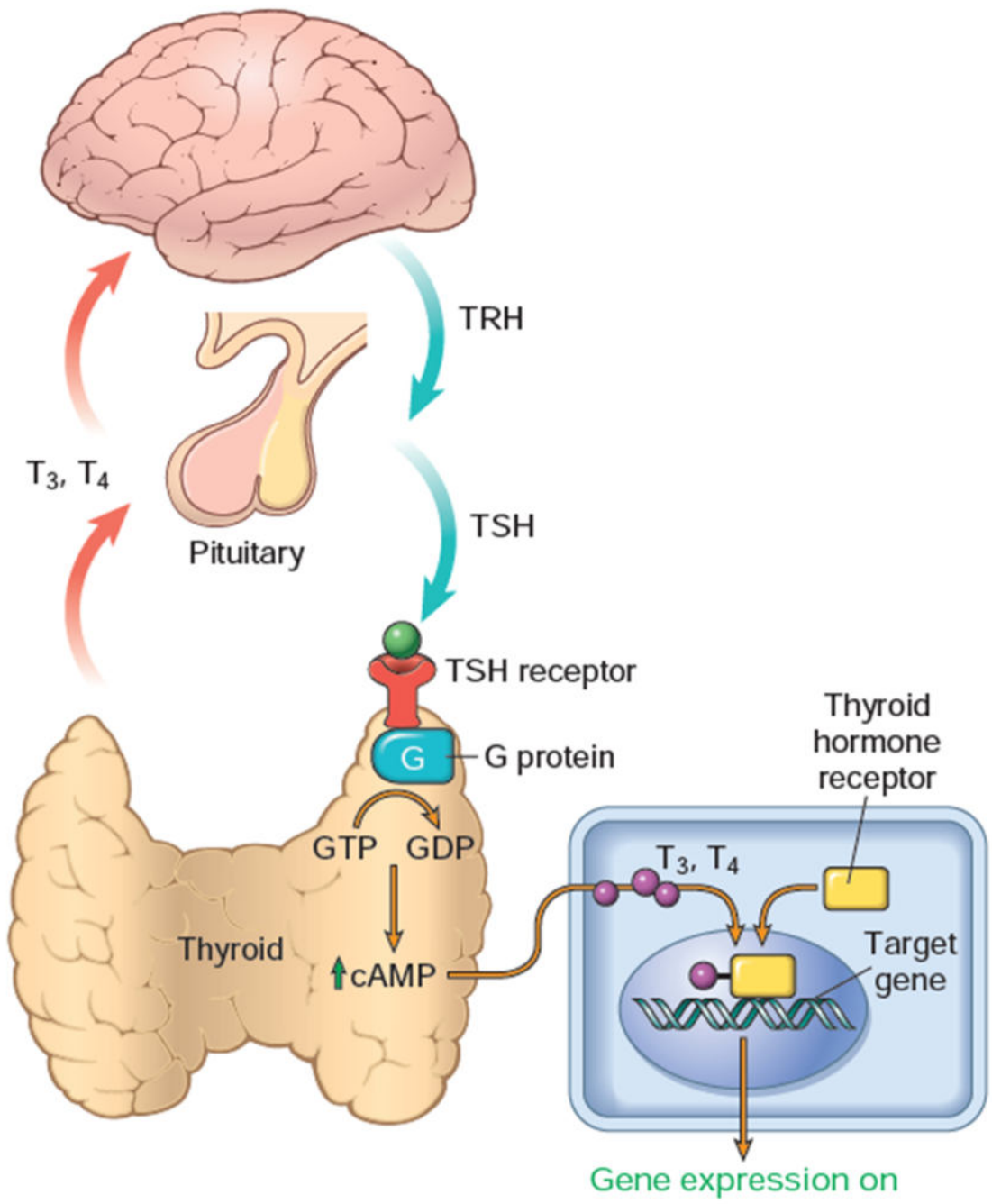
THYROID DISORDER

- Hyperthyroidism
- Hypothyroidism
- Thyroiditis
- Diffuse and Multinodular Goiters
- Neoplasms of the Thyroid
- Congenital cyst
- TFT



- **Hyperthyroidism**-Thyrotoxicosis is a hypermetabolic state caused by elevated circulating levels of free T3 and T4
- Primary
- Secondary
- most common causes of thyrotoxicosis

➢Diffuse hyperplasia of the thyroid associated with Graves disease (approximately 85% of cases)

➢• Hyperfunctional multinodular goiter

➢• Hyperfunctional thyroid adenoma

Table 24-3 Disorders Associated with Thyrotoxicosis

Associated with Hyperthyroidism
Primary
Diffuse hyperplasia (Graves disease)
Hyperfunctioning ("toxic") multinodular goiter
Hyperfunctioning ("toxic") adenoma
Iodine-induced hyperthyroidism
Neonatal thyrotoxicosis associated with maternal Graves disease
Secondary
TSH-secreting pituitary adenoma (rare)*
Not Associated with Hyperthyroidism
Granulomatous (de Quervain) thyroiditis (*painful*)
Subacute lymphocytic thyroiditis (*painless*)
Struma ovarii (ovarian teratoma with ectopic thyroid)
Factitious thyrotoxicosis (exogenous thyroxine intake)

Clinical manifestation-

- weight loss despite increased appetite
- left ventricular dysfunction
- hypermotility, diarrhea, and malabsorption
- Proximal muscle weakness and decreased muscle mass are common (thyroid myopathy)
- osteoporosis

Thyroid storm-

- underlying Graves disease
- during infection, surgery, cessation of antithyroid medication, or any form of stress.
- febrile and present with tachycardia

apathetic hyperthyroidism-

❖**Hypothyroidism**-structural or functional derangement that interferes with the production of thyroid hormone

Table 24-4 Causes of Hypothyroidism

Primary
Genetic defects in thyroid development (*PAX8, FOXE1*, TSH receptor mutations) (rare)
Thyroid hormone resistance syndrome (*THRB* mutations) (rare)
Postablative
Surgery, radioiodine therapy, or external irradiation
Autoimmune hypothyroidism
Hashimoto thyroiditis*
Iodine deficiency*
Drugs (lithium, iodides, *p*-aminosalicylic acid)*
Congenital biosynthetic defect (dyshormonogenetic goiter) (rare) *
Secondary (Central)
Pituitary failure (rare)
Hypothalamic failure (rare)

- Primary
- Secondary

Primary hypothyroidism-

➢Congenital- endemic iodine deficiency

➢Autoimmune-

- **most common** cause of hypothyroidism in **iodine-sufficient** areas of the world
- Hashimoto thyroiditis
- Circulating autoantibodies, including antimicrosomal, antithyroid peroxidase, and antithyroglobulin antibodies

➢Iatrogenic-

- Surgical resection
- Radiation
- drugs

Clinical manifestations of hypothyroidism

- Cretinism
- Myxedema

1.**Cretinism**- congenital hypothyroidism

ETIOPATHOGENESIS-

1.Developmental anomalies

2. Genetic defect in thyroid hormone synthesis

3. Foetal exposure to iodides and antithyroid drugs

4. Endemic cretinism

- CLINICAL FEATURES-slow to thrive, poor feeding, constipation, dry scaly skin, hoarse cry and bradycardia
- rise in TSH level and fall in T3 and T4 levels

- **Myxoedema**-non-pitting oedema due to accumulation of hydrophilic mucopolysaccharides in the ground substance of dermis and other tissues

ETIOPATHOGENESIS.

1.Ablation of the thyroid by surgery or radiation

2. Autoimmune (lymphocytic) thyroiditis (termed primary idiopathic myxoedema)

3. Endemic or sporadic goitre

4. Hypothalamic-pituitary lesions

- CLINICAL FEATURES-cold intolerance, mental and physical lethargy, constipation

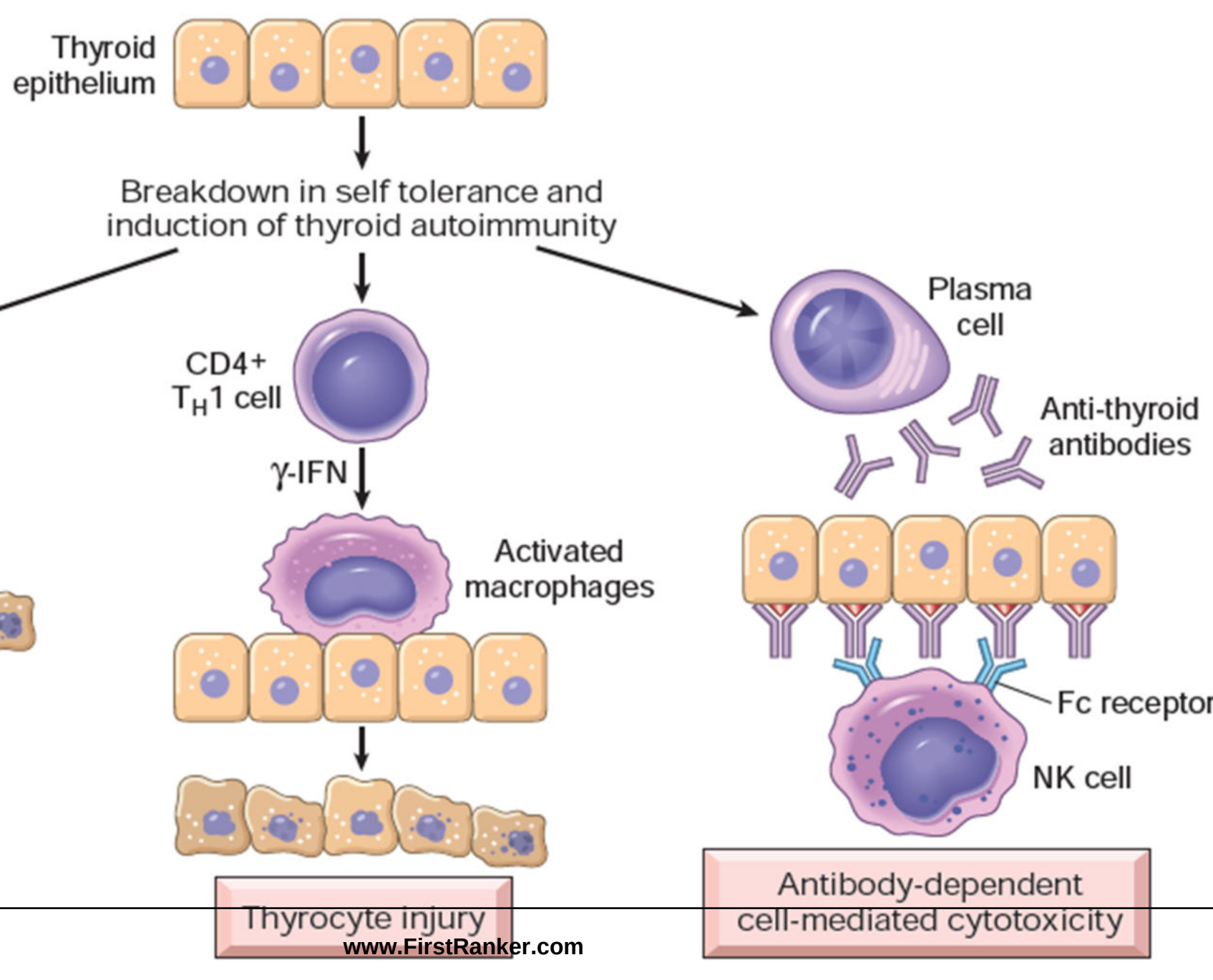
- **Thyroiditis**

1. Hashimoto thyroiditis
2. granulomatous (de Quervain) thyroiditis
3. subacute lymphocytic thyroiditis

- **Hashimoto Thyroiditis**-destruction of the thyroid gland and gradual and progressive thyroid failure.

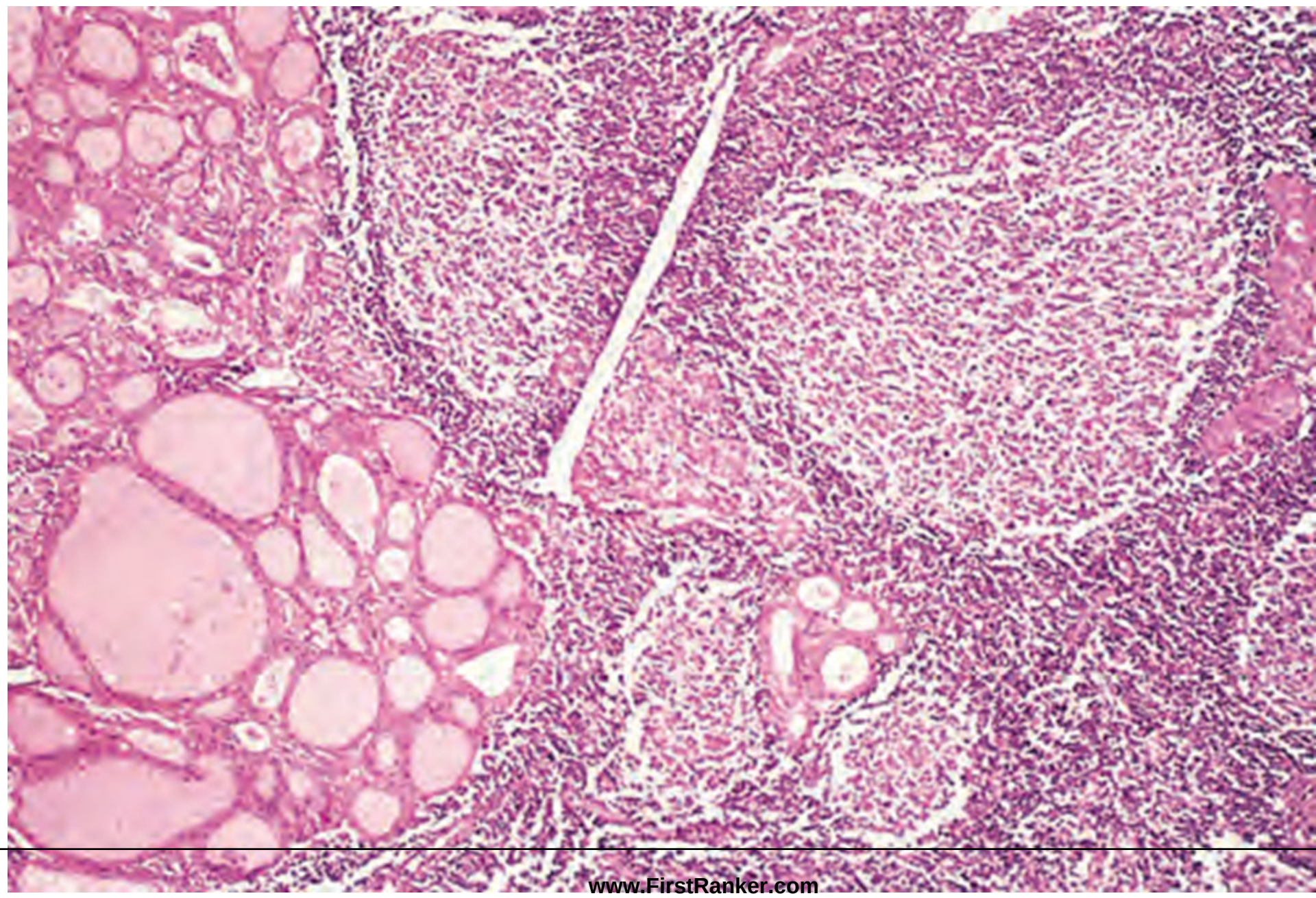
Pathogenesis-

- Anti -thyroglobulin and anti-thyroid peroxidase Ab
- Cytotoxic T lymphocyte-associated antigen-4 (CTLA4) and protein tyrosine phosphatase-22 (PTPN22)



MORPHOLOGY-

- gross-diffusely enlarged
- Cut surface- firm, pale, yellow-tan



Clinical Course.

- Hypothyroidism
- preceded by transient thyrotoxicosis
- Increased risk for developing other autoimmune diseases

- **Subacute Lymphocytic (Painless) Thyroiditis-** subset of HT

similar to Hashimoto thyroiditis, however, fibrosis and Hürthle cell metaplasia are not prominent.

Granulomatous Thyroiditis-

De Quervain thyroiditis

- 40 and 50
- F:M(4:1)

Pathogenesis-

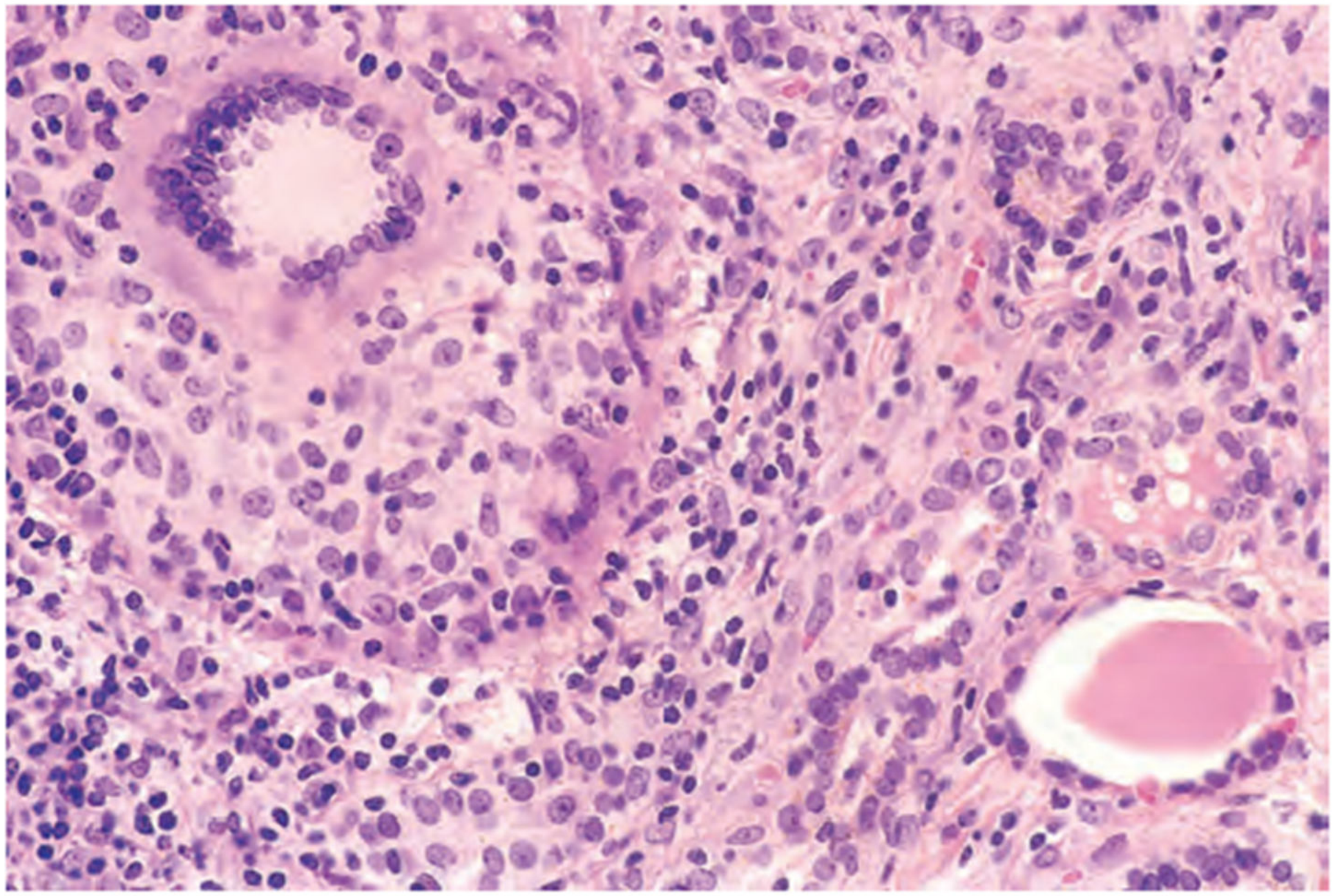
- viral infection

MORPHOLOGIC FEATURES.

- Grossly, asymmetric moderate enlargement
- Cut surface-firm and yellowish-white

Microscopically-vary to the stage

- **acute inflammation**
- **granulomatous** appearance
- advanced cases may show **fibroblastic proliferation**



- **RIEDEL'S THYROIDITIS-**

MORPHOLOGIC FEATURES.

- Grossly-contracted, stony-hard, asymmetric
- Cut section- hard and devoid of lobulations
- Microscopically, there is extensive fibrocollagenous replacement, marked atrophy of the thyroid parenchyma

GRAVES' DISEASE (DIFFUSE TOXIC GOITRE)-

- most common cause of endogenous hyperthyroidism

Clinical findings

- Hyperthyroidism (thyrotoxicosis)
- Diffuse thyroid enlargement
- Ophthalmopathy

ETIOPATHOGENESIS-

- Genetic factor association-HLA-DR3, CTLA-4 and PTPN22
- Autoimmune disease association
- Autoantibodies- against TSH-receptor autoantigen

➢Thyroid-stimulating immunoglobulin (TSI)

➢Thyroid growth-stimulating immunoglobulins

➢TSH-binding inhibitor immunoglobulins

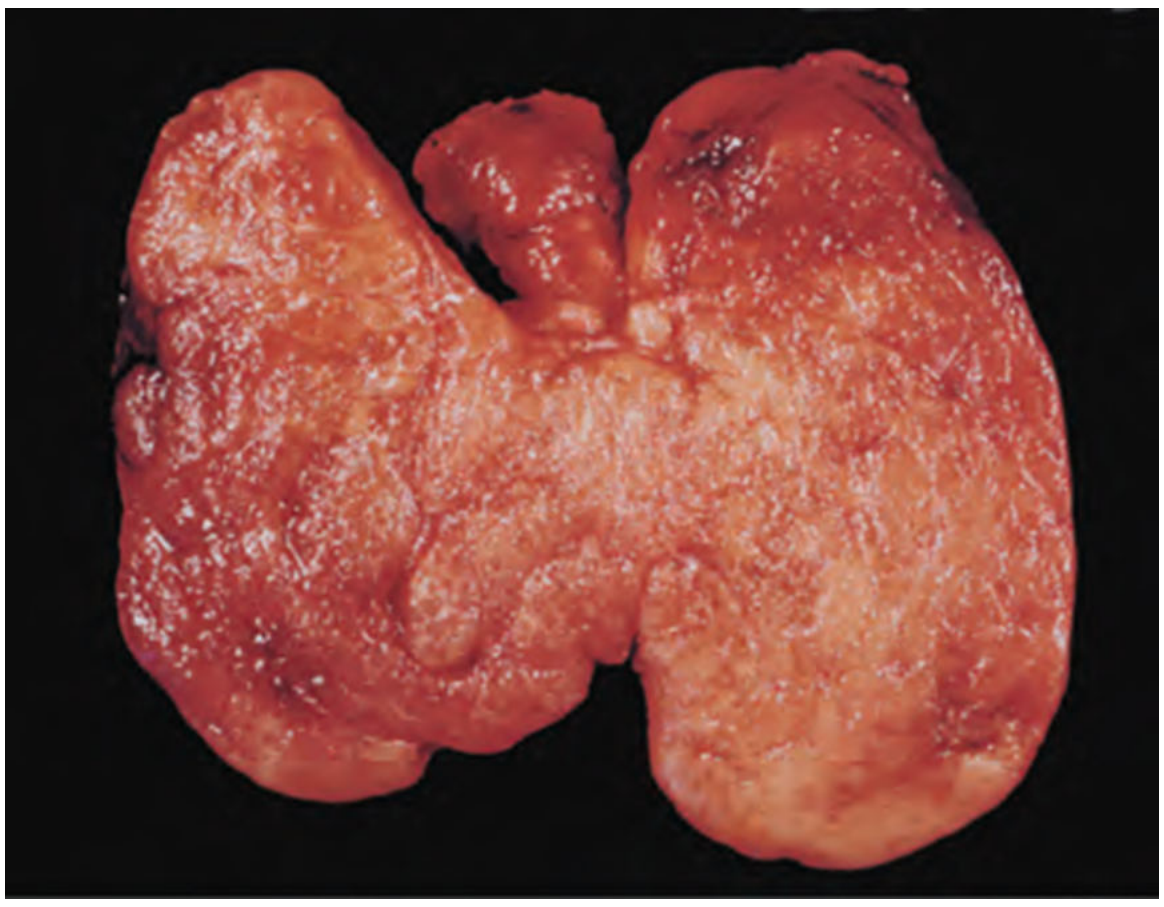
- Other factors-female,stress, and smoking

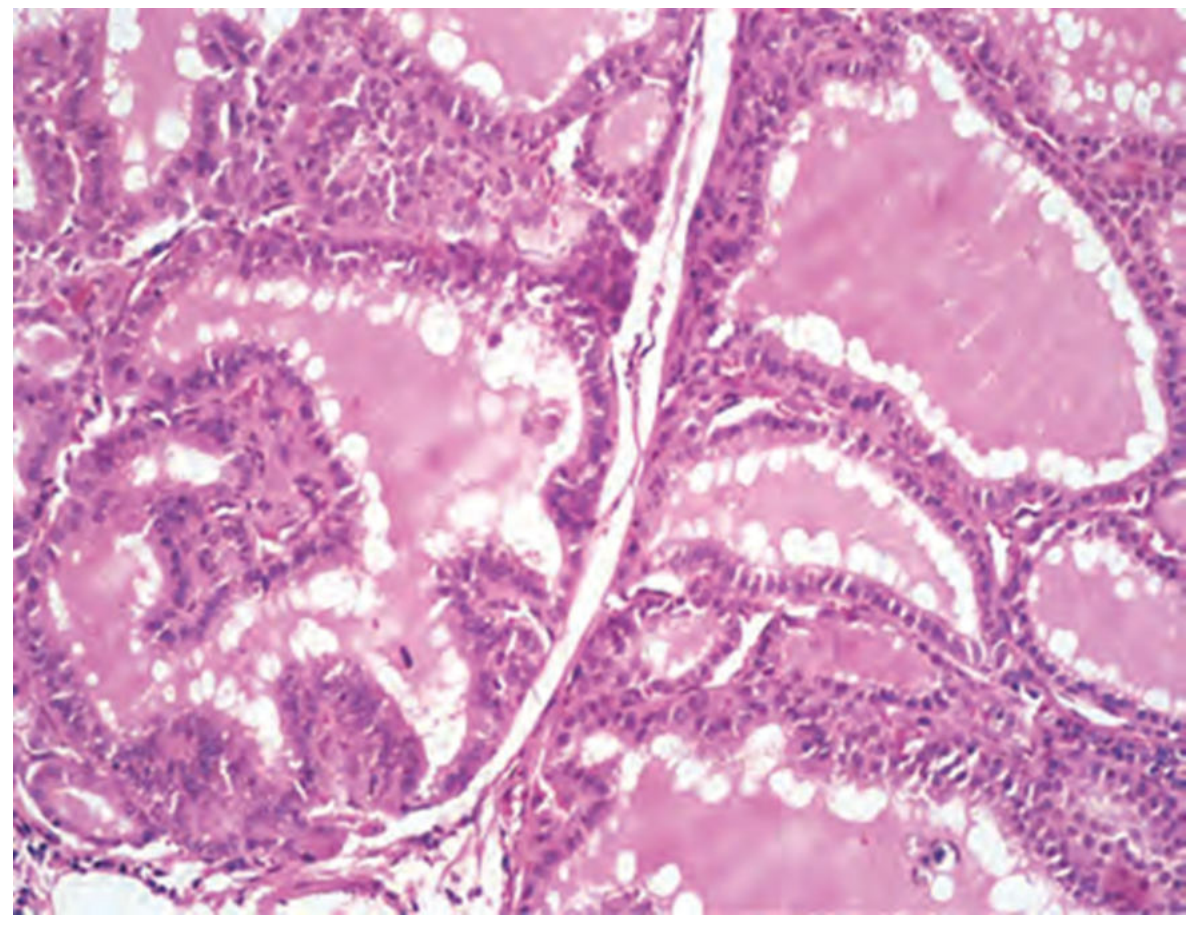
MORPHOLOGIC FEATURES-

- Grossly-moderately, diffusely and symmetrically enlarged
- Cut surface-homogeneous, red-brown and meaty and lacks the normal translucency

Histology-

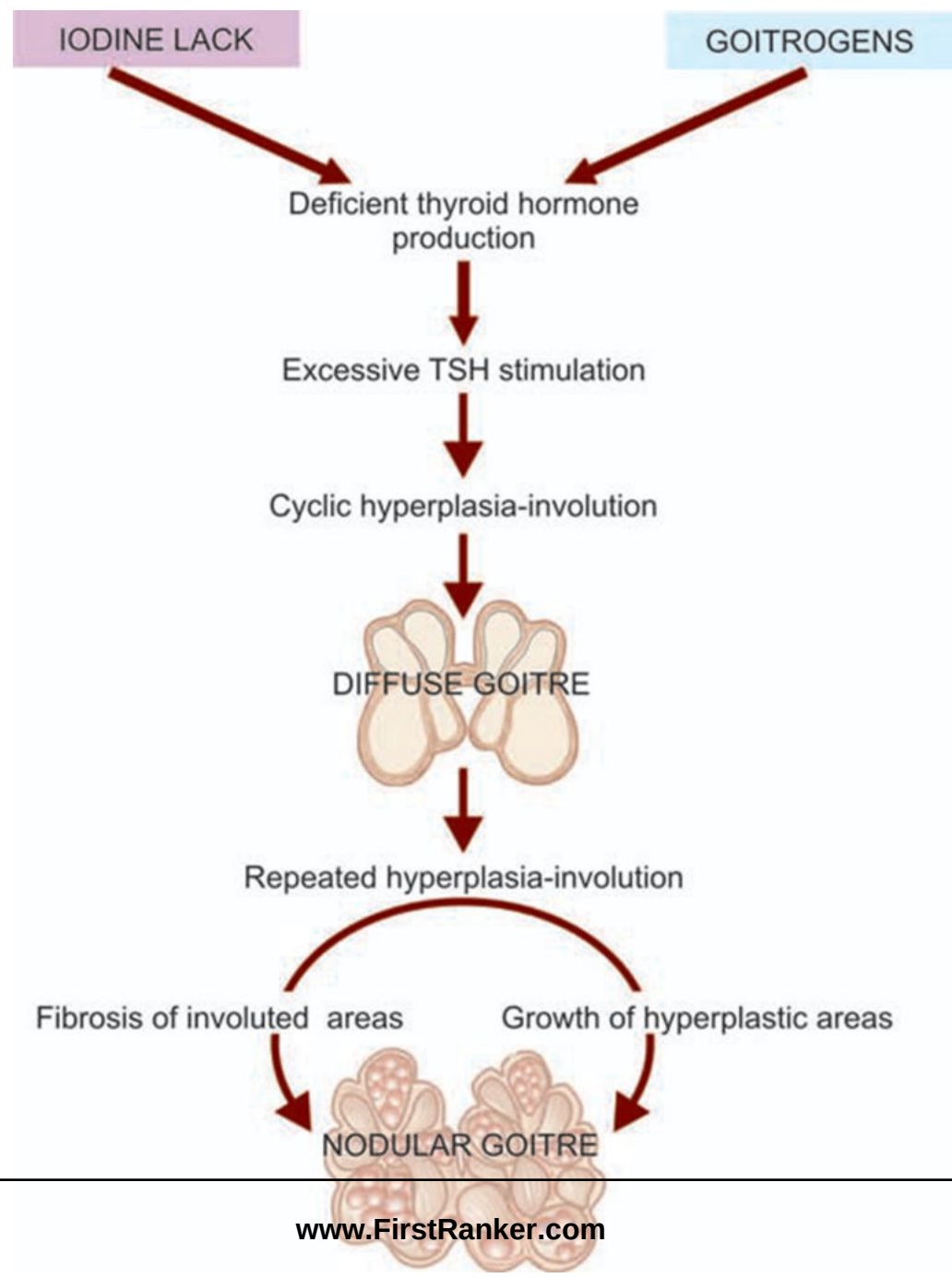
- epithelial hyperplasia
- colloid is markedly diminished
- increased vascularity and accumulation of lymphoid cells





GOITRE-Thyroid enlargement caused by compensatory hyperplasia and hypertrophy of the follicular epithelium in response to thyroid hormone deficiency

- Diffuse goitre (simple nontoxic goitre or colloid goitre).
- Nodular goitre (multinodular goitre or adenomatous goitre).



- ETIOLOGY. Epidemiologically, goitre occurs in 2 forms: endemic, and non-endemic or sporadic.

❑Endemic goitre.

- Endemic zone- more than 10% of the population is termed endemic goitre
- Goitrogens

❑Sporadic (non-endemic) goitre-

- Increased demand as in puberty and pregnancy
- Genetic factors.

➢ germline mutations in DICER1 gene

➢PTEN hamartoma tumor syndrome

- Dietary goitrogenes
- Drug induced goiter
- Hereditary defect in thyroid hormone synthesis and transport
- Inborn errors of iodine metabolism

MORPHOLOGIC FEATURES-

- Gross-moderate enlargement,symmetric and diffuse
- Cut surface-gelatinous and translucent brown

Histologically -stage

- Hyperplastic stage-papillae,new follicles
- Involution stage-large follicles distended by colloid and lined by flattened follicular epithelium

Nodular Goitre (Multinodular Goitre, Adenomatous Goitre)-

- nodular goitre is regarded as the end-stage of long-standing simple goitre.
- tumour-like enlargement of the thyroid gland and characteristic nodularity

MORPHOLOGIC FEATURES.

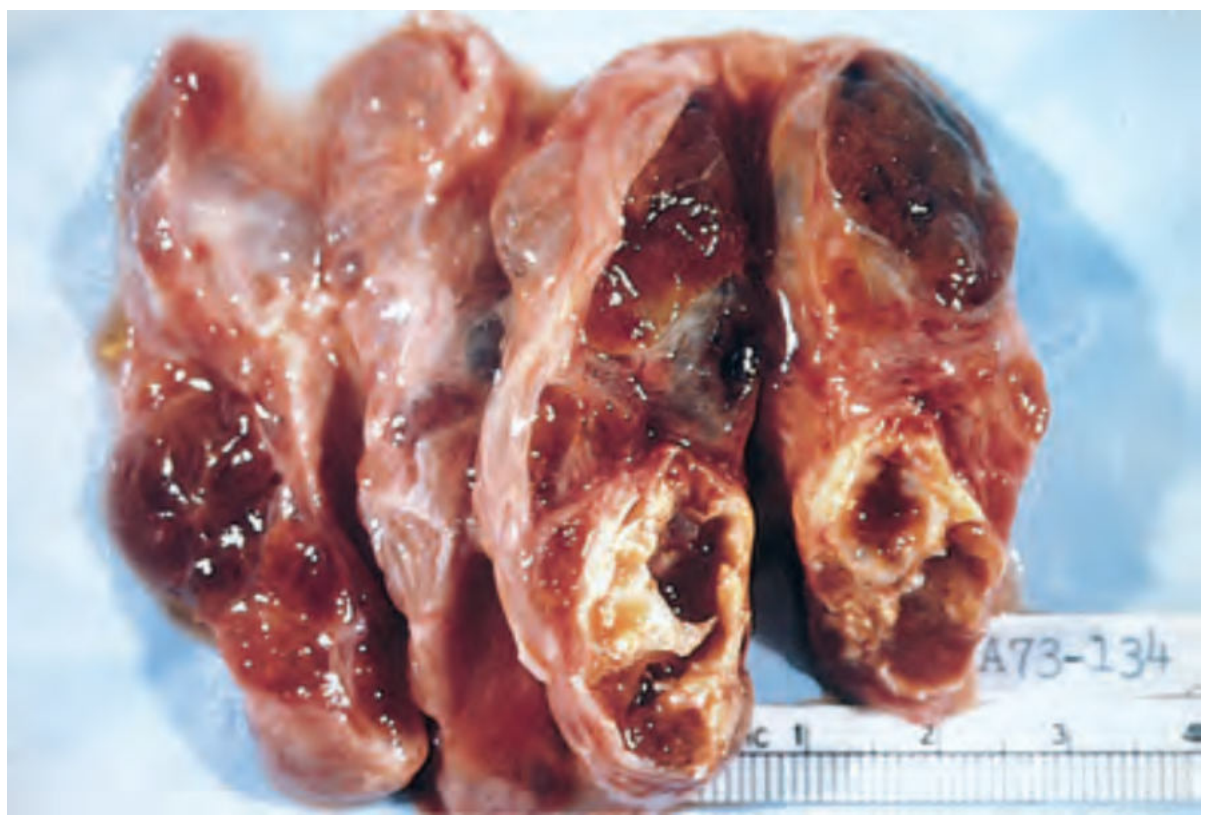
- Grossly, asymmetric and extreme enlargement, weighing 100-500 gm or even more
- Five cardinal macroscopic features are as under

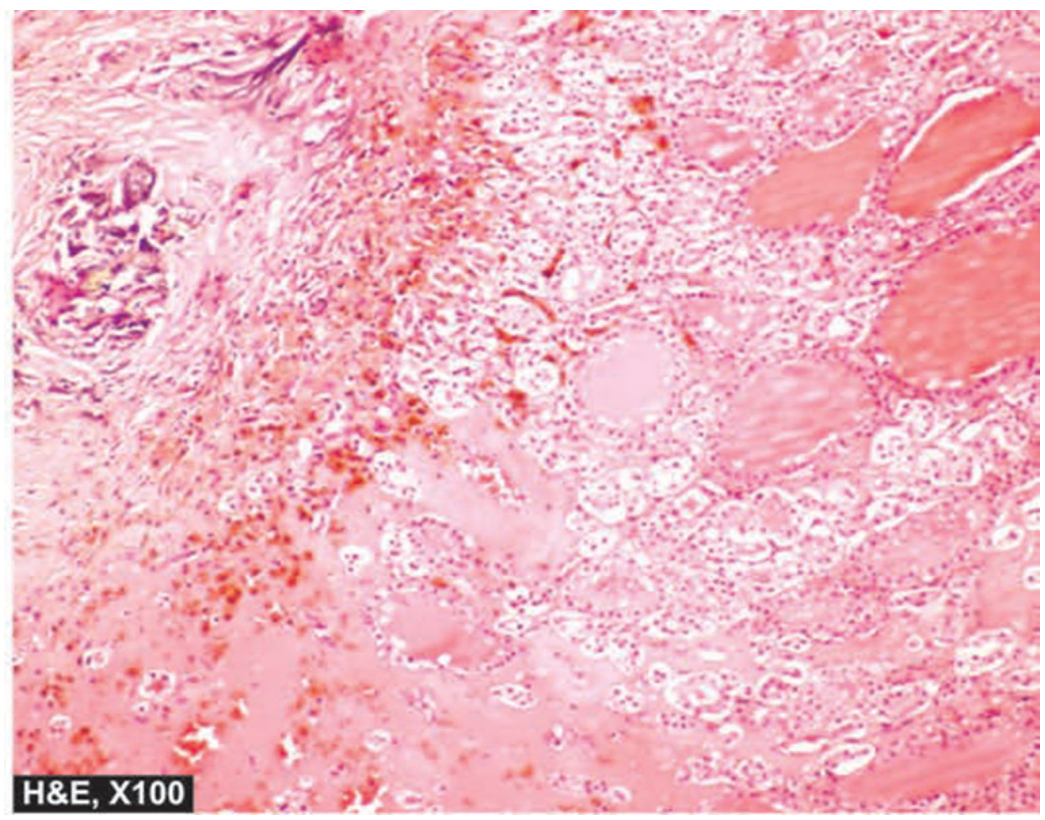
1. Nodularity with poor encapsulation
2. Fibrous scarring
3. Haemorrhages
4. Focal calcification
5. Cystic degeneration

- Cut surface- poorly-circumscribed multinodular

Histologically,

- Partial or incomplete encapsulation of nodules
- follicles varying from small to large
- Areas of haemorrhages
- Fibrous scarring with foci of calcification
- Micro-macrocystic change





THYROID TUMOURS

WHO classification of tumours of the thyroid gland (2017)

Follicular adenoma	8330/0
Hyalinizing trabecular tumour	8336/1*
Other encapsulated follicular-patterned thyroid tumours	
Follicular tumour of uncertain malignant potential	8335/1*
Well-differentiated tumour of uncertain malignant potential	8348/1*
Noninvasive follicular thyroid neoplasm with papillary-like nuclear features	8349/1*
Papillary thyroid carcinoma (PTC)	
Papillary carcinoma	8260/3
Follicular variant of PTC	8340/3
Encapsulated variant of PTC	8343/3
Papillary microcarcinoma	8341/3
Columnar cell variant of PTC	8344/3
Oncocytic variant of PTC	8342/3
Follicular thyroid carcinoma (FTC), NOS	8330/3
FTC, minimally invasive	8335/3
FTC, encapsulated angioinvasive	8339/3
FTC, widely invasive	8330/3
Hürthle (oncocytic) cell tumours	
Hürthle cell adenoma	8290/0
Hürthle cell carcinoma	8290/3
Poorly differentiated thyroid carcinoma	8337/3
Anaplastic thyroid carcinoma	8020/3
Squamous cell carcinoma	8070/3
Medullary thyroid carcinoma	8345/3
Mixed medullary and follicular thyroid carcinoma	8346/3
Mucoepidermoid carcinoma	8430/3
Sclerosing mucoepidermoid carcinoma with eosinophilia	8430/3
Mucinous carcinoma	8480/3
Ectopic thymoma	8580/3
Spindle epithelial tumour with thymus-like differentiation	8588/3
Intrathyroid thymic carcinoma	8589/3
Paraganglioma and mesenchymal/stromal tumours	
Paraganglioma	8693/3
Peripheral nerve sheath tumours (PNSTs)	
Schwannoma	9560/0
Malignant PNST	9540/3
Benign vascular tumours	
Haemangioma	9120/0
Cavernous haemangioma	9121/0
Lymphangioma	9170/0
Angiosarcoma	9120/3
Smooth muscle tumours	
Leiomyoma	8890/0
Leiomyosarcoma	8890/3
Solitary fibrous tumour	8815/1
Hematolymphoid tumours	
Langerhans cell histiocytosis	9751/3
Rosai-Dorfman disease	
Follicular dendritic cell sarcoma	9758/3
Primary thyroid lymphoma	
Germ cell tumours	
Benign teratoma	9080/0
Immature teratoma	9080/1
Malignant teratoma	9080/3
Secondary tumours	

The first four digits indicate the specific histological term; the fifth digit after the slash (/) is the behavior code, including /0 for benign tumours, /1 for unspecified, borderline, or uncertain behavior, /2 for carcinoma in situ and grade III intraepithelial neoplasia, and /3 for malignant tumours

* These new codes were approved by the IARC/WHO Committee for ICD-O

FOLLICULAR ADENOMA-most common

Pathogenesis-Somatic mutations of the **TSH receptor signalling** pathway are found in toxic adenomas, as well as in toxic multinodular goiter.

- TSHR and GNAS mutations,50%
- RAS or PIK3CA (<20%)
- <10% of follicular adenomas harbor PAX8- PPARG fusion genes

MORPHOLOGIC FEATURES.

- Grossly, the follicular adenoma is characterised by four features

1.solitary nodule

2. complete encapsulation

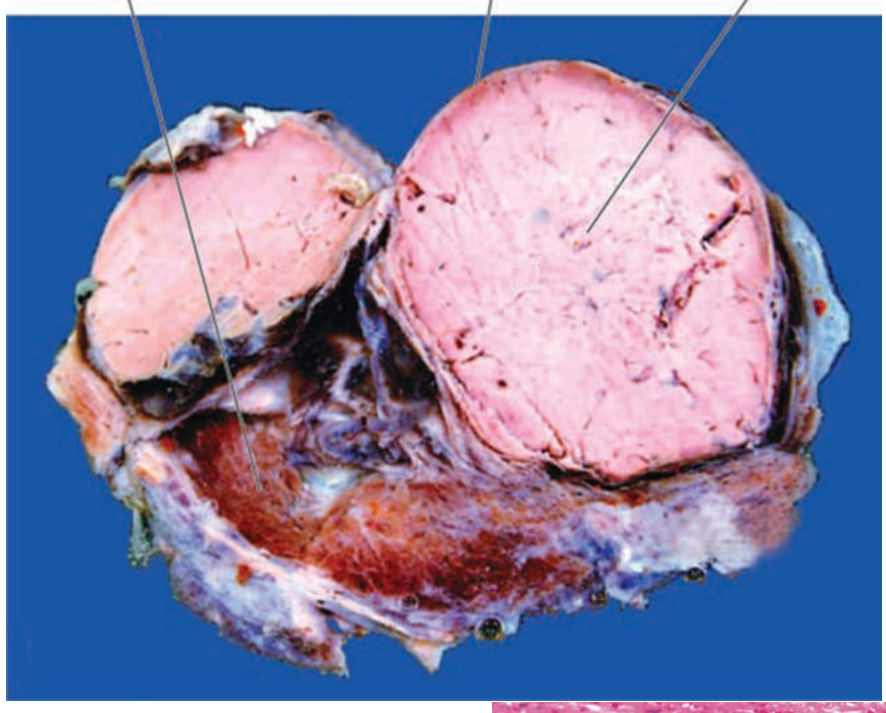
3. clearly distinct architecture inside and outside the capsule

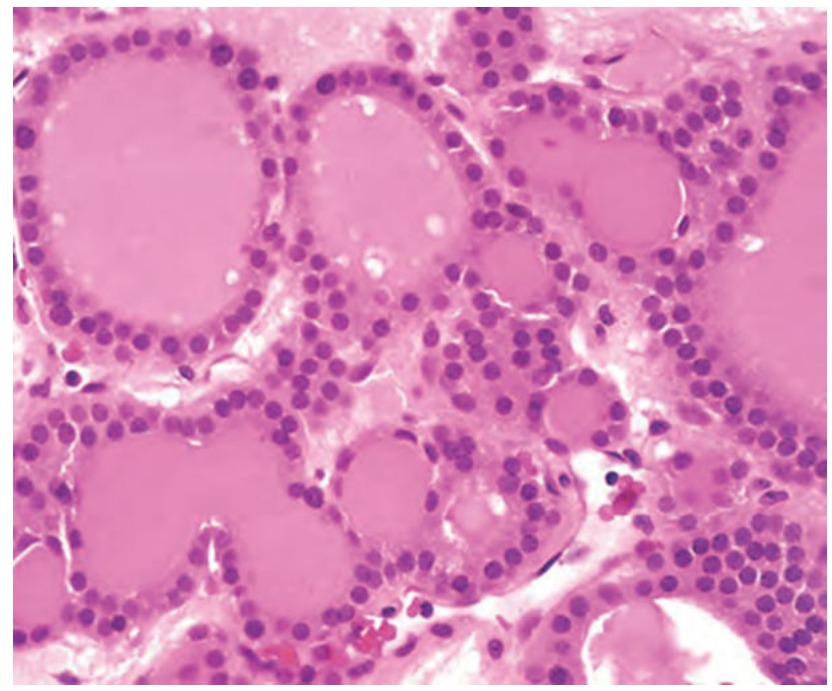
4. compression of the thyroid parenchyma outside the capsule

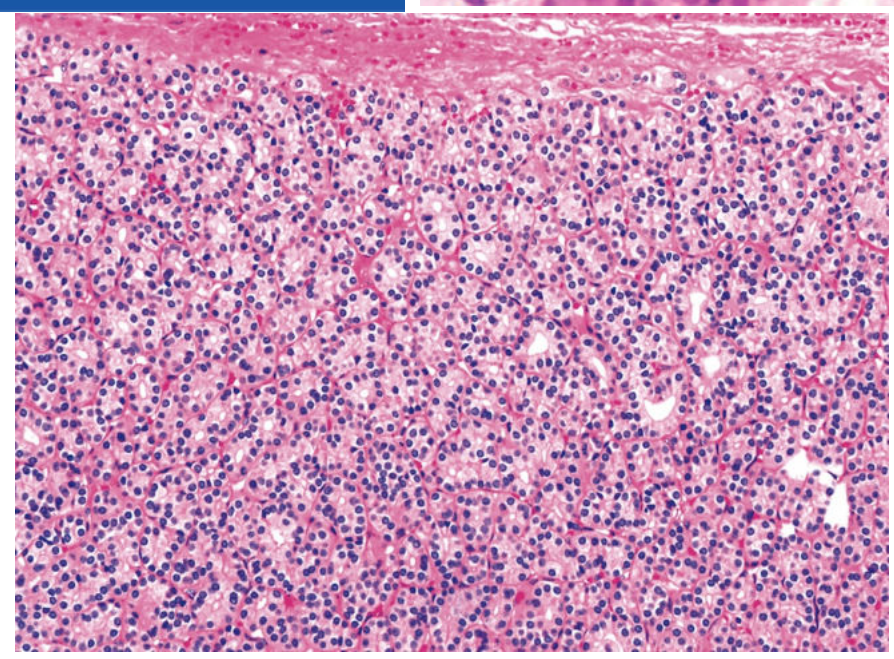
- small ,up to 3 cm in diameter
- cut section-grey-white to red-brown

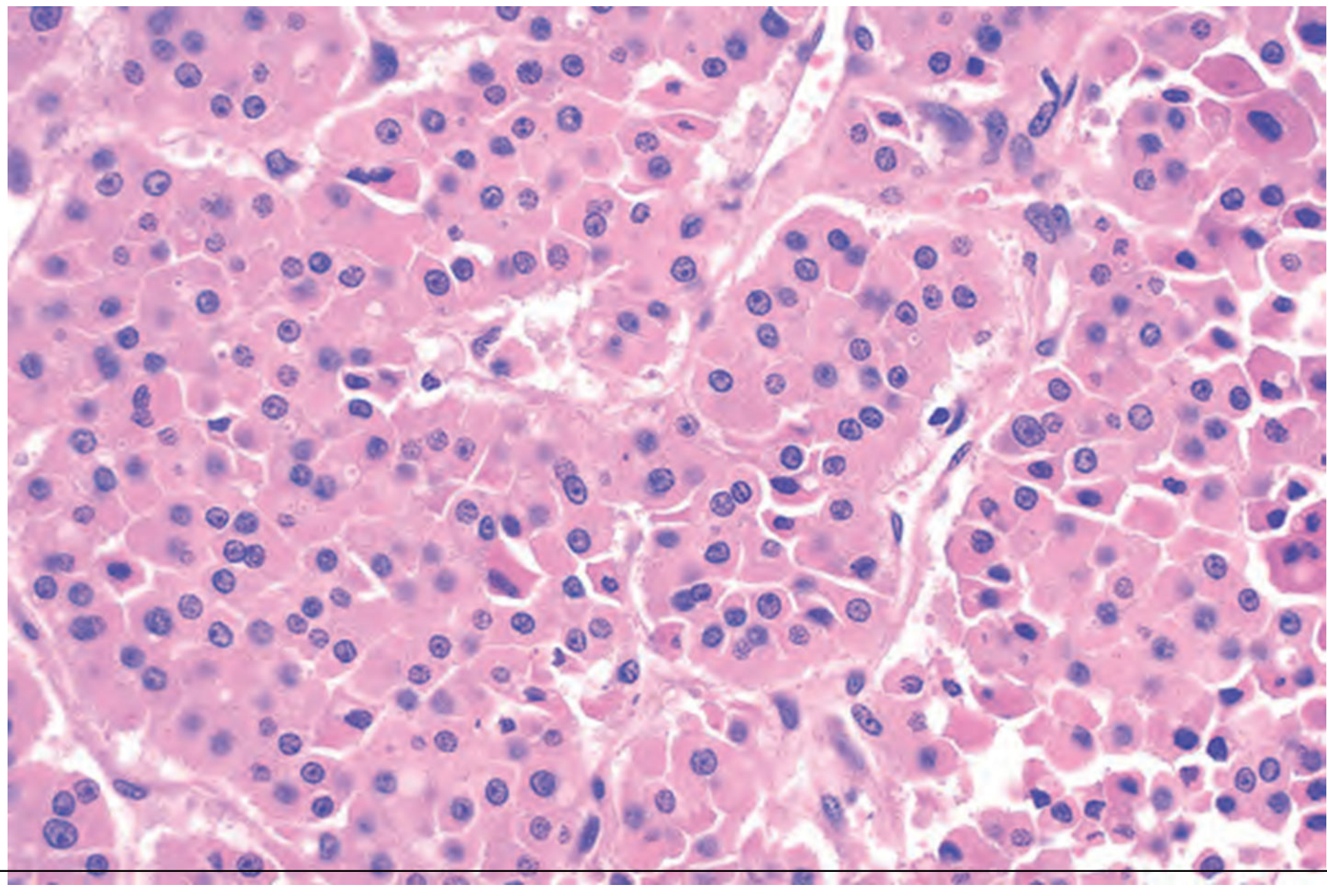
Histologically,

- complete fibrous encapsulation
- epithelial cells forming follicles of various size
- surrounding thyroid tissue shows signs of compression





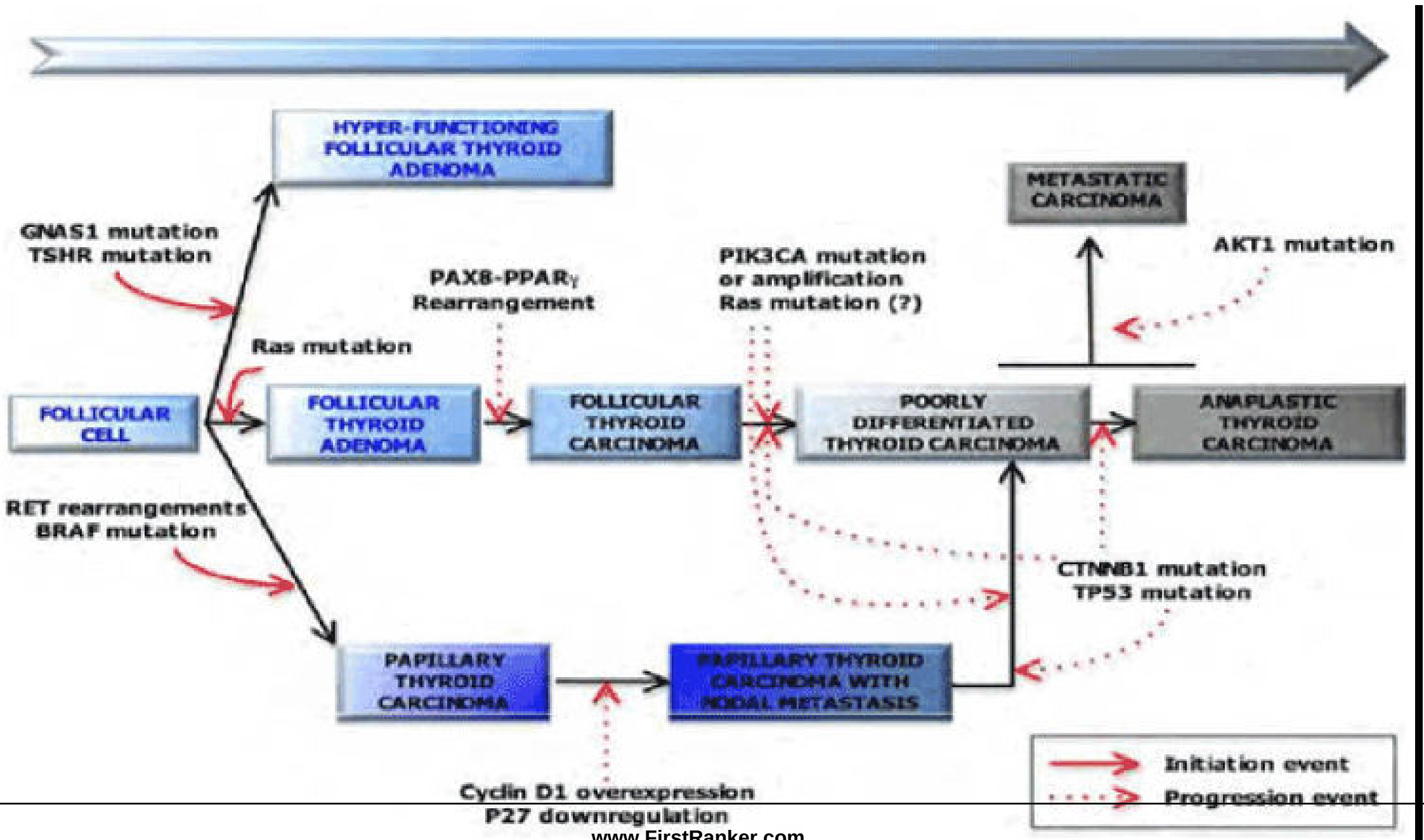




Thyroid Carcinoma

Major subtypes of thyroid carcinoma-

- Papillary carcinoma (>85% of cases)
- Follicular carcinoma (5% to 15% of cases)
- Anaplastic (undifferentiated) carcinoma (<5% of cases)
- Medullary carcinoma (5% of cases)



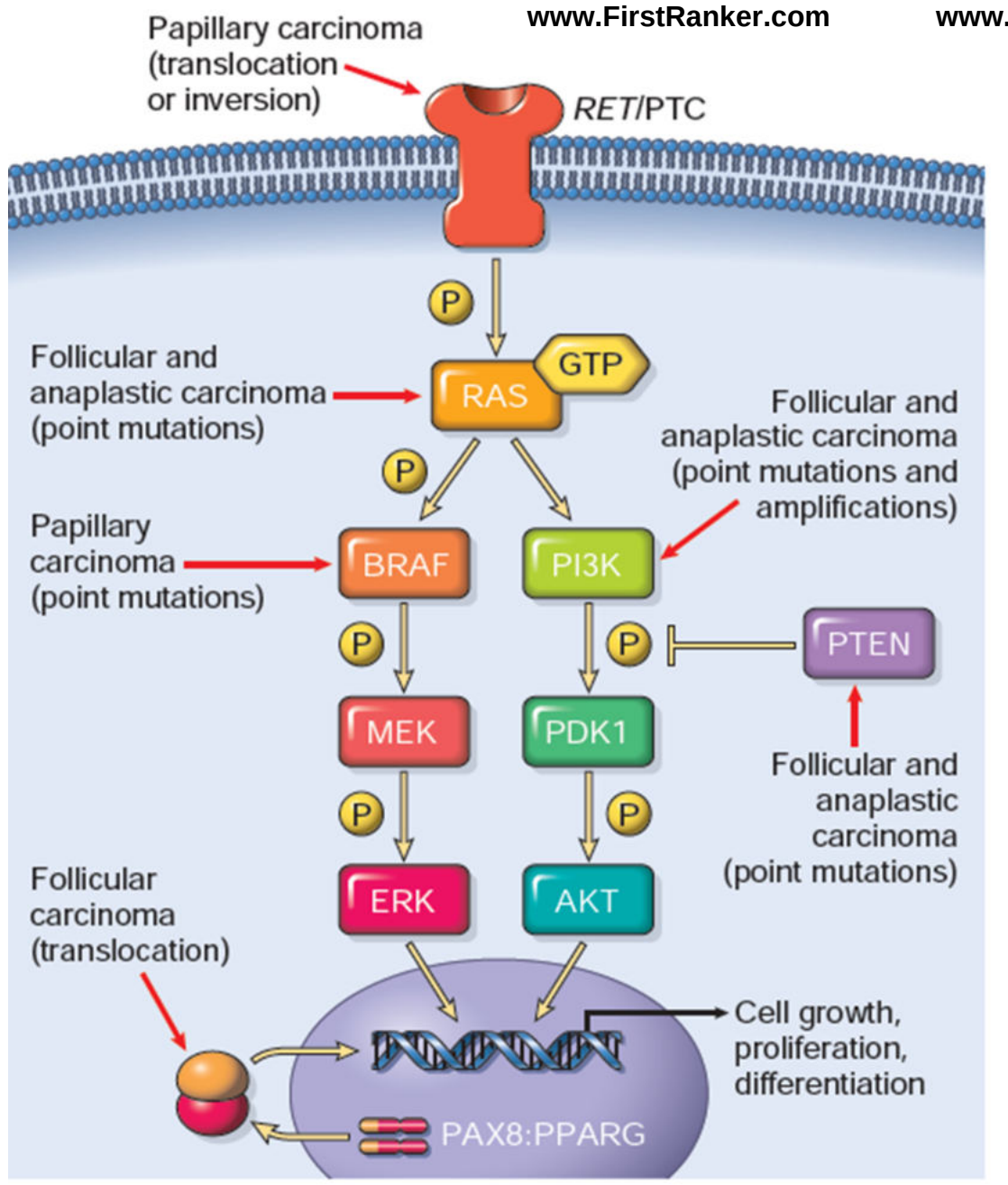


Figure 24-18 Genetic alterations in follicular cell-derived malignancies of the thyroid gland.

Papillary Carcinomas-

- Fusion gene RET/PTC

(RET/papillary thyroid carcinoma) and are present in approximately 20% to 40%

- NTRK1, 5-10%
- BRAF gene, advance stage

Follicular Carcinomas-

- RAS or the PI-3K/AKT
- PIK3CA amplifications
- PTEN, a tumor suppressor gene

Anaplastic (Undifferentiated) Carcinomas-RAS or PIK3CA mutations)
Second hit ,inactivation of TP53 or activating mutations of β-catenin

Medullary Thyroid Carcinomas-

- MEN-2 syndrome
- RET mutations

Papillary Carcinoma-

most common form of thyroid cancer

MORPHOLOGY-

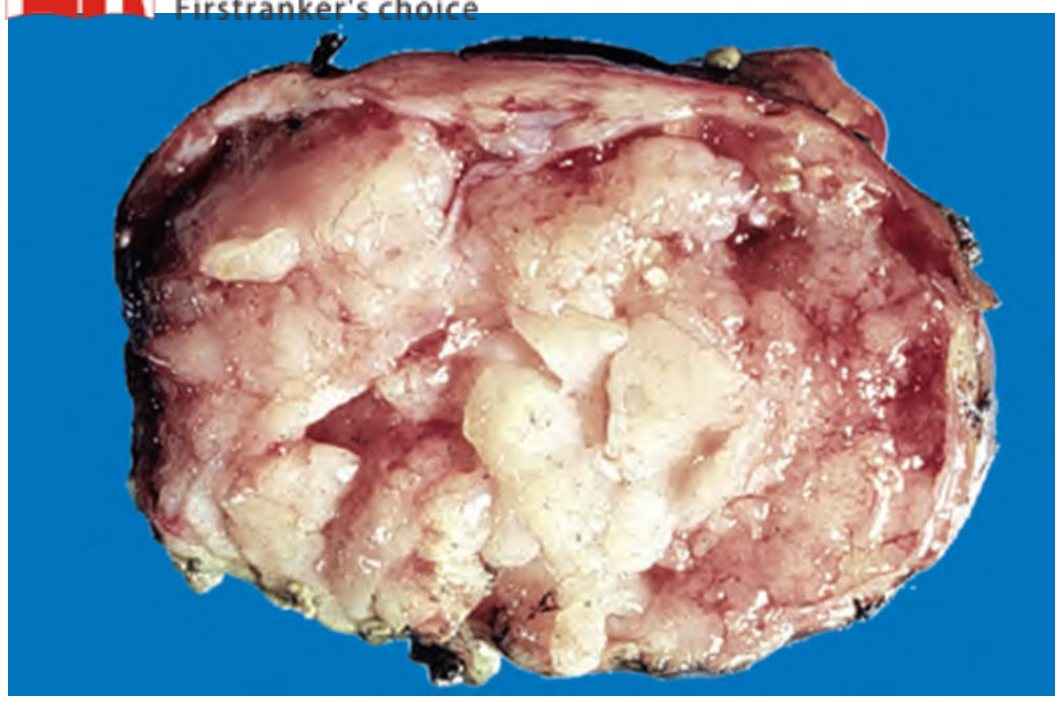
Gross-

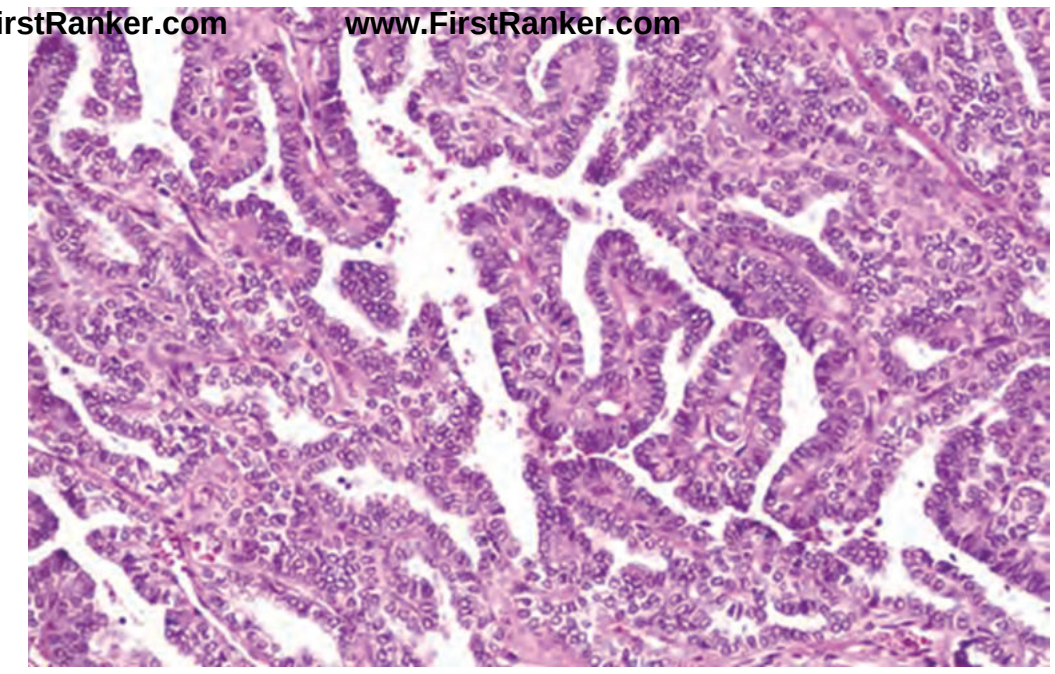
solitary or multifocal

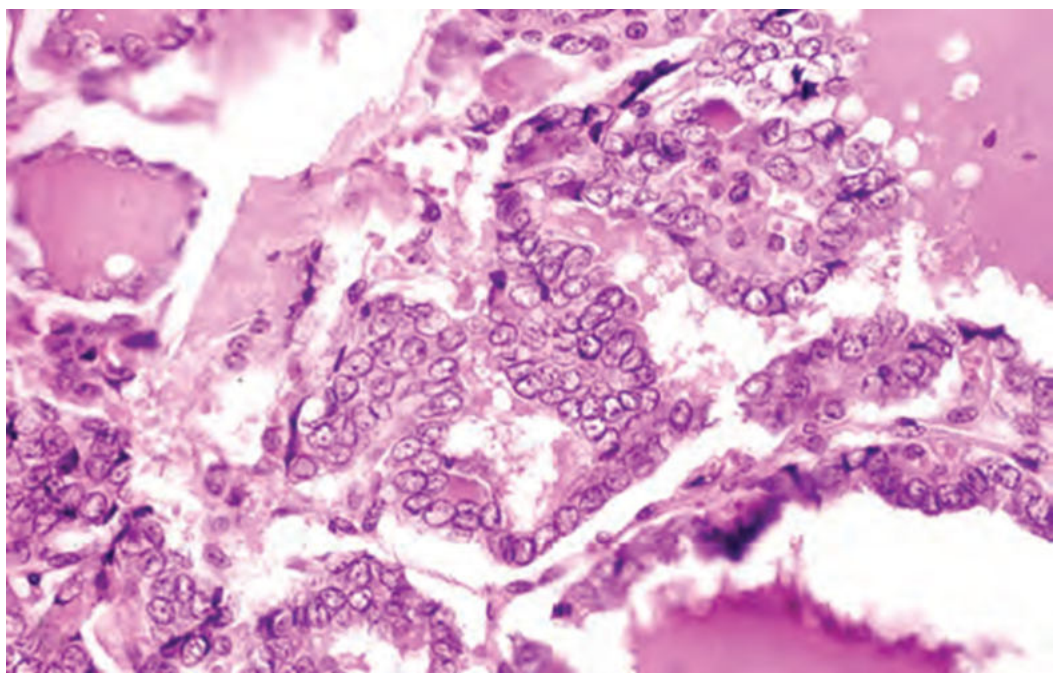
Cut surface-greyish-white, hard, Fibrosis,calcification and papillary foci

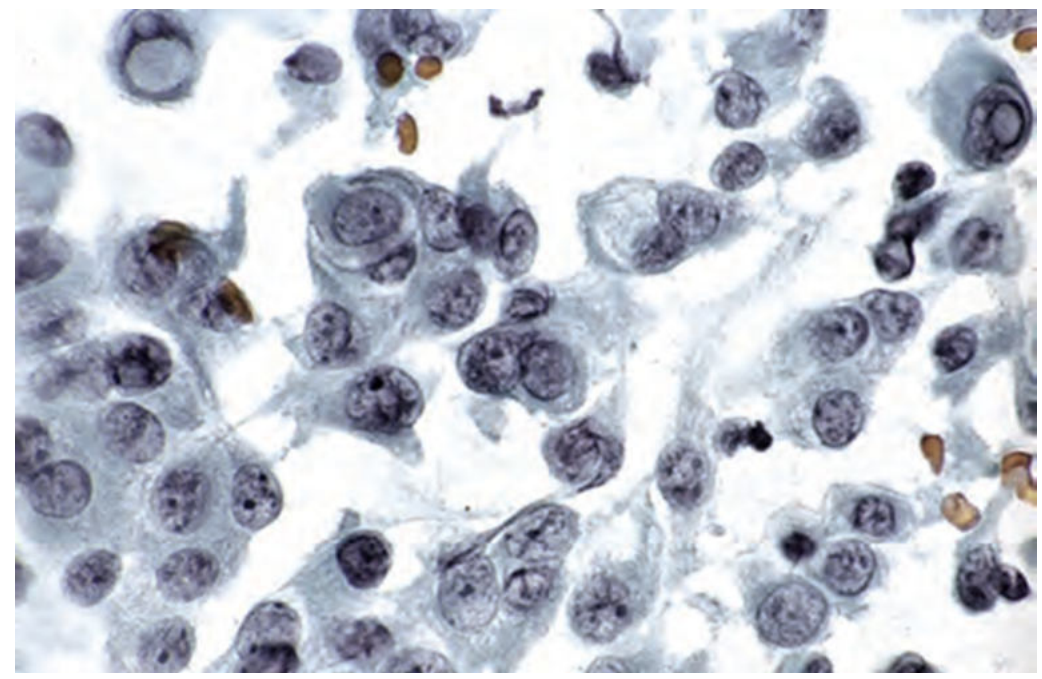
microscopic hallmarks-

- branching papillae
- Ground glass or Orphan Annie eye nuclei,intranuclear cytoplasmic inclusion
- Psammoma bodies



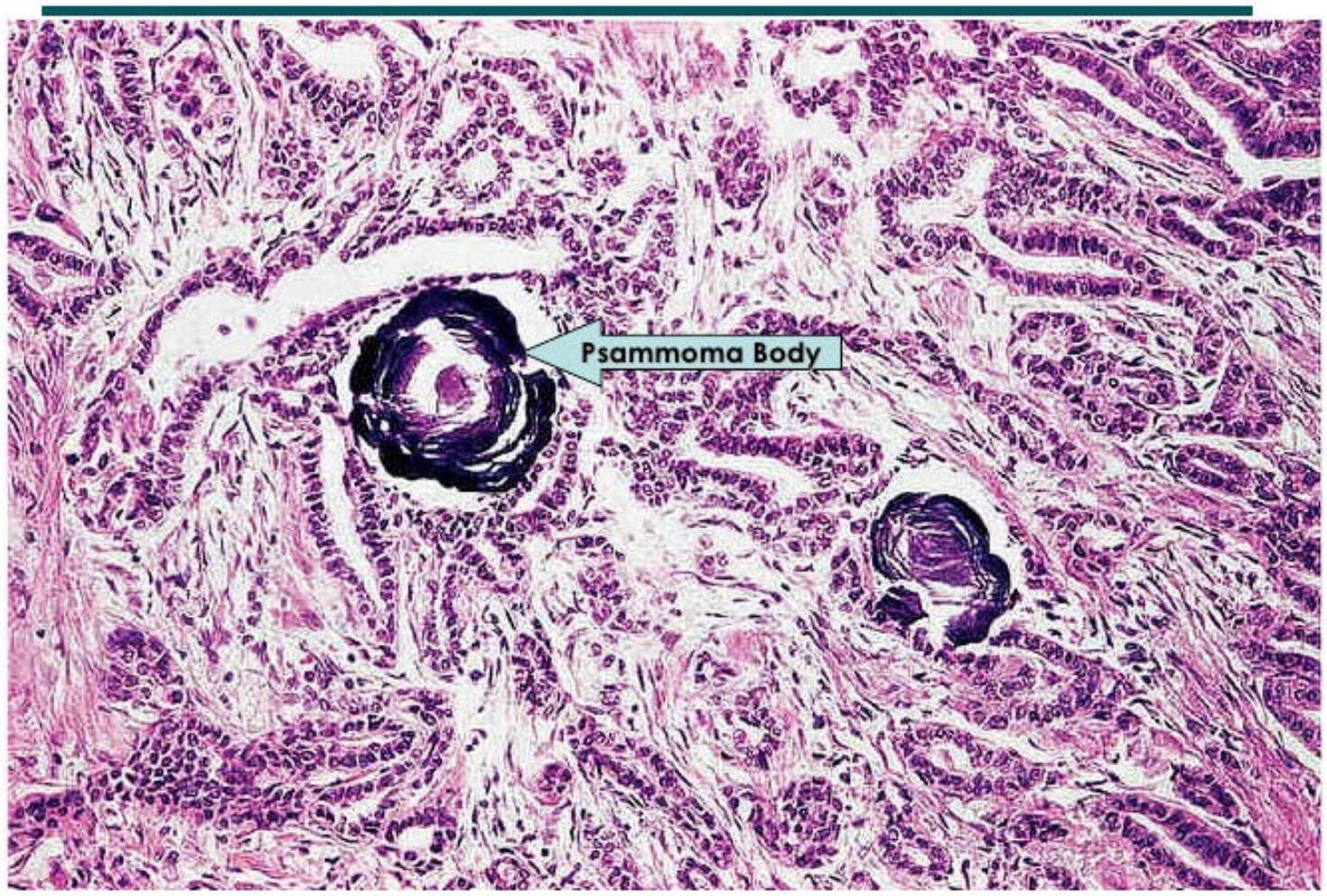






Papillary Carcinoma

Psammoma bodies.



Variants-

- follicular variant
- tall-cell variant
- diffuse sclerosing variant
- papillary microcarcinoma

Follicular Thyroid Carcinoma-

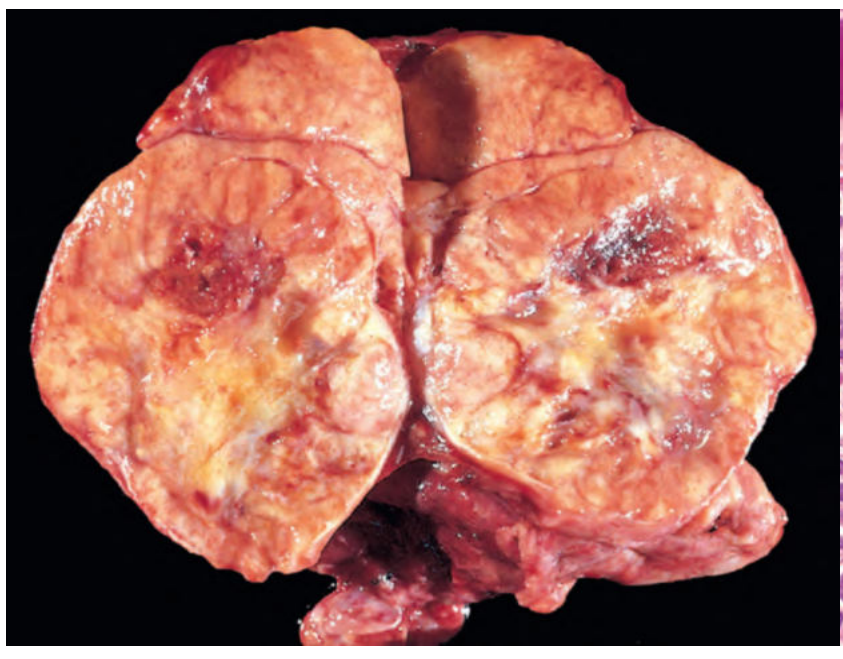
- 5% to 15% of primary thyroid cancers, but are more frequent in areas with **dietary iodine deficiency**

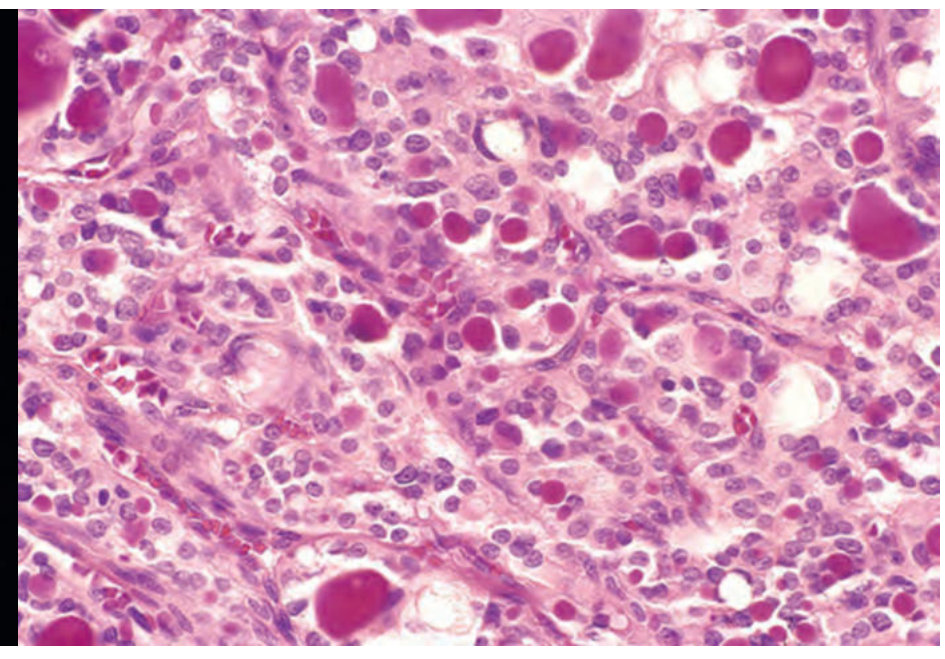
MORPHOLOGY-

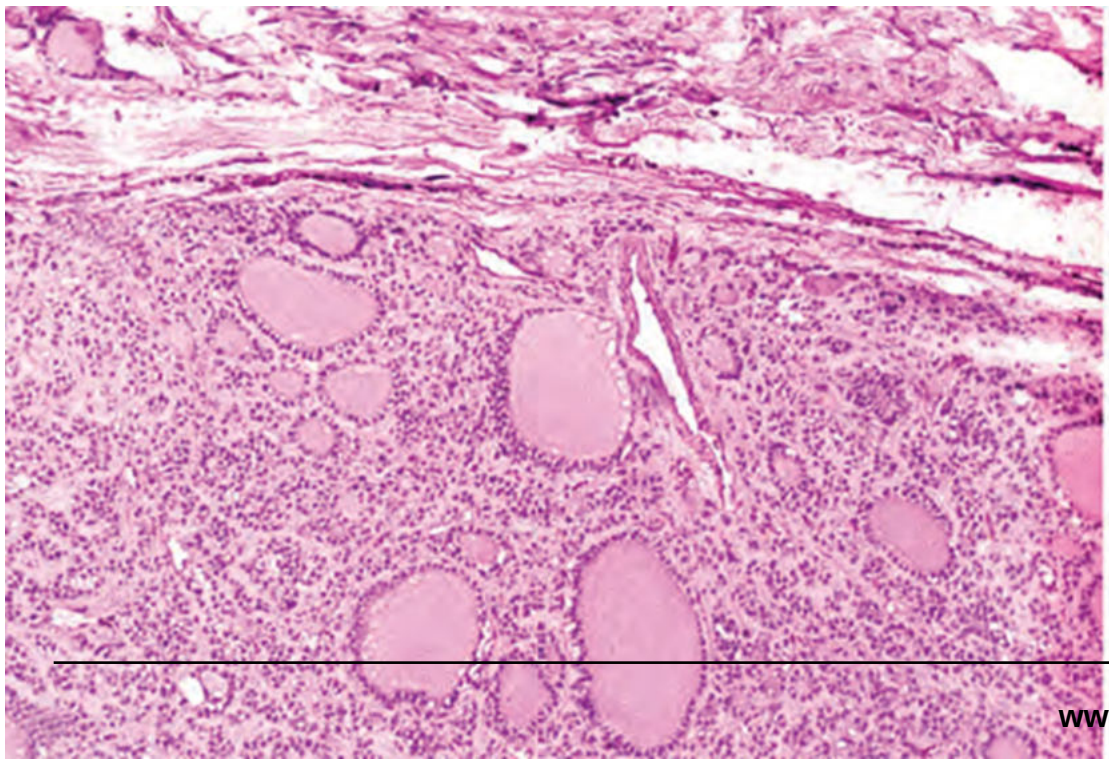
- Solitary nodule
- Cut surface-grey-white with areas of haemorrhages, necrosis and cyst formation

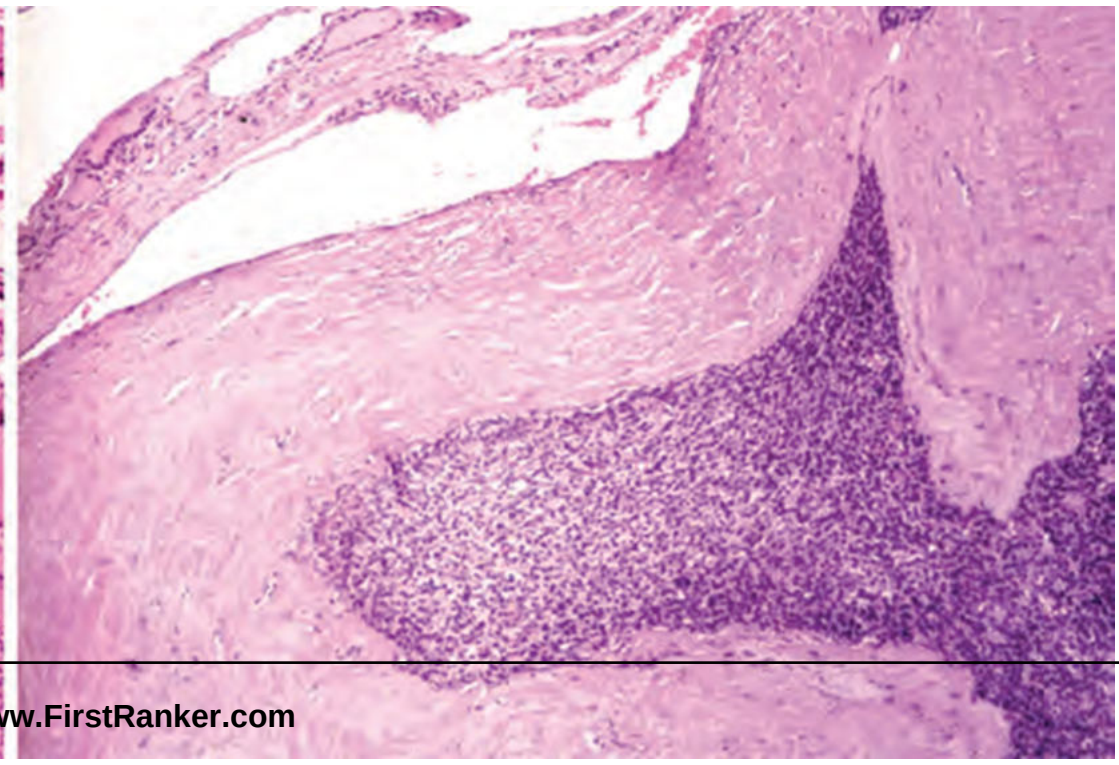
Microscopically,-

- follicles of various sizes,solid trabecular pattern
- Vascular invasion and direct extension
- lymphatic invasion is rare







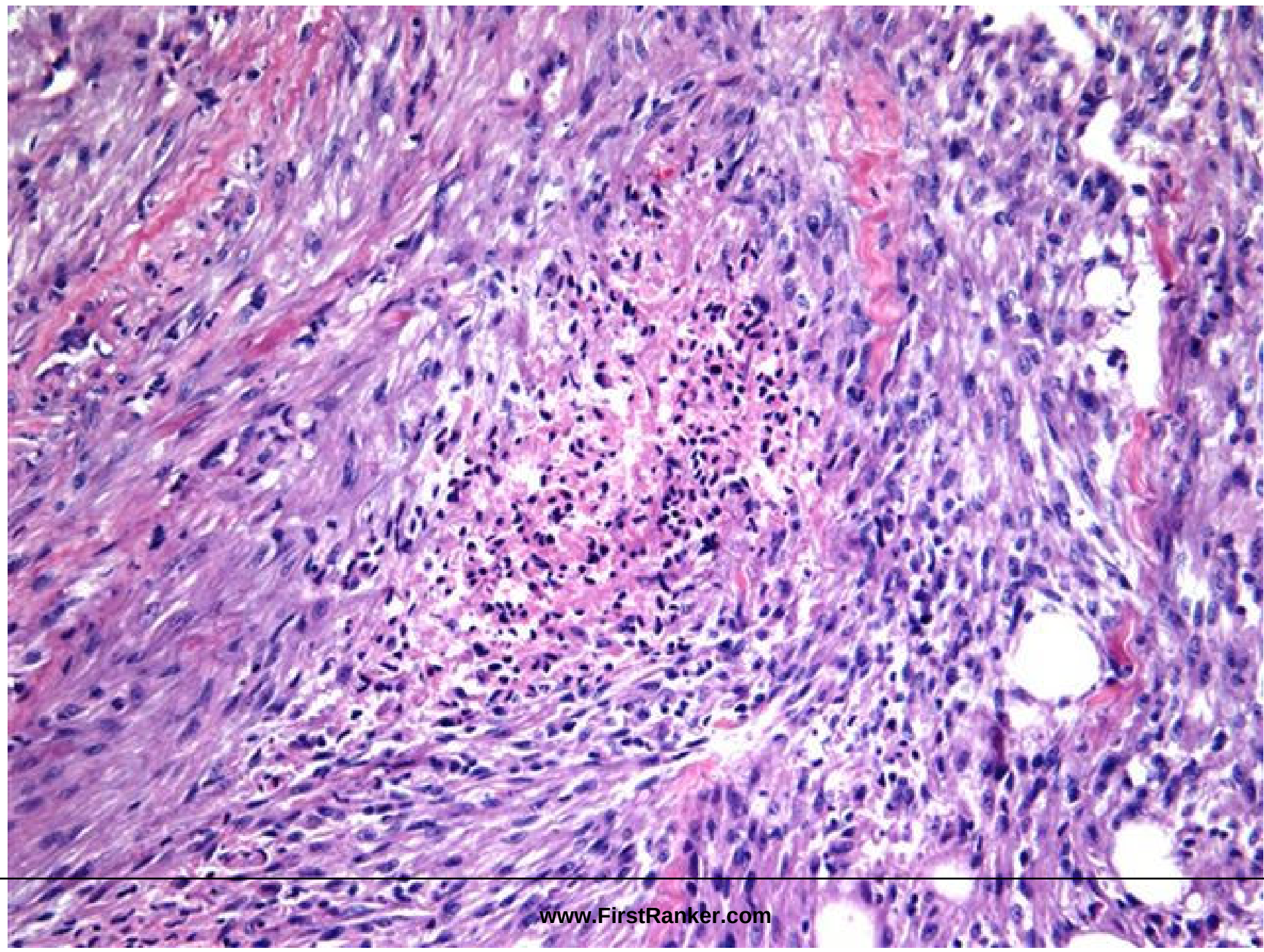


Anaplastic (Undifferentiated) Carcinoma-

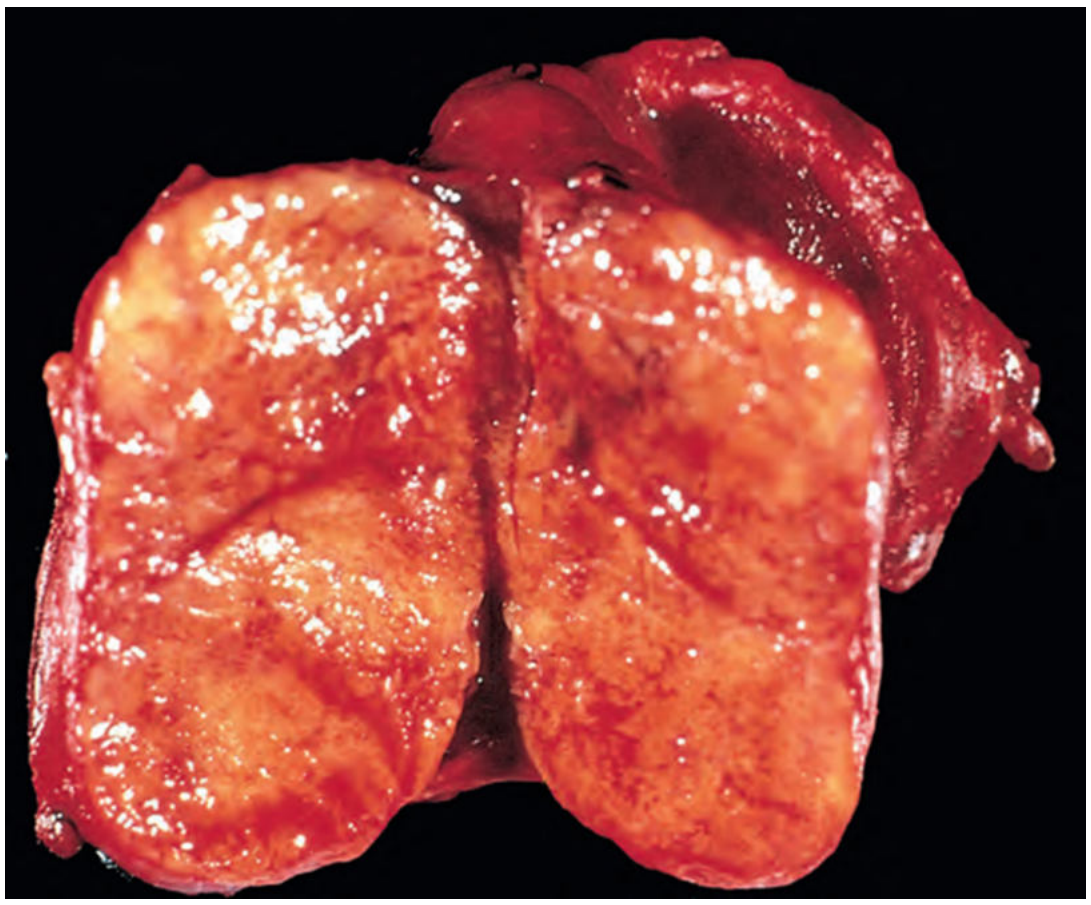
- <5%
- 100% moratality

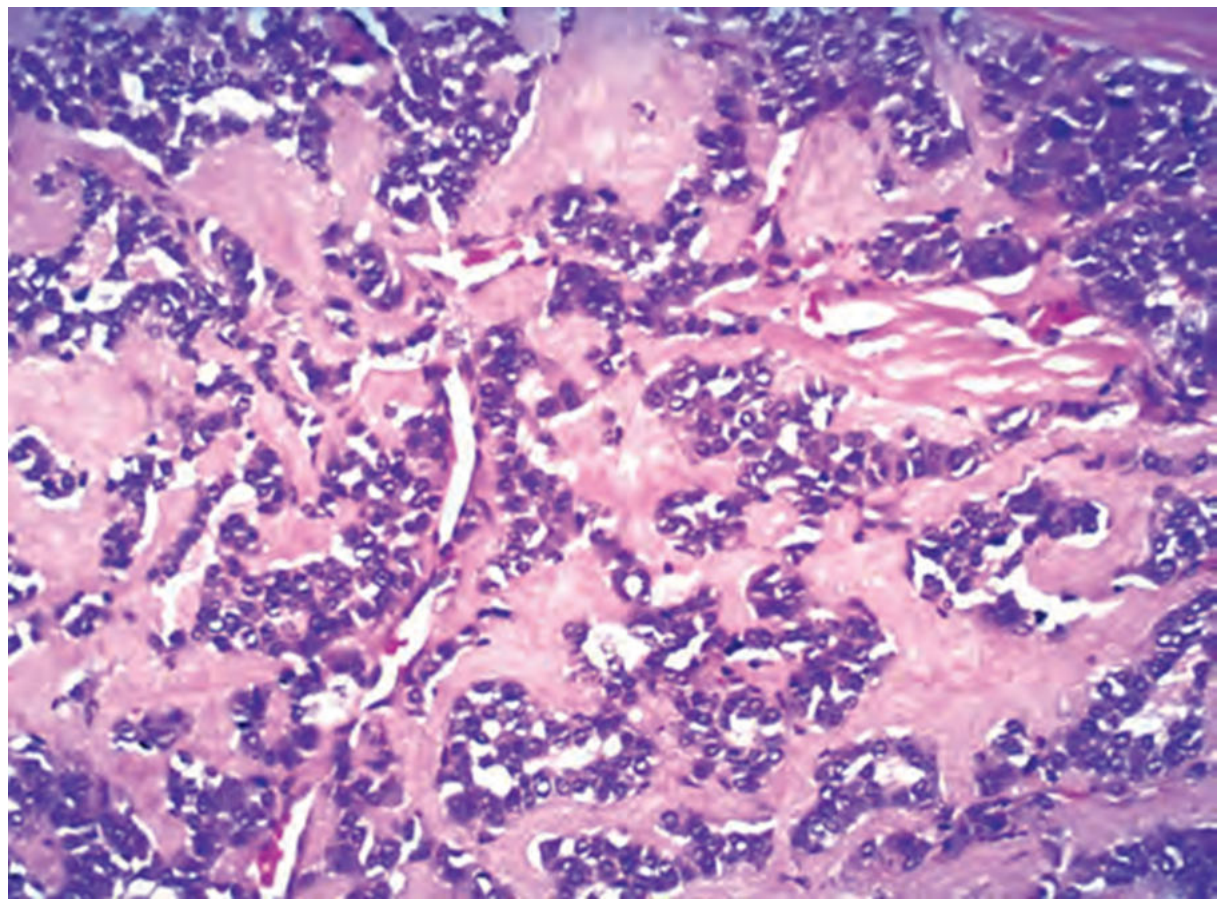
Microscopy-

- pleomorphic giant cells
- spindle cells
- mixed spindle and giant cells



Medullary Carcinoma

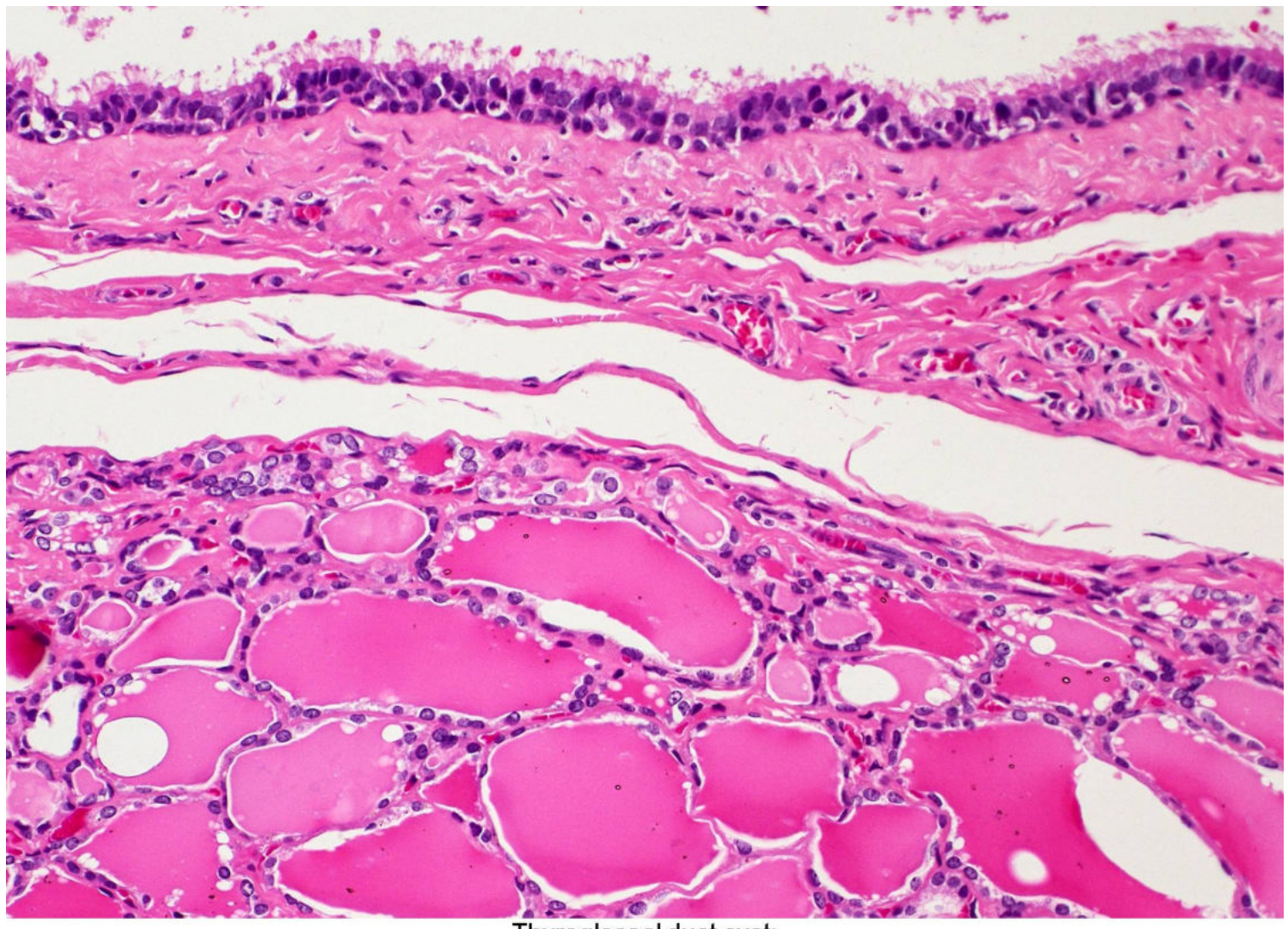




Congenital Anomalies-

Thyroglossal duct cyst

- most common congenital neck mass
- Midline neck



Thyroglossal duct cyst:
thyroid follicles under ciliated epithelium (H&E, high power)