Pathology of the endocrine system.

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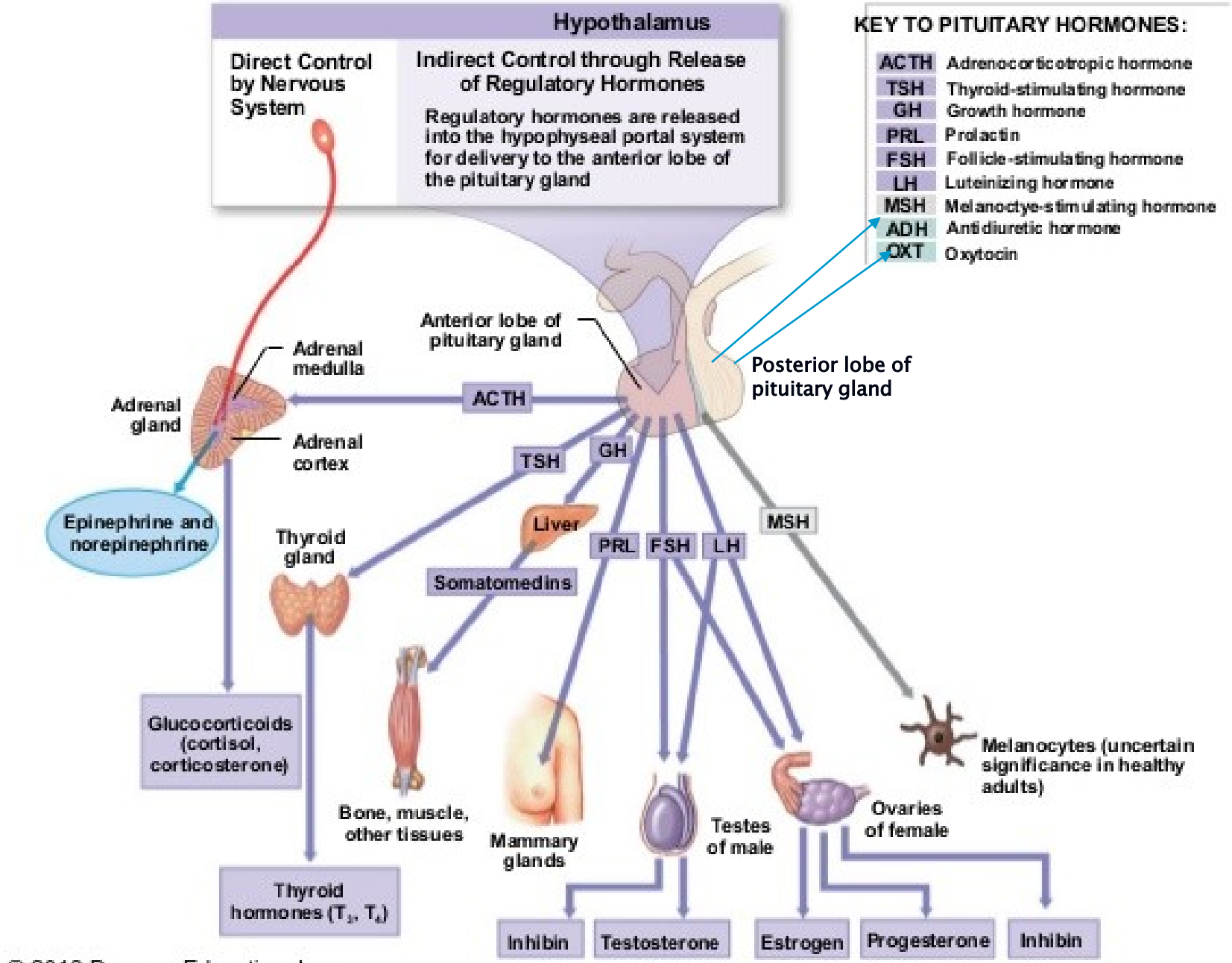

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Pathological basis of endocrine signs and symptoms	
Sign or symptom	**Pathological basis**
Hormone excess (hyperfunction)	Endocrine gland hyperplasia cause by increased trophic stimulus to secretion Functioning neoplasm of endocrine gland
Hormone deficiency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

Pituitary

Adenohypophysis

Hypofunction

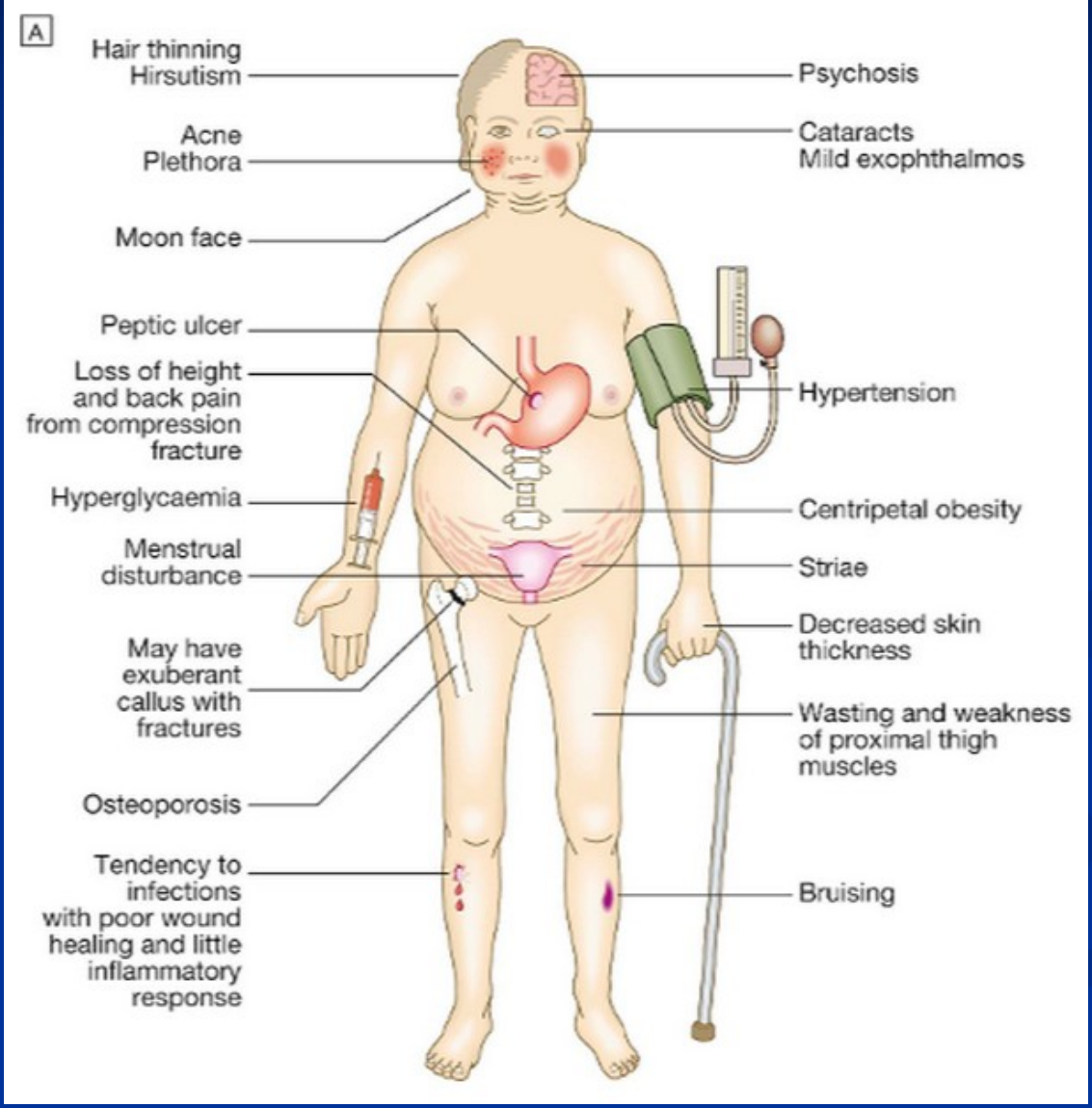
- Due to destruction by tumor or compression; due to hypothalamic reasons
- Due to inflammation (autoimmune); due to genetic abnormalities of hormone synthesis
- Due to ischaemic necrosis, radiation damage or surgical ablation
- Leads to secondary hypofunction of adenohypophyseal dependent endocrine glands (atrophy of gonads, hypothyreosis, hypocorticalism,…)

Hyperfunction

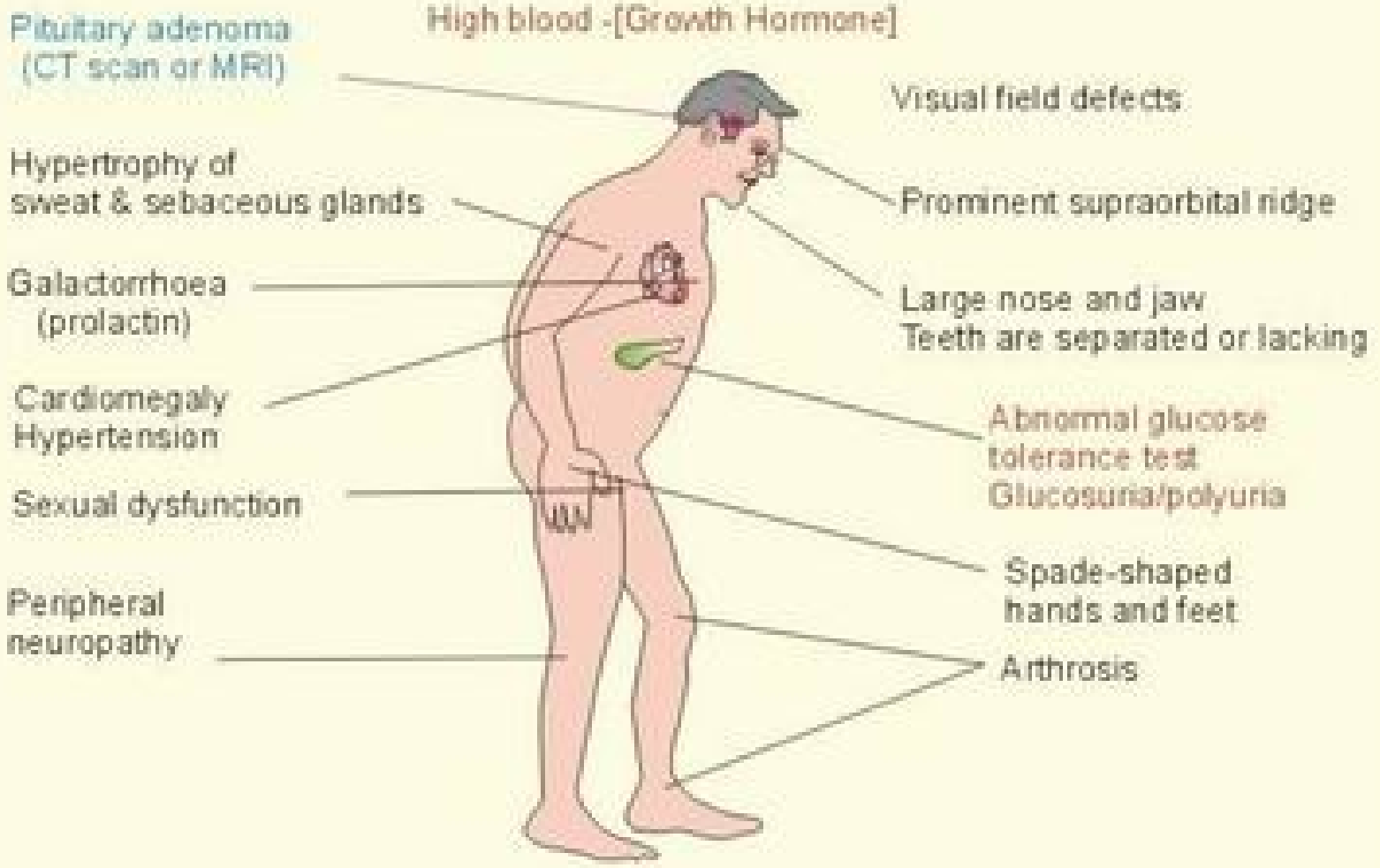
- in adenomas, hyperplasias, due to hypothalamic reasons

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

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,..)
  - 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**

Adrenals

- **Medulla**
- Production of catecholamins (adrenalin, noradrenalin)
- **Tumors:**

- Pheochromocytoma

(symptoms due to excess catecholamine secretion (secondary hypertension with ↑risk of cerebral bleeding), sweating)

- Neuroblastoma

(tumor of children, malignant)

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)

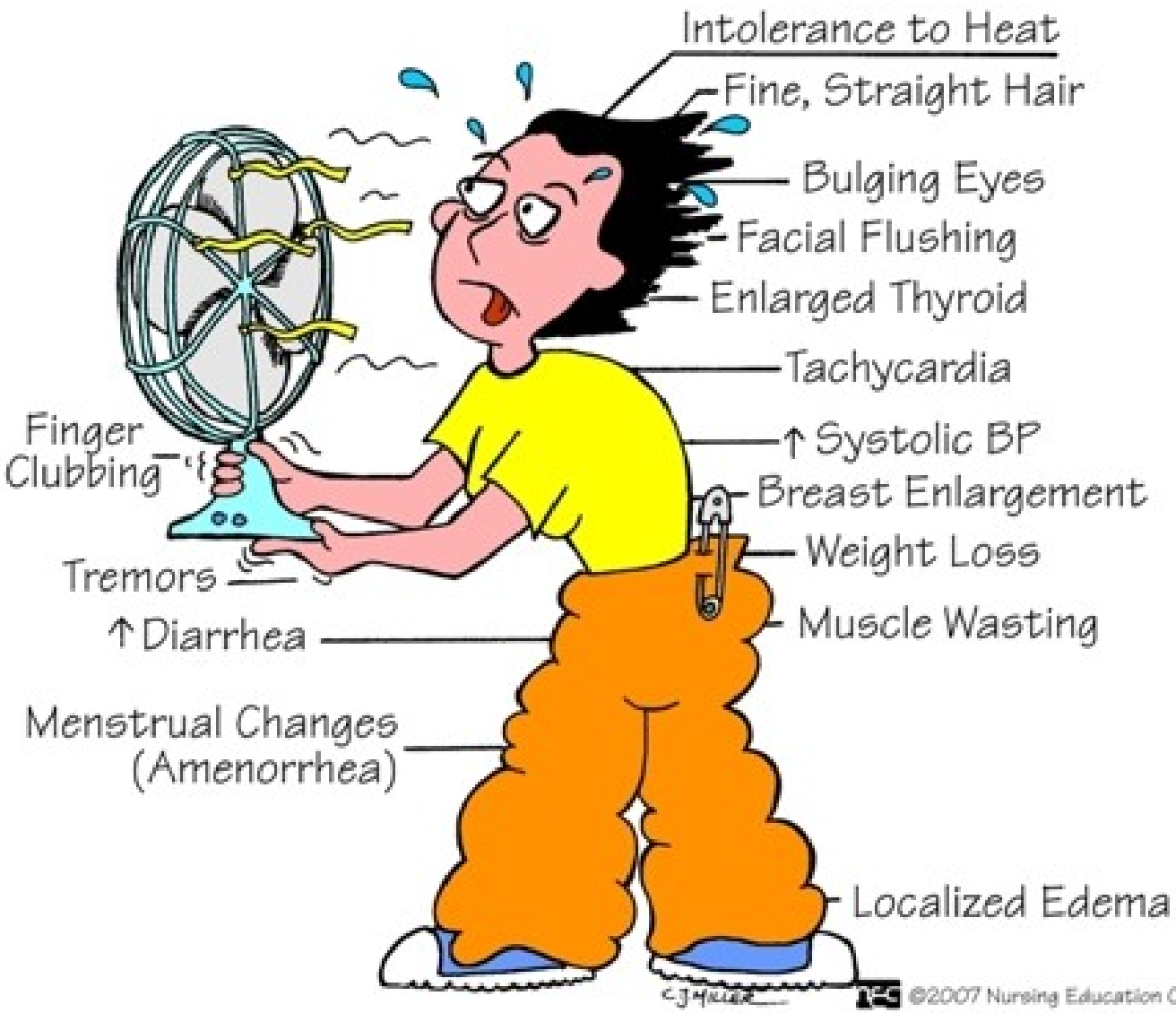
- **Hypofunction**
- Caused by autoimmune adrenalitis, tbc, necrosis of adrenals in sepsis, destruction by tumors,…
- Weight loss, lethargy, hypotension, pigmentation, hyponatraemia

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)

HYPERTHYROIDISM



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HYPOTHYROIDISM

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Goitre
(enlargement of the whole gland)

- **Parenchymatous goitre *vs* colloid goitre**
- **Diffuse vs nodular goitre**

- **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

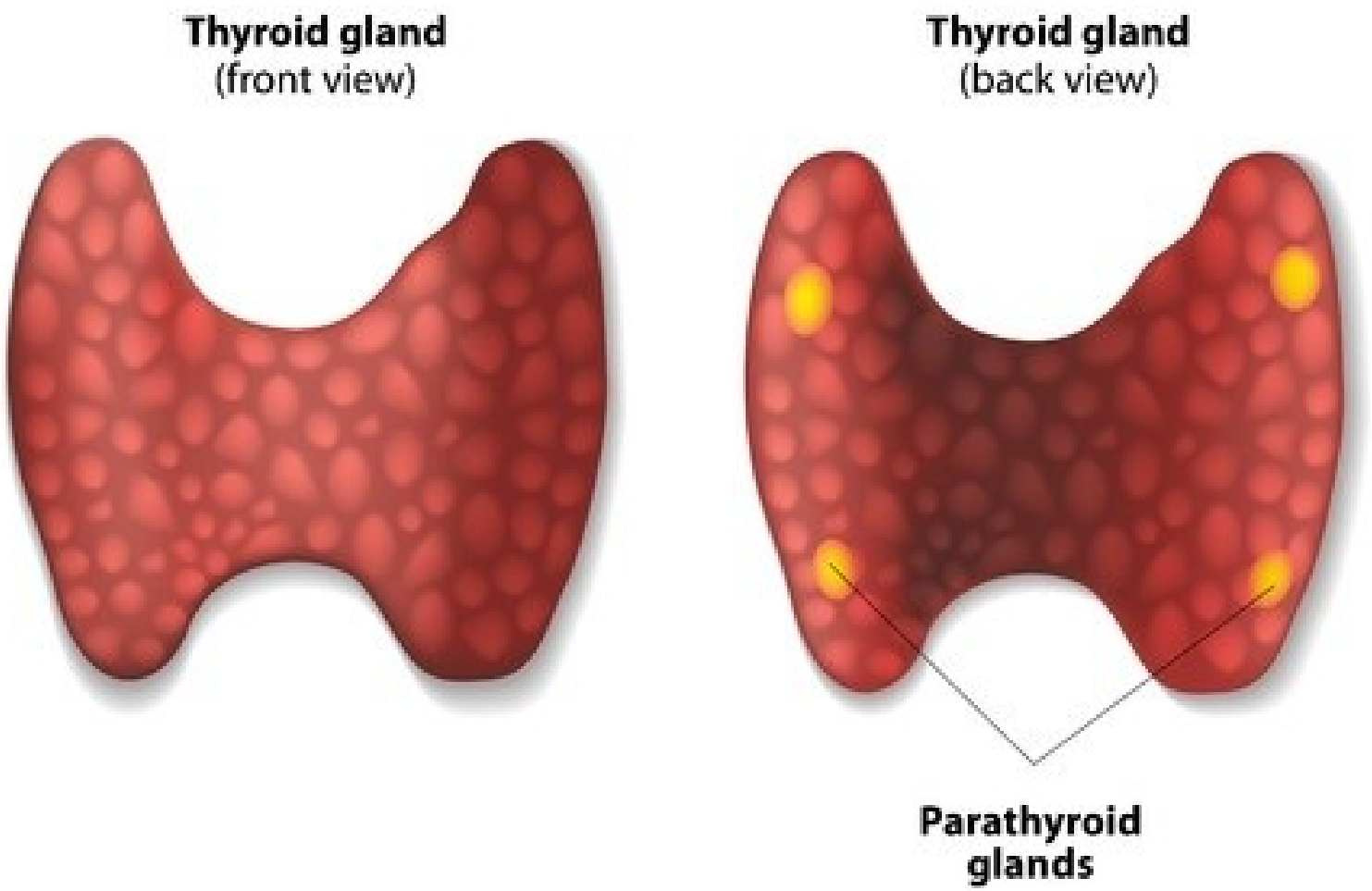
- **Benign**
  - **Follicular adenoma**

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

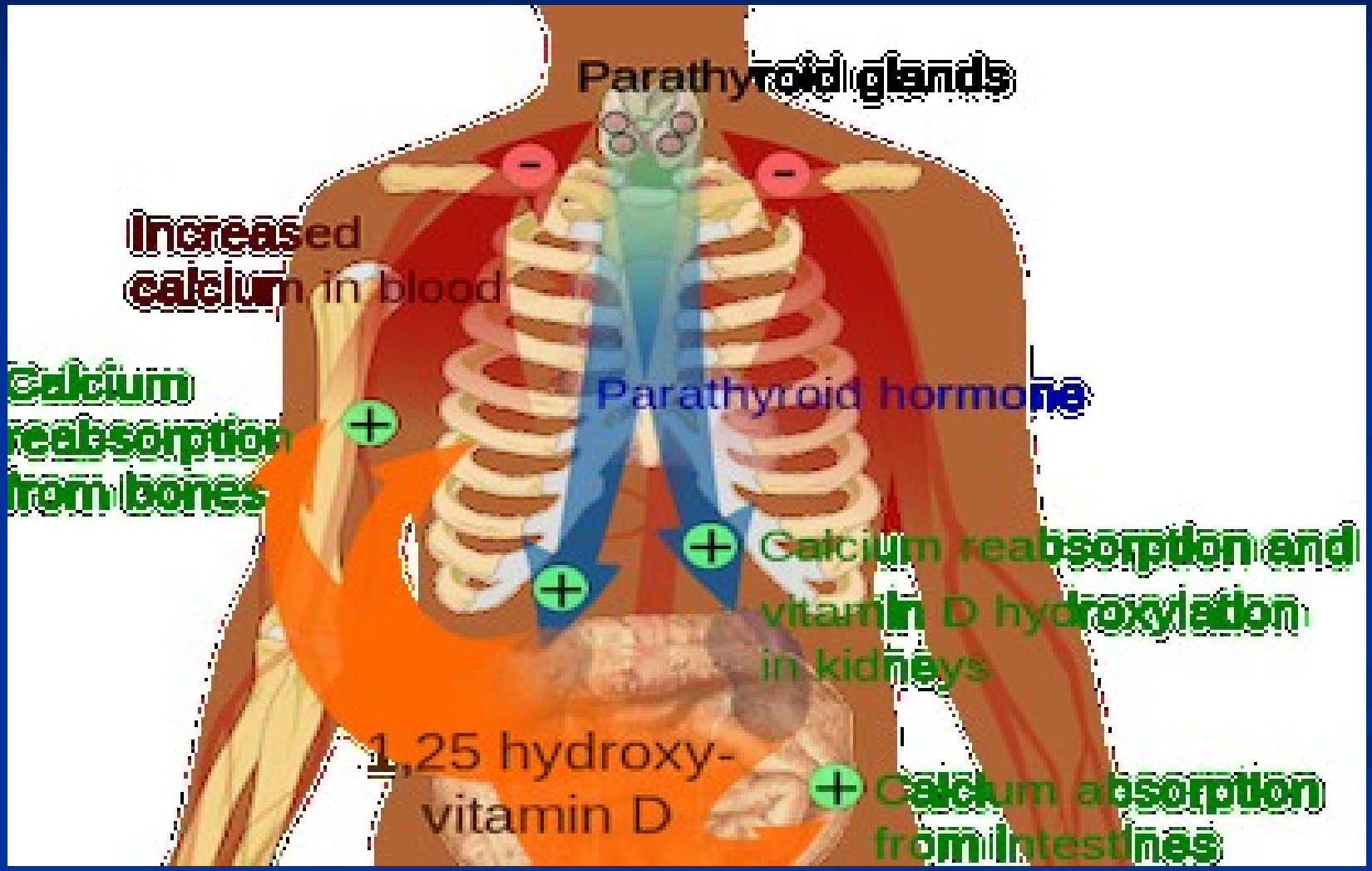
    (lymphoma (usually non-Hodgkin´s lymphomas of B-cell type, variable prognosis)

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

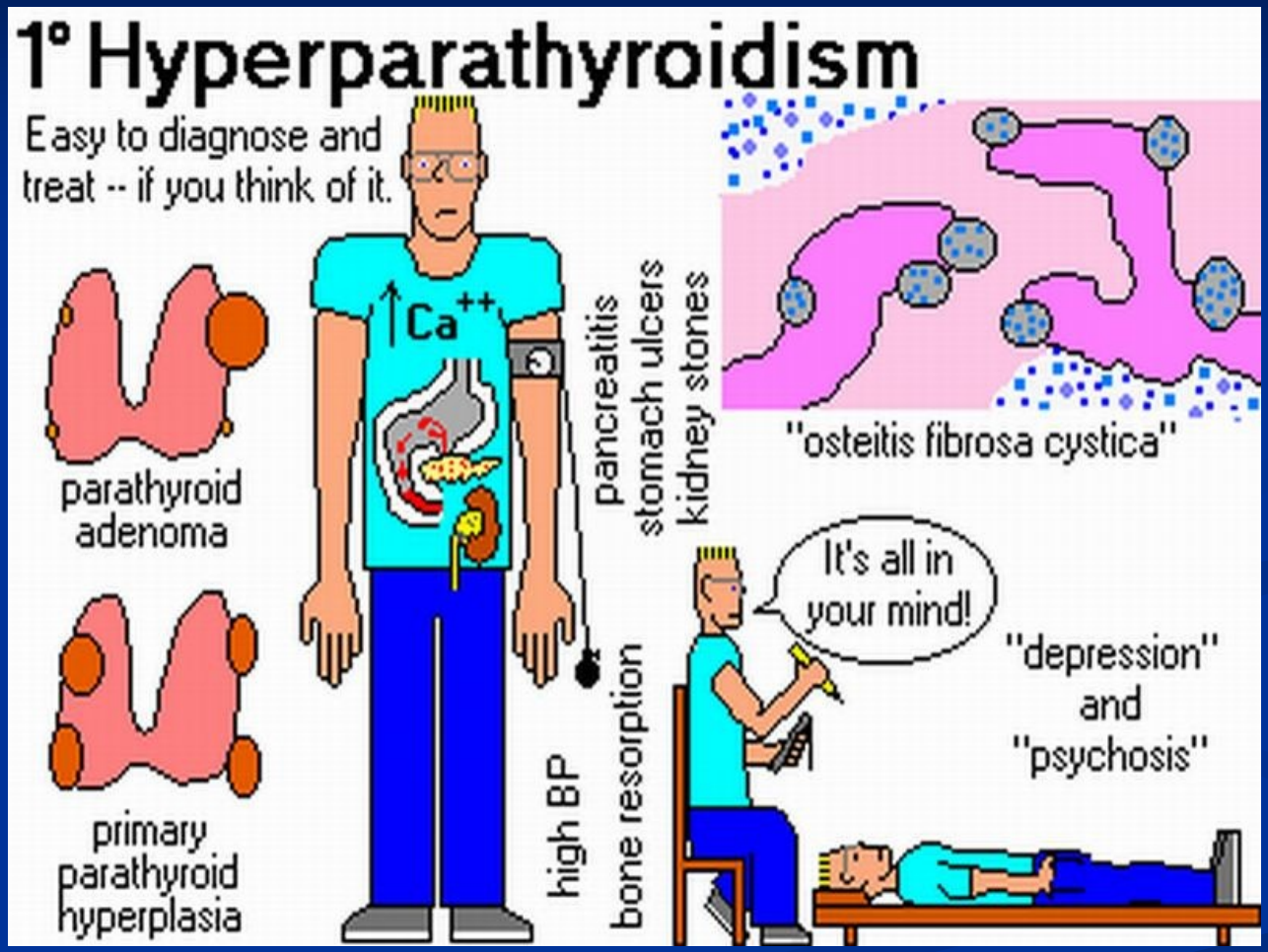
THYROID AND PARATHYROID



Parathyroid



Primary



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

Hypoparathyreoidism

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

- **Caused by:**
  - Removal of or damage of the glands during thyreoidectomy
  - Idiopathic
  - Congenital deficiency

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

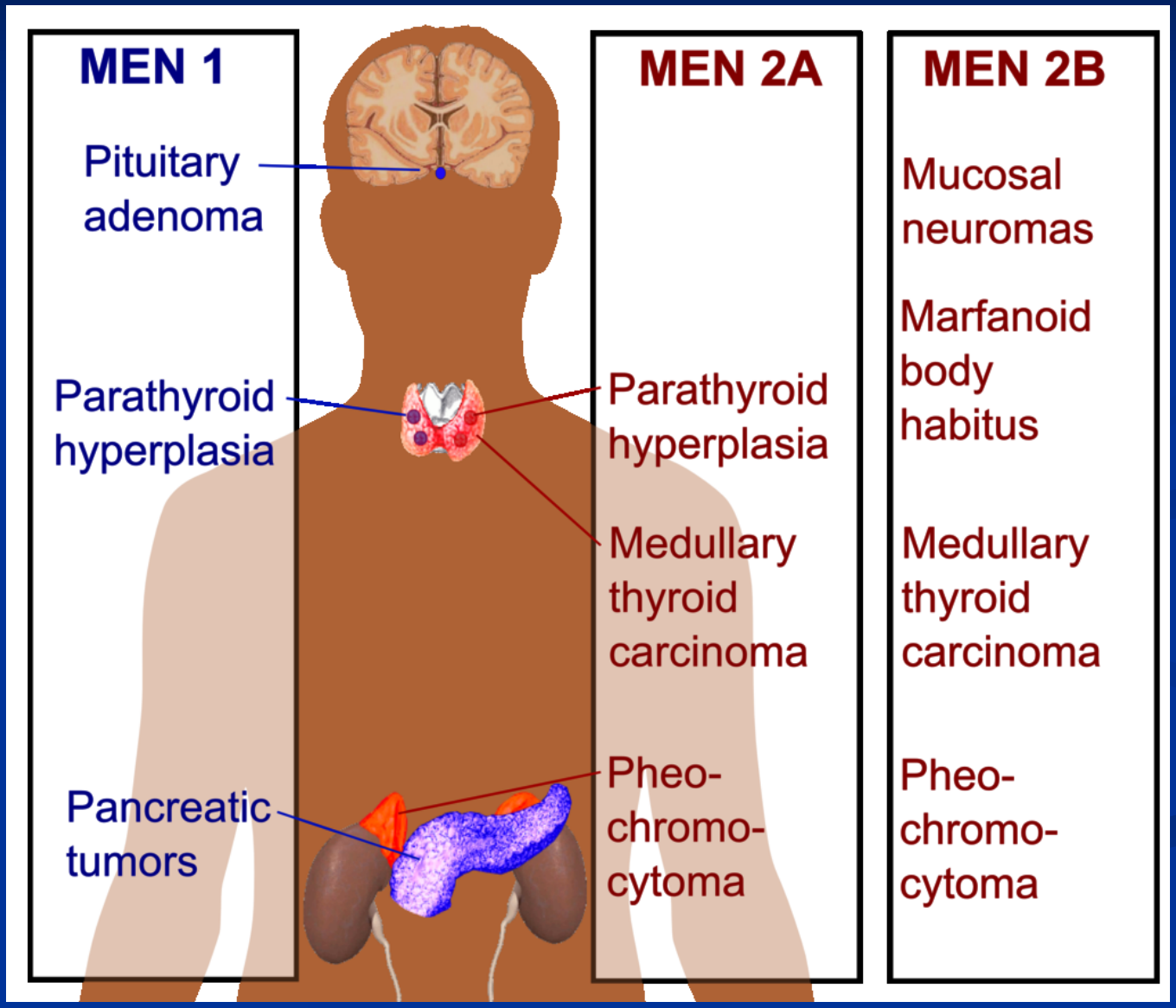
Endocrine pancreas: tumors – islet cell tumors

- Less common than pancreatic adenocarcinoma
- Present with endocrine effects and may 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

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

Multiple endocrine neoplasia (MEN) syndromes



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

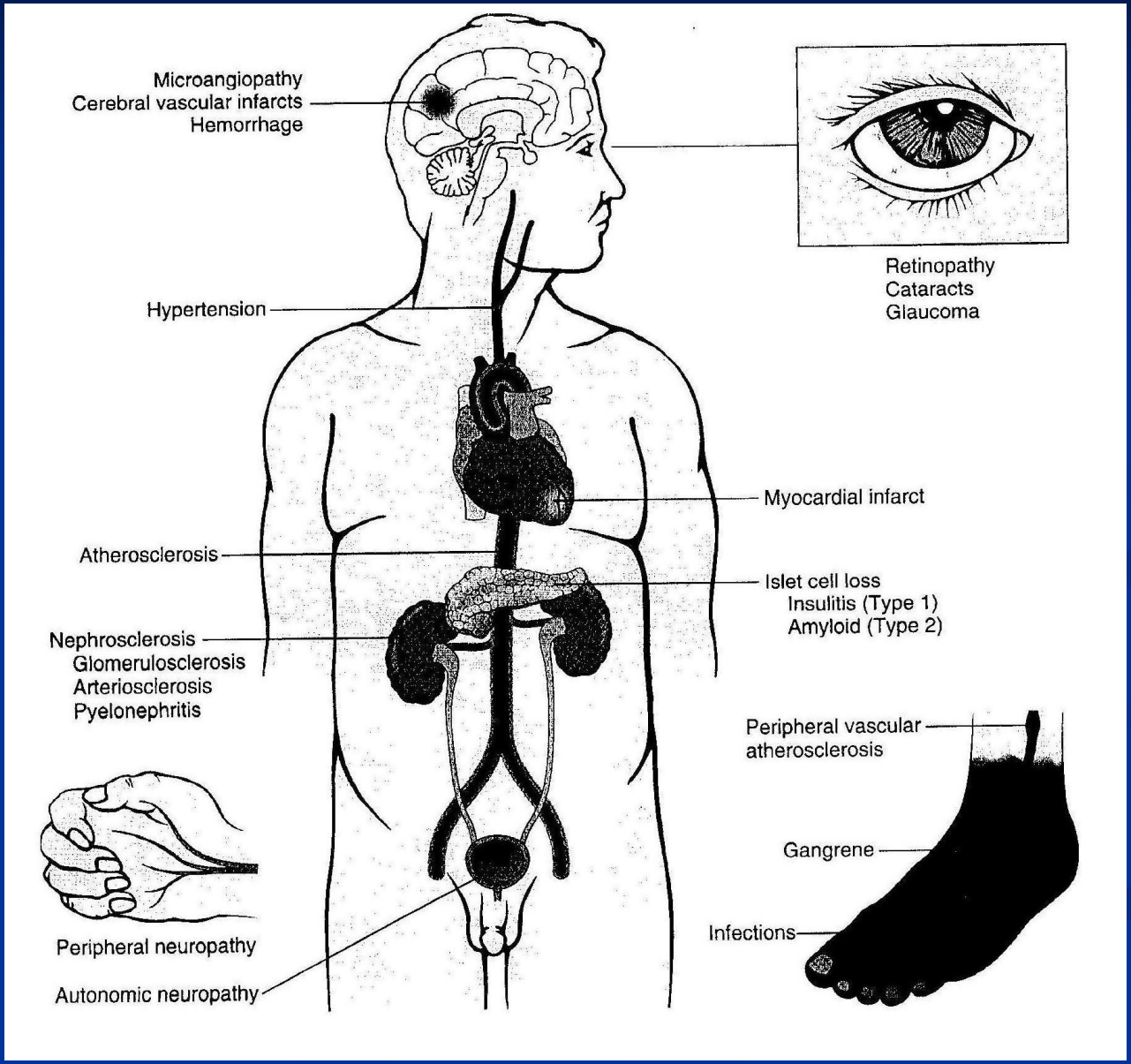
Risk factors for type 1 and type 2 diabetes mellitus
Type 1 DM risk factors
Type 1 DM in a first-degree relative (sibling or parents)
Type 2 DM risk factors
Positive family history
Ethnic origin (black, native americans, hispanic, asian american, pacific islanders)
Obesity
Increasing age
Habitual physical 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: - Myocardial infarction - Cerebrovascular diseases - Ischaemic limbs - Responsible for 80 % of adult diabetic death
Small blood vessels	Endothelial cells and basal lamina damage. 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 Large babies Neonatal hypoglycamia
Skin	Gangrene of extremities Soft tissue lesions (Granuloma annulare, necrobiosis lipoidica)

Complications of diabetes.



Pathology of the skin

Pathological basis of dermatological signs	
Clinical signs	**Pathological basis**
Scaling	Parakeratosis
Erythema	Dilatation of skin vessels
Blisters	Separation of layers of the epidermis or epidermis from dermis
Bruising	Leakage of blood into dermis
Pigmentation	Increased aktivity of melanocytes Increased numbers of melanocytes Endogenous pigment, e.g. Ochronosis Exogenous pigment, e.g. tattoo
Plaques	Increase in epidermal and dermal thickness with cells
Macules	Dilated blood vessels Inflammatory cells Altered pigmentation
Papules	Inflammatory cells Oedema Tumor
Nodules	Epidermal, adnexal and dermal tumors Cysts
Rashes restricted to exposed areas	Photosensitivity Contact eczema
Nail abnormalities	Trauma to nail bed Psoriasis Fungi

Eczema

- a reaction pattern, not a single disease
- several causes
- varied clinical patterns
- histologically: early inflammation and spongiosis, later hyperkeratosis, parakeratosis

Common Eczema Triggers[7]

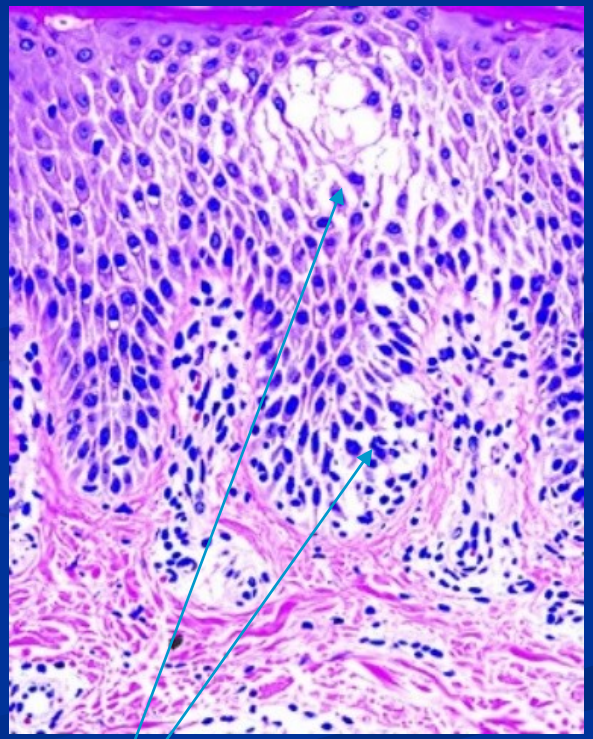
Irritants
- Soaps, detergents
- Disinfectants (chlorine)
- Contact with:
  - Juices from fresh fruits, meats, vegetables
  - Chemicals, fumes on the job

Allergens
- House dust mites
- Pets (cats > dogs)
- Pollens (seasonal)
- Molds
- Dandruff

Microbes
- Certain bacteria ***(Staphylococcusaureus)***
- Viruses
- Certain fungi

Others
- Hot or cold temperatures
  - Heat
  - Humidity
  - Perspiration from exercising
- Foods
- Stress
- Hormones

+ genetic factors



Spongiosis: intercellular oedema

Inflammatory disorders: infections

Viral

- human papillomavirus (verruca vulgaris, genital condyloma accuminatum)
- Pox virus (molluscum contagiosum)
- Herpes virus (herpes zoster: chickenpox, shingles; cold sores (HSV1) and genital herpes (HSV2)
- HIV (Kaposi´s sarcoma)

Bacterial

- Staphylococcal impetigo
- Streptococcal celullitis
- tbc of the skin
- leprosy

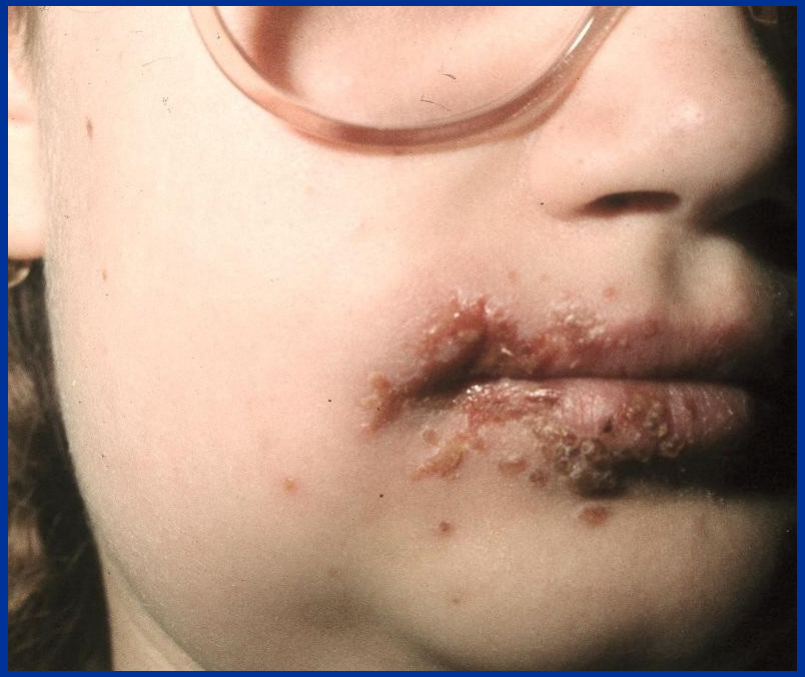
Fungal

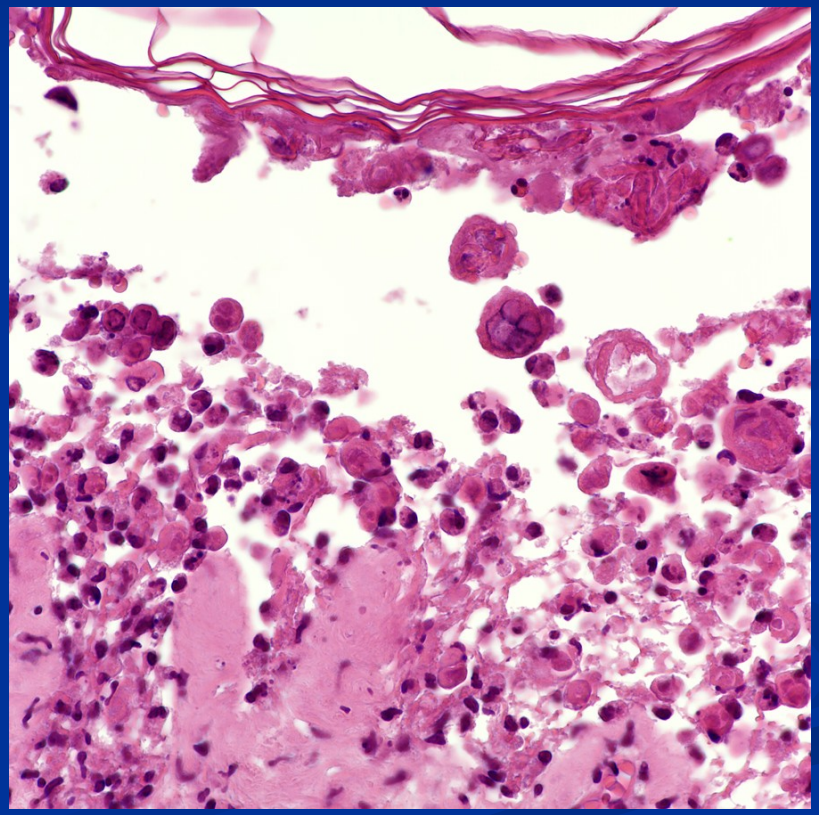
- Tines capitis, pedis, cruris…
- Candida albicans, Trychophyton species,….

Protozoal

- leishmaniasis, amoebiasis, trypanosomiasis

HSV infection

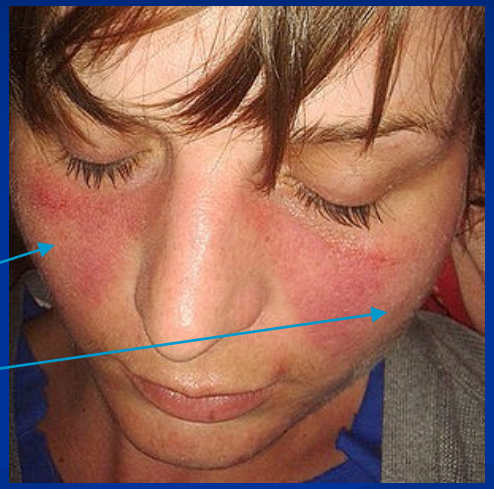




Non-infectious inflammatory diseases

Urticaria (hives, wheals)

- Reaction pattern, oedema =basic lesion
- Clinically itching, swelling
- Caused by plants and animal toxins, physical stimuli, various drugs

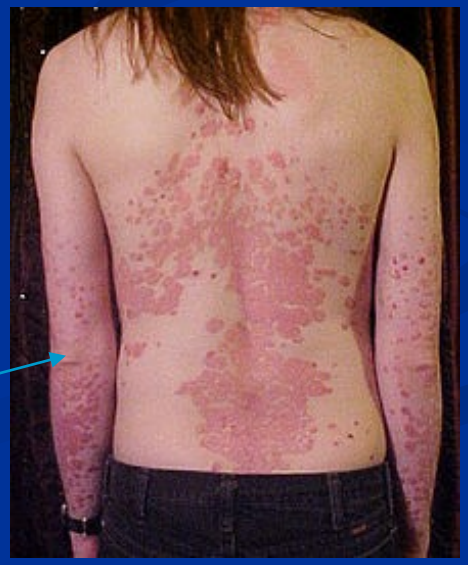


Lupus erythematosus

- Autoimmune disease affecting connective tissue
- Systemic form involves kidneys
- Skin lesions involve epidermis and adnexa

Lichen planus

- Polygonal itchy papules
- Band-like chronic inflammatory infiltrace
- Centred on dermo-epidermal junction

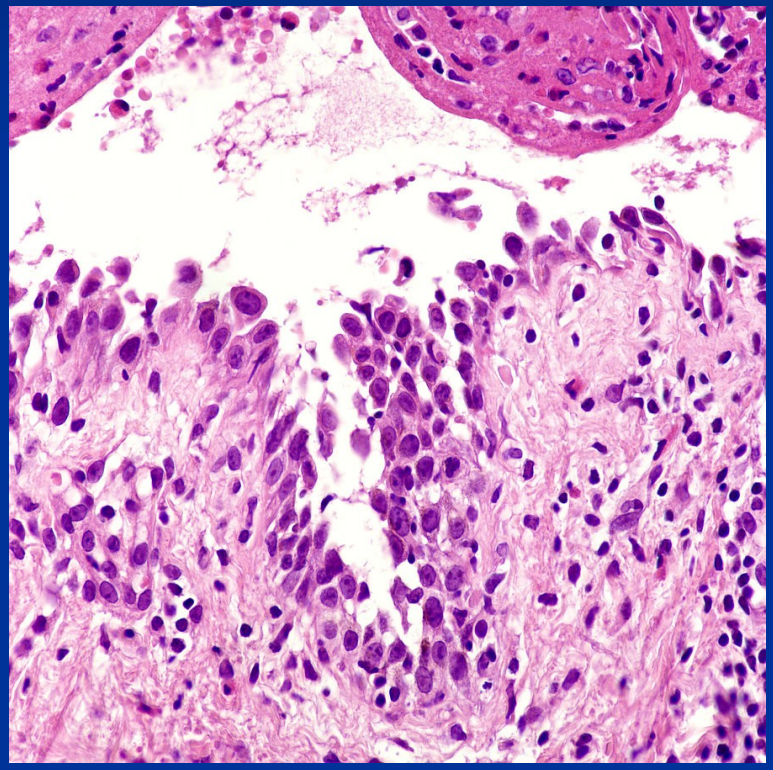


Psoriasis

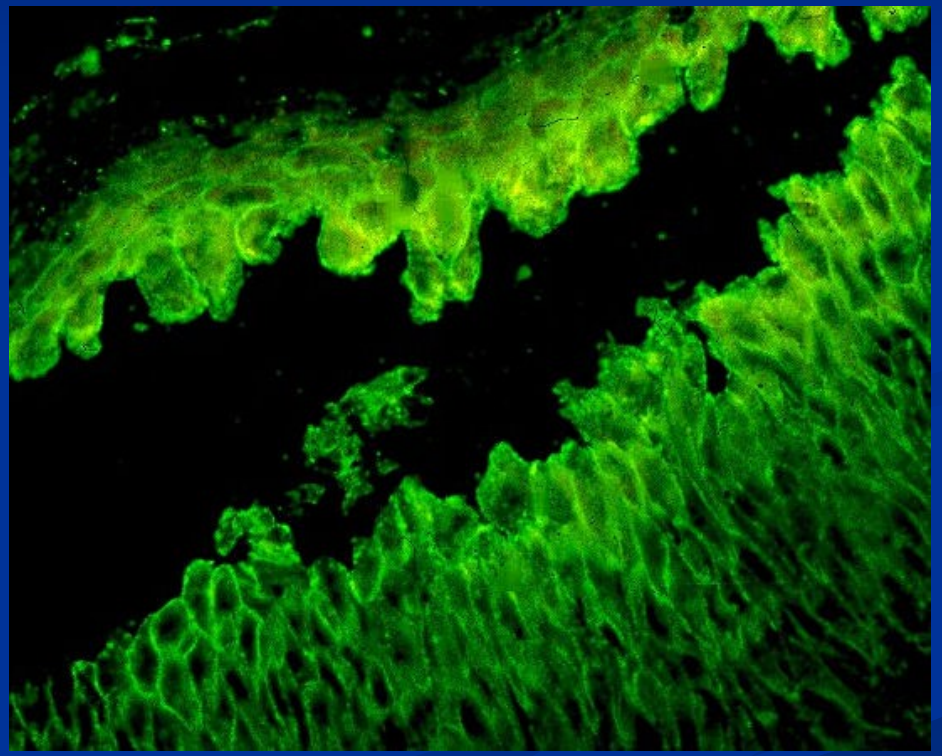
- Genetically determined disease
- Silvery-grey scales of parakeratosis
- Polymorphs enter epidermis but abscesses are sterile

Clinicopathological features of bullous disorders			
Disease	**Location of bullae**	**Immune reaction**	**Clinical feature**
Pemphigus	Intra-epidermal	IgG on intercellular junctions	High mortality
Pemphigoid	Subepidermal	IgG on basement membranes	Elderly patiens
Dermatitis herpetiformis	Subepidermal	IgG on papillary dermis	Associated with coeliac disease

Pemphigus vulgaris

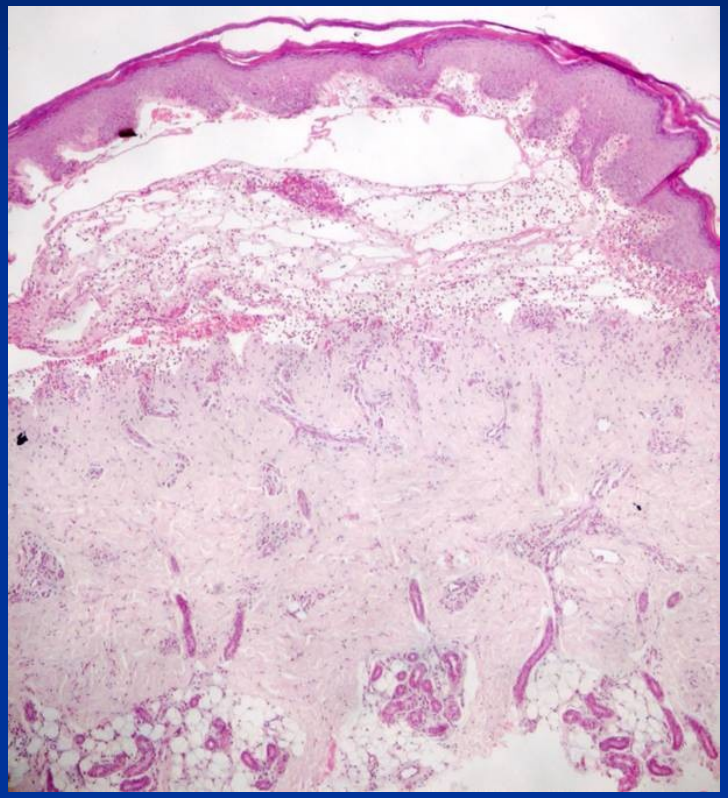


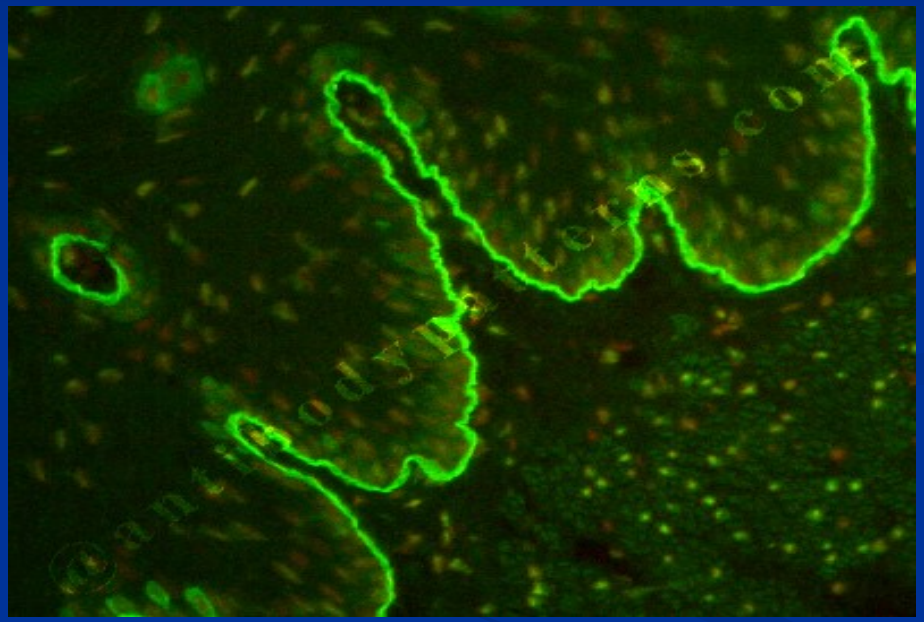
Suprabasal acantolysis, acantolytic bulla



IgG immunopositivita among keratinocytes

Pemphigoid





A – subepidermal bulla
B - linear, continuous deposition of IgG at the dermoepidermal basement membrane zone in perilesional skin

Epidermolysis bullosa

- Inherited disease, 30 types
- Mutations in genes coding specific keratins in the basal epithelial layer (intraepithelial bullae), collagens and other attachement proteins (subepithelial bullae)
- Extreme fragility of the skin
- Mucosae also affected

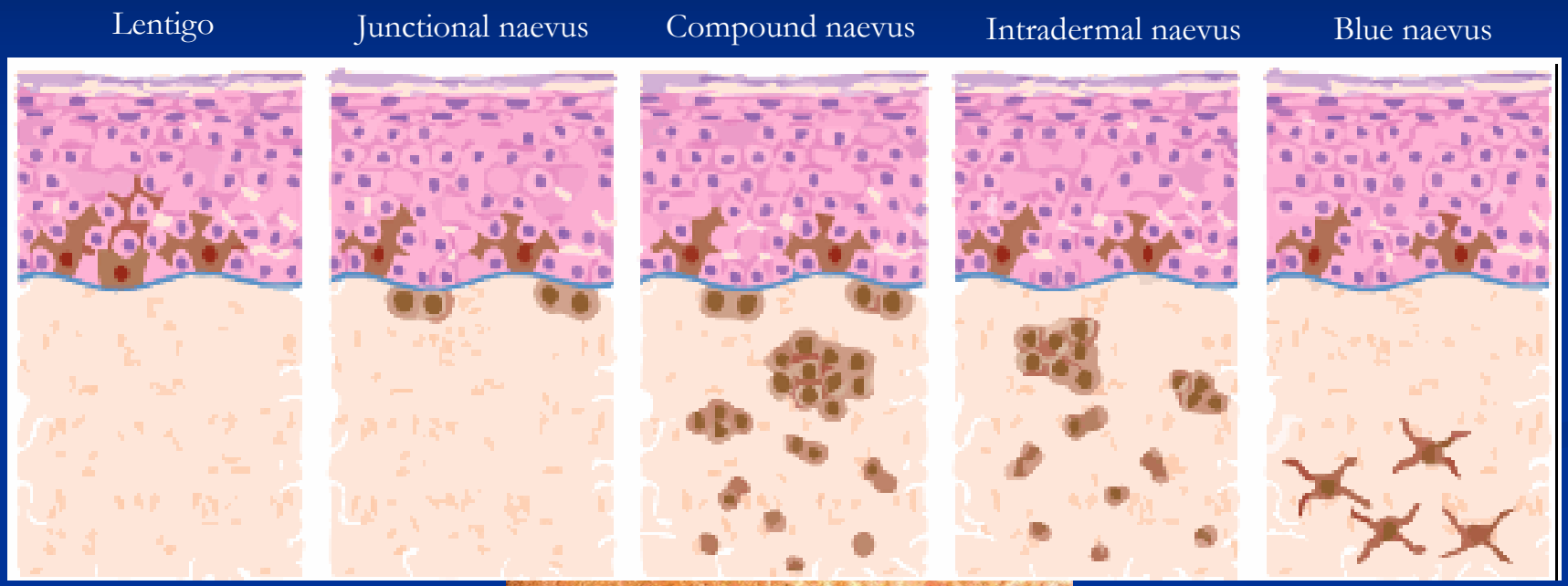
Benign epidermal neoplasms

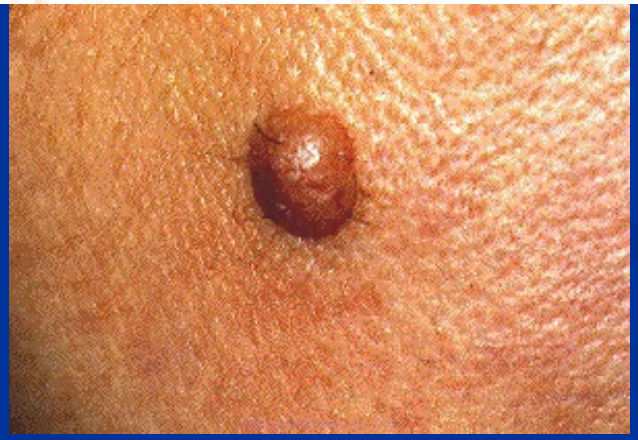
- **Fibroepithelial polyp**
- **Seborrhoic warts/keratosis (basal cell papiloma)**
- **Squamous cell papilloma (often HPV related)**
- **Cysts (epidermal and sebaceous)**

Malignant epidermal neoplasms

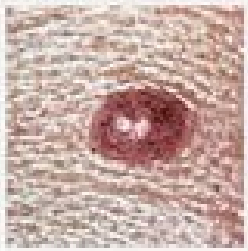
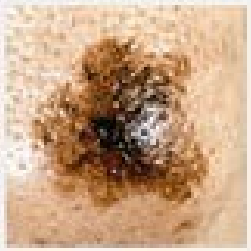
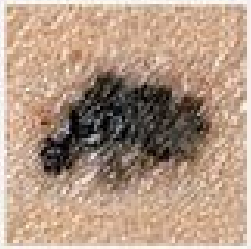
- **Basal cell carcinoma**
  - Very common skin malignancy
  - Related to chronic sun exposure, most commonly on face
  - Locally very invasive, metastasis exteremely rare
- **Squamous cell carcinoma**
  - **Malignant skin neoplasms**
  - Related to chronic sun exposure
  - Locally invasive, metastasis late
- **Actinic keratosis and Bowen´s disease** (=, in situ carcinomapremalignant lesion)

Benign melanocytic naevi





Malignant melanoma

Normal Mole	Melanoma	Sign	Characteristic
		Asymmetry	when half of the mole does not match the other half
		Border	when the border (edges) of the mole are ragged or irregular
		Color	when the color of the mole varies throughout
		Diameter	if the mole's diameter is larger than a pencil's eraser

Photographs Used By Permission: National Cancer Institute

Malignant melanoma

- **Tumor composed of malignant melanocytes**
- **Usually pigmented, but may be amelanotic**
- **Prognosis depends on stage of the disease**
- **Aetiologically associated with fair skin and sunburn**
- **Dysplastic naevus syndrome: familial tendency to melanomas, high risk developing melanomas**
- **Clinicopathological types:**

- Lentigo maligna
- Acral lentiginous melanoma
- Superficial spreading melanoma
- Nodular melanom