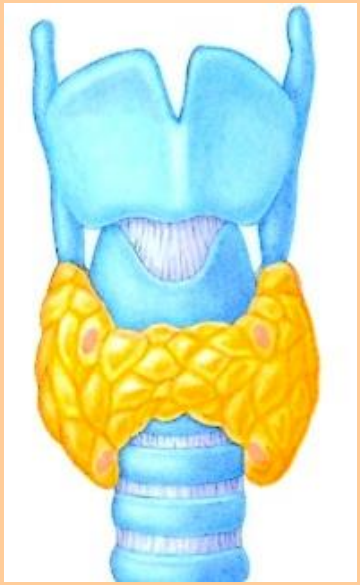
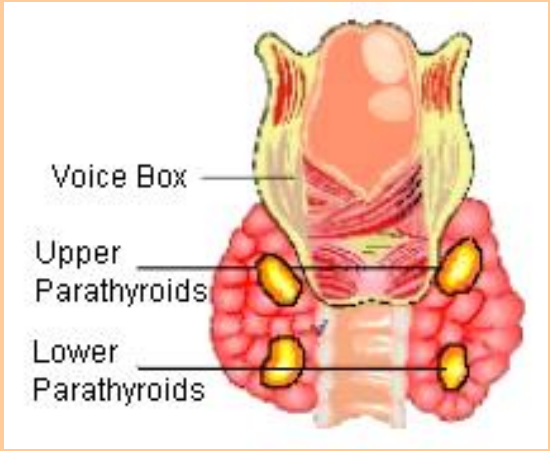
Endocrin pathology

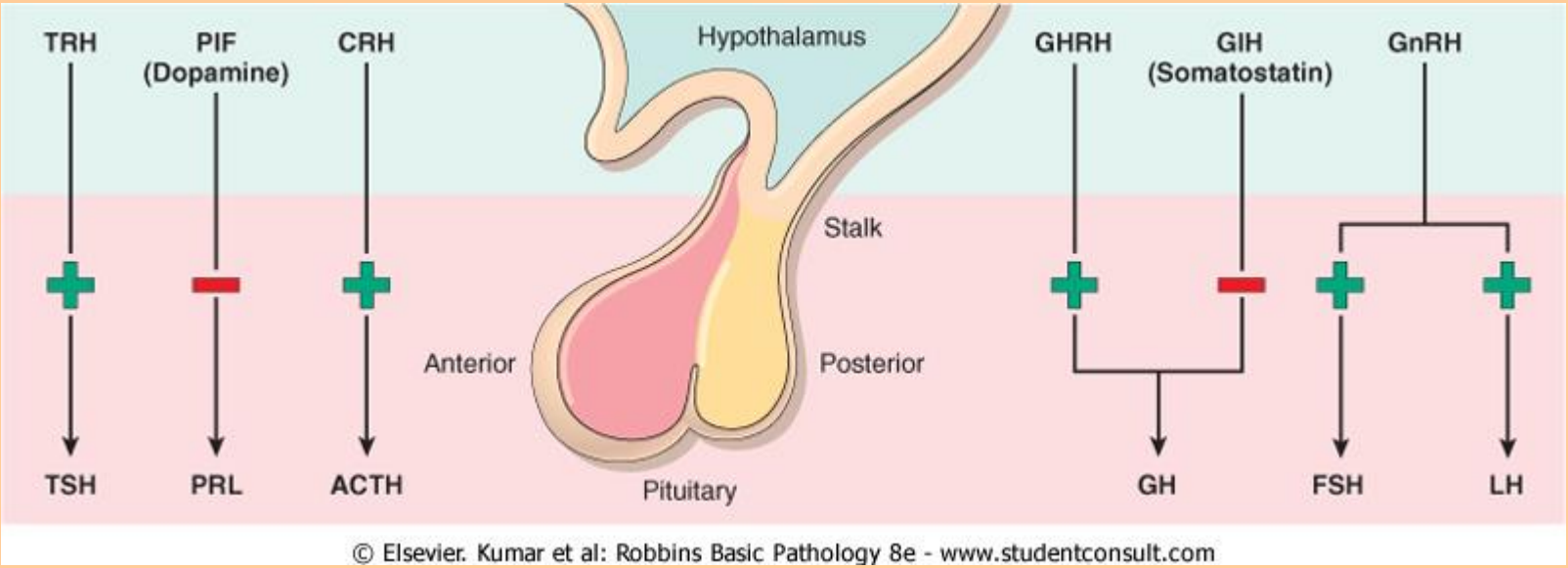
Dr. Zalatnai Attila

Dr. Rácz Gergely



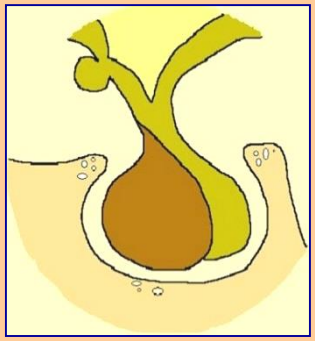


Adenohypophysis



The hypothalamic/pituitary axis. The hypothalamus regulates the secretion of hormones from the adenohypophysis (anterior pituitary gland) by releasing stimulatory (corticotropin-releasing hormone. These in turn modulate the release of six hormones from the anterior pituitary.

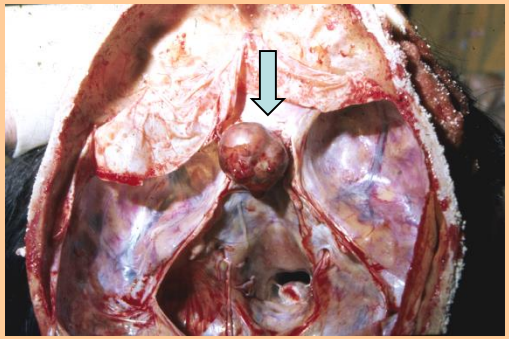
The secretion is controlled by the hypothalamic (releasing) or (inhibitory) factors.

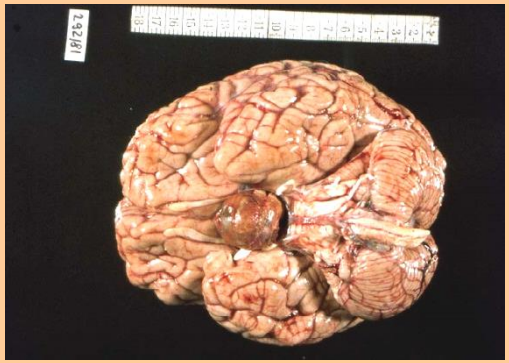


Adenohypophysis

Hyperpituitarismus

Endocrine alterations due to increased trophhormon secretion





Hyperplasia - peregnancy (PRL/GH cells)
risk of infarction (Sheehan-syndrome)

Adenoma - micro/macroadenoma (< 1 cm >)
- basophil, eosinofil, chromophob
- 2/3 hormon secreting, 1/3 inactiv (silent,0-cell)
- Hysto: cellular monomorphism, absence of a reticulin network.

GH-secreting (eosinophil): gigantismus
acromegalia

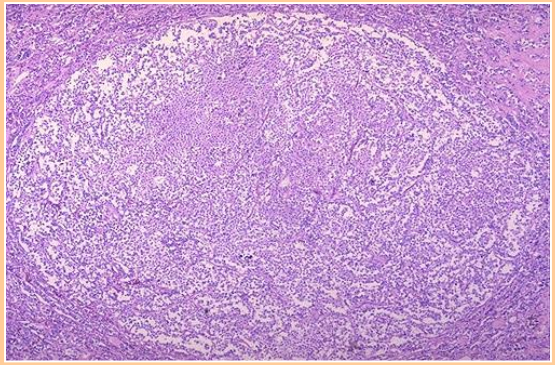
Prolactinoma: commonest type

ACTH-secreting (basophil): Cushing-diseases

TSH, FSH/LH secreting: exeptionally rare

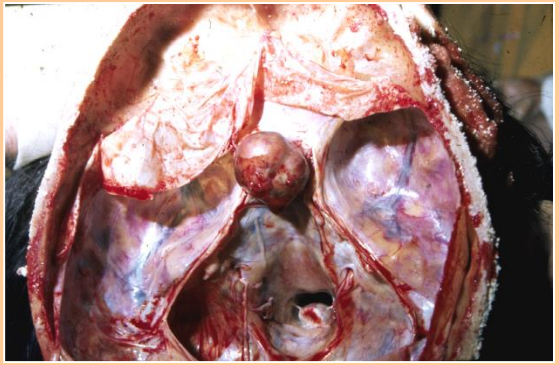
Chromophob adenoma: mass and perssure effect, visual disturbances

Carcinoma: - extrem rare



microadenoma

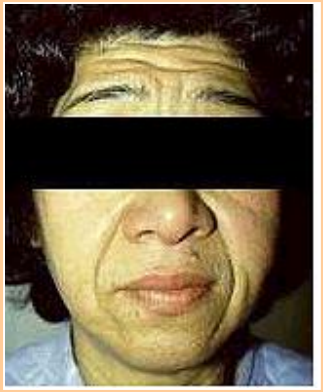
macroadenoma

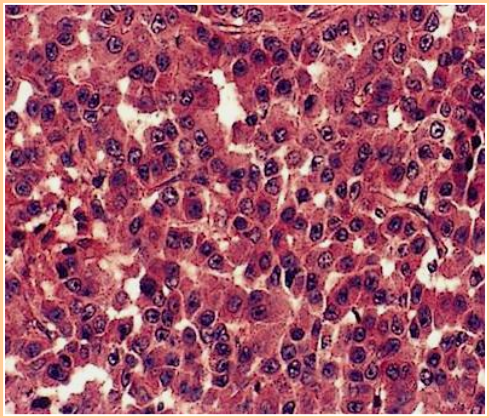


GH-secreting adenoma

Gigantism (children) - before the epiphyses close: increase in body size, with disproportionately long arms and legs

Acromegaly (adults) – after closure of the epiphyses: hyperostosis, prognathism, broadening of the lower face, and separation of the teeth, splachnomegalia

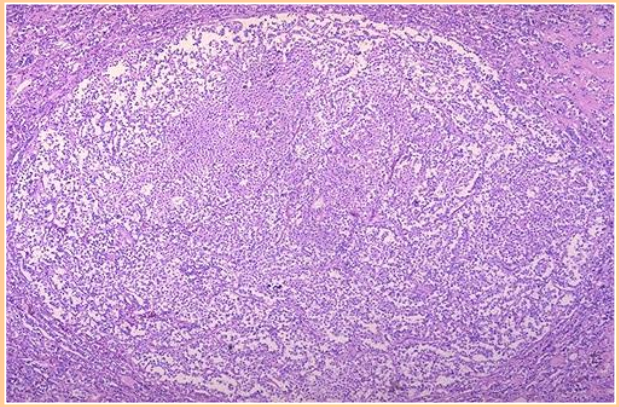


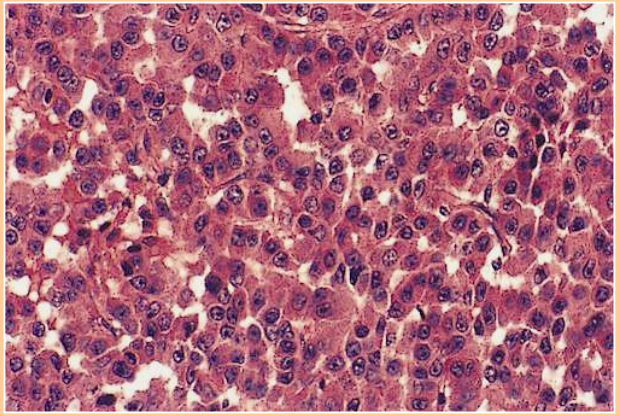


Prolactinoma:

- prolactin-secreting lactotroph adenoma
- most frequent hypophysis adenoma
- 40-50% of of all clinically recognized cases
- functioning adenoma’s 80%-a
- mailnly microadenoma
- female: amenorrhea, galactorrhea,
- male: loss of libido, and infertility

inhibitrory effect LH-hormon secretion

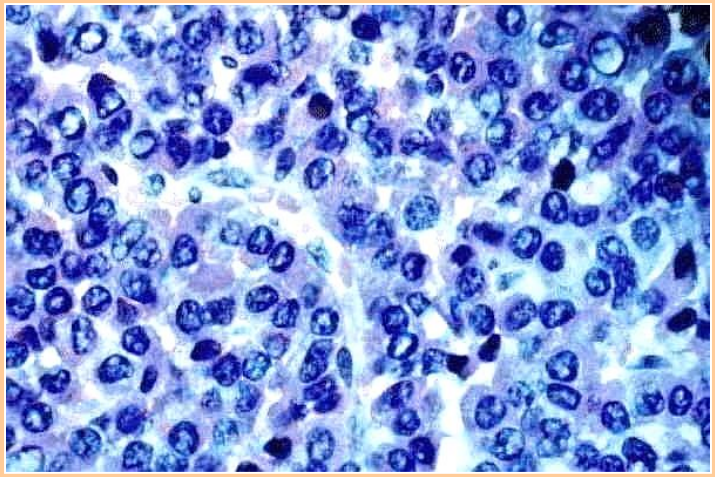


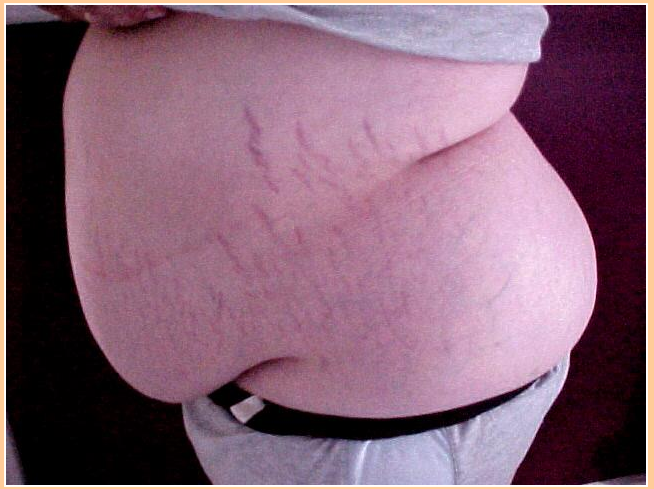


ACTH-secreting adenoma:

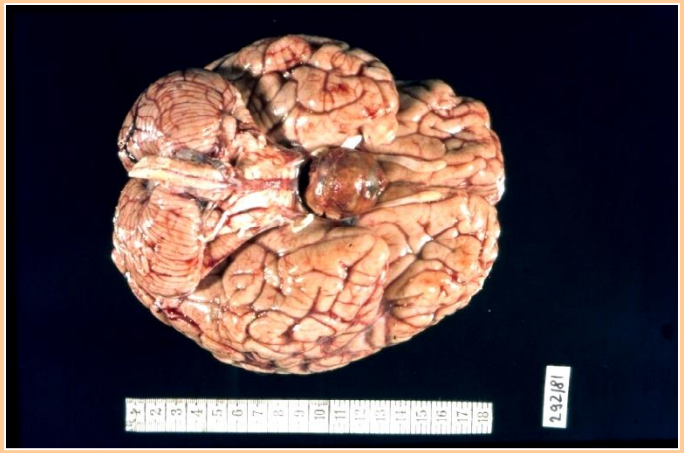
Cushing-syndroma – hypercortisolism

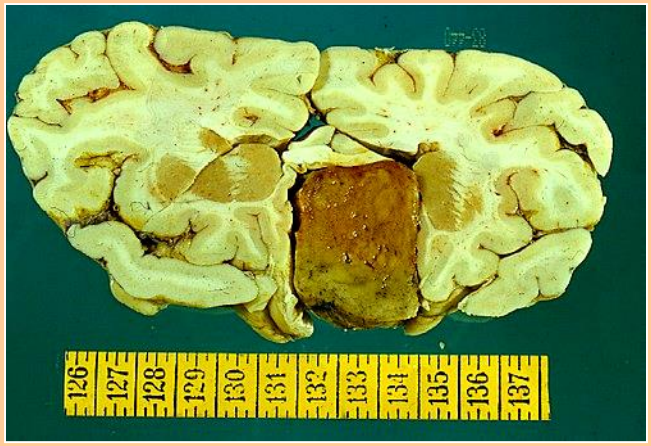
Basophil microadenoma

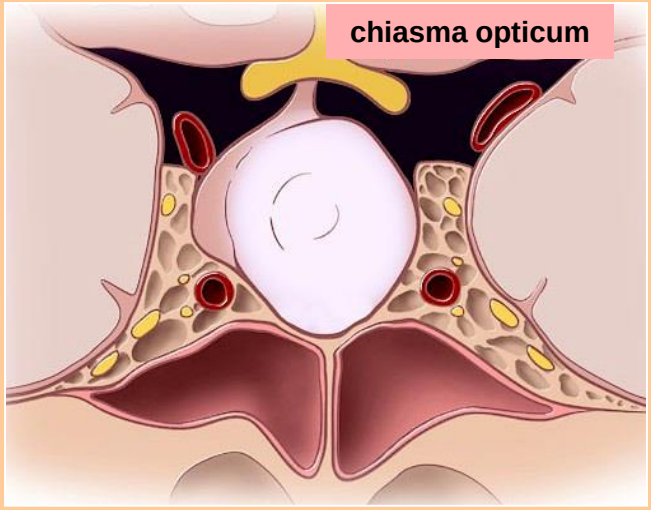




0-cell adenoma
(chromophob cells)







Hypophysis carcinoma

- extrem rare
- extracranial metastasis!

Hypopituitarism:

- panhypopituitarism vagy isolated hormon deficiency
- etiology:

- local destruction, pressure atrophia:

  cromophob adenoma, craniopharyngeoma, metastasis [breast cancer, lung cancer],

- infarction [Sheehan-syndr.], post partum ischaemic necrosis: failure of postpartum lactation ,apathy, amenorrhea, decreased libido
- Hand-Schüller-Christian disease
- Hypothalamus demage disorders
- Inflammation (autoimmun adenohypophysitis, tuberculosis, sarcoisosis)

Clinical manifestations :

Children: growth failure (pituitary dwarfism)

Adult: hypogonadism

Neurohypophysis

- Antidiureticus hormon (ADH)
- Oxitocin

POSTERIOR PITUITARY SYNDROMES :

- ADH deficiency : diabetes insipidus

- Etiology: head trauma, neoplasms, and inflammatory disorders of the hypothalamus and pituitary, and from surgical procedures involving the hypothalamus or pituitary

Designated: central

nephrogenic – caused by renal tubular unresponsiveness to circulating ADH

Clinical manifestations : excretion of large volumes of dilute urine with an inappropriately low specific gravity. Serum sodium and osmolality are increased as a result of excessive renal loss of free water, esulting in thirst and polydipsia.

- The syndrome of inappropriate ADH : SIADH

-- Etiology: secretion of ectopic ADH by malignant neoplasms (SCLC), local injury to the hypothalamus or neurohypophysis

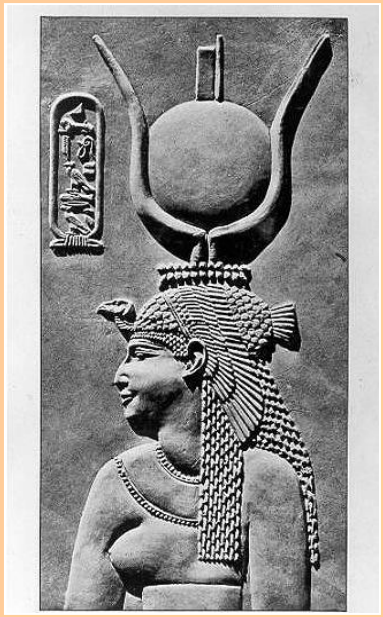
The clinical manifestations : are dominated by hyponatremia, cerebral edema, and resultant neurologic dysfunction. Although total body water is increased, blood volume remains normal, and peripheral edema does not develop.

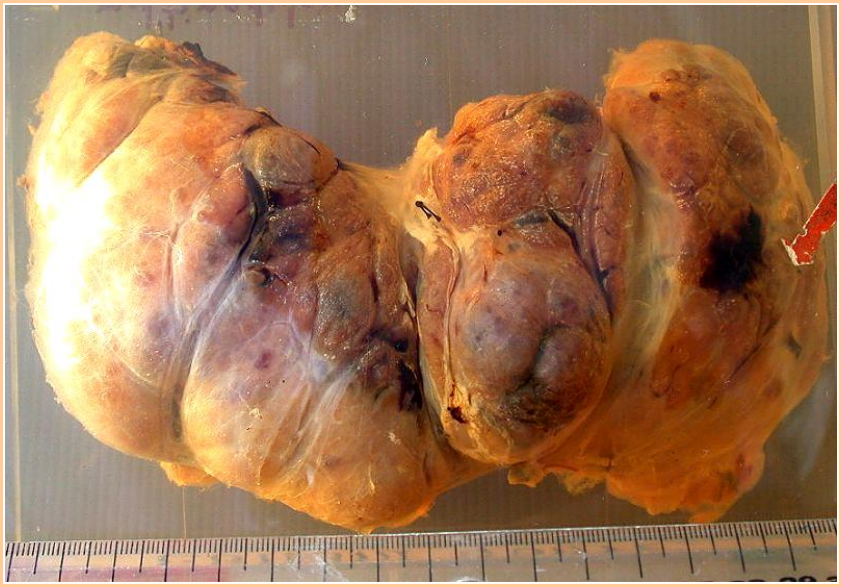
Thyroid gland

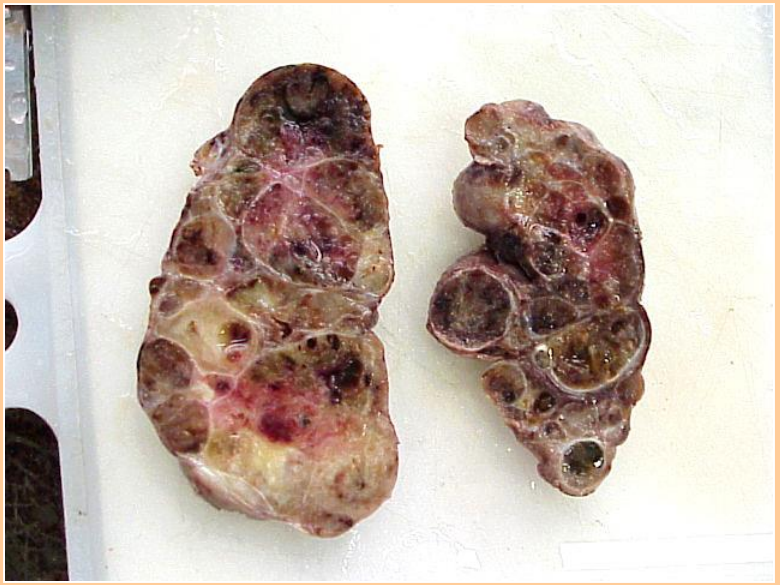
Enlargement: goiter

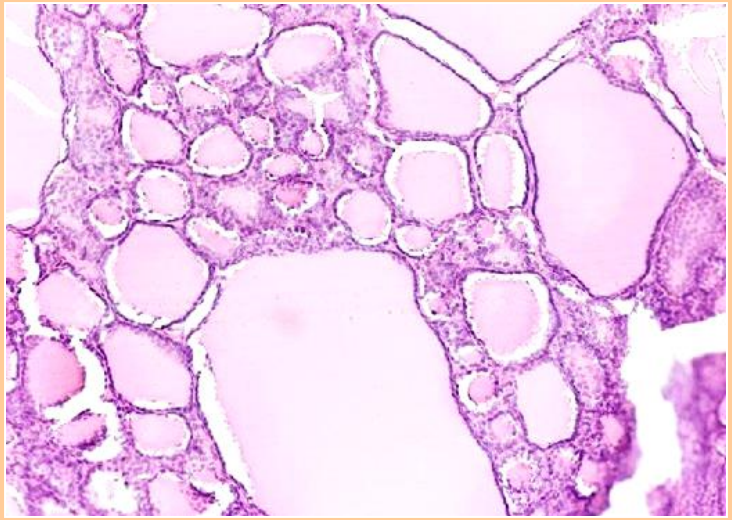
- normofunction, hyperfunction, hypofunction
- diffuse, (multi)nodular

Diffuse and multinodular goiters are the result of impaired synthesis of thyroid hormone, most often caused by dietary iodine deficiency.









Thyreotoxicosis

- Disorders with thyreoid hyperfuncions

Primary

Diffuse toxic hyperplasia (Graves)

Hyperfunctional nodulary goiter

Hyperfunctional (toxic) adenoma

Secundary

TSH-secreting hypophysis adenoma (rare)

- Disorders without thyreoid hyperfunction

Subacute granulomatosus thyreoiditis (de Quervain)

Subacute lymphocytic thyreoiditis

Struma ovarii (teratoma)

Exogen tiroxin

Thyreotoxicosis

- Cinical manifestations : the hypermetabolic state induced by thyroid hormone and overactivity of the sympathetic nervous system.

- Constitutional symptoms : The skin of thyrotoxic individuals tends to be soft, warm, and flushed because of increased blood flow and peripheral vasodilation to increase heat loss; heat intolerance and excessive sweating are common. Increased sympathetic activity and hypermetabolism result in weight loss despite increased appetite.

- Cardiac: peripheral oxygen requirements. Older adult patients with preexisting heart disease may develop congestive heart failure.

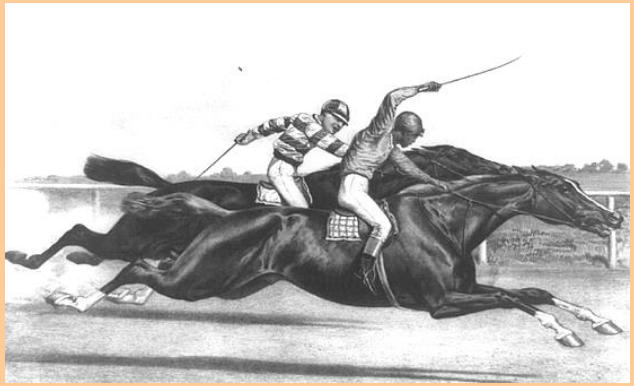
- Gastrointestinnal symptoms: Stimulation of the gut results in rapid transit time (hypermotility), which can cause fat malabsorption and steatorrhea.

- Ocular changes: A wide, staring gaze and lid lag are present because of sympathetic overstimulation

- **Thyroid storm :** the abrupt onset of severe hyperthyroidism. Thyroid storm is a medical emergency, as a significant number of untreated patients die of cardiac arrhythmias.

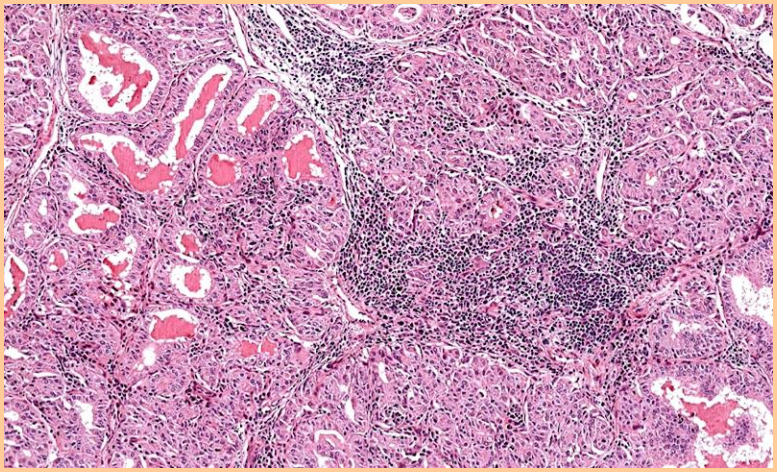
- Apathetic hyperthyroidism : thyrotoxicosis occurring in older adults, in whom the typical features of thyroid hormone excess often are blunted. The underlying thyroid disease is usually detected during laboratory workup for unexplained weight loss or worsening cardiovascular disease.

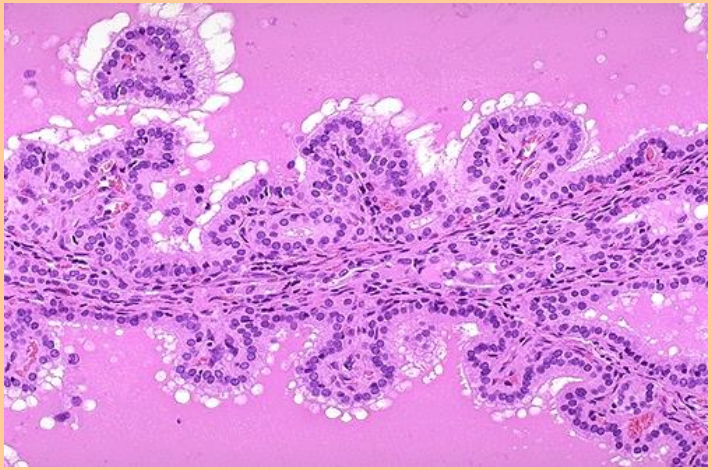
Thyreoid gland



Basedow (Graves) – disease

- Common in females, 20-40 years
- autoimmun disorder
- autoantibodies against the TSH receptor that bind to, and stimulate, thyroid follicular cells independent of endogenous trophic hormones.
- - The triad: diffuse hyperplasia of the thyroid, ophthalmopathy, and dermopathy
- Neck mass, breathing and swallowing problems





Hypothyreodism

- Hypothyroidism is caused by structural or functional derangements that interfere with thyroid hormone production.

Primary

- Iatrogenic hypothyroidism
- Hormonsynthesis congenital disturbances
- Endemic deficiency of dietary iodine
- Autoimmune thyroid disese (Hashimoto-thyreoiditis)
- Side effect of medication, drugs (litium, iodine)

Secundary (Central)

- Hypophysis and hypothalamus diseases:
  - Pituitary failure
  - Hypothalmic failure

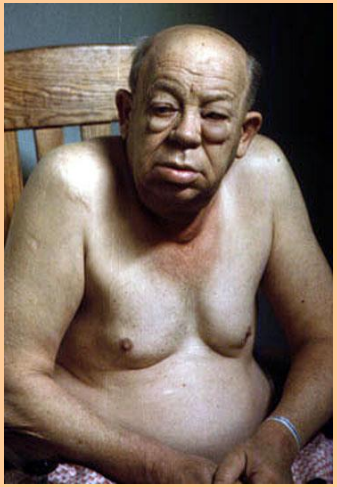
Hypothyreosis

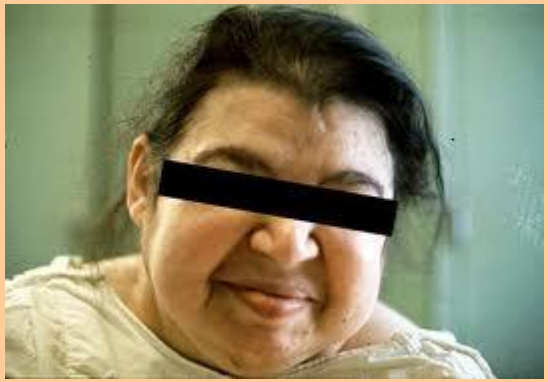
- Clinical manifestation: cretenism and myxoedema

-Caused by structural or functional derangements that interfere with thyroid hormone production.

- Cretenism: refers to hypothyroidism developing in infancy or early childhood. This disorder formerly was common where dietary iodine deficiency is endemic

- Myxoedema: older children and adults
- generalized fatigue, apathy, and mental sluggishness, which may mimic depression. Decreased sympathetic activity results in constipation and decreased sweating.
- The skin is cool and pale because of decreased blood flow.
- Reduced cardiac output contributes to shortness of breath and decreased exercise capacity, two frequent complaints.



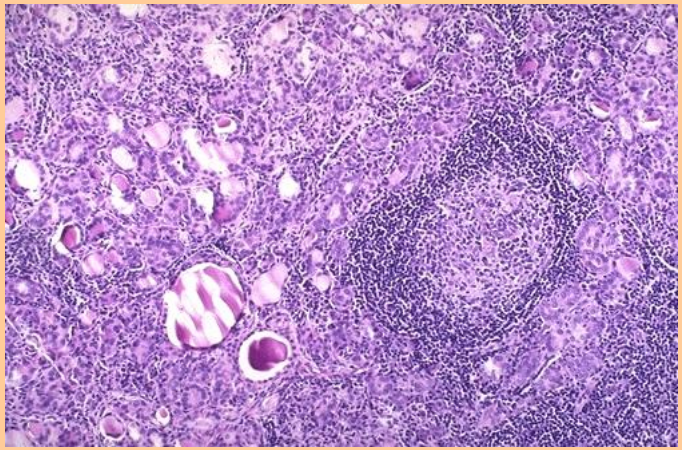


Thyroid gland

Thyreoiditis Acute is rare!

Chronic: not iodene defficiency area the most common case of hypothyreodism.

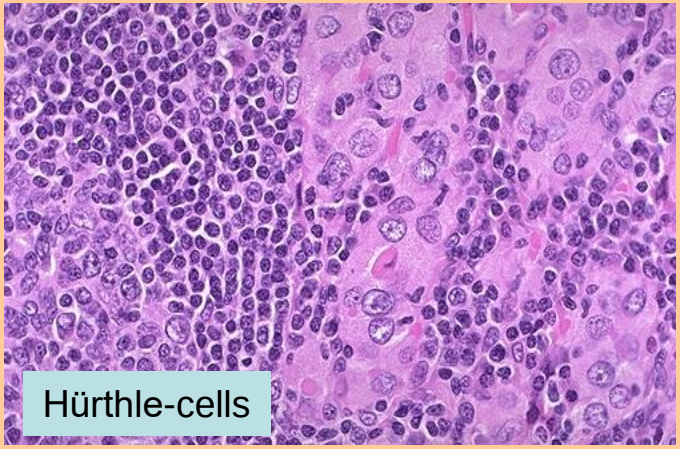
- Hashimoto-thyreoiditis (autoimmun)
initial hyperthyreosis → hypothyreosis
simmetric, moderate nodular goiter, later MALT!

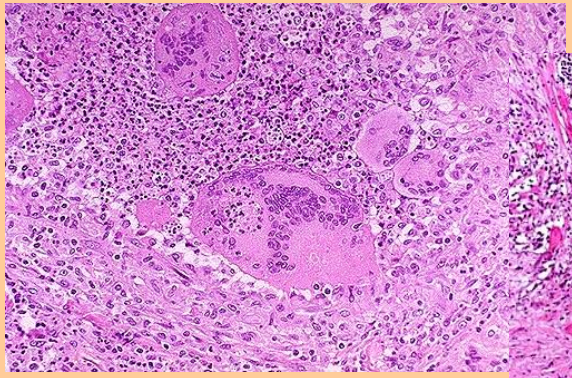


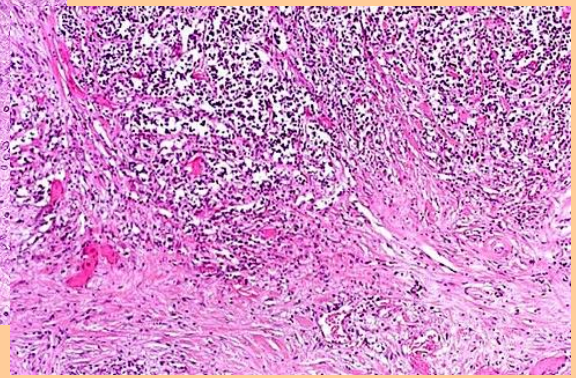
- De Quervain (granulomatosus) - a selflimited disease, probably secondary to a viral infection, and is characterized by pain and the presence of a granulomatous inflammation in the thyroid.

- Chronic lymphocytic thyreoiditis – a self-limited disease that often occurs after a pregnancy (postpartum thyroiditis), typically is painless, and is characterized by lymphocytic inflammation in the thyroid.

- Riedel-goiter, Palpitation thyreoditis







Tyroid neoplasms

Benign

follicular adenoma

(solitary,capsule)

Malignant

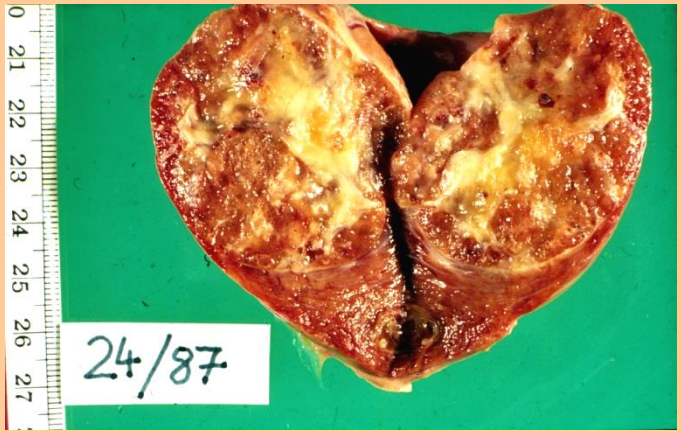
follicular carcinoma 10-20%

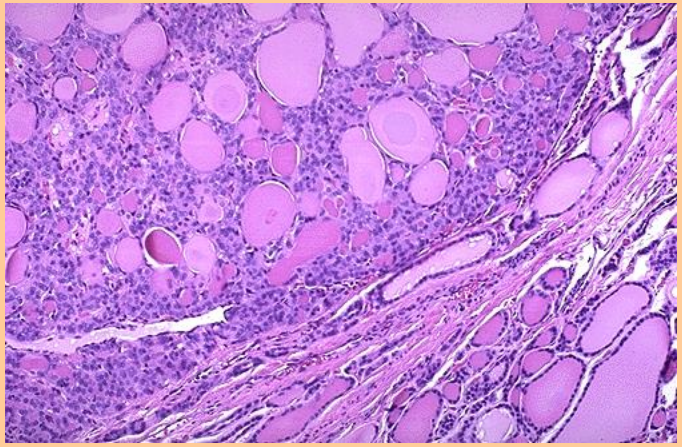
papillary carcinoma 5-85%

medullary carcinoma 5%

anaplastic carcinoma 5%

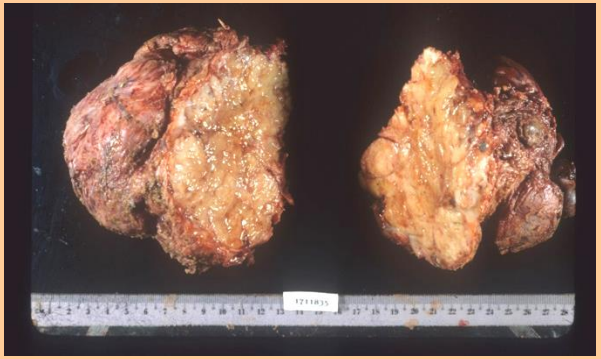
malignant lymphoma (B-)

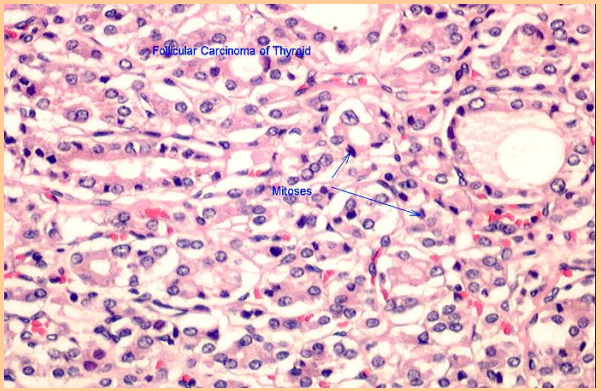




Thyroid – malignant neoplasms

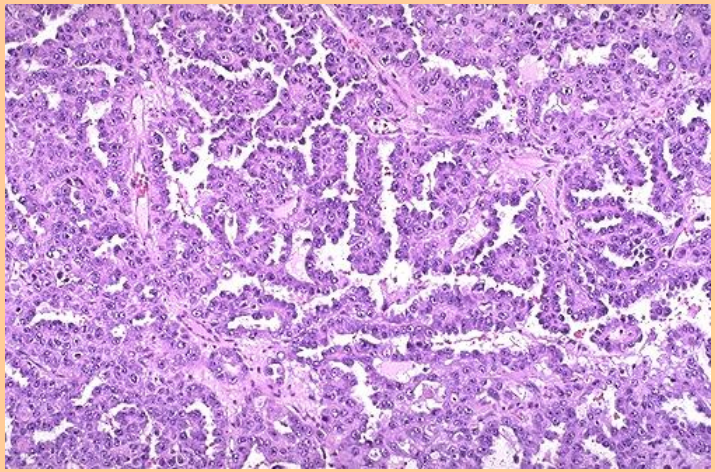
Carcinoma folliculare

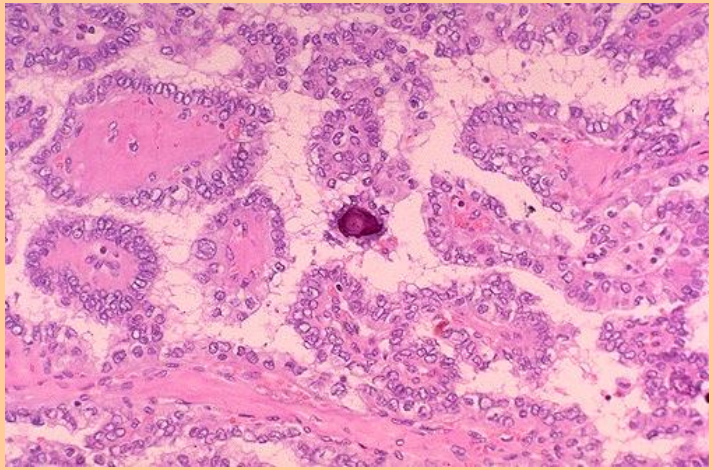




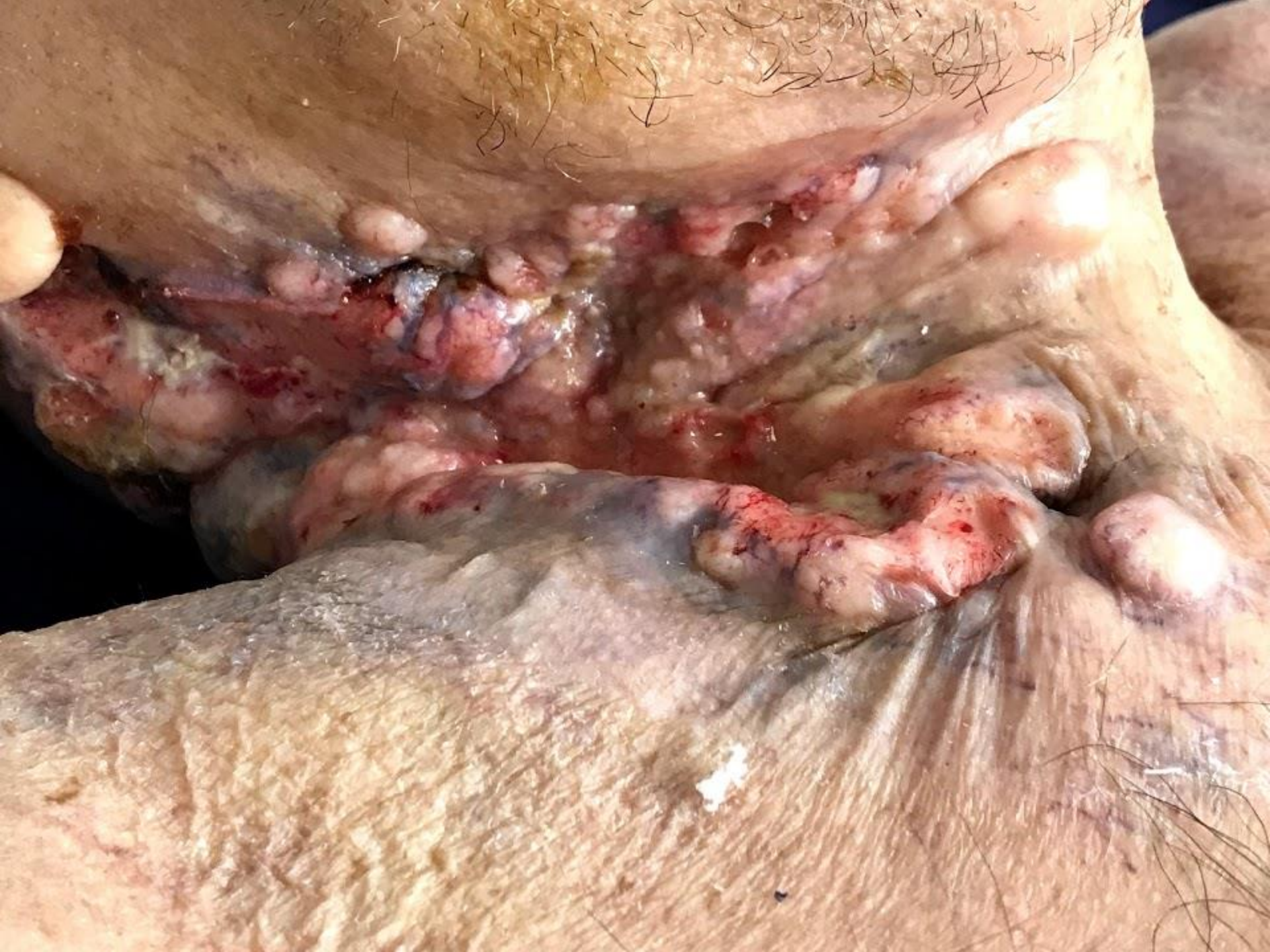
Haematogen metastasis!

Carcinoma papillare



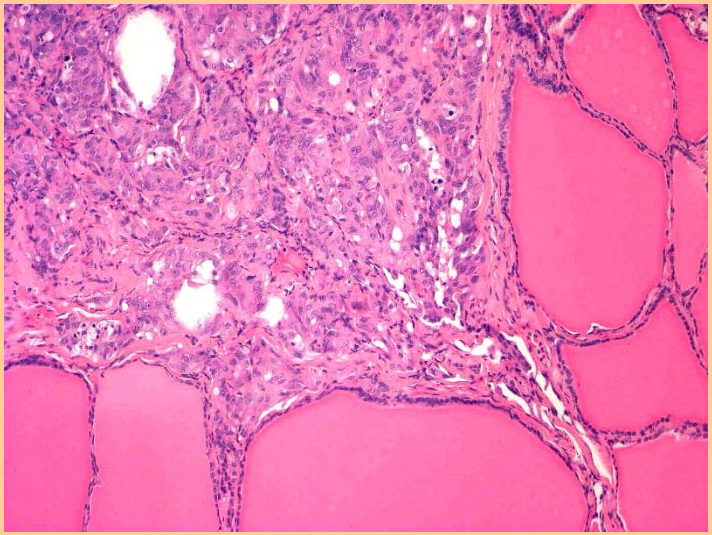


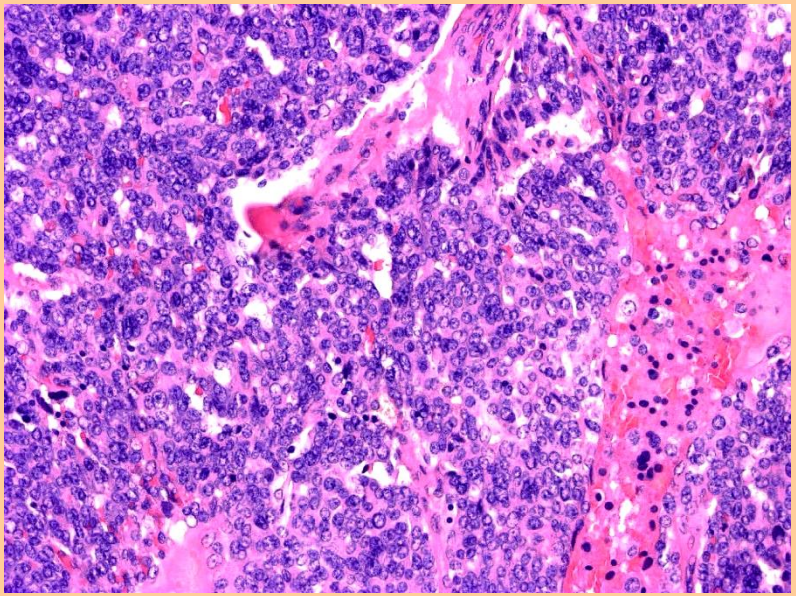
Lymphogen metastasis!

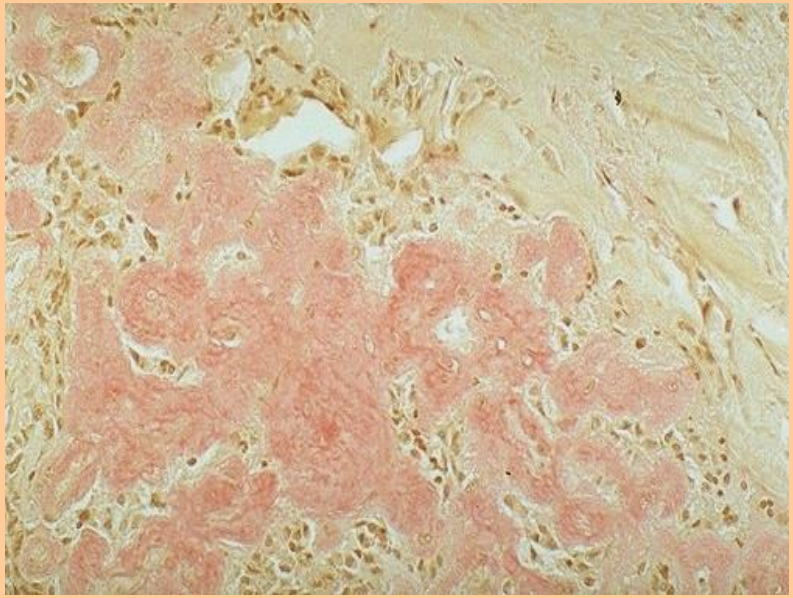


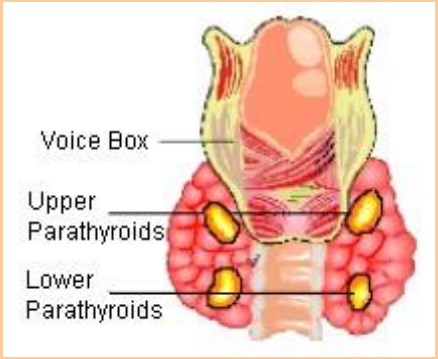
Thyroid - carcinoma medullare

- parafollicular (C-cell) origin
- citokeratin és kromogranin A +
- stromal amyloid (AE amyloid)
- MEN-2 syndrom (*Ret*-mutation)
- calcitonin-secretion, hypocalcaemia
- lymphogen metastasis







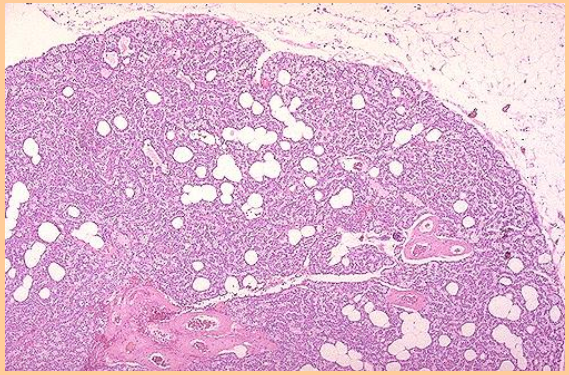


Parathyreoid gland

Hyperplasia – all 4 glands are involved, 10-15%

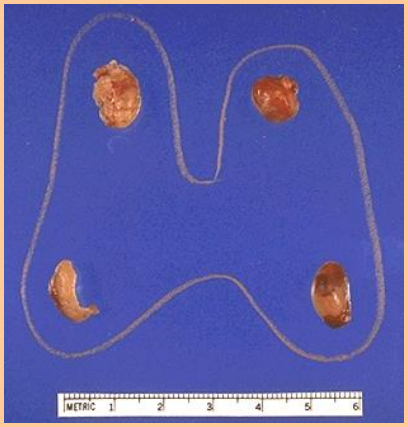
Adenoma – 1 glands, rest atrophy , 75-80%

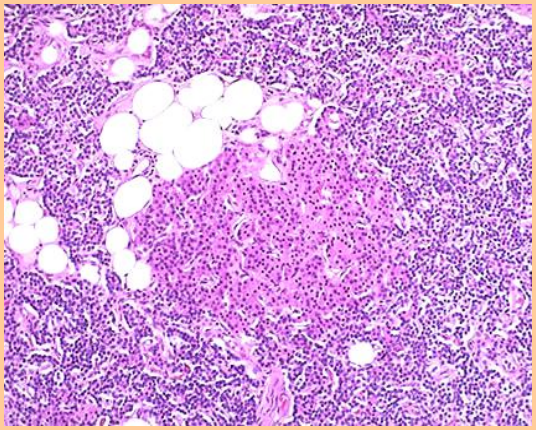
Carcinoma – infiltrative, hard less than 5%

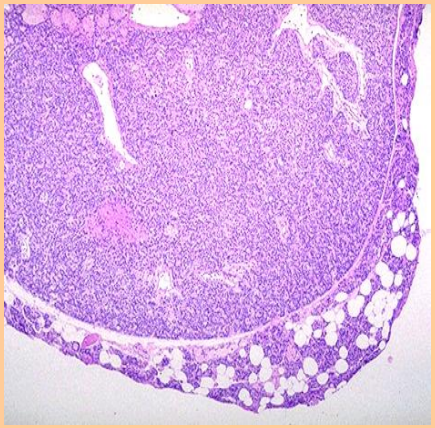


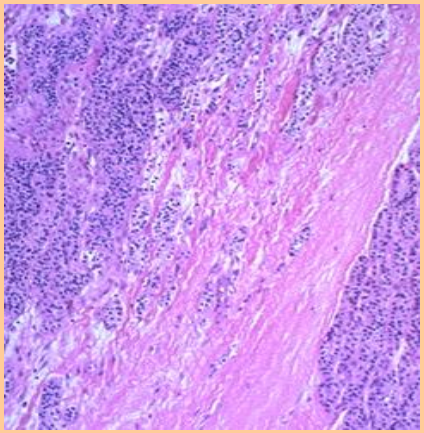
Hyperparathyreoidism- HYPERCALCEMY!

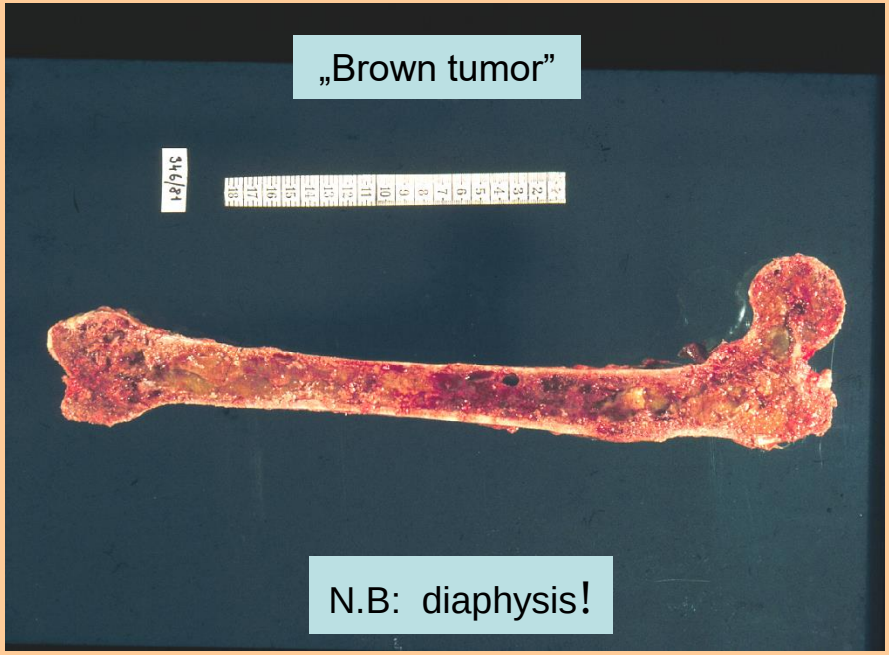
- osteodystrophia fibrosa cystica generalisata sec. Recklinghausen
- metastatic calcification (heart, stomach, nephrocalcinosis)
- nephrolithiasis, obstrucion- abdominal pain, colica
- depressio, lethargy, muscular weekness

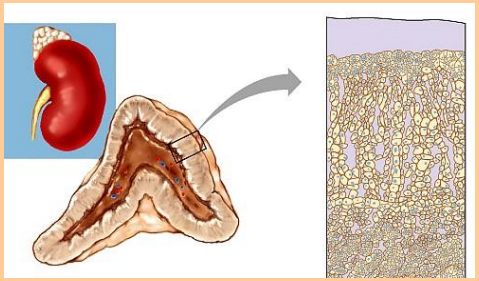









„Brown tumor”
346/81
N.B: diaphysis!



Adrenal gland

Congenital: ectopic (kidney, ovarium)

Apoplexia: Waterhouse-Friderichsen syndroma

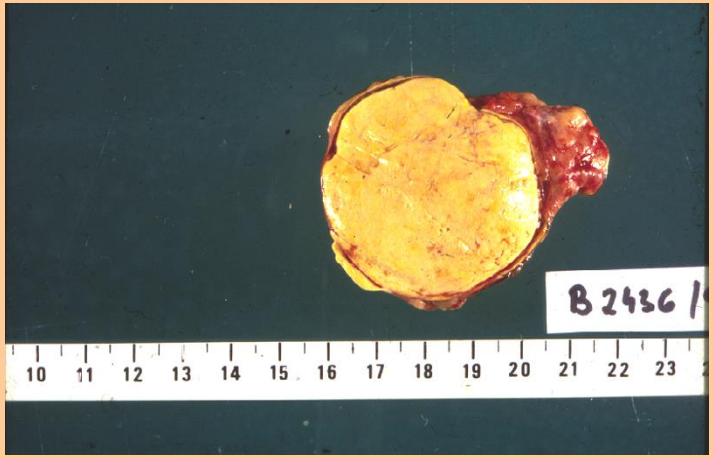
Congenital adrenal hyperplasy (adrenogenitalis syndrom)

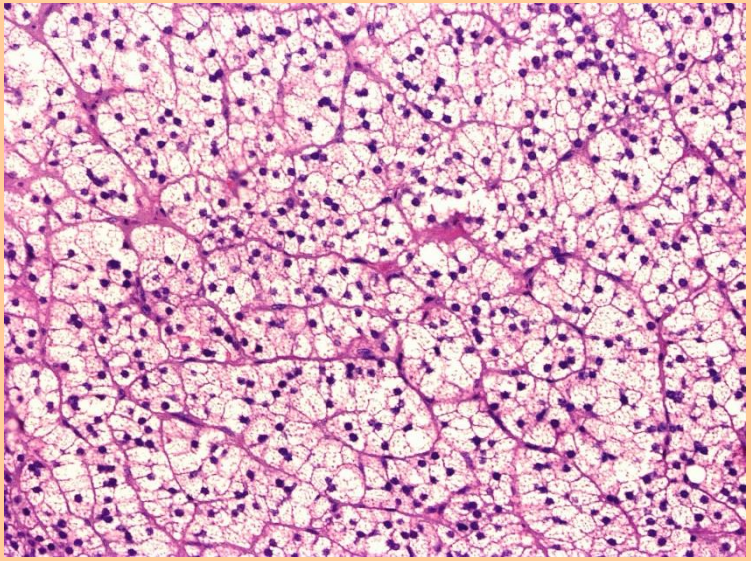
Hyperplasy, nodosus hyperplasy

Adenoma: functional (hormon secteting) non-functional

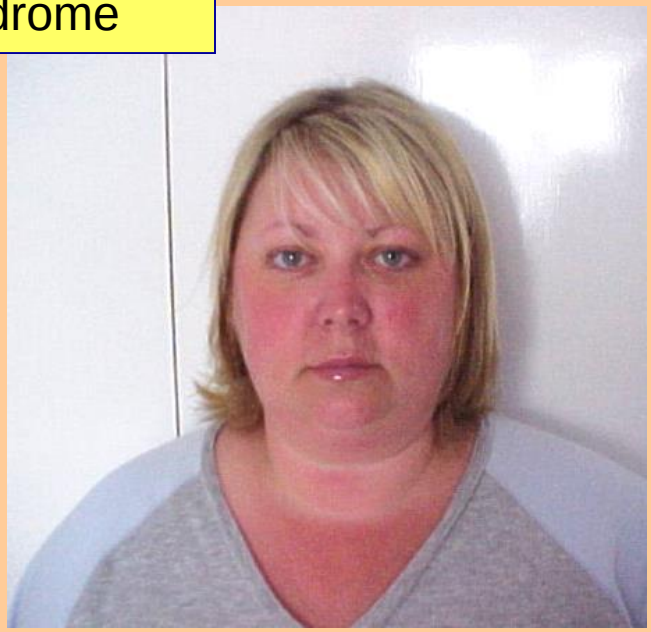
- glycocorticoid: Cushing-syndroma
- mineralocorticoid: Conn-syndroma

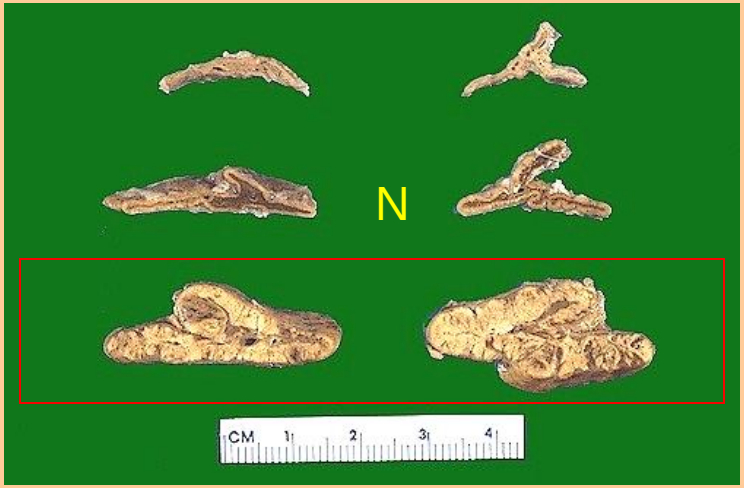
Myelolipoma

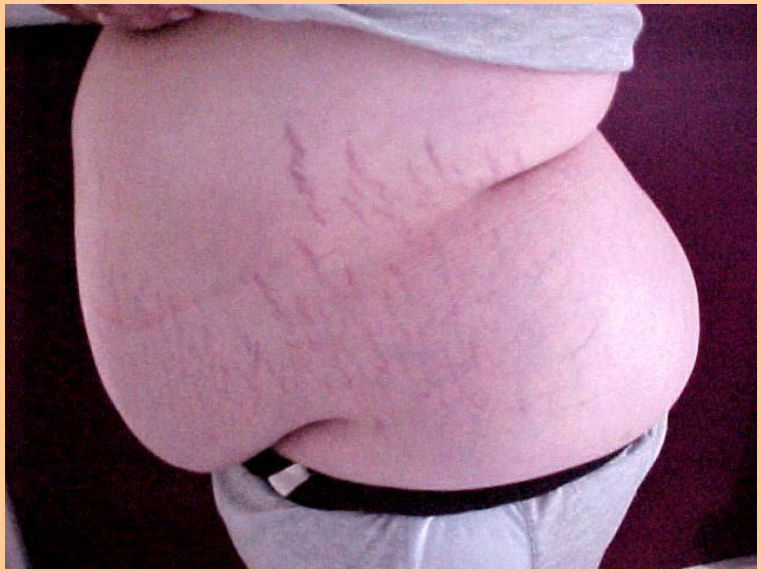




Cushing-syndrome







ADRENOCORTICAL INSUFFICIENCY (HYPOADRENALISM)

Primary adrenocortical insufficiency can be

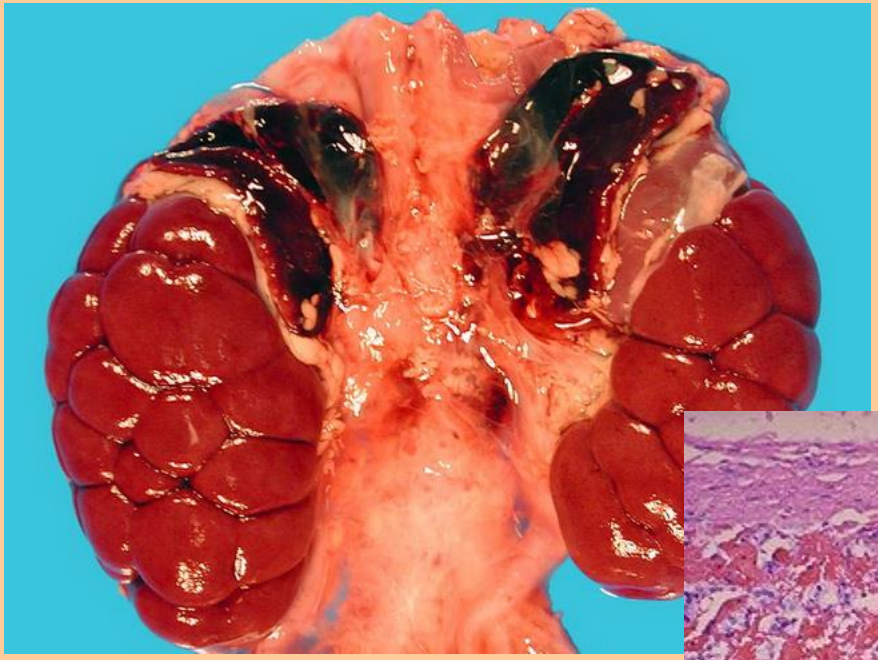
- acute (Waterhouse-Friderichsen syndrome)
- chronic (Addison-disease).

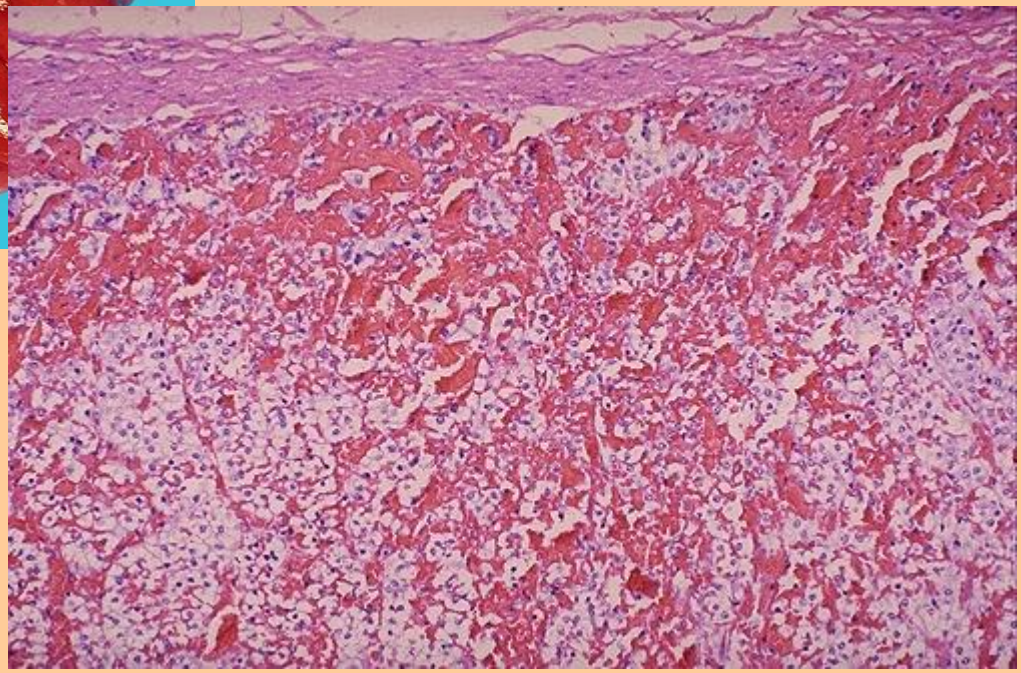
- Chronic adrenal insufficiency in the Western world most often is secondary to autoimmune adrenalitis, which occurs in the context of autoimmune polyendocrine syndromes.

- Tuberculosis and infections due to opportunistic pathogens associated with the HIV-virus

- Tumors metastasis
-
- Patients typically present with fatigue, weakness, and gastrointestinal disturbances. Primary adrenocortical insufficiency also is characterized by high ACTH levels with associated skin pigmentation.

Waterhouse-Friderichsen syndrome

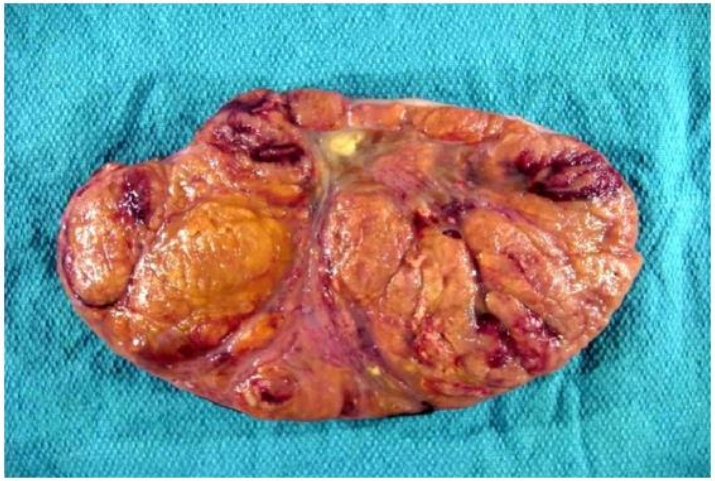


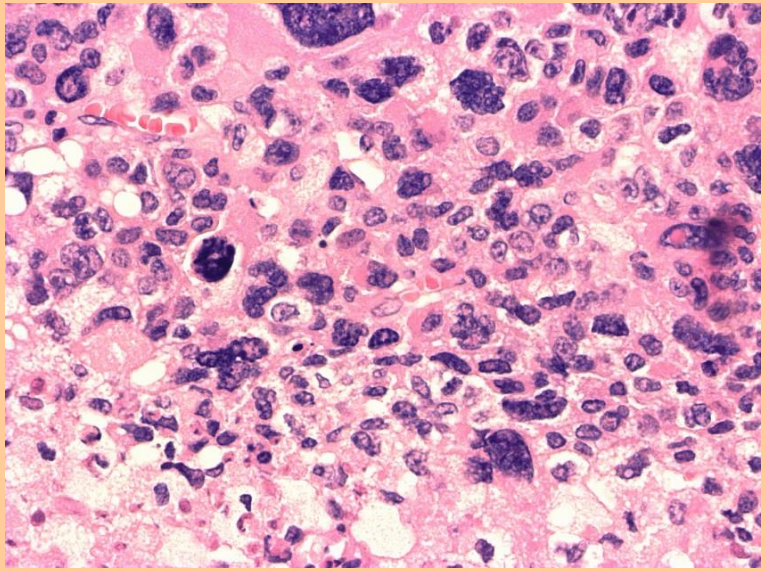


ADRENOCORTICAL MALIGNANT NEOPLASMS

Primary: Adrenocortical carcinoma

- rare neoplasms
- may occur at any age, including in childhood.
- large, invasive lesions that efface the native adrenal gland.
- On cut surface, adrenocortical carcinomas typically are variegated, poorly demarcated lesions containing areas of necrosis, hemorrhage
- Microscopic examination typically shows these tumors bizarre, pleomorphic cells
- Adrenal cancers have a strong tendency to invade the adrenal vein, vena cava, and lymphatics.
- Metastases to regional and periaortic nodes are common, as is distant hematogenous spread to the lungs and other viscera.
- The median patient survival is about 2 years





Secundary: metastasis

- carcinomas metastatic to the adrenal cortex are significantly more frequent than a primary adrenocortical carcinoma. LUNG CC!!!

Tumors of the adrenal medulla

Phaeochromocytoma:

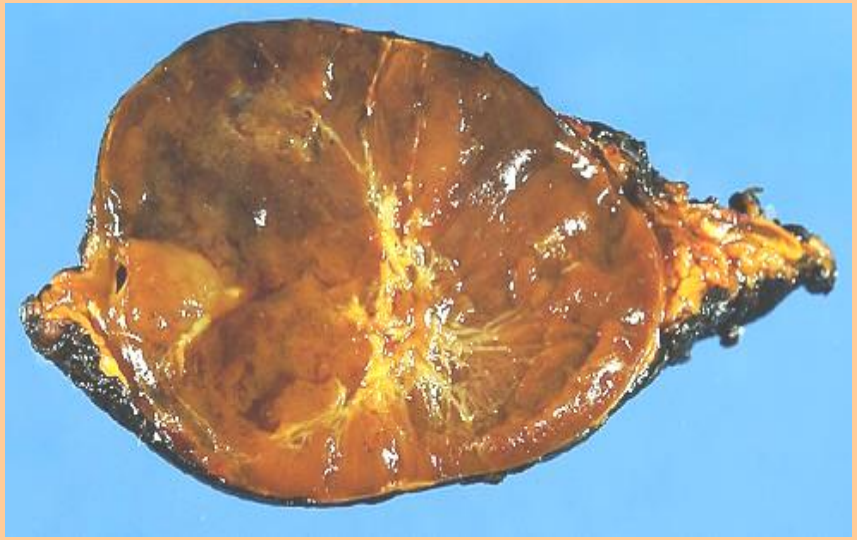
- composed of chromaffin cells, which, like their nonneoplastic counterparts, synthesize and release catecholamines

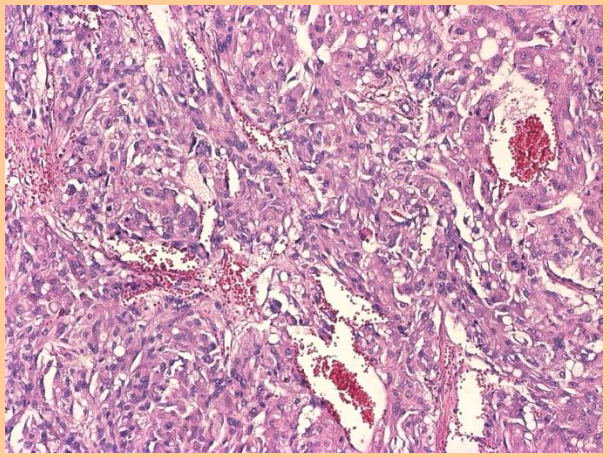
- circumscribed lesion

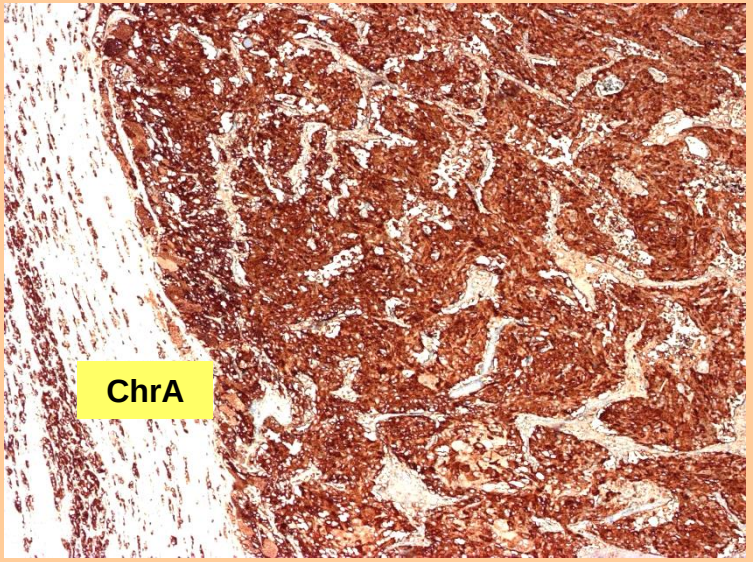
- special importance because, give rise to a surgically correctable form of hypertension.

- Pheochromocytomas usually subscribe to a convenient “rule of 10s”:

- 10% of pheochromocytomas are extraadrenal, where they usually are called *paragangliomas*, rather than pheochromocytomas.
- 10% of adrenal pheochromocytomas are bilateral; this proportion may rise to 50% in cases that are associated with familial syndromes.
- 10% of adrenal pheochromocytomas are malignant, although the associated hypertension represents a serious and potentially lethal complication of even benign tumors.

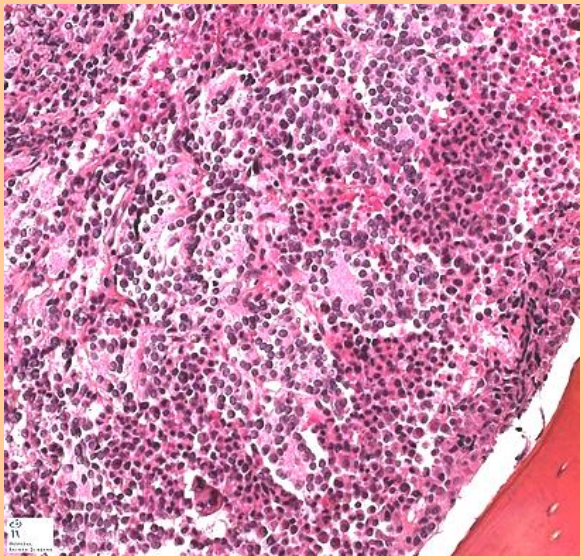


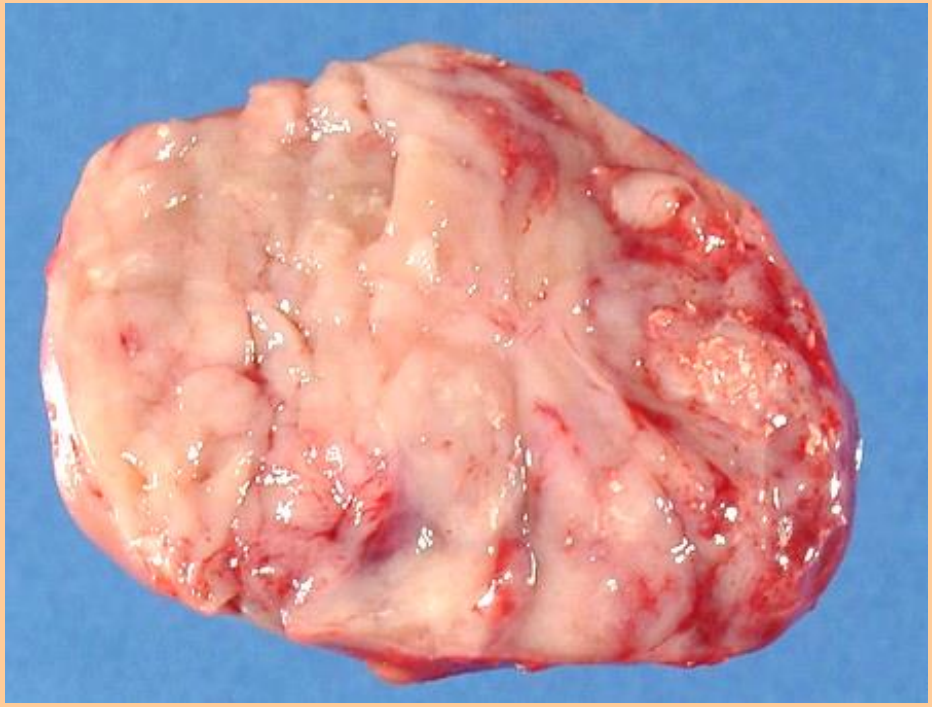


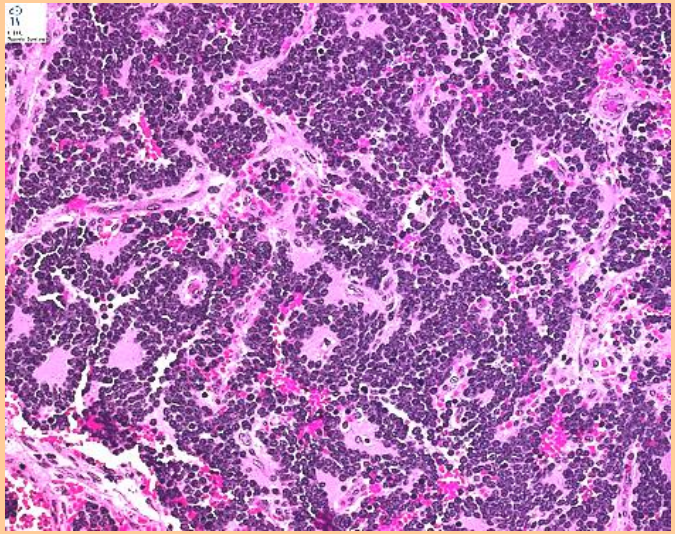


Neuroblastoma

- most common extracranial solid tumor of childhood
- most neuroblastomas are sporadic
- occur most commonly during the first 5 years of life and may arise during infancy
- they are most common in the abdomen
- „penaut" tumors
- N-myc protooncogen overexpession (25% - poor prognosis)
- Lymphogen and haematogen metastasis
-Neuroblastoma – ganglioneuroblastoma - ganglioneurinoma!







Multiple Endocrine Neoplasia (MEN) Syndromes)

Definition: The MEN syndromes are a group of inherited diseases caused by proliferative lesions (hyperplasias, adenomas, and carcinomas) of multiple endocrine organs.

- These tumors occur at a younger age than that typical for sporadic cancers.
- They arise in multiple endocrine organs, either synchronously (at the same time) or metachronously (at different times).
- Even in one organ, the tumors often are multifocal.
- These tumors are usually more aggressive and recur in a higher proportion of cases than similar endocrine tumors that occur sporadically.

MULTIPLE ENDOCRINE NEOPLASIA TYPE 1

MEN-1 syndrome is caused by germ line mutations in the MEN1 tumor suppressor gene, which encodes a protein called Menin.

Menin is a component of several different transcription factor complexes, and loss of Menin function leads to deregulation of the corresponding binding partners, promoting endocrine neoplasia.

Organs most commonly involved are the parathyroid, the pancreas, and the pituitary—the “3 Ps.”

MULTIPLE ENDOCRINE NEOPLASIA TYPE 1

Parathyroid. Primary hyperparathyroidism is the most common manifestation of MEN-1 (80%–95% of patients) and is the initial manifestation of the disorder in most patients, appearing in almost all by 40 to 50 years of age. Parathyroid abnormalities include hyperplasia and adenomas.

Pancreas. Endocrine tumors of the pancreas are the leading cause of death in MEN-1. These tumors usually are aggressive and present with metastatic disease. Pancreatic endocrine tumors often are functional (i.e., secrete hormones). Zollinger-Ellison syndrome, associated with gastrinomas, and hypoglycemia, associated with insulinomas, are common endocrine manifestations.

Pituitary. The most frequent pituitary tumor in patients with MEN-1 syndrome is a prolactinoma. In some cases, acromegaly develops in association with somatotropin-secreting tumors (GH adenoma).

MULTIPLE ENDOCRINE NEOPLASIA TYPE 2

MEN-2 syndrome actually comprises two distinct groups of disorders that are unified by the occurrence of activating (i.e., gain-of-function) mutations of the RET proto-oncogene at chromosomal locus 10q11.2.

A strong genotype-phenotype correlation has been recognized for the MEN-2 syndromes, and differences in mutation patterns account for the variable features in the two subtypes.

MEN-2 is inherited in an autosomal dominant pattern.

Multiple Endocrine Neoplasia Type 2A

• Thyroid: Medullary carcinoma of the thyroid develops in virtually all untreated cases, and the tumors usually occur in the first 2 decades of life. The tumors commonly are multifocal, and foci of C cell hyperplasia can be found in the adjacent thyroid. Familial medullary thyroid cancer is seen in a variant of MEN-2A, without the other characteristic manifestations listed here. In comparison with MEN-2, familial medullary carcinoma typically occurs at an older age and follows a more indolent course.

• Adrenal medulla: Adrenal pheochromocytomas develop in 50% of the patients; fortunately, no more than 10% of these tumors are malignant.

• Parathyroid: Approximately 10% to 20% of patients develop parathyroid gland hyperplasia with manifestations of primary hyperparathyroidism.

Multiple Endocrine Neoplasia Type 2B

- Primary hyperparathyroidism does not develop in patients with MEN-2B.
- Pheochromocytoma + medullary thyroid cancer
- Extraendocrine manifestations are characteristic in patients with MEN-2B.

These include ganglioneuromas of mucosal sites (gastrointestinal tract, lips, tongue) and a marfanoid habitus, in which overly long bones of the axial skeleton give an appearance resembling that in Marfan syndrome.