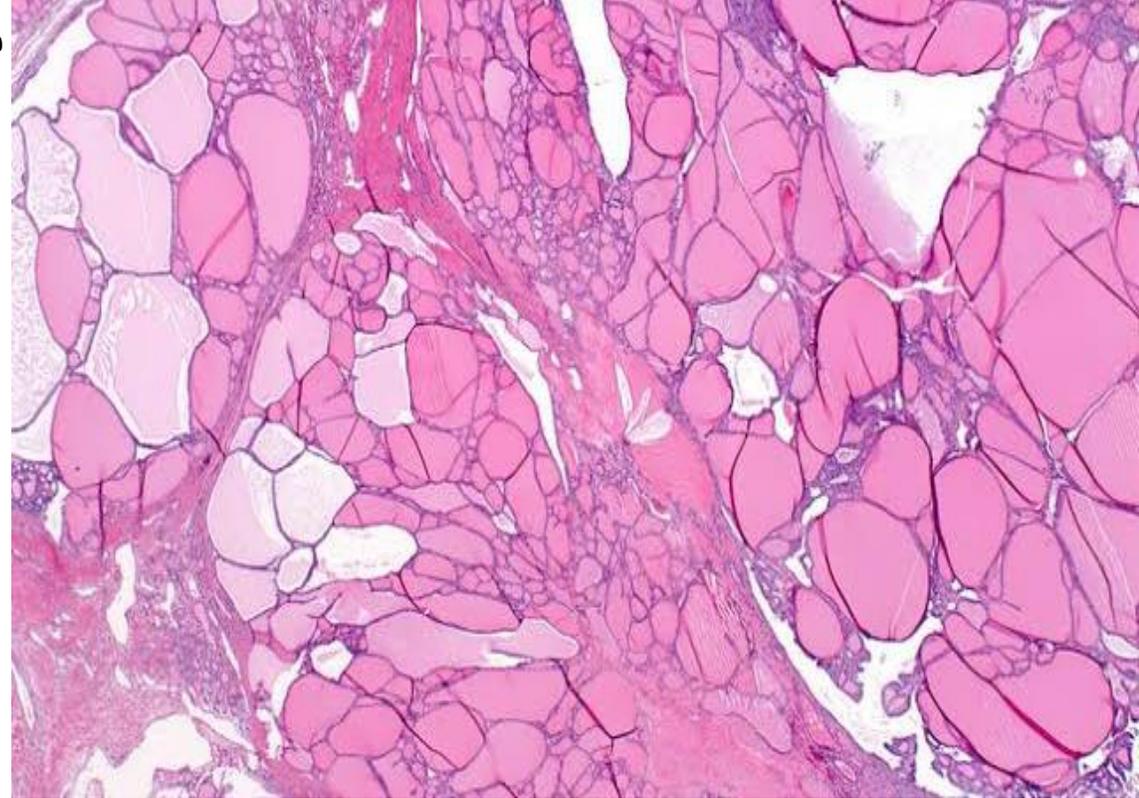


Nodules

Simple (Nontoxic) Goiter

Microscopic

- Nodular thyroid gland separated by fibrous tissue.
- Hyperplastic nodules, tall columnar follicular epithelium, papillary structures, formation of small new follicles.
- Involuted nodules, large follicles distended by colloid and lined by flat follicular epithelium. Large colloid-containing follicles may fuse to form colloid cysts.
- Calcification, chronic inflammation, hemorrhage & cystic degeneration are common in the old standing cases.



Simple (Nontoxic) Goiter

Complications

- Pressure effects: on trachea, esophagus and recurrent laryngeal nerve
- Some of these nodules may become hyper functioning and cause hyperthyroidism (no exophthalmos)
- Malignancy: rare in 2% of cases



Pathology

Neoplastic thyroid diseases

Classification of thyroid tumors

□ Primary thyroid tumors

➤ Epithelial tumors

○ Benign epithelial tumors

- Follicular Adenoma.
- Hurthle cell Adenoma.
- NIFTP (Non-invasive follicular thyroid neoplasm with papillary like nuclear features).
- Hyalinizing trabecular tumor.

○ Malignant epithelial tumors

- Follicular carcinoma
- Papillary carcinoma
- Medullary carcinoma
- Anaplastic carcinoma

➤ Mesenchymal tumors

➤ Hematolymphoid tumors

□ Metastases (rare)

Follicular Adenoma

Most common benign thyroid gland tumor.

Grossly, the follicular adenoma is characterized by four features:

1. Solitary nodule.
2. Complete encapsulation.
3. Difference between inside and outside the capsule.
4. Compression of the thyroid tissue outside the capsule.

Hemorrhage, fibrosis and cystic change are common.



1.0 cm

Follicular Adenoma

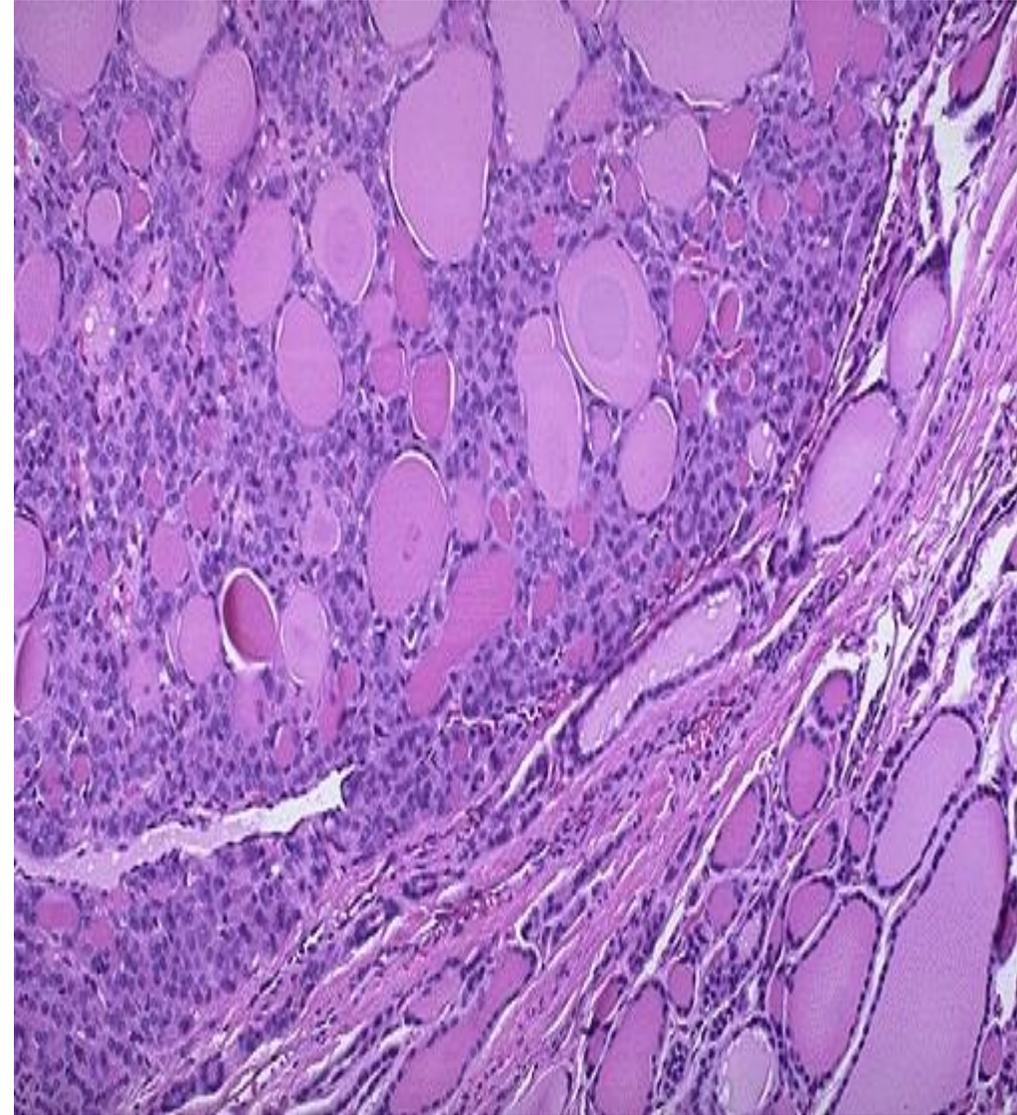
Microscopically

Complete fibrous capsule

The tumor is formed of thyroid follicles (large or small) containing colloid (abundant or scanty).

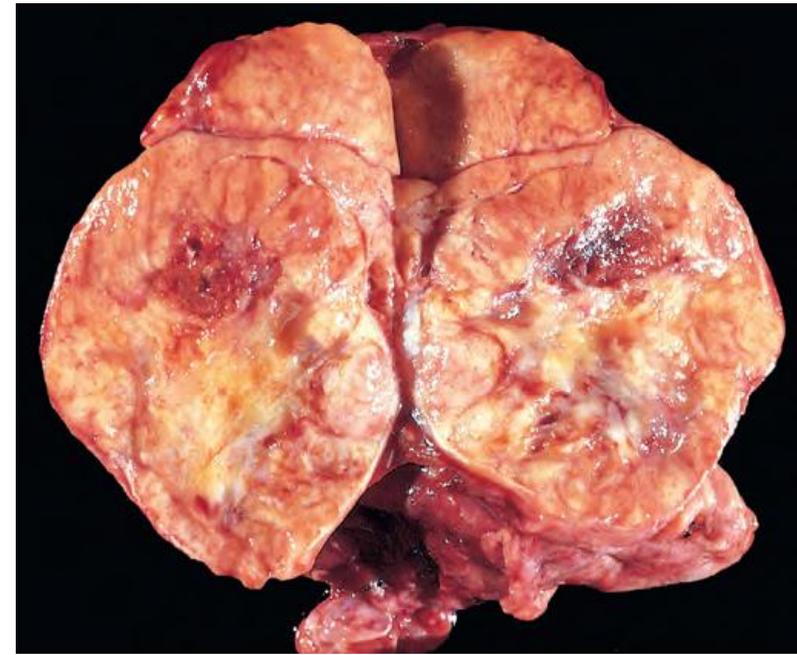
* **Hurthle cell type:** the follicles are lined by oncocytic cells (Cells with abundant granular eosinophilic cytoplasm and central rounded vesicular nuclei).

Careful evaluation of the capsule to differentiate follicular adenomas from follicular carcinomas, which demonstrate capsular and/or vascular invasion.



Follicular carcinoma

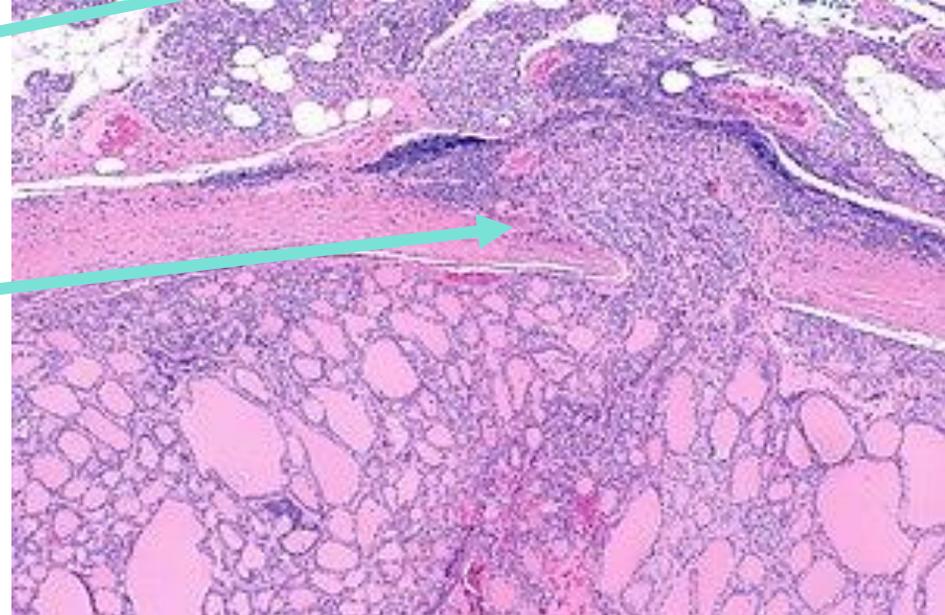
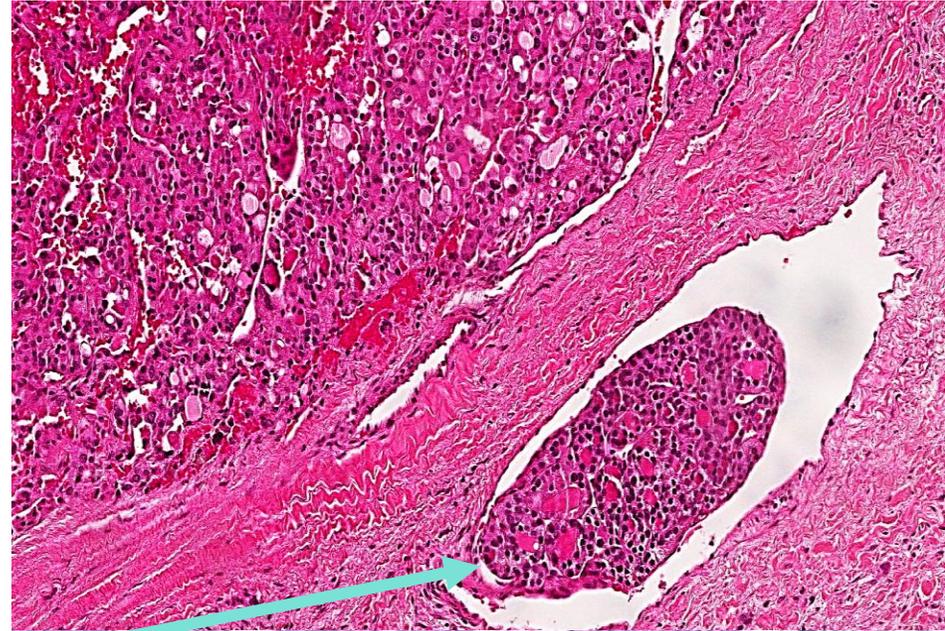
- The second most common type of thyroid carcinoma (10-15%).
- Common in females.
- Blood spread to distant sites (lung, bone).
- Worse prognosis than papillary thyroid carcinoma.
- **Grossly**, it appears as well-defined, encapsulated tumor. On cut section, it is soft and pale tan to pink with areas of hemorrhages, necrosis, cyst formation and bulges from within its capsule.



Follicular carcinoma

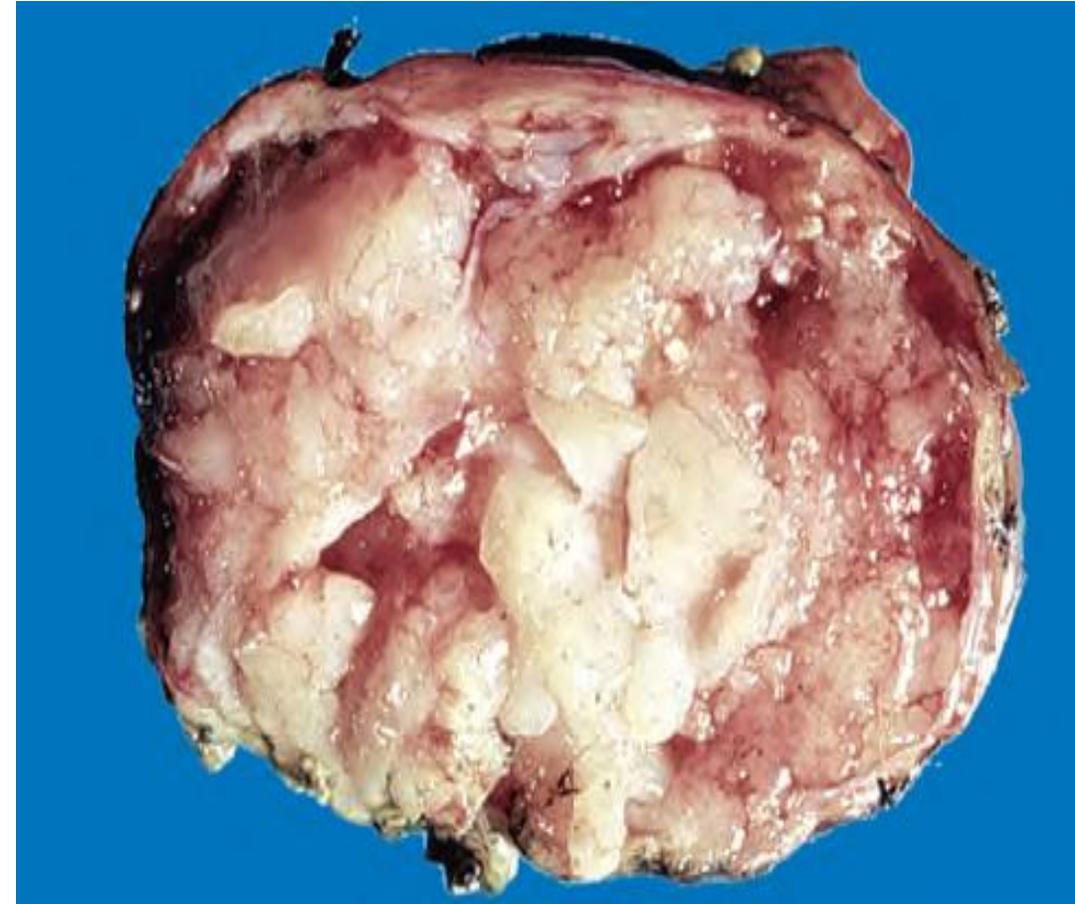
Microscopically, resembles follicular adenoma.

The principal distinction from adenoma is at the interface of the capsule and normal parenchyma by demonstration of **invasion of blood vessels** in region of capsule or by finding **capsular invasion**.



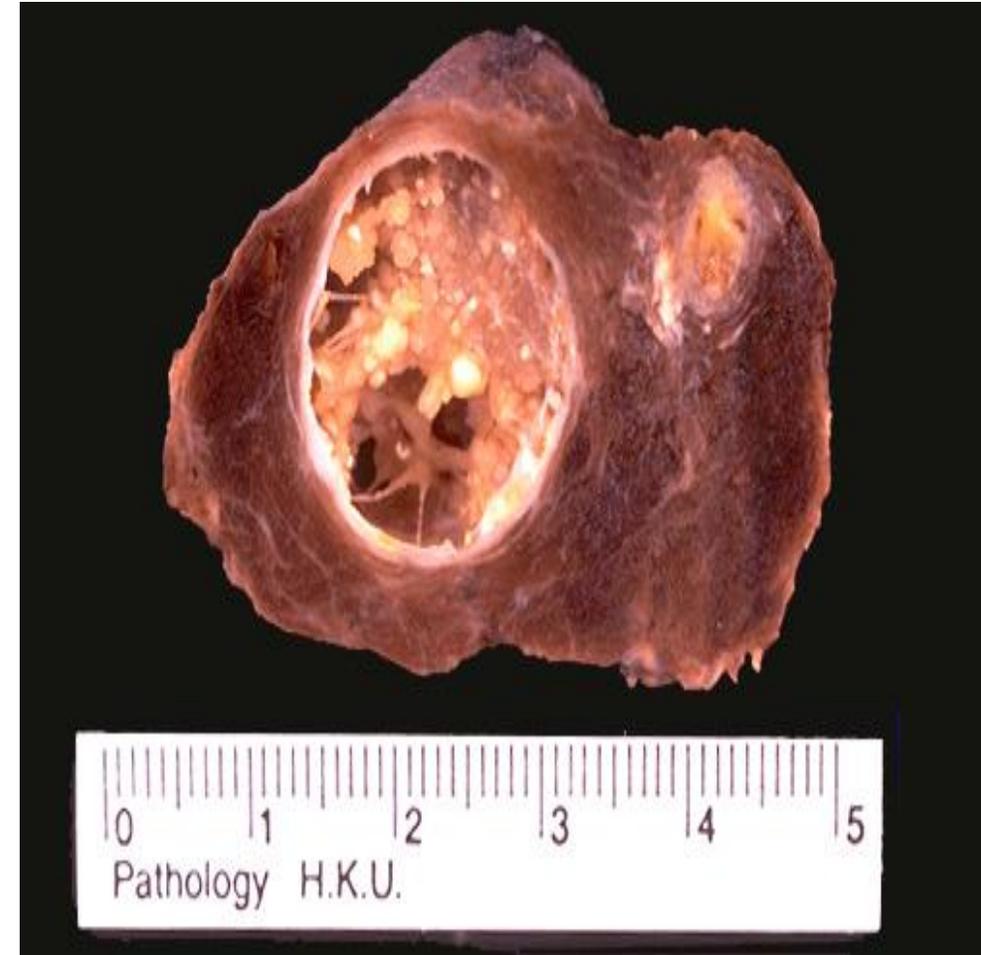
Papillary thyroid carcinoma

- The most common type of thyroid carcinoma (75-85%).
- It can occur at all ages including children.
- Common in females.
- Lymphatic spread to cervical lymph nodes.
- Good prognosis.



Papillary thyroid carcinoma

- **Grossly**, ranges from microscopic foci < 1 cm to large nodule up to 10 cm in diameter, can be multicentric with firm consistency. Cut surface is greyish-white.
- Sometimes the tumor is transformed into cyst, into which numerous papillae projection.



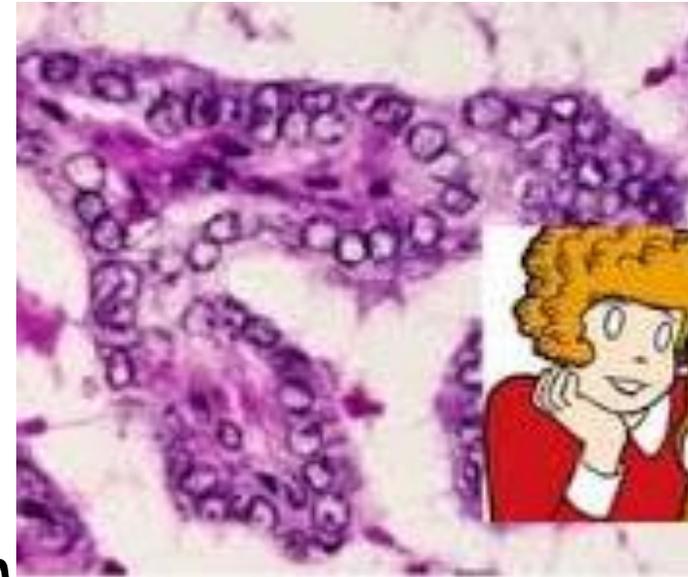
Papillary thyroid carcinoma

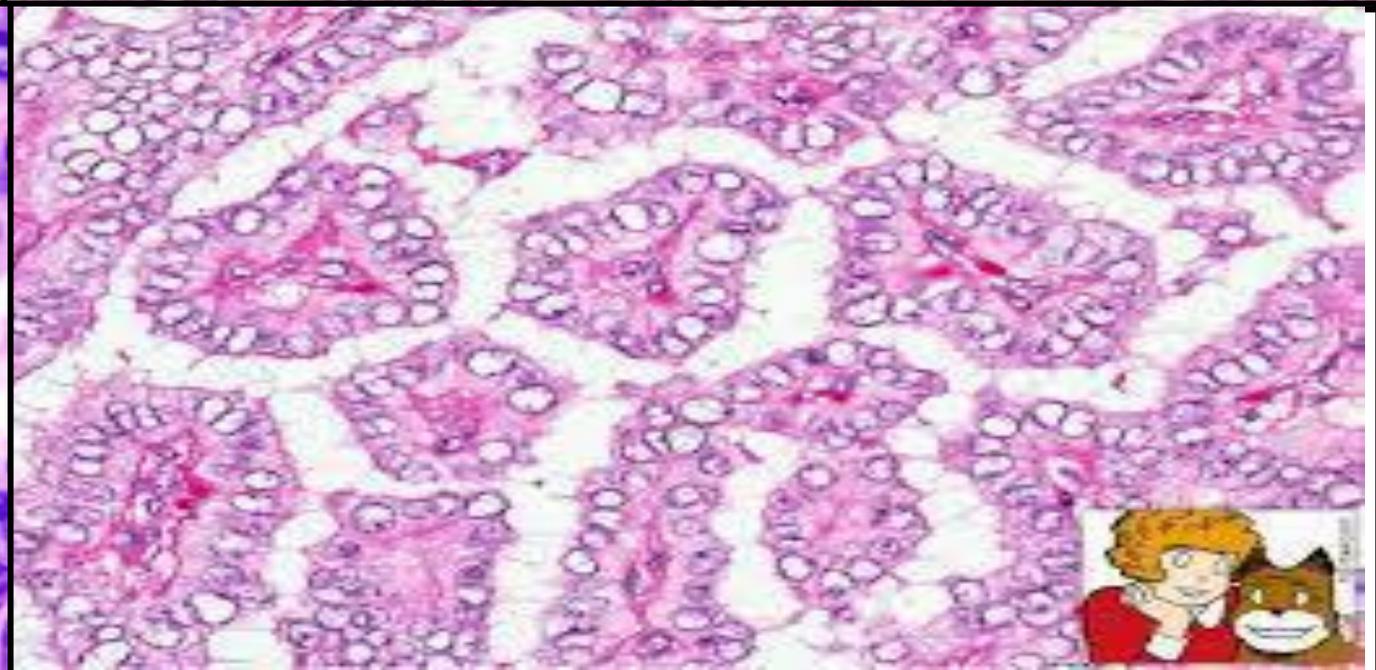
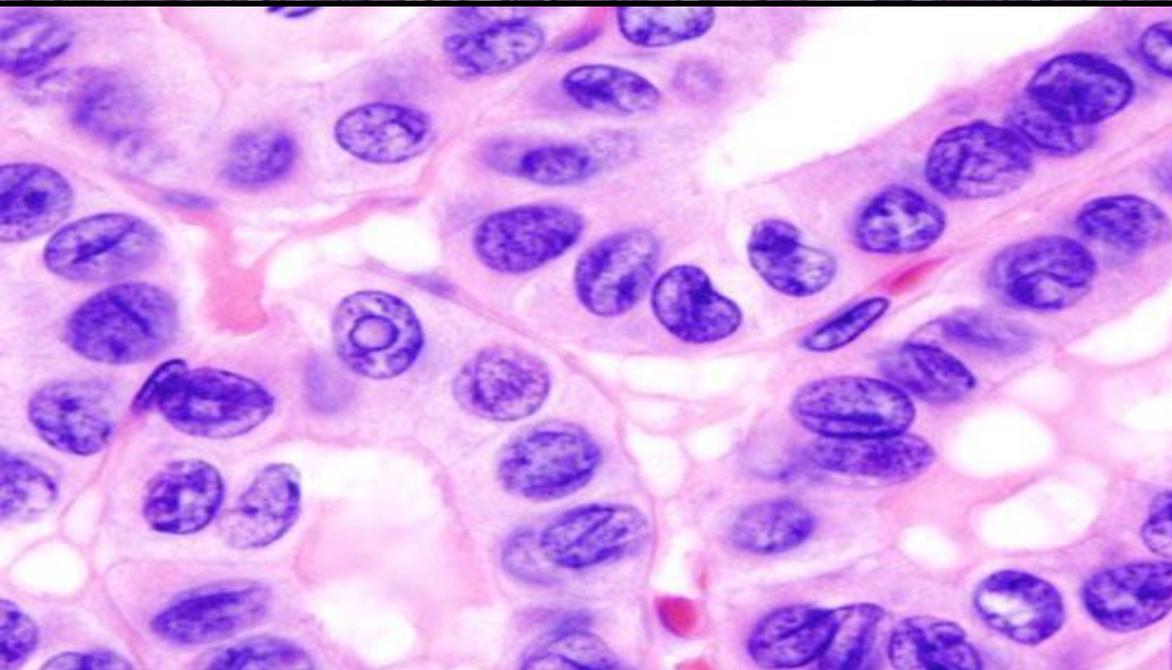
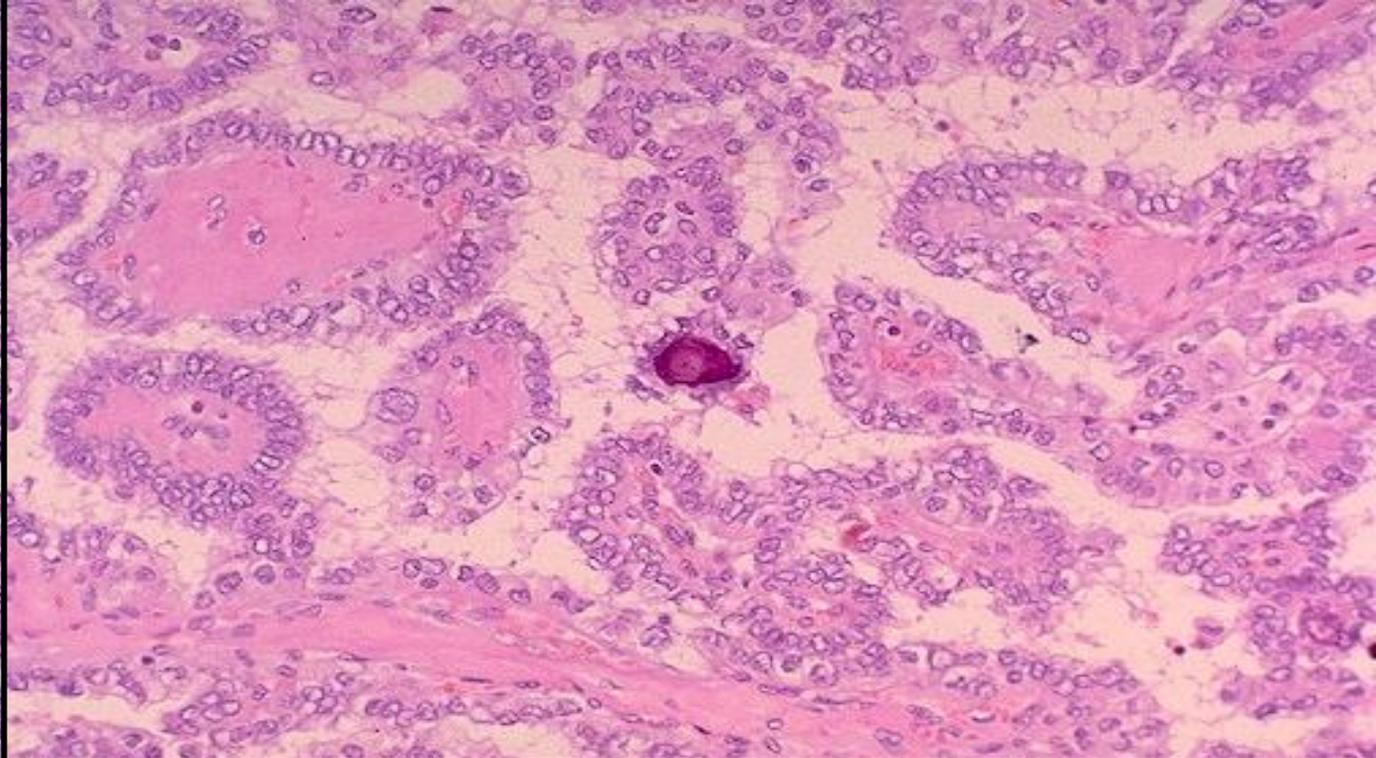
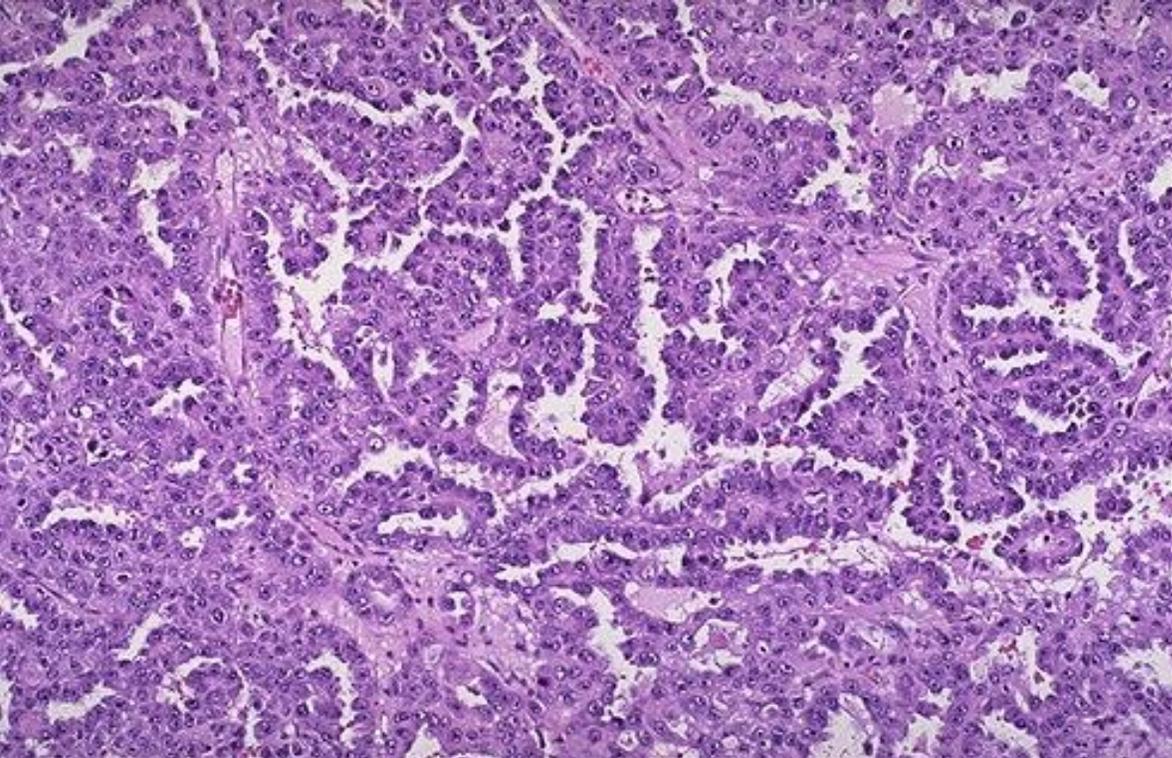
- **Microscopically,**

- ❖ Papillary structures with thin fibrovascular cores.
- ❖ Psammoma bodies: Concentrically calcified structures.

- **Nuclear features:**

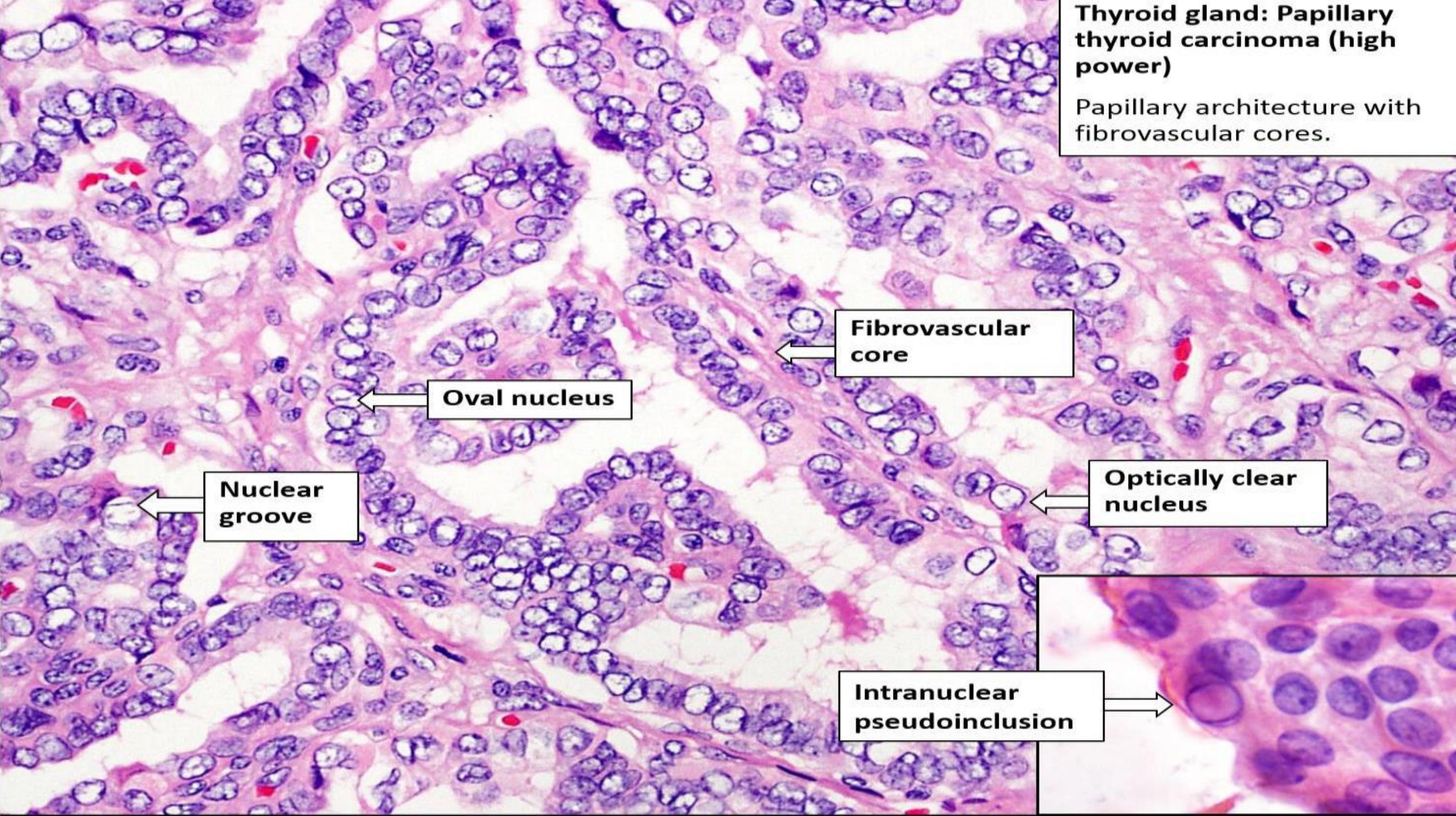
- ✓ Glassy/ground glass nuclei (Orphan Annie nuclei, washed out nuclei): very finely dispersed chromatin.
- ✓ Pseudo-inclusions: invaginations of the cytoplasm may give the appearance of intranuclear inclusions.
- ✓ Grooved nuclei.
- ✓ Crowded & overlapping nuclei





Thyroid gland: Papillary thyroid carcinoma (high power)

Papillary architecture with fibrovascular cores.



Fibrovascular core

Oval nucleus

Nuclear groove

Optically clear nucleus

Intranuclear pseudoinclusion

Medullary thyroid carcinoma

- This tumor is derived from **C cells** or **parafollicular cells**.
- They secrete **calcitonin**.
- The disease can be **sporadic** or **familial**, Patients with the familial medullary carcinoma have **MEN type 2 syndrome**, which includes medullary carcinoma, adrenal pheochromocytoma and parathyroid adenoma.
- The mean age of patients is 50 years, but familial cases appear earlier (mean age, 20 years).
- Both lymphatic and blood spread occurs.
- Worse prognosis.

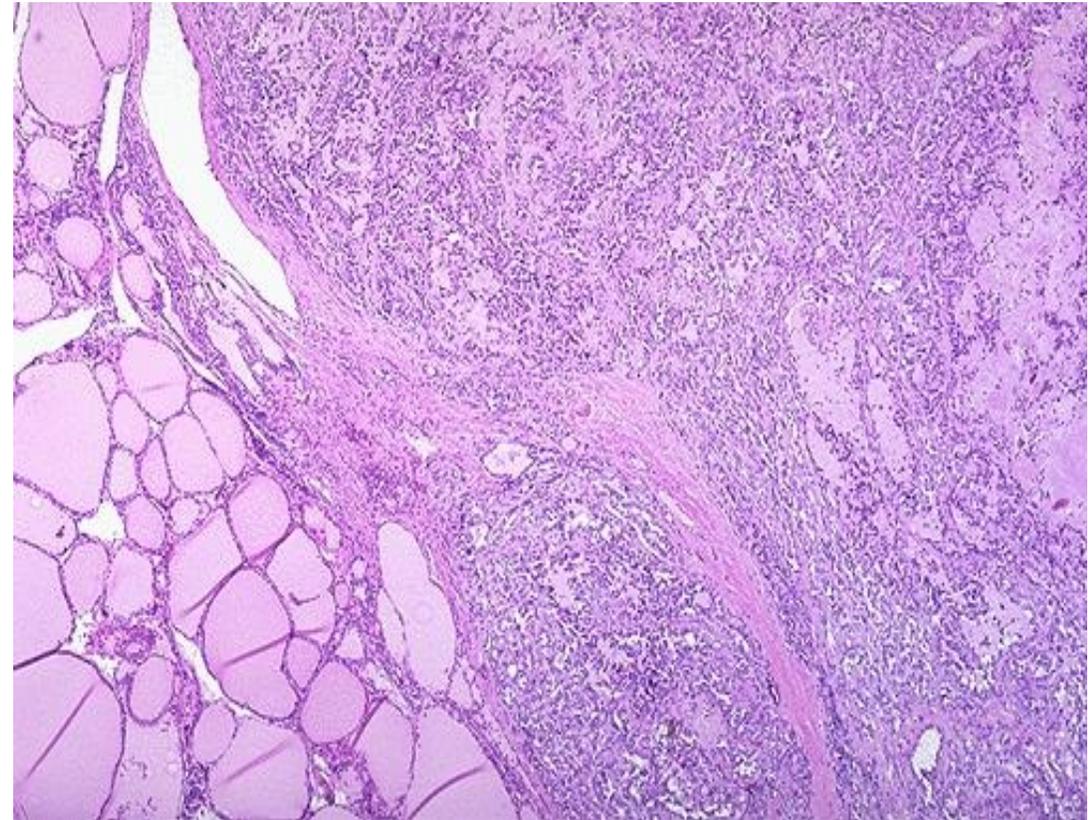
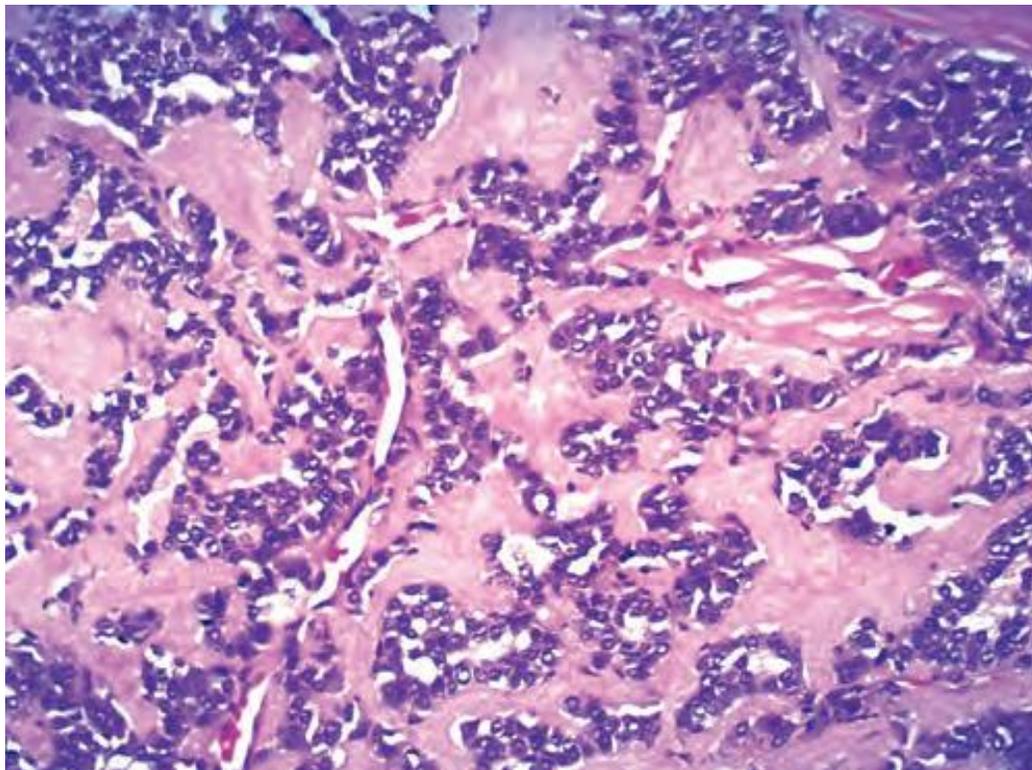
Medullary thyroid carcinoma

- *Grossly*, It is usually single nodule not encapsulated, but are usually circumscribed.
- Cut surface is firm and grayish white.
- In MEN type 2, tumors are often multicentric and bilateral.



Medullary thyroid carcinoma

- **Microscopically**, it is composed of nests, trabeculae, and sheets of spindle/polygonal cells.
 - The stroma contains **amyloid material**.

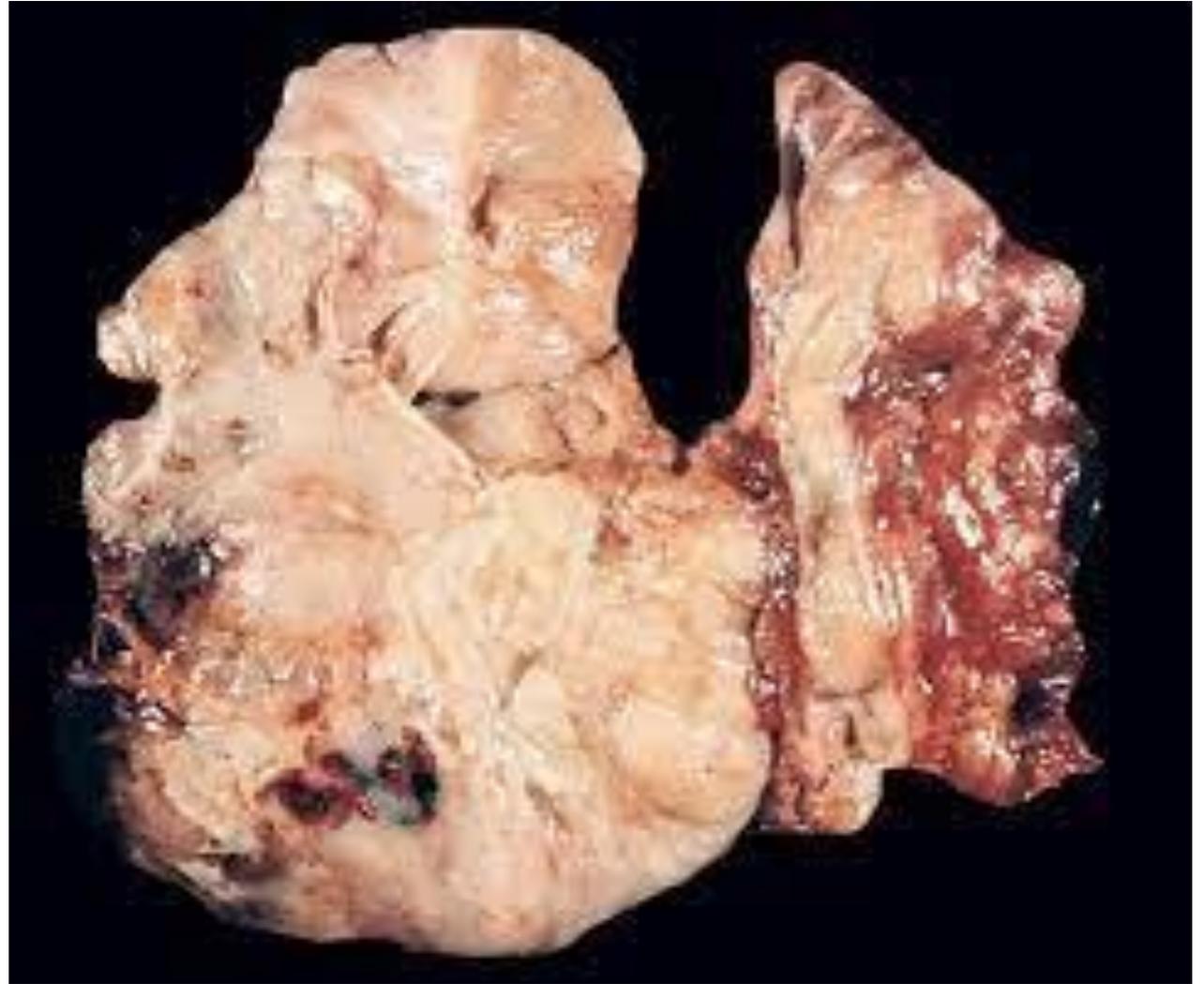


Anaplastic thyroid carcinoma

- They are **undifferentiated tumors** of the thyroid follicular epithelium.
- **Rare**, less than 5% of thyroid carcinomas.
- The tumor is predominantly found in **old age**.
- The features at presentation are usually those of extensive invasion of adjacent soft tissue, neck muscles and structures of the neck.
- Both lymphatic and blood spread occurs.
- **Worse prognosis.**

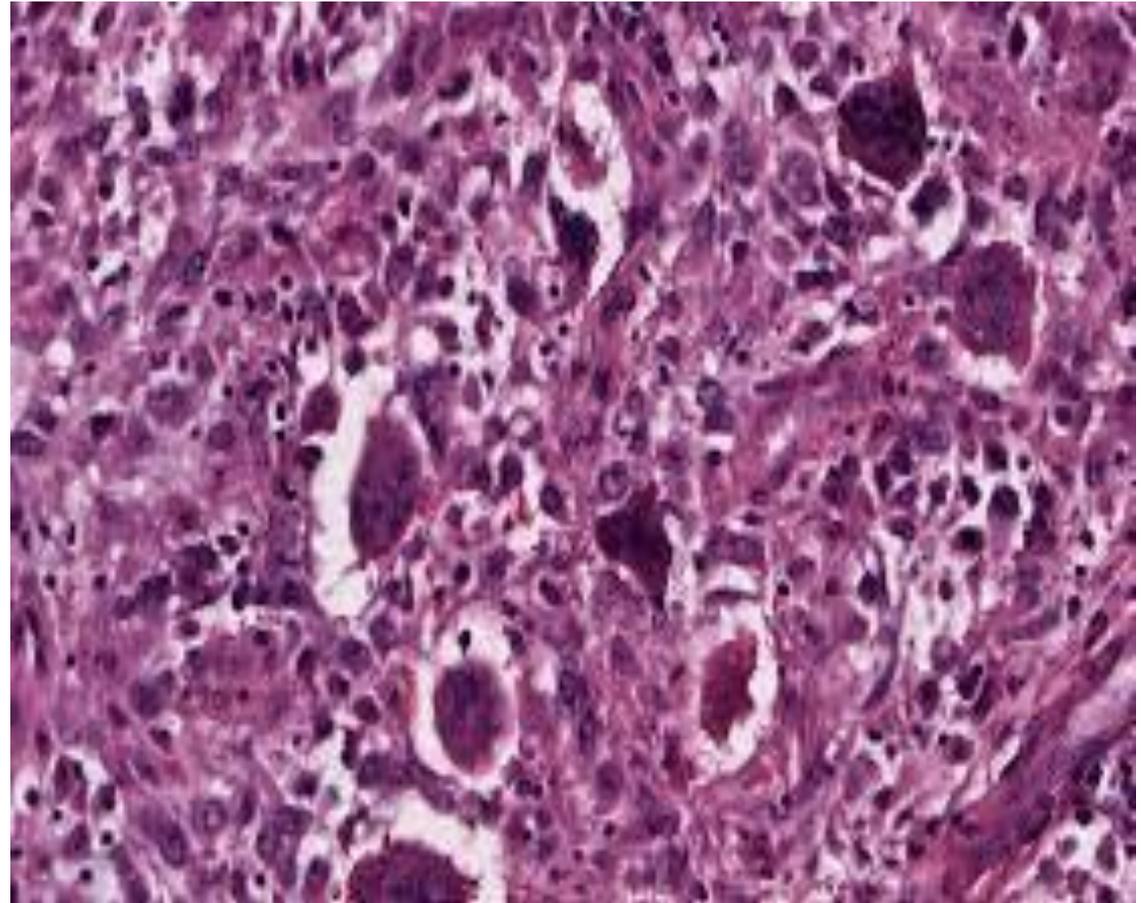
Anaplastic thyroid carcinoma

- **Grossly**, A huge infiltrative lesion. It is hard, and grayish-white and show areas of necrosis and hemorrhage.



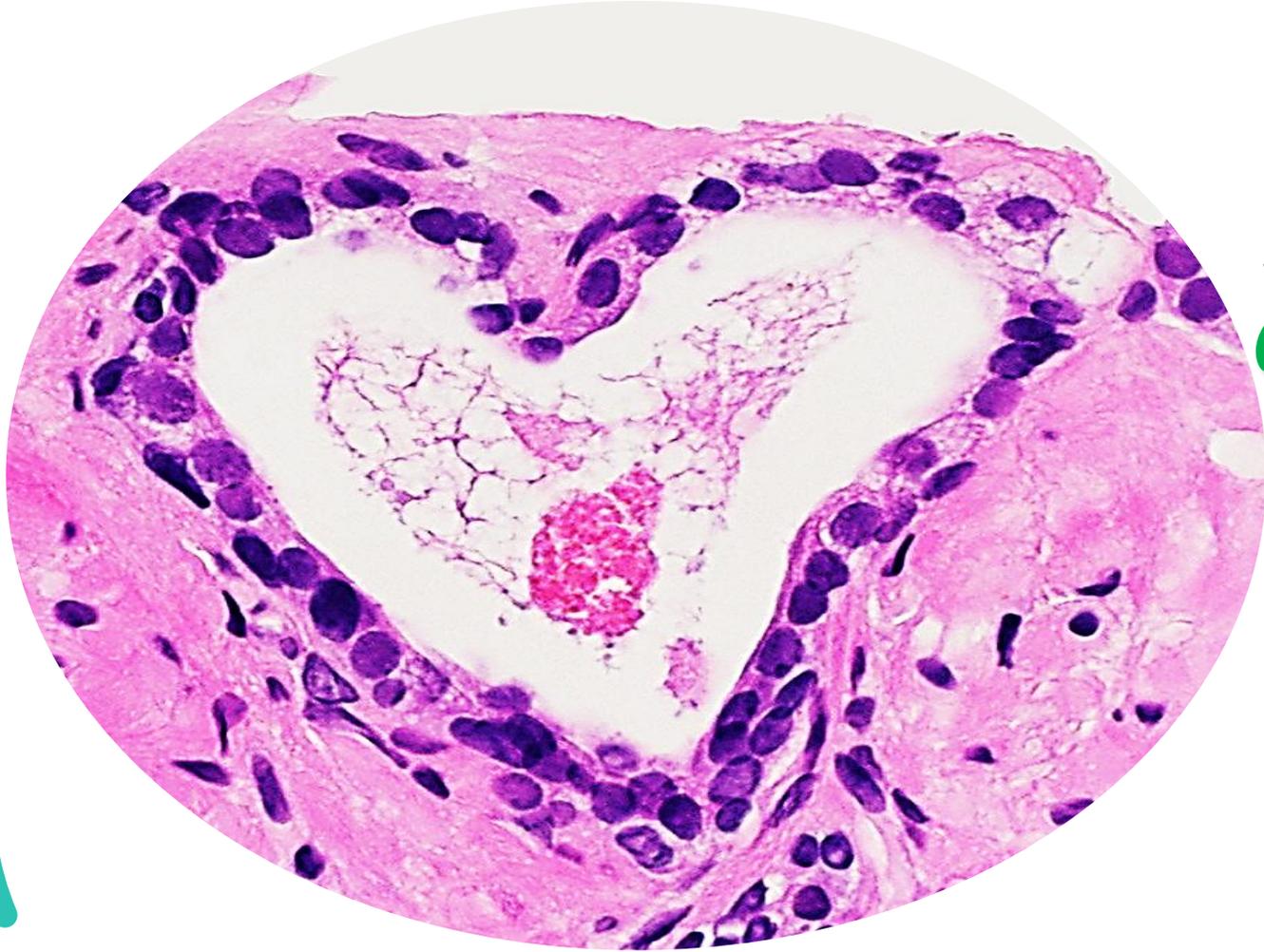
Anaplastic thyroid carcinoma

- **Microscopically**, It is composed of highly malignant spindle or giant cells, showing marked pleomorphism and numerous mitotic figures.



Test example

- Mention definition of Sheehan syndrome?
- Mention causes of hypopituitarism
- Causes of Addisons disease
- mention the outcome of diabetic microangiopathy
- Define goiter, and mention its classification?
- Mention the gross examination of multinodular goiter?
- Describe nuclear feature of papillary thyroid carcinoma?.



Thank you