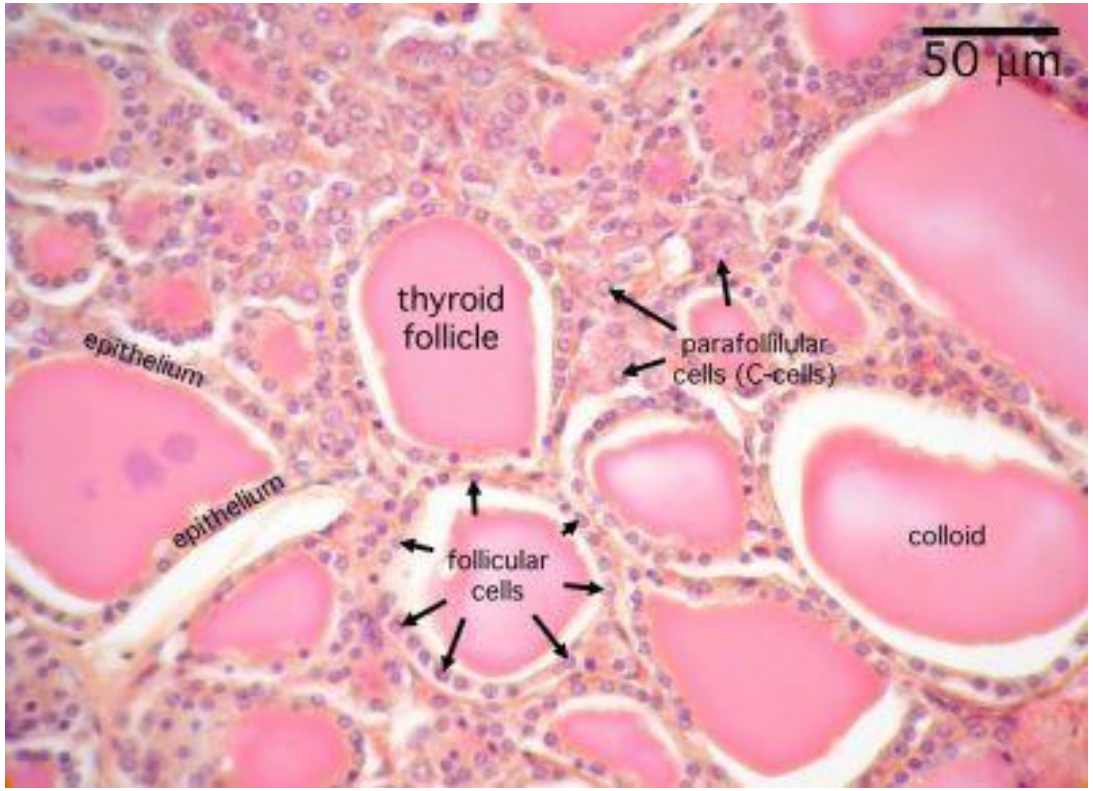
Pathology of the endocrine system

Endocrine system

A. Endocrine organs
    1. Pituitary gland
    2. Pineal gland
    3. *Thyroid gland*
    4. *Adrenal glands*
    5. Parathyroid glands
B. Organs with partial endocrine functions
    1. Pancreas
    2. Gonads
C. Diffuse neuroendocrine system

(endocrine cells with diffuse localization; gastrointestinal tract, bronchi)

Thyroid gland



Cells:

- Follicular epithelial cells
- Parafollicular C-cells located sparsely between the follicles

Pathology of the thyroid gland

- Functionally:
  - Hyperfunction = **Hyperthyroidism**
  - Hypofunction = **Hypothyroidism**
- Morphologically:
  - Hyperplasia: goiter (diffuse or multinodular)
  - Inflammatory diseases – thyreoiditis
    - Infective - rare
    - Autoimmune (Hashimoto, Graves) - common
    - Other etiology (palpation)
  - Neoplasms (benign, malignant)

Hyperthyroidism

- Hyperfunction of the thyroid
- Primary hyperthyroidism - causes:
  - Graves disease
  - Multinodular goiter
  - Hyperfunctional adenoma
  - (Early phase of Hashimoto thyroiditis)
- Secondary hyperthyroidism - causes :
  - TSH producing pituitary gland tumor, iatrogenic

- Characteristic symptoms
  - Variable enlargement of the thyroid gland → no strict correlation with the size of the thyroid
  - Increased metabolism, sympathicotonia
  - Palpitation

Hypothyroidism

- Hypofunction of the thyroid
- Primary, secondary and tertiary causes
  - Primary:
    - Late phase of Hashimoto thyroiditis
    - Iatrogenic (resection, irradiation, drugs)
    - Other (hemochromatosis, amyloidosis, sarcoidosis)
  - Secondary: absence of TSH (pituitary diseases)
  - Tertiary: absence of TRH (hypothalamic diseases)
- Clinical presentations:
  - Myxedema (adults)
  - Cretinism (infants)

Hyperplasia- Goiter

Multinodular goiter

- Predominantly in elderly patients
- Permanent increase of TSH levels (ex. iodine deficiency)
  Follicular epithelial cells have varying responsiveness to TSH, in different areas there is different intensity of hyperplasia
- As the TSH levels are changing hyperplasia and involution present alternately
- Degenerative changes are characteristic (hemorrhage, scarring, calcification, cystic degeneration)
- Functionally, most commonly normofunctional
- Sometimes some of the nodules is hyperfunctional
  toxic multinodular goiter – *Plummer's disease*

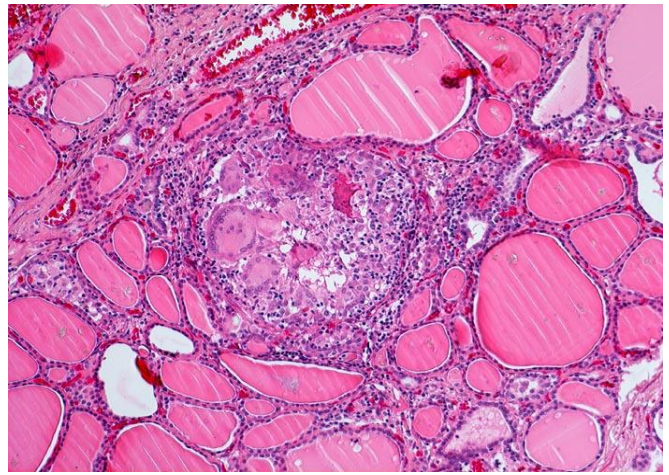
Hyperplasia- Goiter

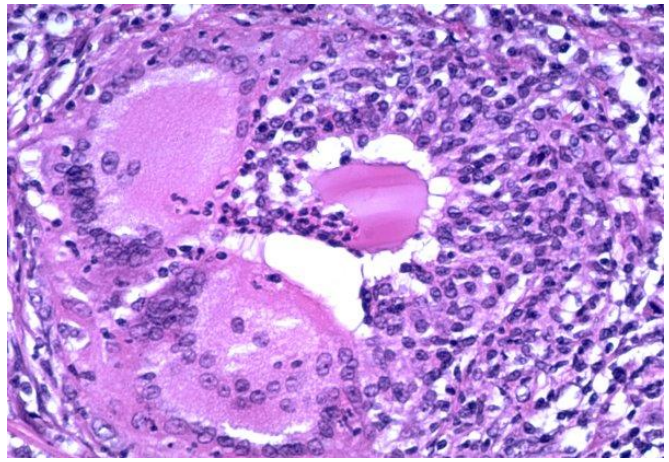
Diffuse goiter

- Functionally, it can be euthyroid, hyperthyroid or hypothyroid
- **Graves disease:**
  - Most common
  - Autoimmune thyroiditis
  - Hyperfunction
- Endemic goiter:
  - Due to decreased iodine intake permanent TSH hypersecretion occurs with diffuse hyperplasia
  - normofunction or hypofunction
- Enzymopathies
  - Hypofunction

de Quervain's thyroiditis

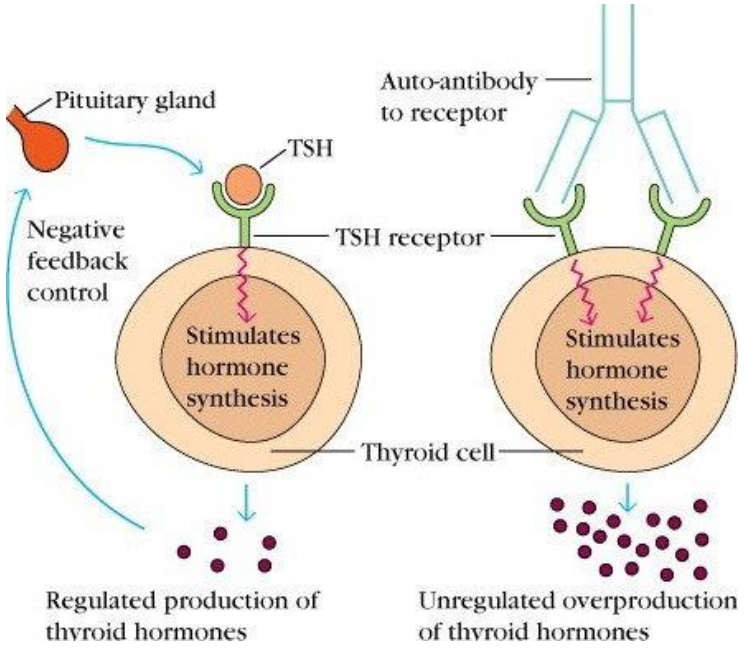
- Subacute granulomatous thyroiditis
- Diffuse enlargement
- Viral etiology
- Young and middle-aged women
- Painful! Can be accompanied with transient fever
- In acute phase microabscesses, follicular damage present – colloid gets into the interstitium
- Later lymphoplasmocytic infiltration, histiocytes foreign body reaction to the colloid – granulomas, giant cells
- Spontaneous healing





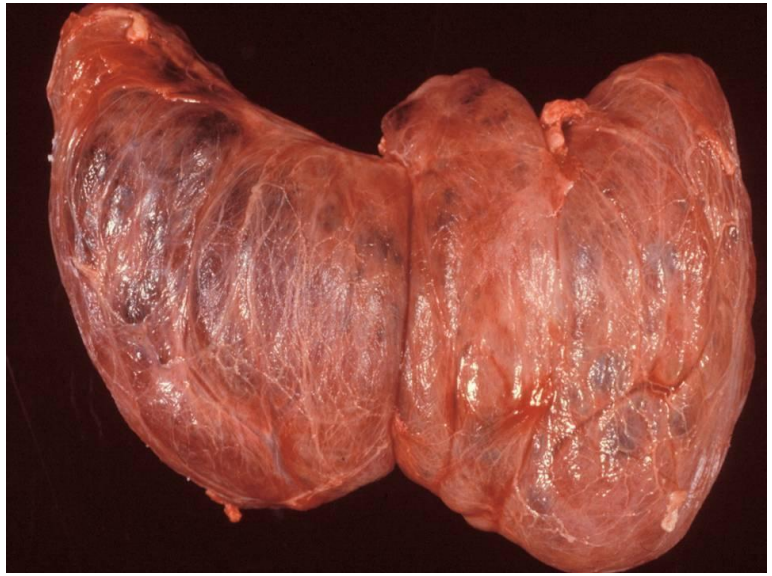
Graves disease

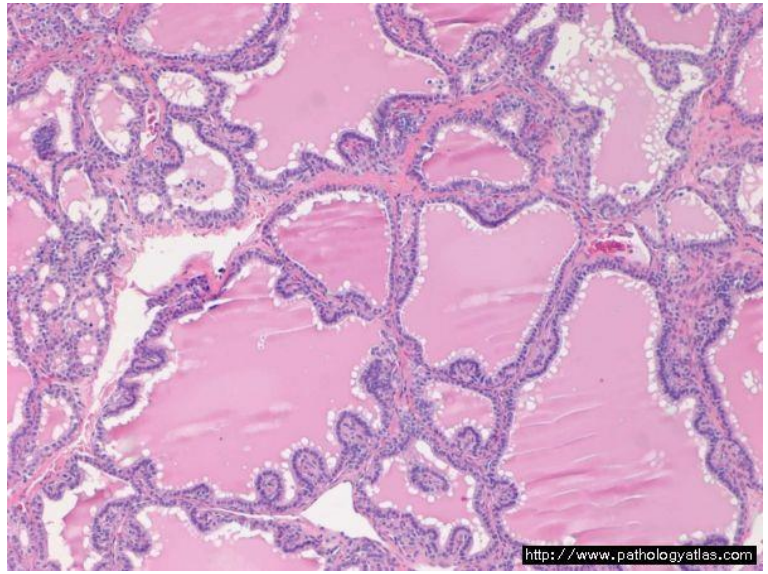
- Autoimmune disease
- Autoantibodies to TSH receptors
- Most common between the age of 20 and 40
- More common in women
- Genetic factors play an important role in pathophysiology: associated with HLA-B5 and DR3 haplotypes



Graves disease

- Enlarged, firm, hyperemic thyroid
- Hypertrophy and hyperplasia of follicular epithelia
- Bulging of hyperplastic follicular epithelium into the follicular lumen:
  Sanderson polster
  papillary structures without fibrovascular core (←→papillary cc.)
- High, cylindrical follicular epithelial cells
- Lymphocytic aggregates





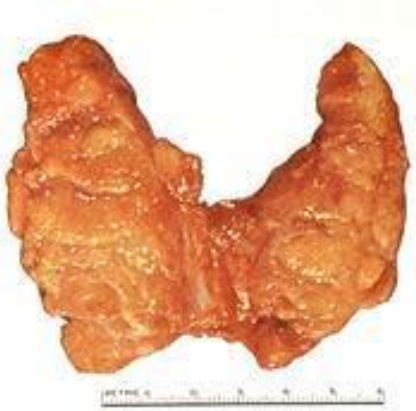
Hashimoto thyroiditis

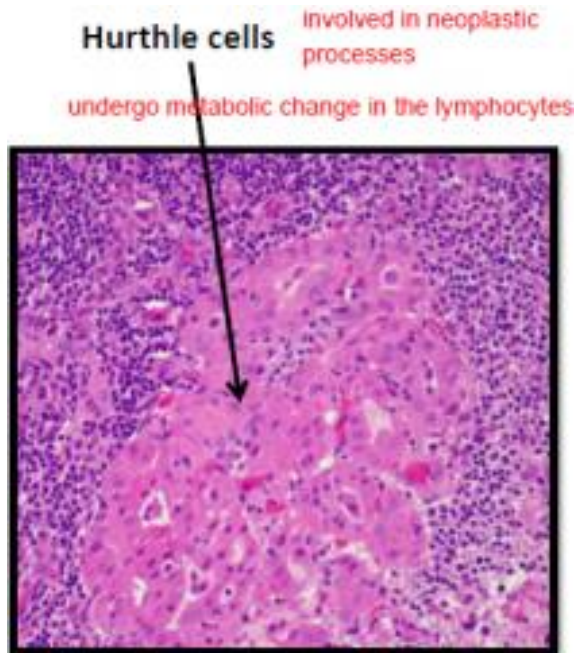
- Functionally, in early phase transient hyperfunction is followed by normofunction - eventually hypofunction develops
- Most commonly in middle-aged patients
- More common in women
- Anti-Tg and anti-TPO autoantibodies (humoral immune response)
- T-cell dysfunction (cellular immune response)
- HLA-DR3 and DR5 association

Hashimoto thyroiditis

- The thyroid is normal in size, pale in color
- Lymphocytic aggregates with germinal centers, lots of plasma cells
- The amount of colloid and the number of epithelial cells decrease
- The cytoplasm of remaining epithelial cells gets acidophilic. Oncocytic cells – ***Hurthle cells*** (increased number of mitochondria)
- After long term progression interstitial fibrosis occurs with atrophy

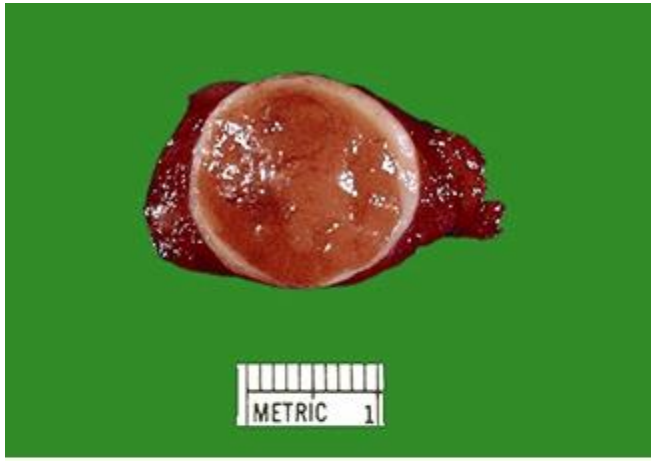
In Hashimoto thyroiditis thyroid neoplasms more frequently occur: follicular adenoma, follicular carcinoma, papillary carcinoma, B-cell lymphoma**!**

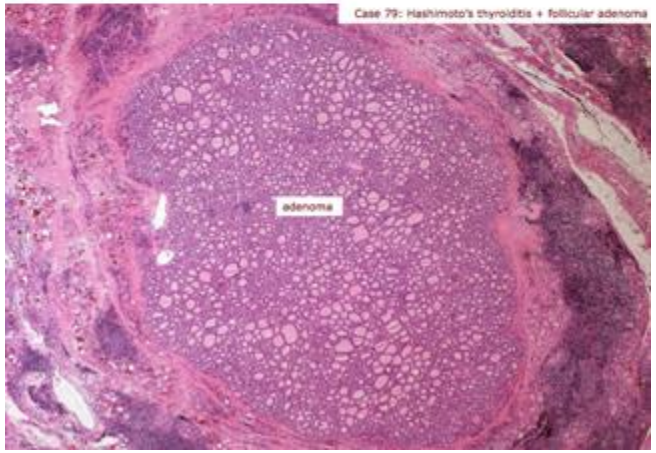




Neoplasms of the Thyroid
Follicular neoplasms

- Majority are benign: follicular adenomas
- Solitary, spherical, en*capsulated lesion,* well demarcated
- Size, colour (gray-white to red-brown), cut surface appearance(hemorrhage, fibrosis, cystic change) varies
- Microscopical appearance also varies: macro- and microfollicular type, Hürthle cell adenoma, atypical and papillary (rare) type adenomas
- *Criteria of malignancy – not cytologic!!:*
  - *Loss of capsule integrity and/ or* vascular invasion = follicular carcinoma

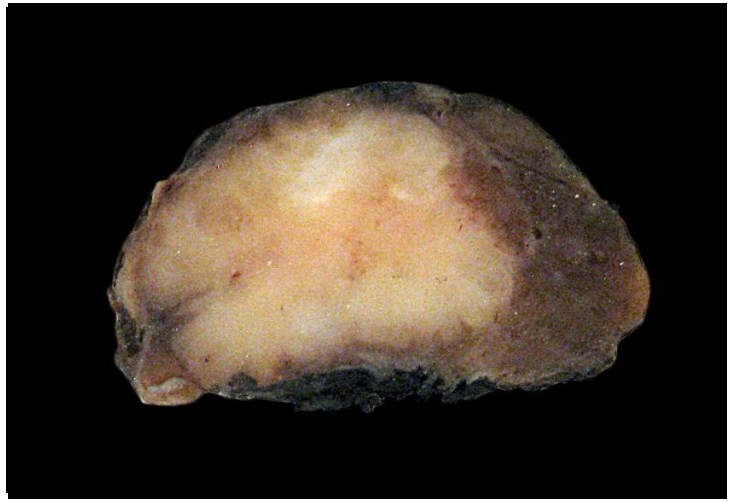


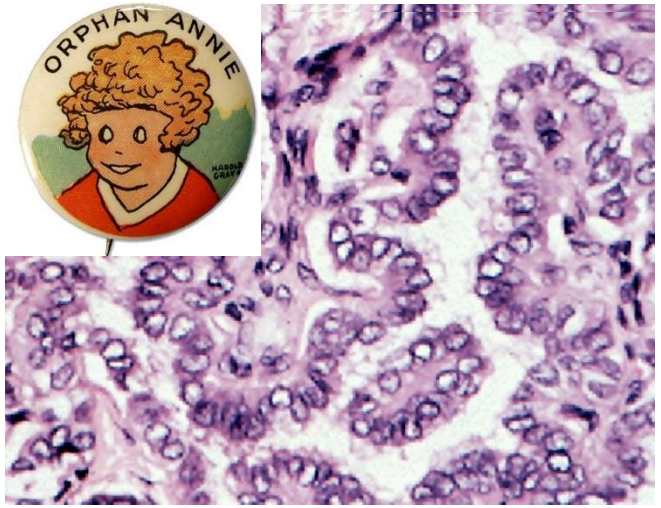


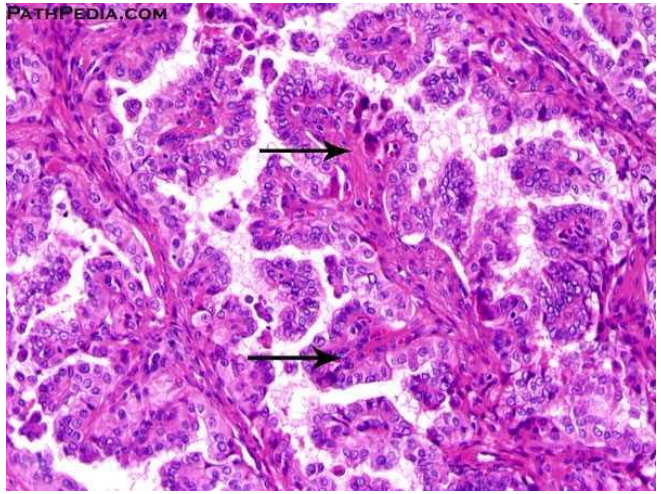
Malignant neoplasms
Papillary carcinoma

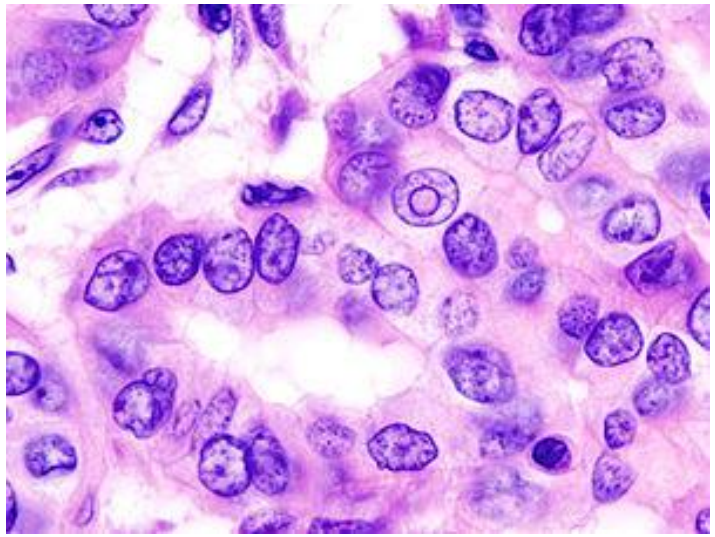
- Tumor cells are derived from the thyroid follicular epithelium
- Most common form of thyroid cancer, most often occurs in young adults (women)
- Good prognosis
- Often multifocal
- Lymphogenic metastasis (cervical lymph nodes) – can develop early on, but can be treated surgically
- Macroscopic appearance: gray-white nodule with ill-defined margins
- Histological criteria – cytomorphology!!!
  - Nuclear features:
    - Enlarged nuclei containing finely dispersed chromatin, optically clear appearance (Orphan Annie eye nuclei)
    - Nuclei are overlaping, arranged with long axes in parallel alignment
    - Invaginations of the cytoplasm: intranuclear pseudo-inclusions and grooves (coffee bean nucleus)
  - Structure:
    - Contains papillary and follicular architecture in variable proportions
    - Branching papillae, having a fibrovascular stalk, psammoma bodies are often present

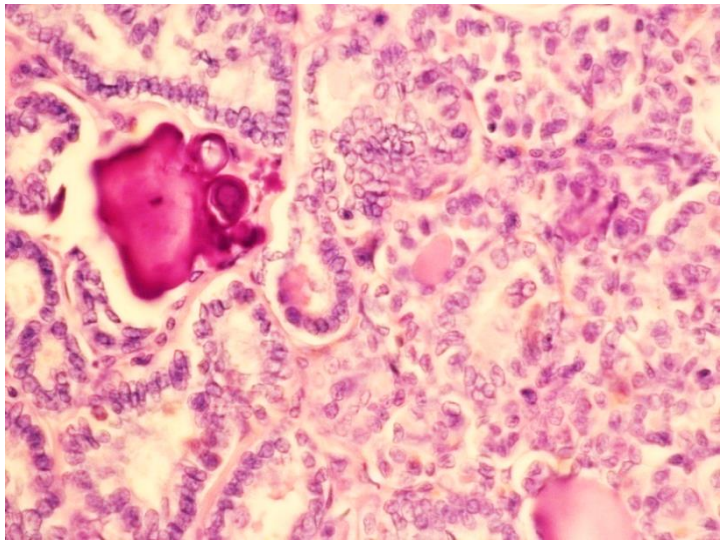
Malignant neoplasms
Papillary carcinoma









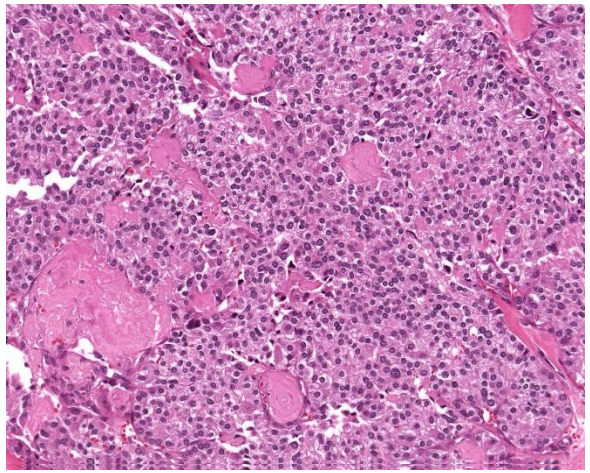


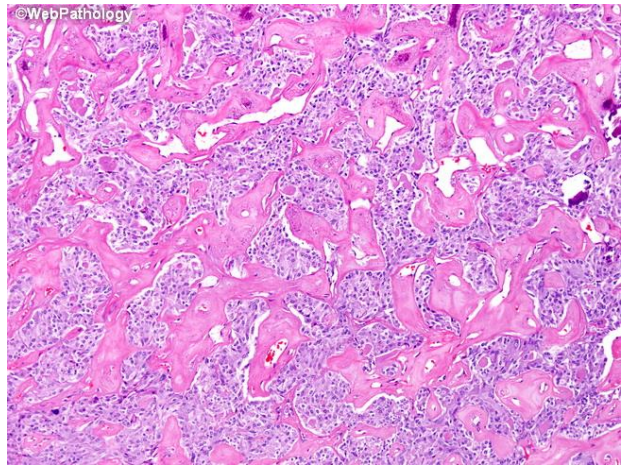
Malignant neoplasms
Anaplastic carcinoma

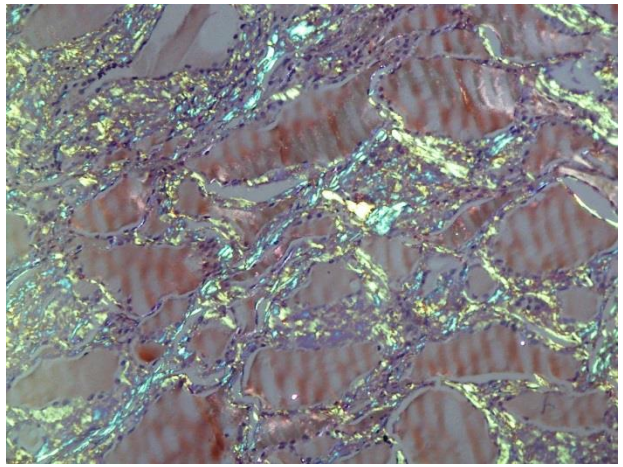
- Elderly patients
- Very poor prognosis
- Rapidly enlarging mass, infiltrates adjacent neck structures
- Extensive metastasis
- Variable morphology, highly anaplastic cells

Malignant neoplasms
Medullary carcinoma

- Derived from the parafollicular C cells
- Small, neuroendocrine tumorcells
- Solitary nodule
- Amyloid deposits are often present
- Present individually or with other endocrine tumors (always present in MEN2-syndrome → preventive thyreoidectomy in childhood)

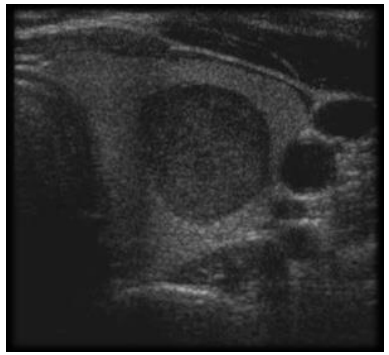


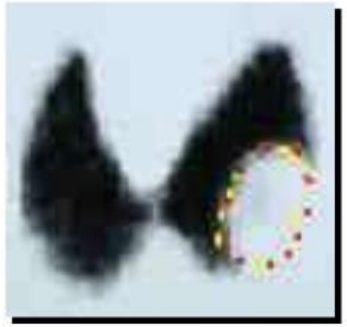




Examination of a soliter nodule

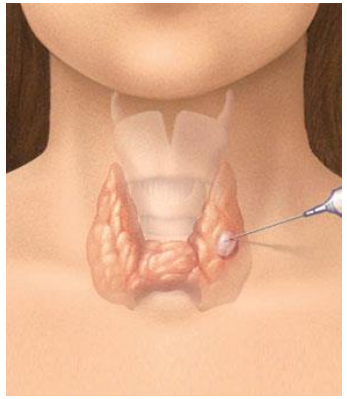
Usually discovered on ultrasound





Scintiscan: cold masses are alarming

FNAB



Risk of malignancy

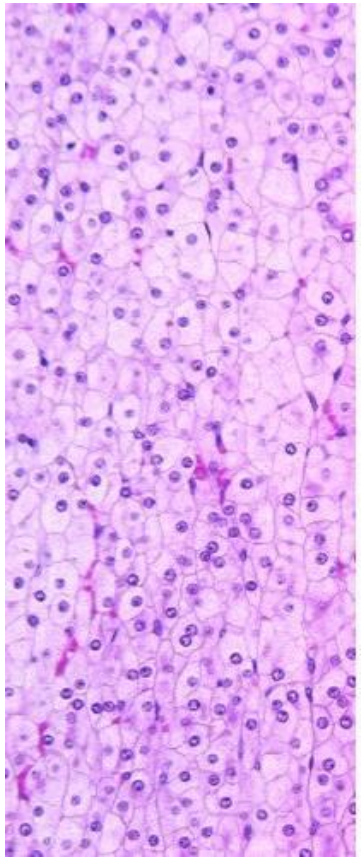
Benign	0-3 %
Atypia of undetermined significance *OR* Follicular lesion of undetermined significance	5-15 %
Suspicious for a follicular neoplasm	15-30 %
Suspicious for malignancy	60-75 %
Malignant	97-99 %

The Bethesda System for Reporting Thyroid Cytopathology Edmund S. Cibas, MD,1 and Syed Z. Ali, MD2

Adrenal glands

Consist of cortex (mesodermal origin) and medulla (neuroectodermal origin)

Cortex:



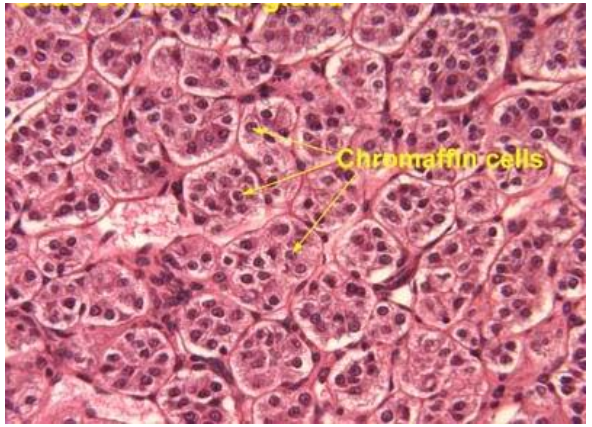
Zona glomerulosa:
mineralocorticoids
regulated by *RAAS*

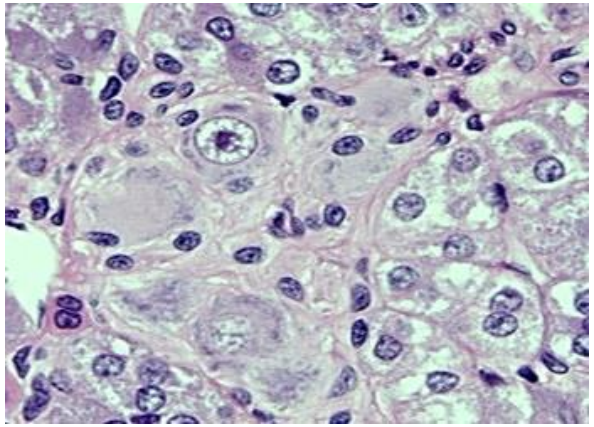
Zona fasciculata:
glucocorticoids
regulated by *ACTH*

Zona reticularis:
sex steroids
regulated by *ACTH*

Medulla:

Part of the sympathetic nervous system
Secretes catecholamines
Chromaffin cells containing catecholamines
Dispersed ganglion cells





Pathology of adrenal cortex

Functional

- **Hyper**function
  - glucocorticoids: Cushing-sy.
  - mineralocorticoids: Conn-sy.
  - androgenes: adrenogenital syndromes
- **Hypo**function**:**
  - chronic: Addison disease – autoimmune disease
  - acute (rapid withdrawal of steroids, necrosis e.g. Waterhouse- Friedrichsen sy.)

Pathology of adrenal cortex

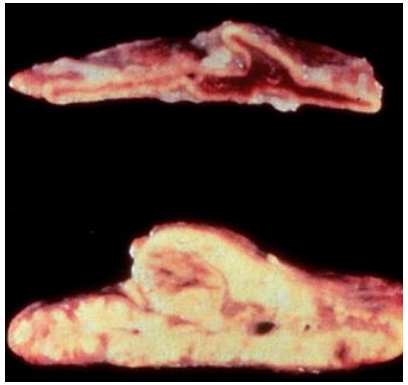
Morphologic

- Atrophy (endogenous ACTH suppression)
  - Exogenous cortisol
  - Functioning (cortisol secreting) benign and malignant neoplasms of the adrenal cortex
- Hyperplasia
- Neoplasms
  - Benign (adenoma)
  - Malignant
    - Primary: carcinoma (very rare)
    - Secundary: carcinoma of the lung, stomach, esophagus, liver and biliary tracts, kidney (often)

Adrenocortical hyperplasia

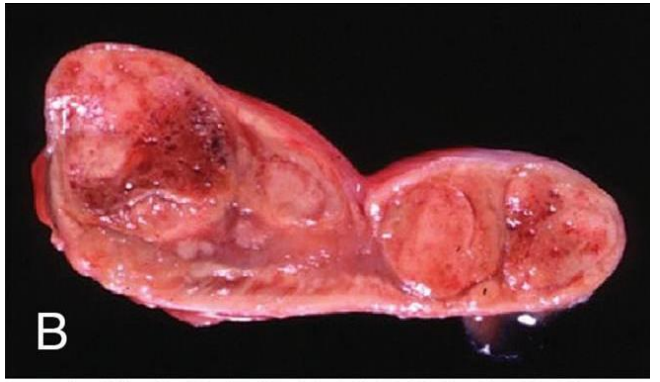
Diffuse hyperplasia

- Cortex is diffusely thickened, sulfur yellow
- Cause:
  - ACTH-dependant Cushing-sy



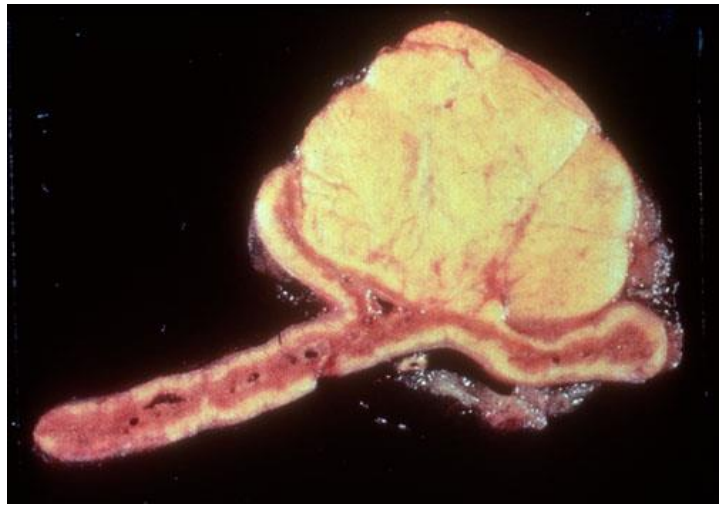
Nodular hyperplasia

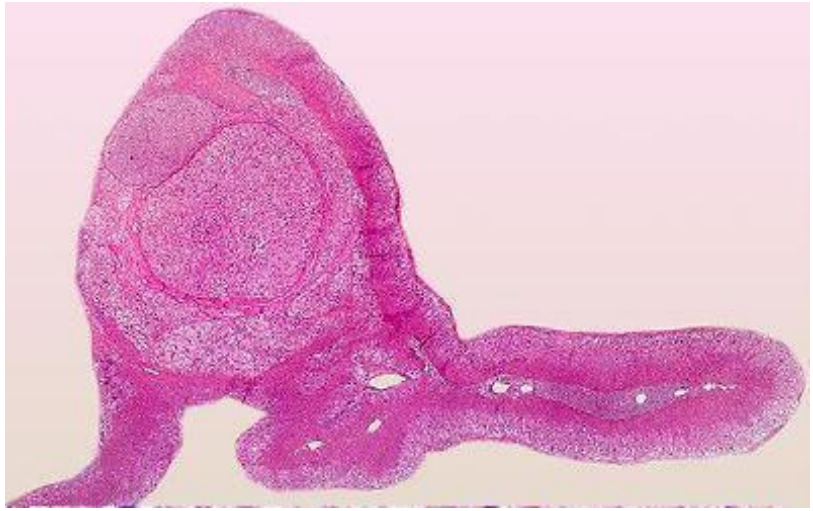
- Hyperplastic nodules
- Not encapsulated
- causes:
  - ACTH-independent
  - Bilateral idiopathic hyperaldosterinism
  - Congenital adrenal hyperplasia



Benign neoplasms
Adrenocortical adenomas

- Unilateral
- Spherical nodule
- Functional and nonfunctional forms
- Sulfur yellow





Adrenal medulla -Phaeochromocytoma

- Adrenal phaeochromocytoma cells are derived from chromaffin cells (extraadrenal: paragangliomas)
- Synthesize and release catecholamines
- Sympaticotonia
  - Hypertension (secunder hypertension, paroxysmal episodes)
  - Tachycardy
  - Elevated blood sugar levels
- Diagnosis: increased urinary excretion of metanephrines
- 90 % benign, without metastasis
- 90 % sporadic, 10% familiar
  - MEN sy
  - NF-1
  - Struge-Weber sy
  - Von Hippel Lindau sy