# Pathology of the endocrine system.

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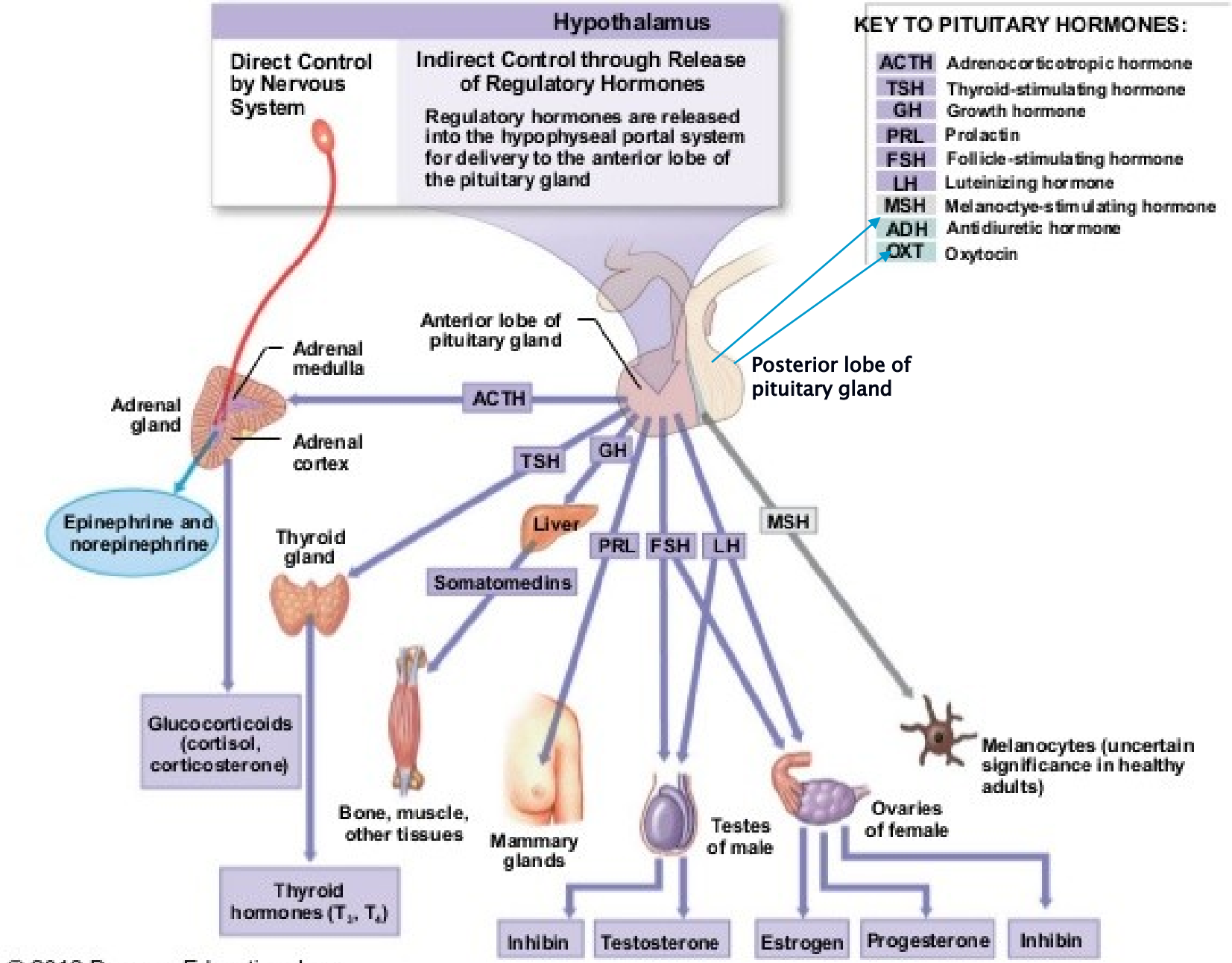
- Pituitary gland
- Thyroid
- Parathyrois
- Adrenal gland
- Endocrine pancreas



| Pathological basis of endocrine signs and symptoms | |
|---|---|
| **Sign or symptom** | **Pathological basis** |
| **Hormone excess (hyperfunction)** | Endocrine gland hyperplasia cause by increased trophic stimulus to secretion<br>Functioning neoplasm of endocrine gland |
| **Hormone deficiency (hypofunction)** | Endocrine gland atrophy due to loss of trophic stimulus to secretion<br>Destruction of endocrine gland by inflammation, ischamia or non-functioing tumor |
| **Diffuse enlargement of gland** | Inflammatory cell infiltration<br>Hyperplasia |

# Pituitary

- **Adenohypophysis**
- **Hypofunction/partial or panhypopituitarism**
  - Due to destruction by tumor or compression, Rathke's cleft cyst; due to hypothalamic reasons
  - Due to inflammation (autoimmune); due to genetic abnormalities of hormone synthesis
  - Due to ischaemic necrosis, radiation damage or surgical ablation
  - Leads to secondary hypofunction of adenohypophyseal dependent endocrine glands (atrophy of gonads, hypothyreosis, hypocorticalism,…)

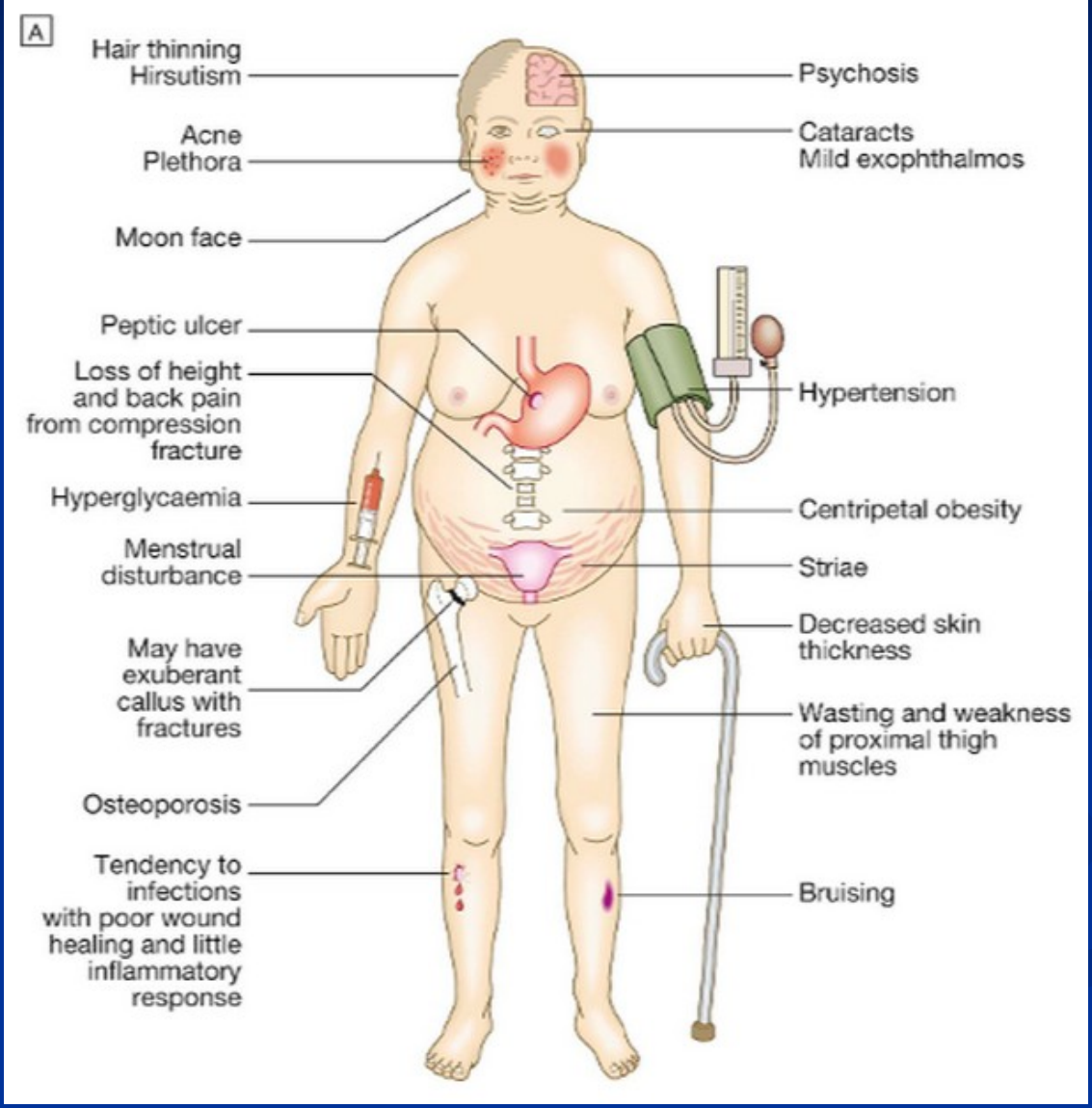
- **Hyperfunction/hyperpituitarism**
  - in adenomas, carcinomas, hyperplasias, due to hypothalamic reasons

# Adenomas of the adenohypophysis

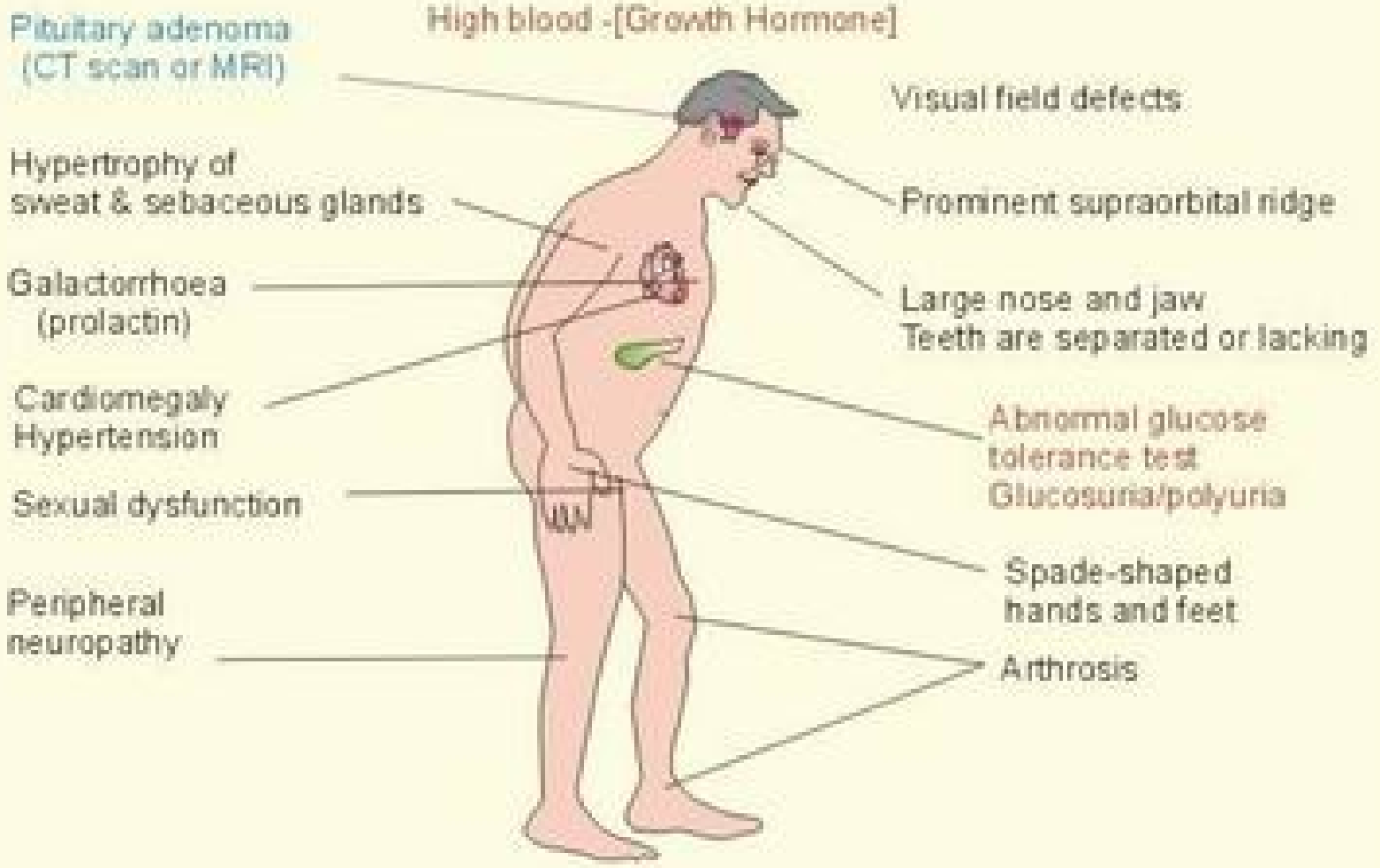
| Adenoma type | Clinical picture |
|---|---|
| Prolactinoma | Commonest type, produces galactorrhoea and menstrual disturbances |
| GH-secreting | Produces gigantism in children and acromegaly in adults |
| ACTH-secreting | Produces Cushing syndrome |
| Others | Exceptionally rare (TSH-, FSH-, LH- secreting) |
| | Plurihormonal |
| | Hormonally non-functioning |

Association with MEN-1 syndrome!

# Cushing syndrome



# Acromegaly


High blood -[Growth Hormone]
Pituitary adenoma
(CT scan or MRI)
Visual field defects
Hypertrophy of
sweat & sebaceous glands
Prominent supraorbital ridge
Galactorrhoea
(prolactin)
Large nose and jaw
Teeth are separated or lacking
Cardiomegaly
Hypertension
Abnormal glucose
tolerance test
Glucosuria/polyuria
Sexual dysfunction
Spade-shaped
hands and feet
Peripheral
neuropathy
Arthrosis

# Neurohypophysis

- **Antidiuretic hormone (ADH)**
- **ADH deficiency – diabetes insipidus (DI)**
  - Due to hypothalamus damage (trauma, tumor, inflammation.. due to hypothalamic reasons)
  - Polyuria, polydipsia
  - In peripheral forms of DI the renal tubules insensitive to ADH
- **Excess ADH**
  - Usually due to ectopic production by tumors (neuroendocrine carcinomas of the lung)
- **Oxytocin**

# Hypothalamic suprasellar tumors

- **Gliomas**

- **Craniopharyngeoma**

- usually benign, malignisation rare; from the Rathke´s cleft epithelial rests
- children (5-15 years; endocrinopathies) + 2nd peak in 6th decase
- solid, cystic or multilocular

# Adrenals

- **Medulla**

- Production of catecholamins (adrenalin, noradrenalin)

- **Tumors:**

- Pheochromocytoma

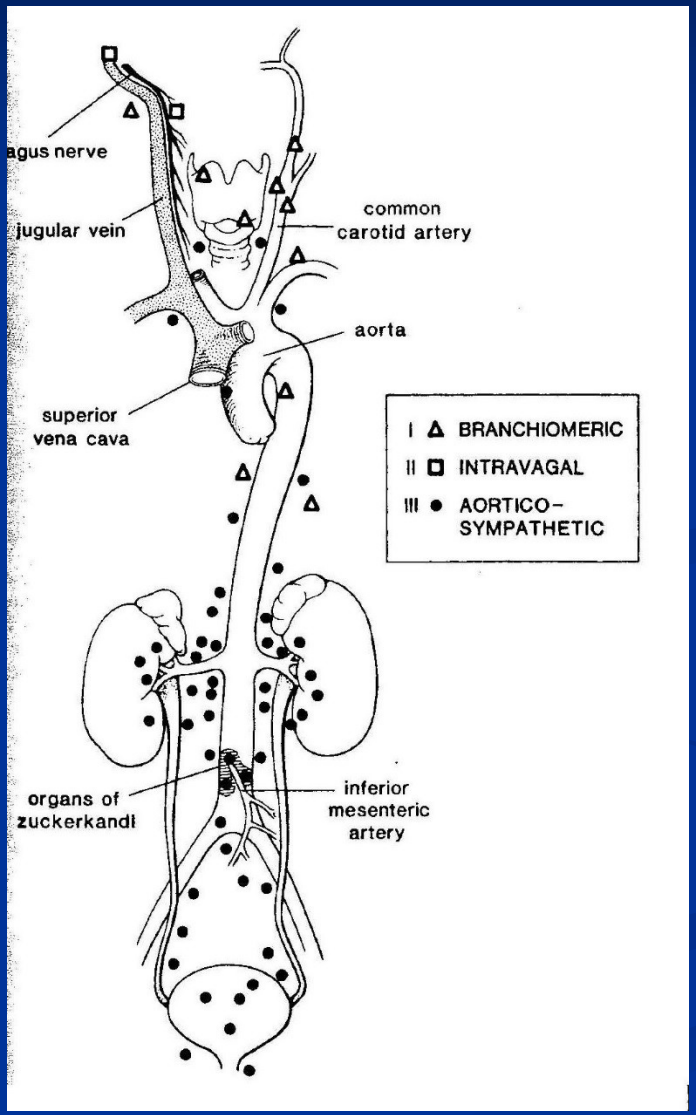
- symptoms due to excess catecholamine secretion (secondary hypertension with ↑risk of cerebral bleeding), sweating)
- Adrenal or extraadrenal, uni or bilateral, assoc. with MEB 2A and 2B (10 %)
- 10 % with malignant biological behavior

- Neuroblastoma

(tumor of children, malignant)

- Ganglioneuroblastoma, ganglioneuroma

# Extraadrenal system of chromaffine paraganglia



# Adrenals

- **Cortex**
- Production of glucocorticoids,mineralocorticoids, sex steroids
- **Hyperfunction:**
- Cushing syndrome

(excess secretion of ACTH, tumors of adrenals, treatment by steroids

- Conn´s syndrome

(overproduction of mineralocorticoids: retention of water, hypertension, muscular weakness, arrhythmias)

- **Hypofunction**
- Caused by autoimmune adrenalitis, tbc, necrosis of adrenals in sepsis, destruction by tumors,…
- Weight loss, lethargy, hypotension, pigmentation, hyponatraemia

# Thyroid

- **Hyperthyroidism**
- Syndrome due to excess T3 and T4
- Very rarely due to excess TSH
- Caused by Grave´disease/thyreoiditis, in which the thyroid stimulating autoantibodies are produced
- Rarely due to functioning adenoma or toxic nodular goiter

- **Hypothyroidism (myxoedema)**
- Syndrome due to insufficient circulating T3 and T4
- If congenital , causes cretenism
- Commonest cause is Hashimoto´s thyreoiditis (=autoimmune thyreoiditis)

# Causes of thyreotoxicosis

- **Primary associated with hyperthyreoidism**
  - Diffuse toxic hyperplasia (m. Graves-Basedow)
  - Hyperfunctional (toxic) nodulat goiter
  - Hyperfunctional (toxic) adenoma
  - Hyperfunctional thyreoidal carcinoma
  - Iodine induced hyperthyreoidismus
  - Neonatal thyreotoxicosis (of mothers with m. G-B)

- **Secondary associated with hypertyreoidismem**
  - TSH producing pituitary adenoma
  - TRH overproduction

- **Without association with hyperthyreoidism**
  - Subacute granulomatous thyreoiditis
  - Chronic lymphocytic thyreoiditis
  - Struma ovarii (mature ovarial teratoma)

# Hypothyreoidismus:

## A) congenital - cretenismus

(endemic (in iodine defficiency); sporadic (due to enzymatic defect)

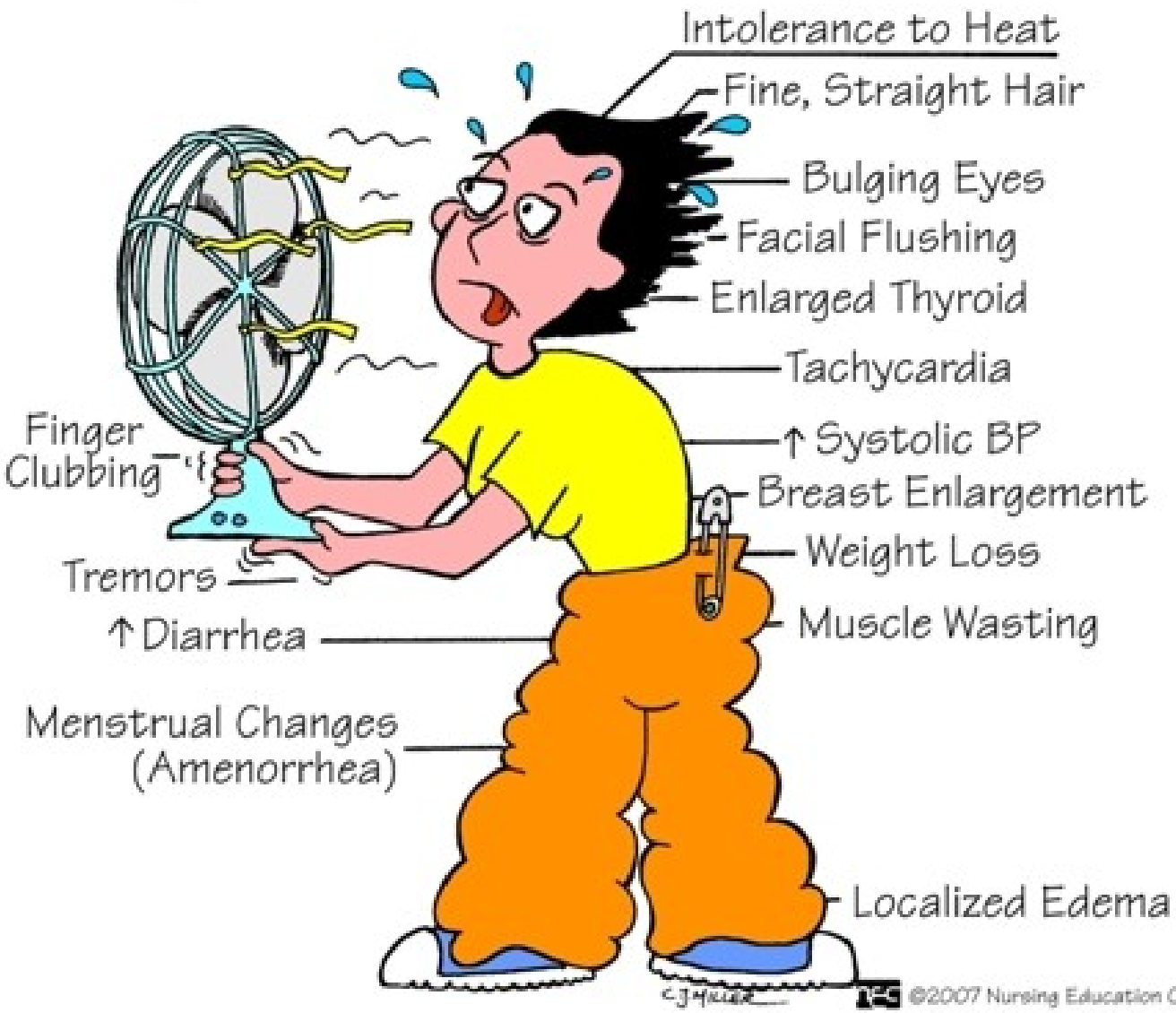
## B) aquiered – myxoedema

- **Clinical signs of cretenism:**
  - Impaired physical growth and mental development, hypomimic face, tongue protrusion, umbilical hernia

- **Clinical signs of myxoedema**
  - Accumulation of mucosubstances in corium (and viscerally)
  - Hypercholesteroĺaemia, accelerated AS
  - Dry cold skin, gruff voice, muscle weakness, prone to hypotermia, dry hair, brittle nails, oligo –amenorea, obesity, psychic disorders - depression,….
  - Coma with hypothermia, circulaton failure

- **Causes**
  - **Primary**
  - Developmental (dysgenesis: mutation in genes for TSH-receptor, TTF)
  - Genetically caused resistence to thyreoidal hormones
  - Surgical ablation, radiation
  - Autoimmunne thyreoiditis
  - Iodine deficiency
  - Congenital biosynthetical defect (dyshormonogenetic goiter)
  - Drugs – thyreostatic
  - **Secundary and tertiary** (hypothalamic anf hypophyseal reasons)

# HYPERTHYROIDISM



# HYPOTHYROIDISM

# M. Graves-Basedow
## (diffuse parenchymatous toxic (hyperfunctional) goitre)

- F>M, 2nd to 4th decade, genetically predisposed
- Autoimmune disease: stimulating autoantibodies against TSH receptor
- Hyperthyreoidism+infiltrative ophtalmopathy-exophthalmos (T cells, oedema, GAGs, adipocytes) +(pretibial myxoedema)
- Diffuse hypertrophy and hyperplasia
- „too many follicular cells and too little colloid“
- Surgical removal or radioiodine ablation

# Thyroiditis

- **Chronic autoimmune lymphocytic thyroiditis (Hashimoto´s)**
- F:M = 10:1
- Genetic predisposition
- CD8+ cytotoxic T cells mediated cell death; cytokines mediated cell death
- Autoantibodies against TSH receptor, thyreoglobulin, peroxidase – antibody-dependent cell-mediated cytotoxicity (ADCC)
- Enlarged thyroid, lymphoplasmocytic infiltrate, lymphatic follicles, oncocytic transformation of thyreocytes, fibrotisation
- Often assoc. with other autoimmune diseases
- Increased risk of malignant lymphoma (MALToma) and carcinom of the thyroid

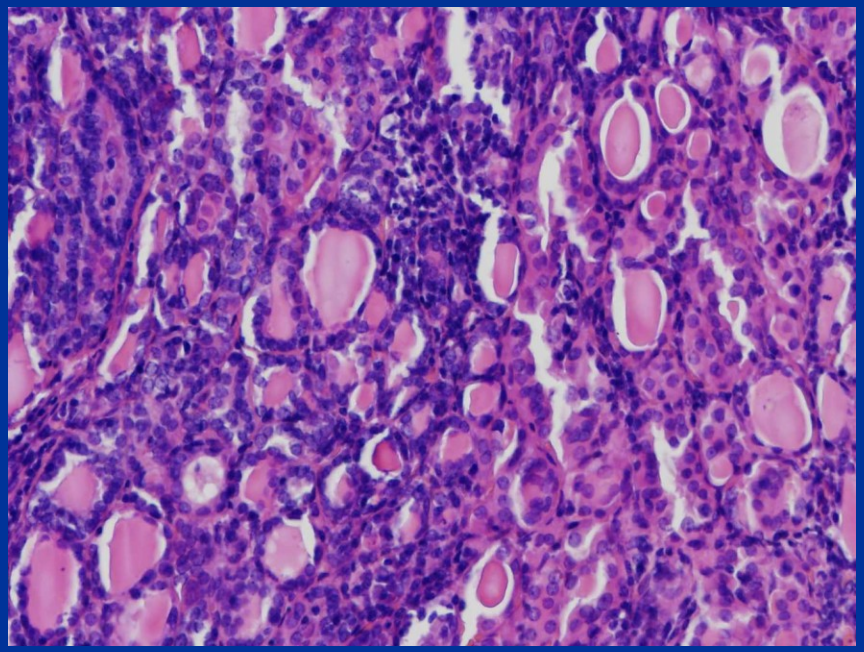
# Thyroiditis

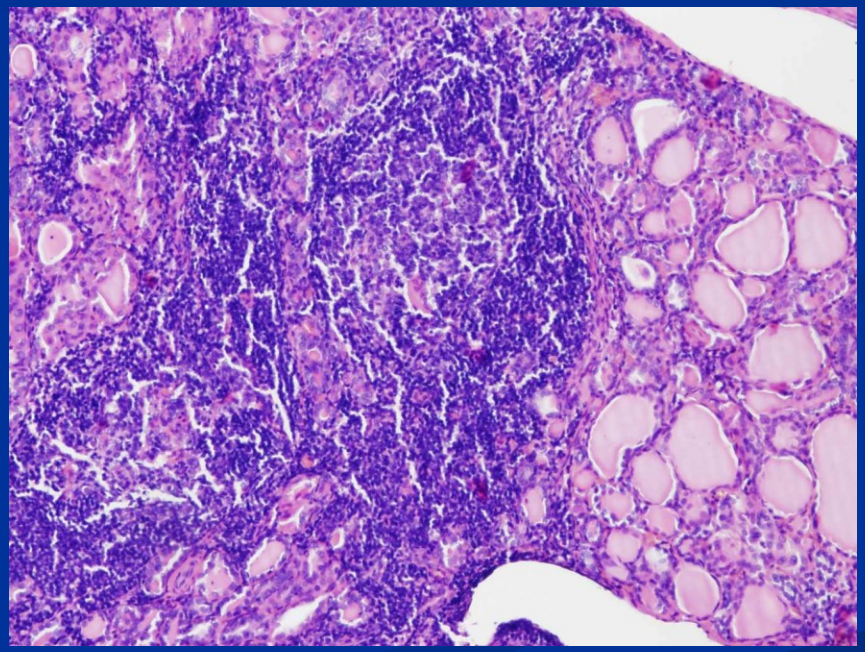
- **Subacute granulomatous thyroiditis (de Quervainova)**
- F:M = 3-5:1
- virus-induced host tisuue damage? cytotoxic T lymphocytes
- Painfully enlarged thyroid, fever, fairly abrupt onset
- Focal disruptions nad necroses of follicules, granulocytic and granulomatous reactions, fibrotisation)

- **Chronic sclerosing thyroiditis (Riedl´s)**
- Fibrotising inflammation involving thyroid and also surrounding tissues and organs (stenosis of trachea, paresis of n. recurrens, hypothyroidism)
- Systemic connective tissue disease (IgG4 assoc.?), fibrotising Hashimoto´s thyroiditis?, idiopathic fibrosis?

- **Subacute lymphocytic thyroiditis (often post partum thyroiditis)**

# Chronic autoimmune lymphocytic thyroiditis (Hashimoto´s thyroiditis)





# Sclerosing lesions associated with IgG4

- Autoimmune pancreatitia
- Sclerosing cholangitis
- Lymphoplasmocytic sclerosing cholecystitis
- Sclerosing sialoadenitis
- Idiopathic retroperitoneal fibrosis (M. Ormond)
- Inflammatory pseudotumor of the liver, lung, pituitary gland
- Tubulointerstitial nephritis assoc. with IgG4
- Interstitial pneumonia assoc. With IgG4
- Sclerosing prostatitis
- **Sclerosing thyreoiditis**

- M>F; immunosuppressive therapy response (steroids)
- Imitation of neoplastic lesions
- Sclerosing lesions with lymphoplasmocytic infiltrates, irregular fibrotisation, obliterative phlebitis, IgG4+ plasma cells.
- Increased risk of malignant lymphoma

# Goitre
## (enlargement of the whole gland)

- **Parenchymatous goitre *vs* colloid goitre**
- **Diffuse vs nodular goitre**
- **Hypofunctional vs hyperfunctional vs eufunctional**

- **Aetiology**
  - Iodine deficiency, due to endemic goitre or food faddism
  - Rare inherited enzyme defects in T3 and T4 synthesis
  - Drugs that induce hypothyroidism

# Thyroid tumors

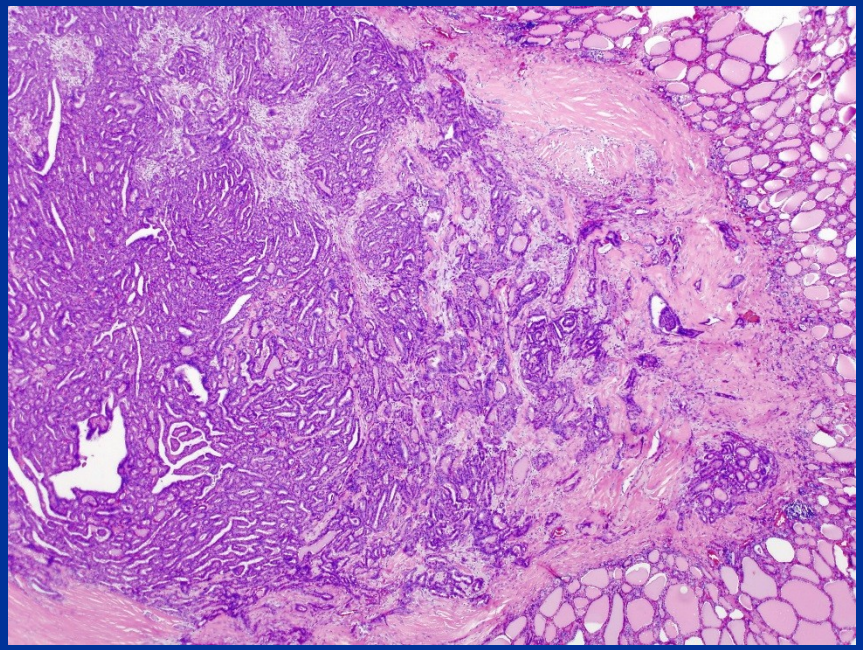
- **Benign**
  - **Follicular adenoma**

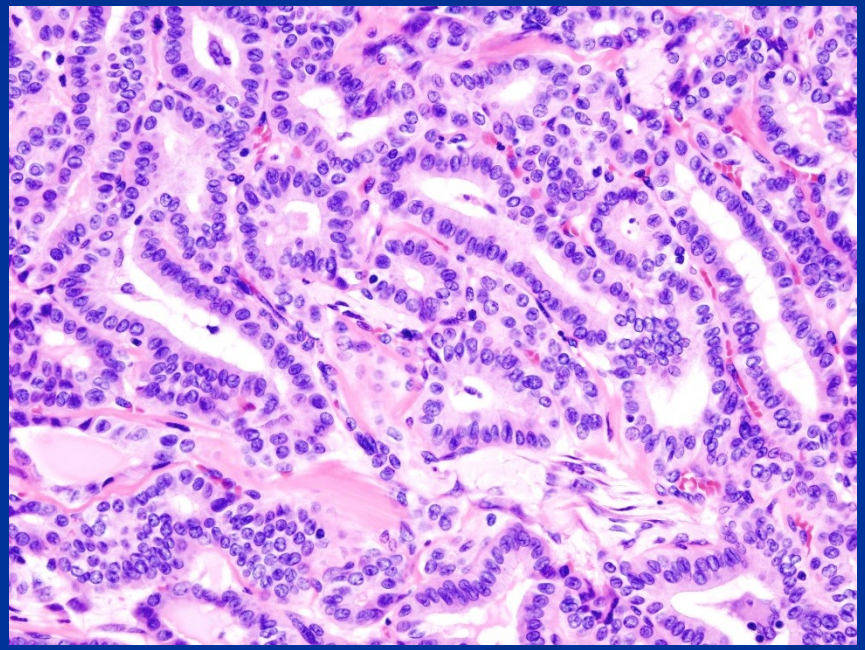
- **Malignant**
  - **Carcinoma**
  - **Lymphoma**

    (lymphoma (usually non-Hodgkin´s lymphomas of B-cell type, variable prognosis)

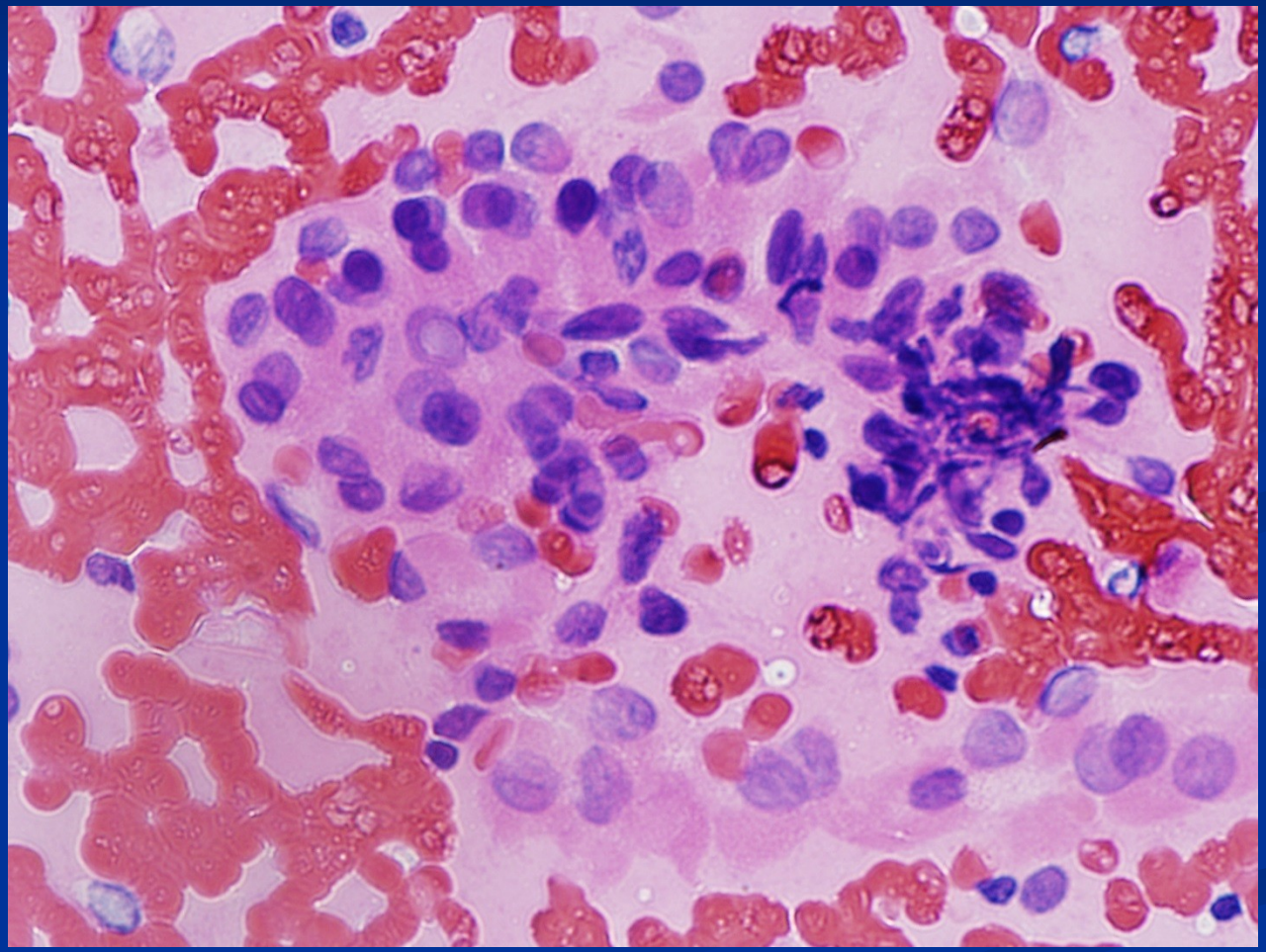
| Carcinoma of the thyroid | | | | |
|---|---|---|---|---|
| **Type** | **Proportion of all cases (%)** | **Typical age range** | **Mode of spread** | **Prognosis** |
| **Papillary** | 60-70 | Children, young adults | Lymphatic, to lymph nodes | Excellent |
| **Follicular** | 20-25 | Young-middle age | Haematogenous, to bones | Good |
| **Anaplastic** | 10-15 | Elderly | Aggressive local extension | Very poor |
| **Medullary** | 5-10 | Usually elderly, also familial case (MEN sy) | Local, lymphatic, haematogenous | Variable, more aggressive in familial cases |

# Papillary carcinoma of the thyroid



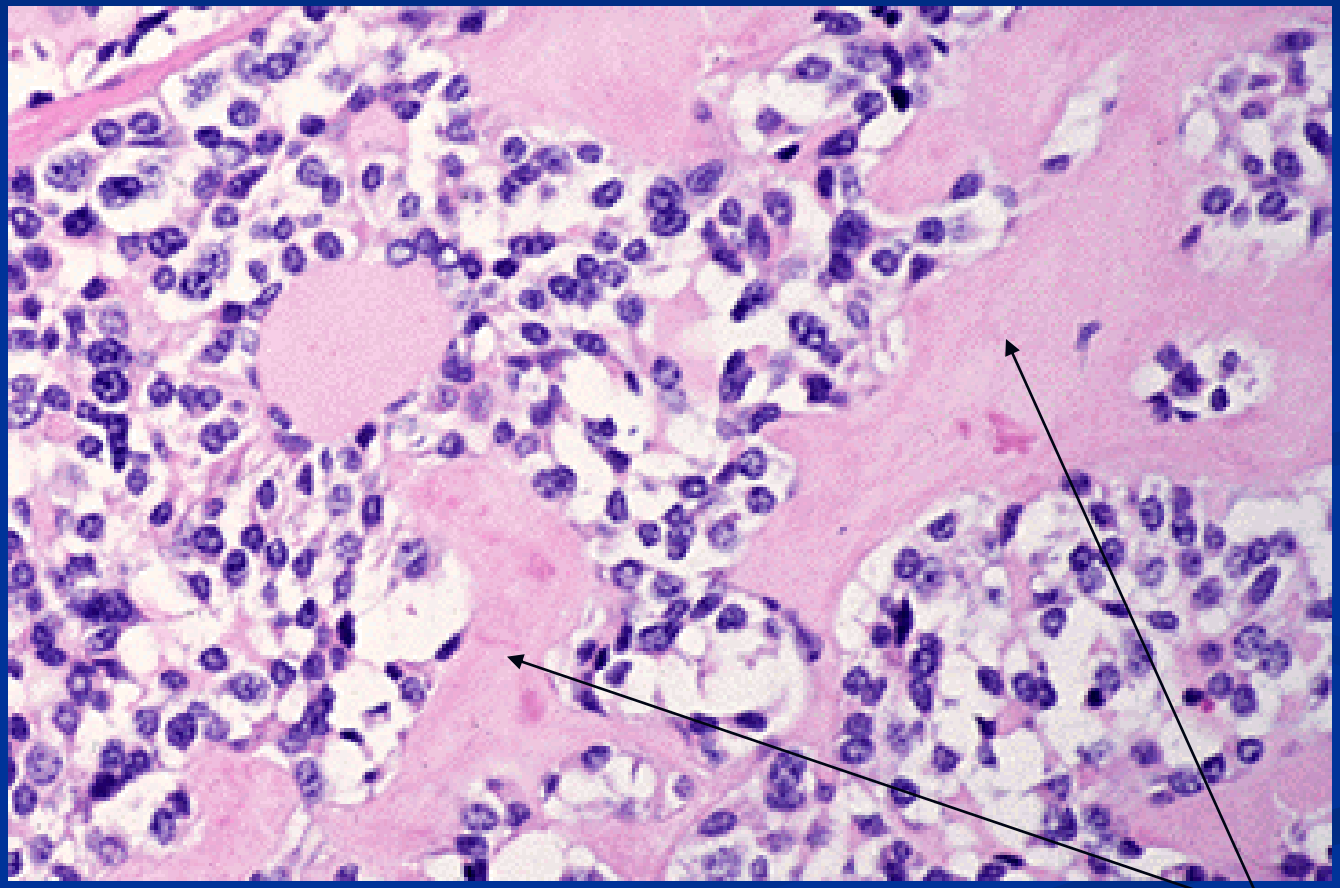


# Papillary carcinoma of the thyroid

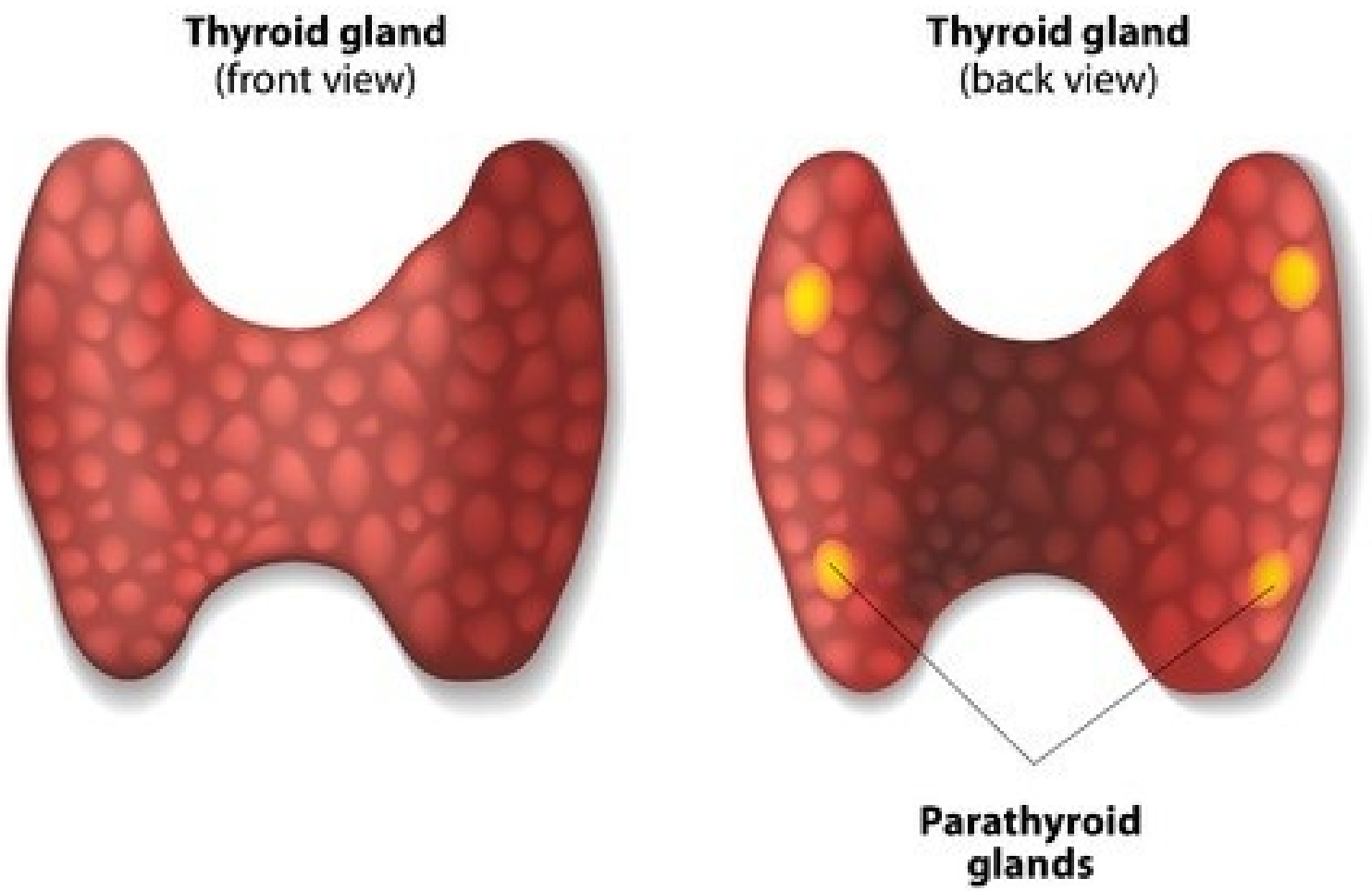


FNAB

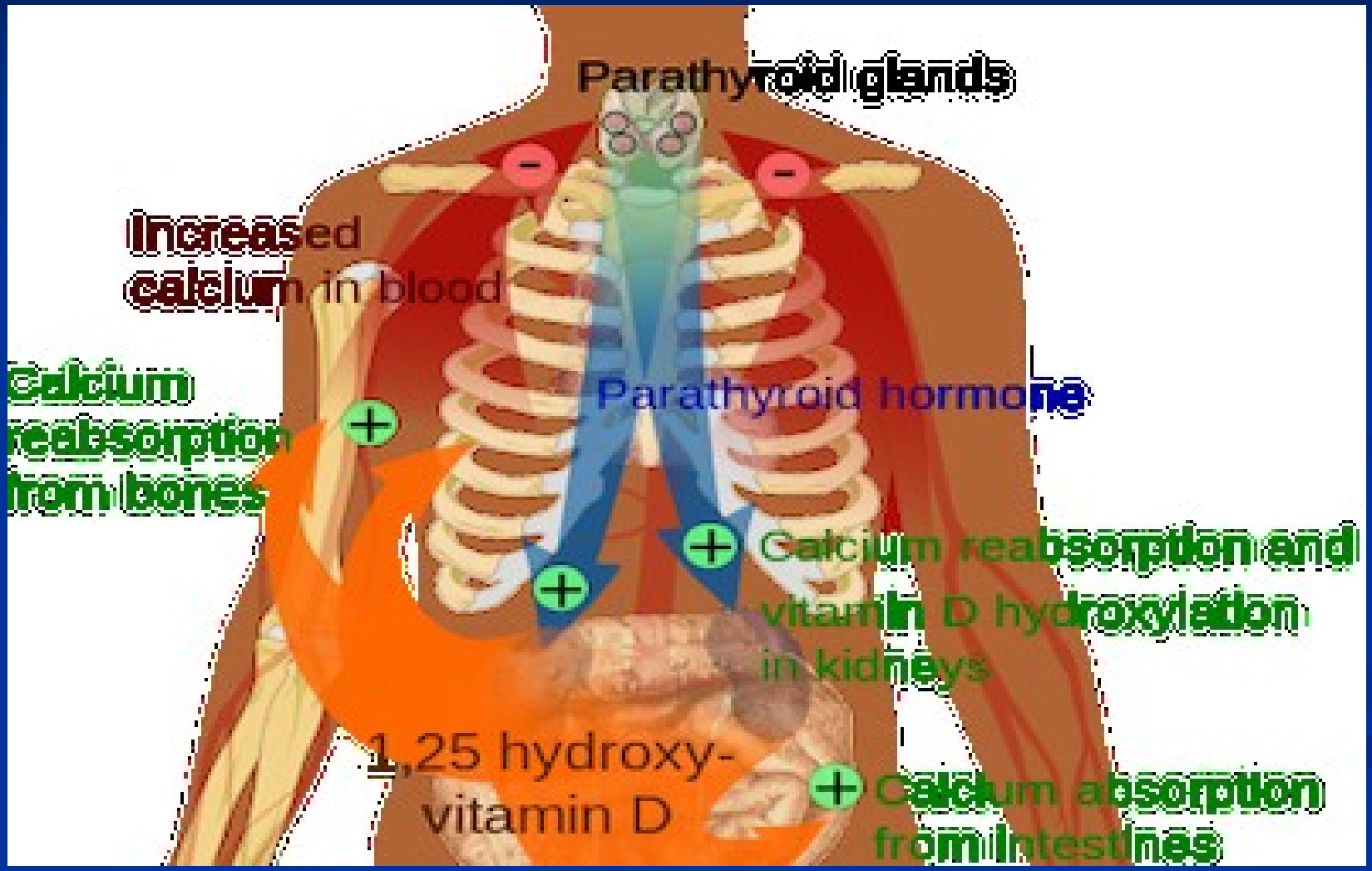
# Medullary carcinoma of the thyroid



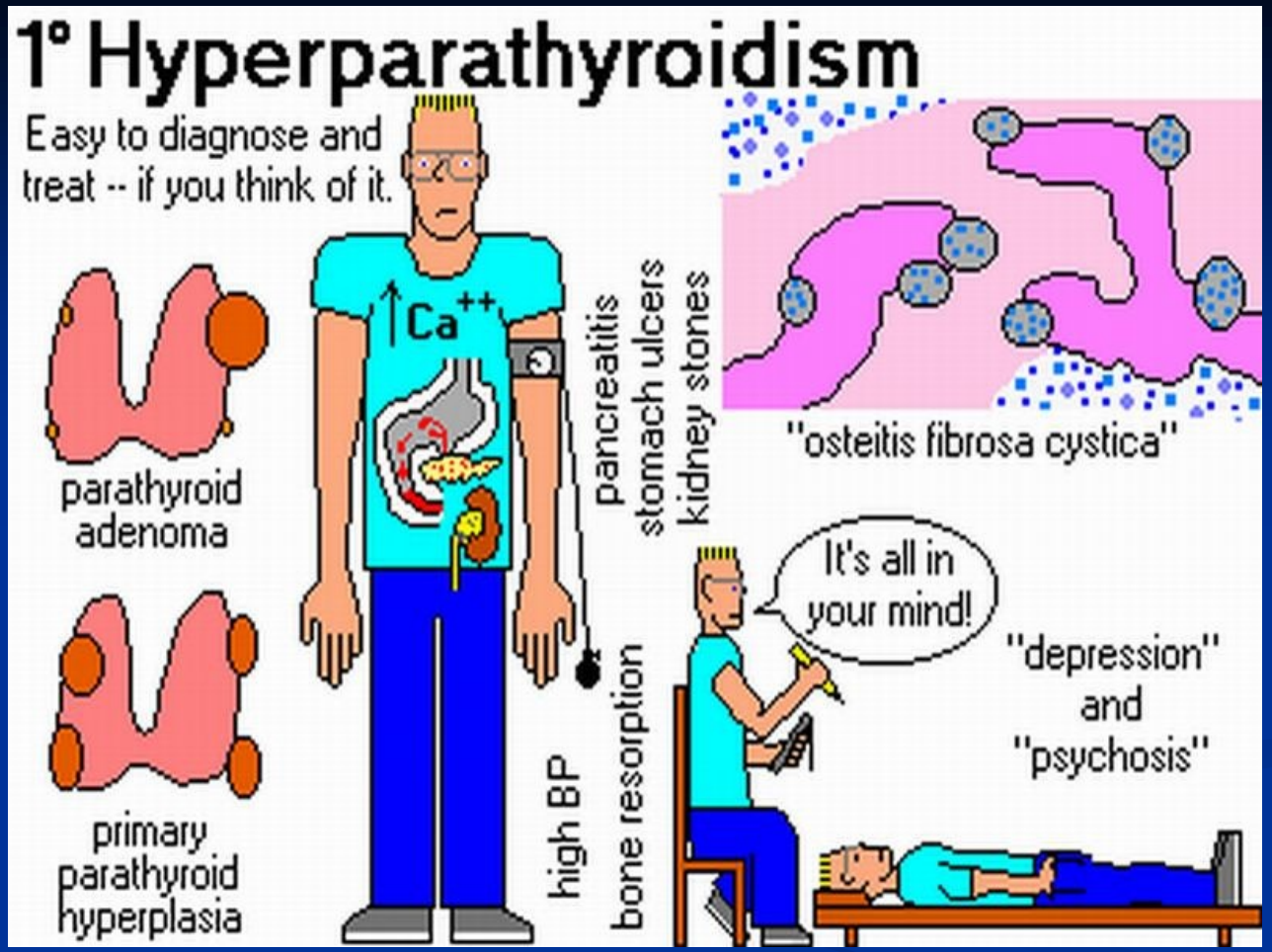
# THYROID AND PARATHYROID



# Parathyroid



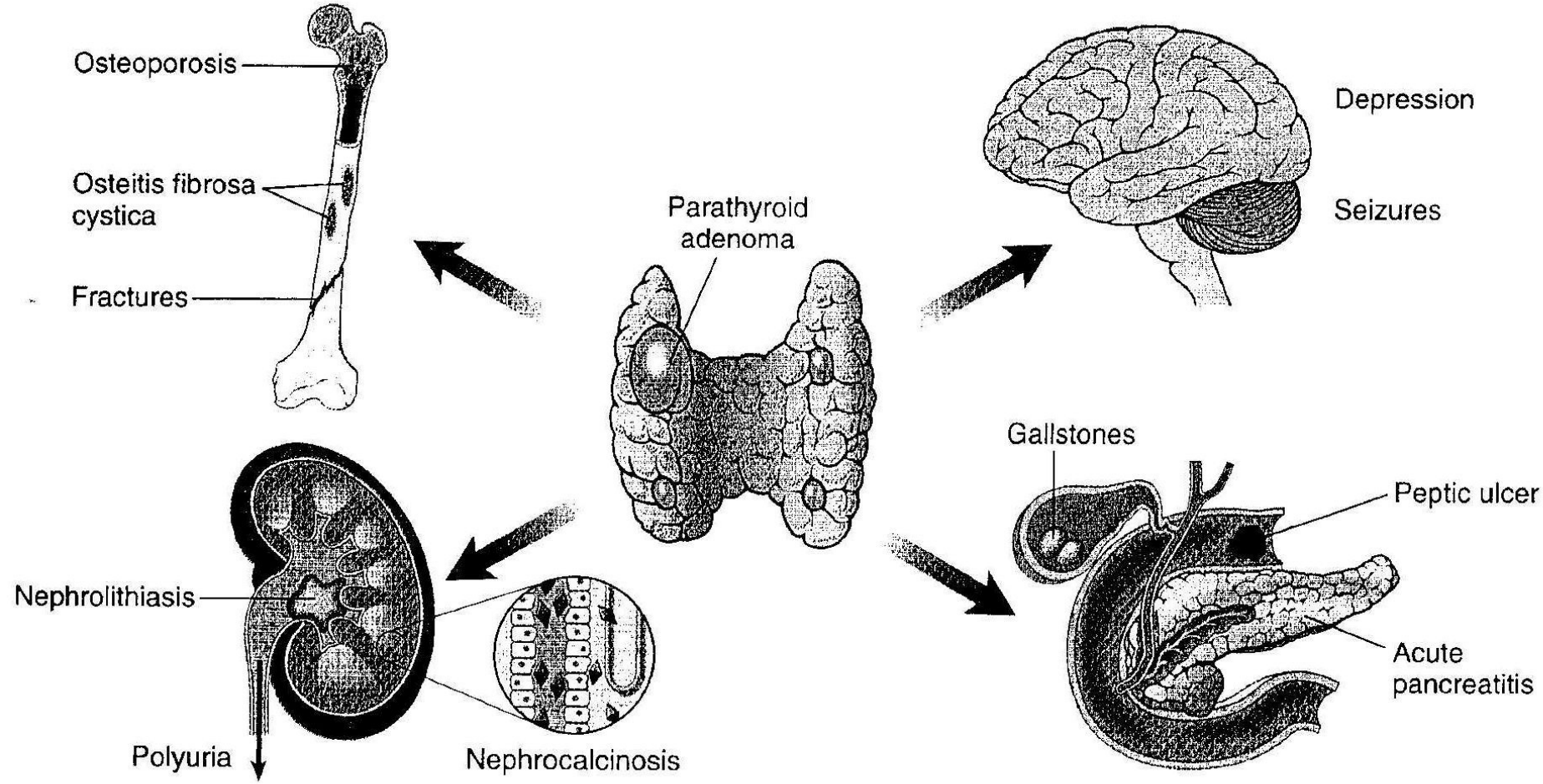
# Primary



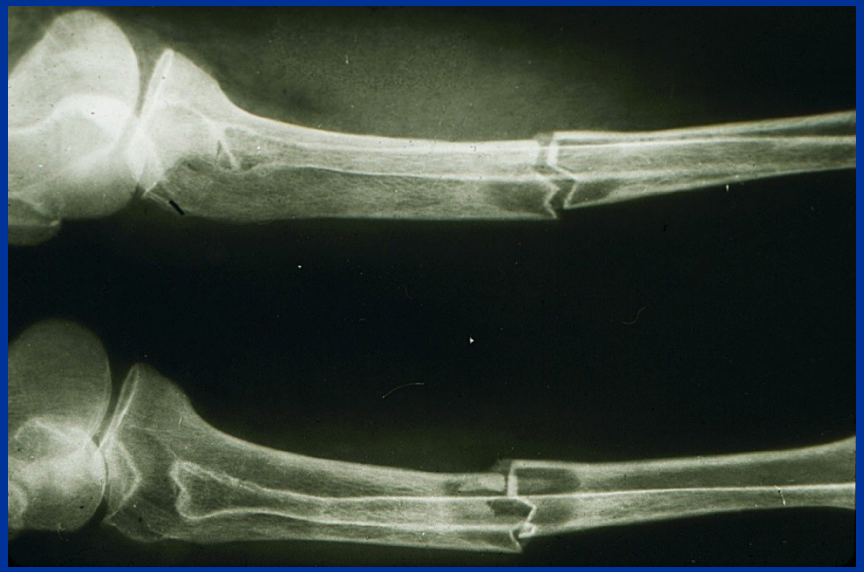

**Secondary hyperparathyreoidsm**: a physiological response to hypocalcaemia (e.g. in malabsorption, renal failure)

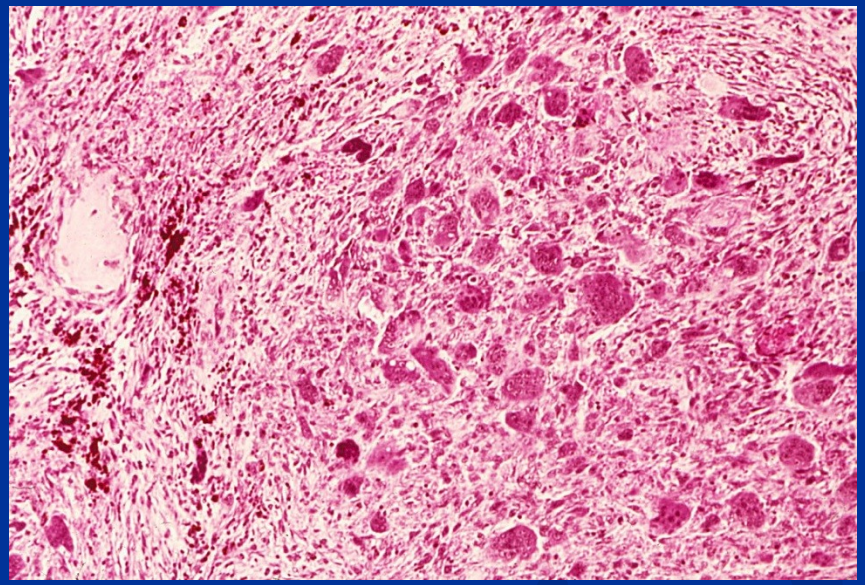
MEN 1, MEN 2

# Clinical signs of hyperparathyreoidismu



# Pathological fracture and brown pseudotumor





# Hypoparathyreoidism

- **Causes hypocalcaemia**
- Tetany (spasm of the skeletal muscle)
- Convulsions
- Paraesthesiae
- Psychiatric disturbances
- Rarely cataracts and brittle nails

Pseudohyperthyreoidism
- Insensitivity of peripheral tissues to PTH
- Usually genetically caused

- **Caused by:**
- Removal of or damage of the glands during thyreoidectomy
- Idiopathic, autoimmune (also as a part of polyendocrine syndrome)
- Congenital hypoplasia or aplasia (Di George syndroma)
- Congenital deficiencies

Other causes of hypocalcaemia: chronic renal failure, vitamin D deficiency, excess loss during lactation

# Endocrine pancreas:
## islet cell tumors – neuroendocrine neoplasias

- Less common than pancreatic adenocarcinoma (1-2 % of pancreatic tumors)

- Present with endocrine effects and can be malignant:
- **Insulinoma:** hypoglycaemia due to hypersecretion of insulin
- **Glucagonoma:** secondary diabetes and skin rash
- **Gastrinoma:** hypersecretion of gastric acid due to gastrin action resulting in severe peptic ulcerations
- ….others (somatostatinoma, VIPoma, serotoninoma, with ectopic hormonal production (ACTH, calcitonin)
- Non-functional
- Microadenoma (<0,5 cm)

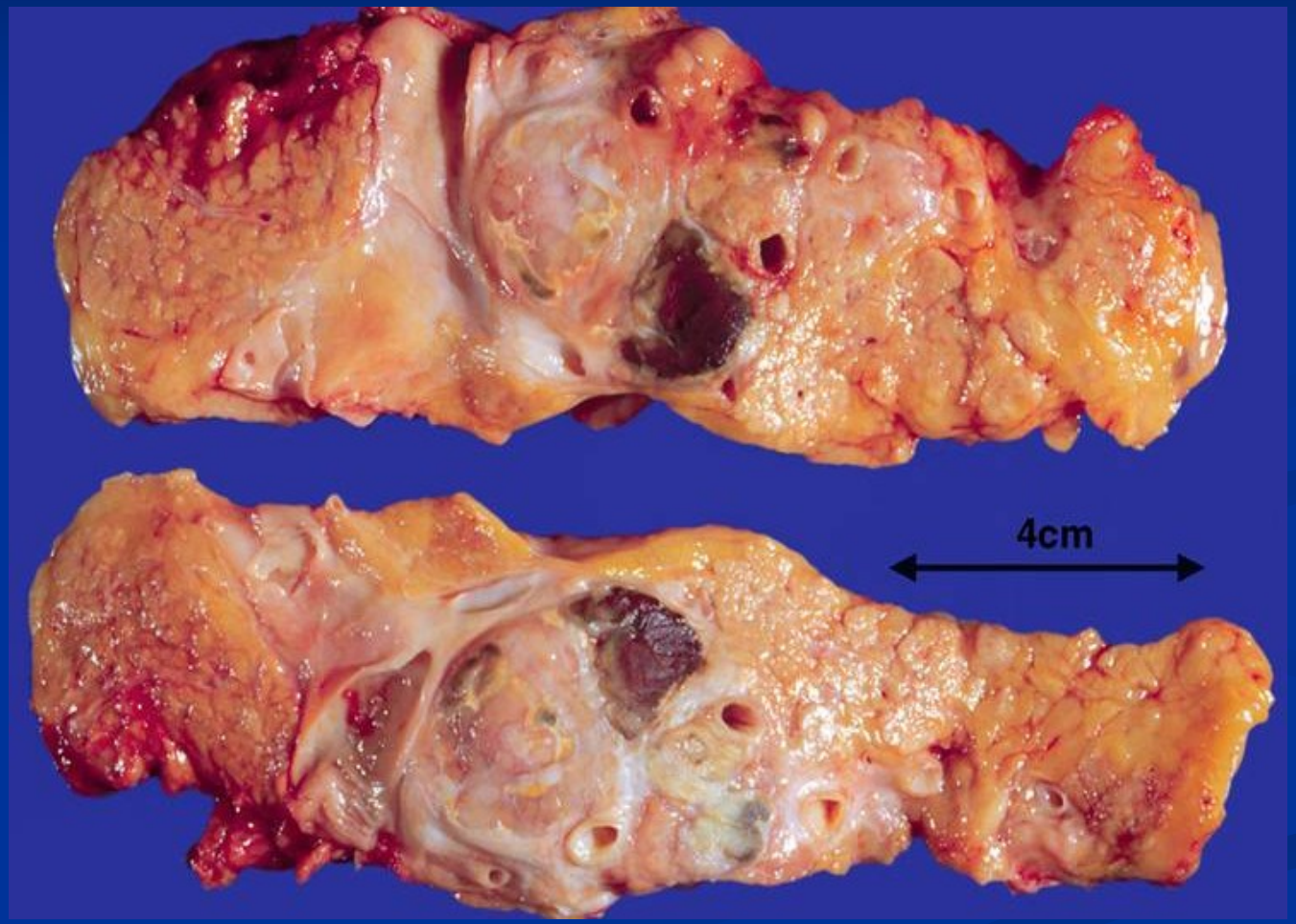
**Islet cell tumor and gastrinomas may occur as a part of inherited MEN (multiple endocrine neoplasia) syndrome.**

# Neuroendocrine neoplasias – tumors of the endocrine pancreas

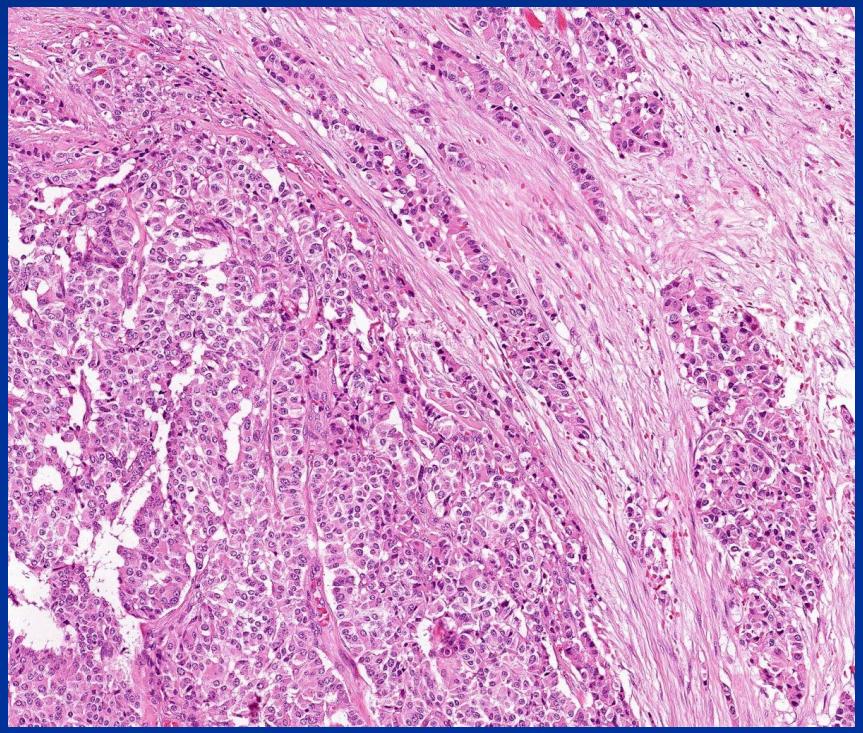
- Neuroendocrine tumor (NET)
  - Non-functional pancreatic NET (NET G1, G2)
  - NET G1
  - NET G2
  - NET G3 (from WHO 2017)

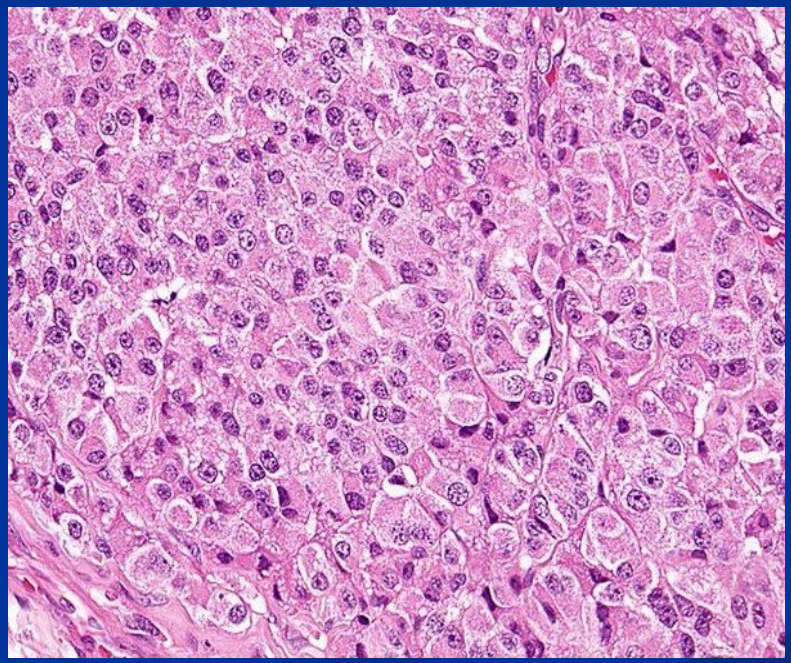
- Neuroendocrine carcinoma (NEC)
  - Large cell type NEC
  - Small cell type NEC

# Neuroendocrine neoplasia of the pancreas.

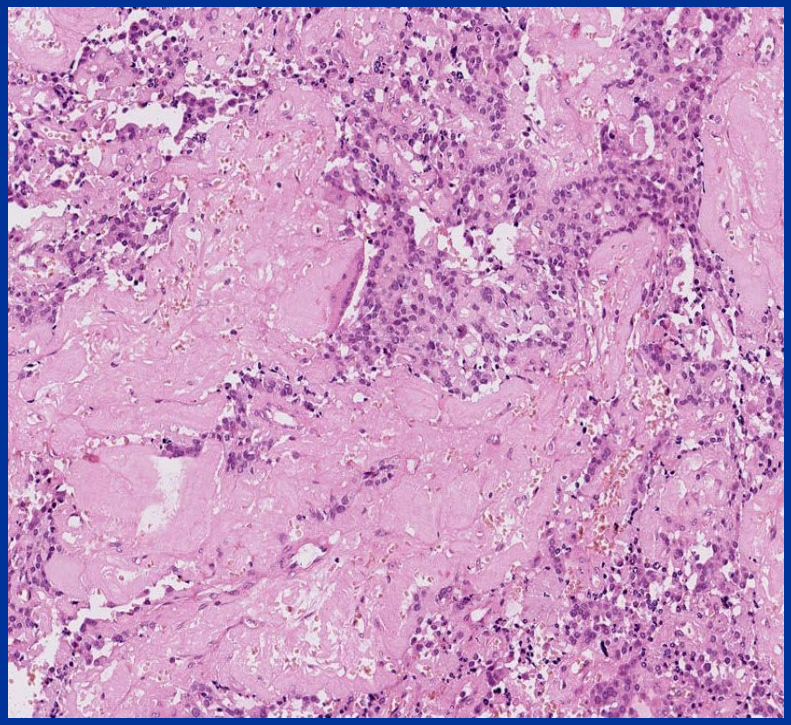


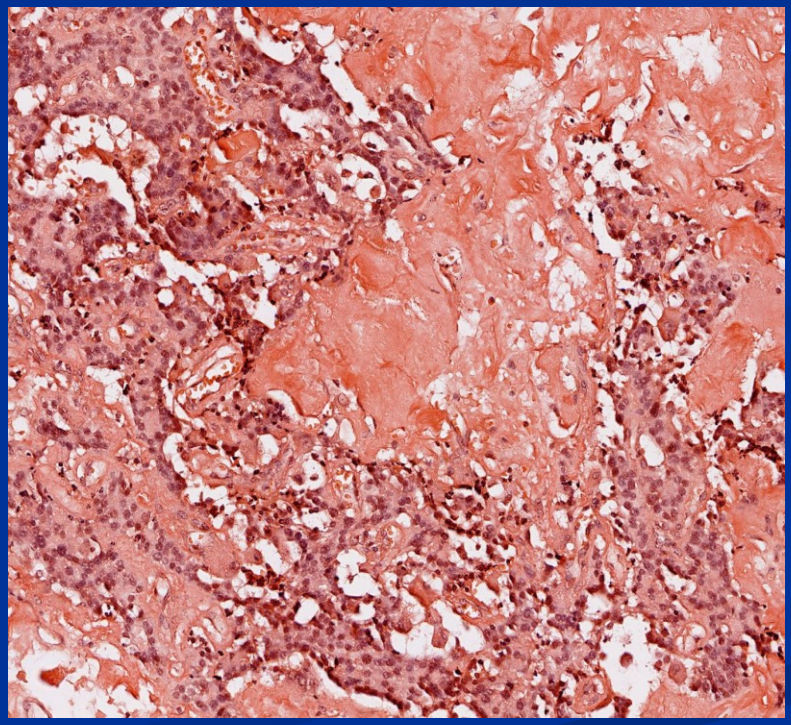
# Neuroendocrine neoplasia of the pancreas.





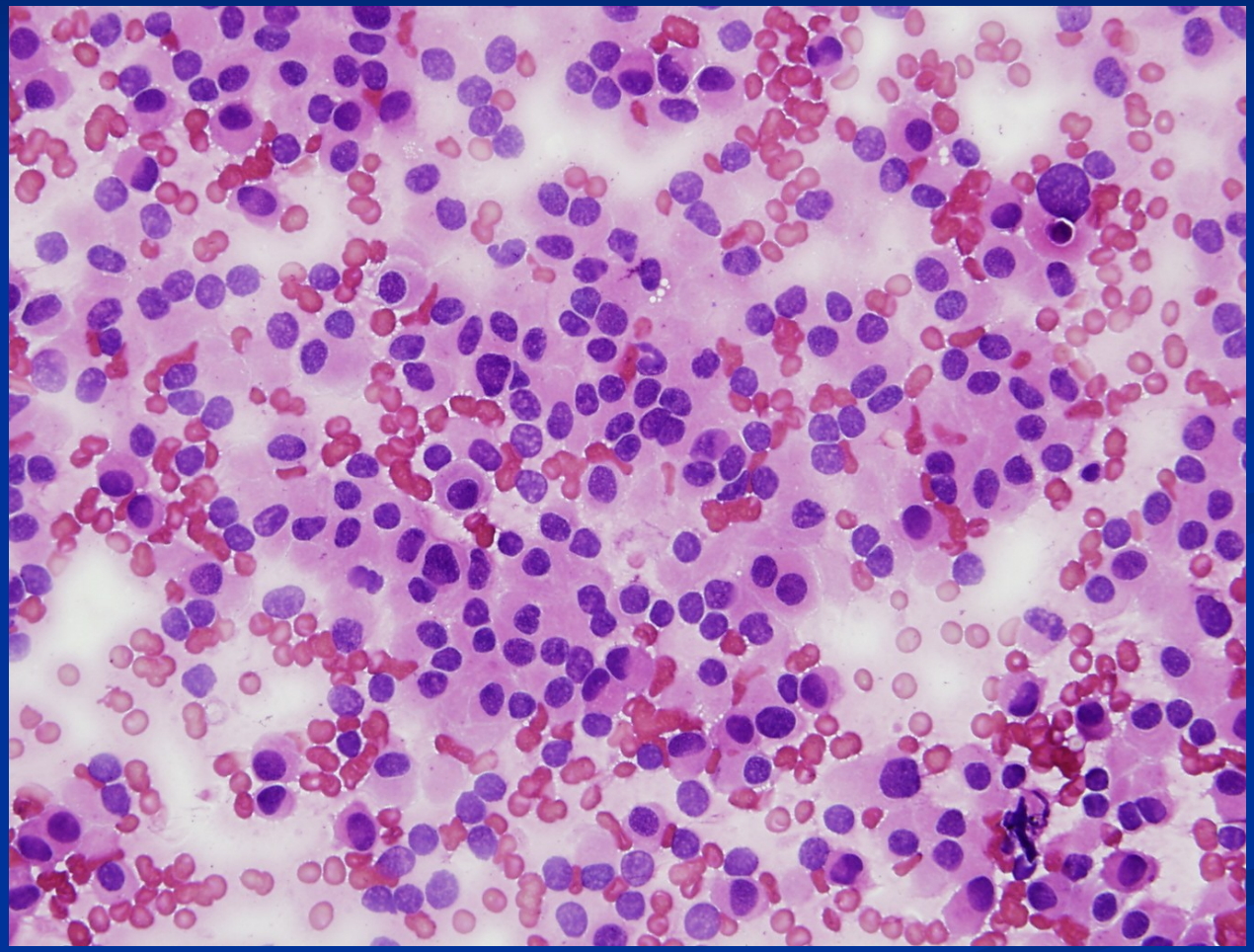
# Amyloid deposits in insulinoma



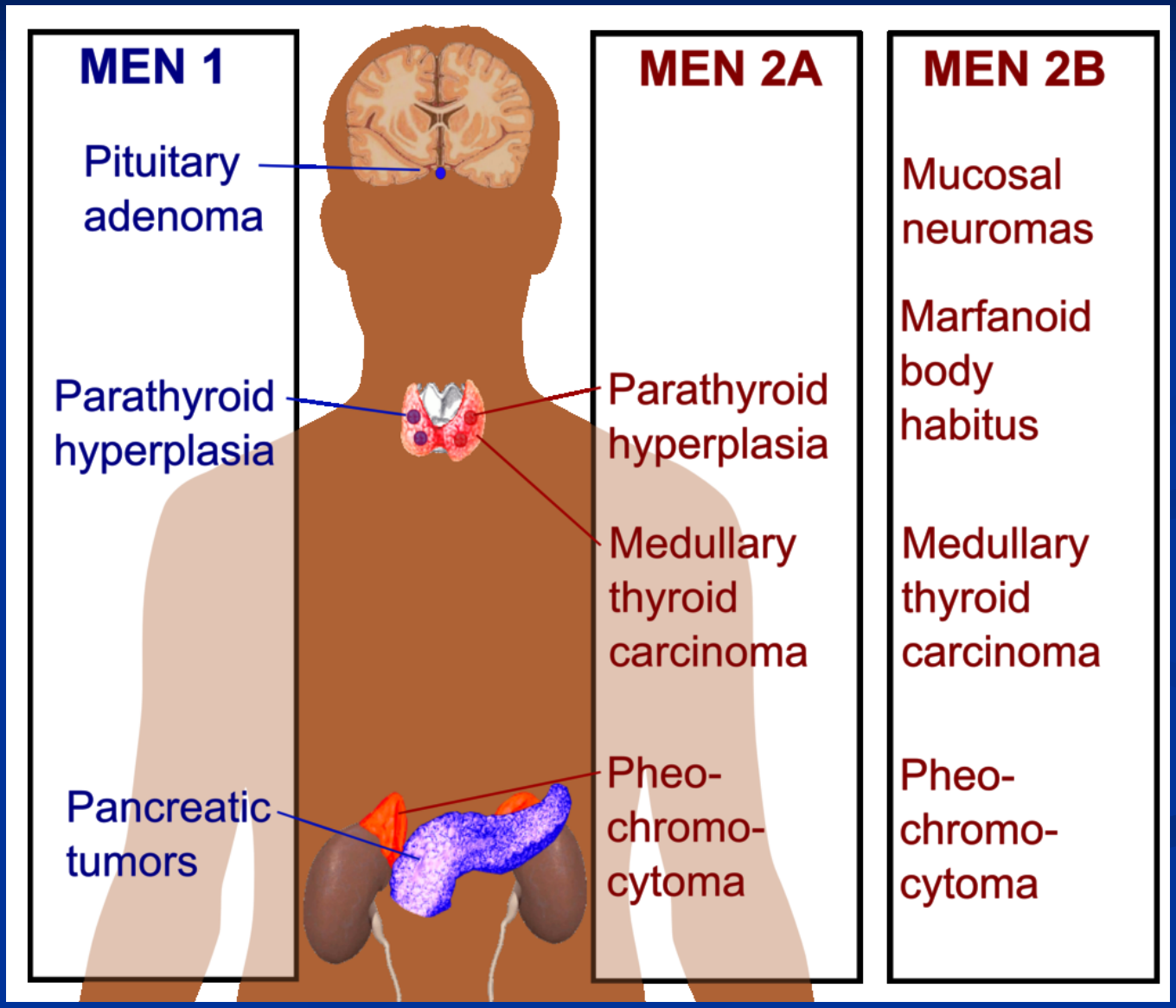


# FNAB

## cytology of neuroendocrine neoplasia of the pancreas.



# Multiple endocrine neoplasia (MEN) syndromes



# Diabetes mellitus

## (group of metabolic disorders sharing the common sign– hyperglycemia)

- **Type 1**
  - Immune mediated destruction of B cells
  - Autoimunne IDDM in genetically predisposed patients + environmental factors (viruses)
- **Type 2**
  - Insulin rezistent, with relative or absolute insulin deficiency
  - Genetics; obesity, life style
- **Genetically caused defects of B cells functions**
  - „maturity-onset diabetes of the young“ (mutations in different genes)
  - „mitochondrial diabetes“ (mutations in mtDNA; oxidative phosphorylation failures)
- **Genetically caused defects in insulin function**
  - Insulin gene, insulin receptor gene mutations, defects of proinsulin conversion
- **Disorders of exocrine pancreas**
  - Chronic pancreatitis
  - Pancreatectomy
  - Pancreatic neoplasia
  - Cystic fibrosis
  - Haemochromatosis

# Diabetes mellitus

## (group of metabolic disorders sharing the common sign– hyperglycemia)

- **Endokrinopathies**
  - Acromegaly
  - Cushing syndroma
  - Hyperthyreoidismus
  - Glucagonoma, feochromocytoma
- **Infections**
  - CMV
  - Coxackie virus B
- **Drugs**
  - Glucocorticoids, hormones of thyroid, alpha interferon, proteases inhibitors, thiazids, phenytoin, …
- **Genetic syndromas assoc. with DM**
  - Down syndroma
  - Klienefelter syndroma
  - Turner syndroma
- **Gestational DM**

| Differences between types of diabetes mellitus (DM: abnormal metabolic state characterised by glucose intolerance due to inadequate insulin action) | | |
|---|---|---|
| **Features** | **Type 1 (ketosis-prone, juvenile onset, insulin-dependent)** | **Type 2 (not ketosis-prone, maturity onset, non-insulin-dependent)** |
| **Age of onset** | Usually <20y | Usually <40y |
| **Proportion of all cases** | <10 % | >90% |
| **Type of onset** | Abrupt (acute or subacute) | Gradual |
| **Etiological factors** | Possible viral/autoimmune, resulting in destruction of islet cells | Obesity associated insulin resistence |
| **HLA asocciation** | Yes (=genetic predisposition in DM) | No |
| **Insulin antibodies** | Yes | No |
| **Body weight at onset** | Normal or thin, obesity uncommon | Majority are obese (80%) |
| **Endogenous insulin production** | Decreased (little or none) | Variable (above or below normal) |
| **Ketoacidosis** | May occur | Rare |
| **Treatment** | Insulin, diet, exercise | Diet, oral hypoglycemic agents, exercise, insulin, and weight control |

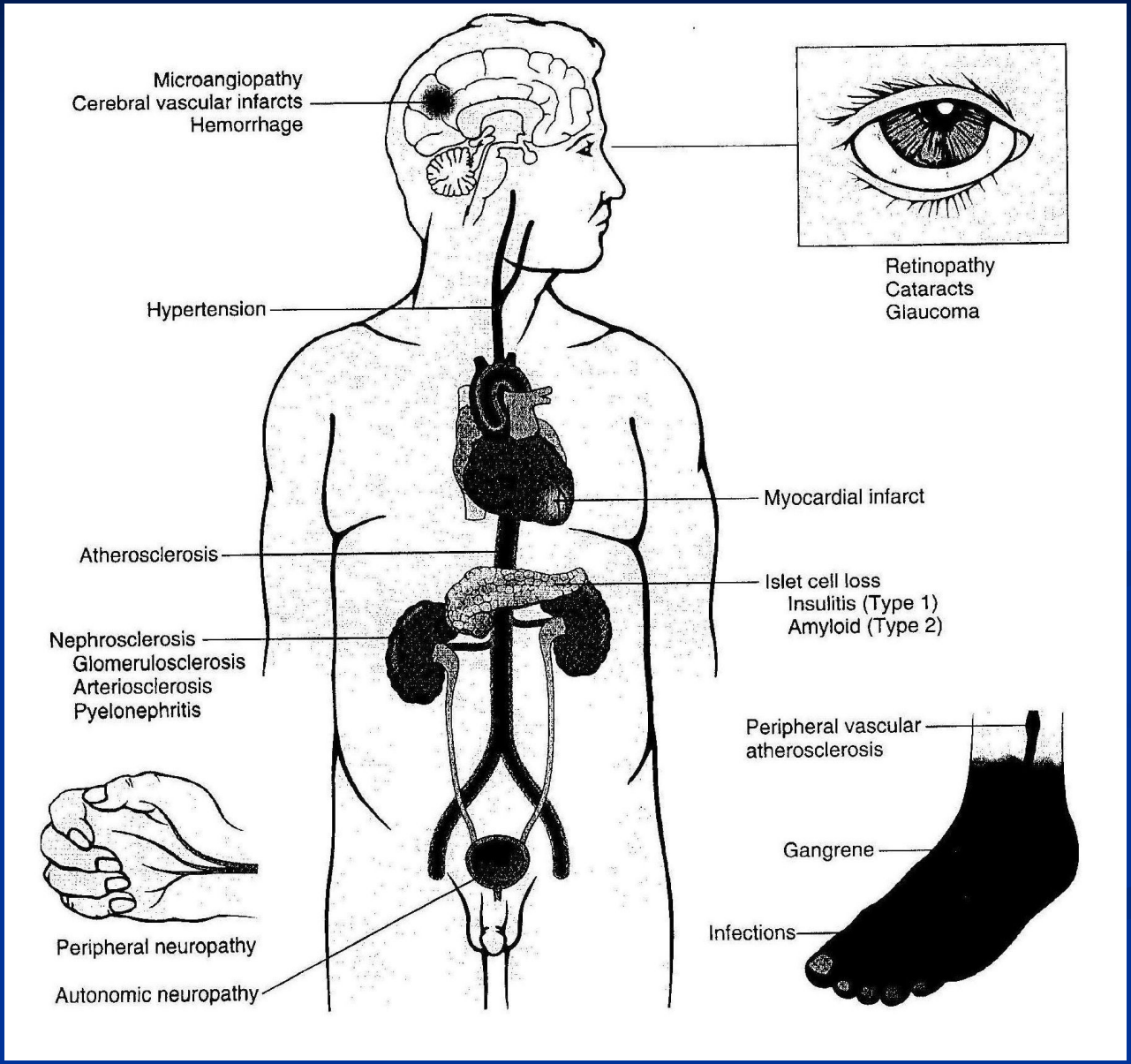
| Risk factors for type 1 and type 2 diabetes mellitus |
| --- |
| **Type 1 DM risk factors** |
| Type 1 DM in a first-degree relative (sibling or parents) |
| **Type 2 DM risk factors** |
| Positive family history |
| Ethnic origin (black, native americans, hispanic, asian american, pacific islanders) |
| Obesity |
| Increasing age |
| Habitual physical inactivity, sedentary lifestyle |
| History of gestational DM |
| Other clinical conditions assoc. with insulin resistence (e.g. polycystic ovary syndrome) |
| History of vasular diseases |
| Previously identified impaired fasting glucose or impaired glucose tolerance |
| Hypertension |
| HDL cholesterol level <35mg/dL and/or triglyceride level ≥250mg/dL |
| Cigarette smoking |

# Cardinal clinical signs of DM at diagnosis

- Polyuria
- Polydipsia
- Polyphagia, excessive hunger (in type 1)
- Weight loss (in type 1)
- Recurrent blured vision
- Ketonuria (in type 1)
- Weakness, fatigue, dizziness
- Often asymptomatic (type 2)

| Complications of diabetes | |
|---|---|
| **Situation** | **Complication** |
| **Large blood vessels** | Accelerated arteriosclerosis leading to:<br>- Myocardial infarction<br>- Cerebrovascular diseases<br>- Ischaemic limbs<br>- Responsible for 80 % of adult diabetic death |
| **Small blood vessels** | Endothelial cells and basal lamina damage.<br>Retinopathy (major cause of blindness), nephropathy |
| **Peripheral nerve** | Diabetic neuropathy (v.s. due to disease of small vessels supplying the nerves) |
| **Neutrophils** | Susceptibility to infection |
| **Pregnancy** | Pre-eclamptic toxaemia<br>Large babies<br>Neonatal hypoglycamia |
| **Skin** | Gangrene of extremities<br>Soft tissue lesions (Granuloma annulare, necrobiosis lipoidica) |

# Complications of diabetes.



*Thank you for your attention…*