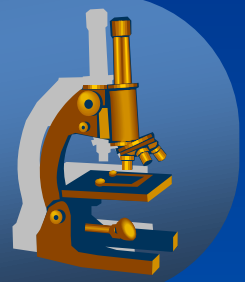
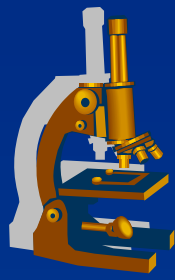
# General pathology III.



Inflammation II. (proliferative, granulomatous).

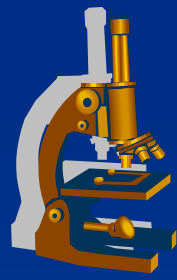
Progressive changes.

General oncology.



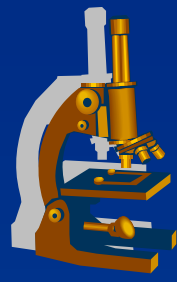
# *Inflammation II.*

# Proliferative inflammation



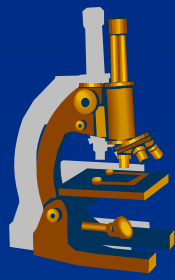
- Healing (reparation) of defects (wound, regressive changes, postinflammatory etc.) → granulation tissue → scar
- often pronounced in chronic inflammation
- primary proliferative inflammation uncommon (fibromatosis)
- reactive fibro/myofibroblastic lesions
  - ⇨ ***proliferation of myofibroblasts, occasionally forming tumour-like masses***
    - nodular fasciitis, myositisossificans – may be posttraumatic, often idiopathic

# Chronic inflammation



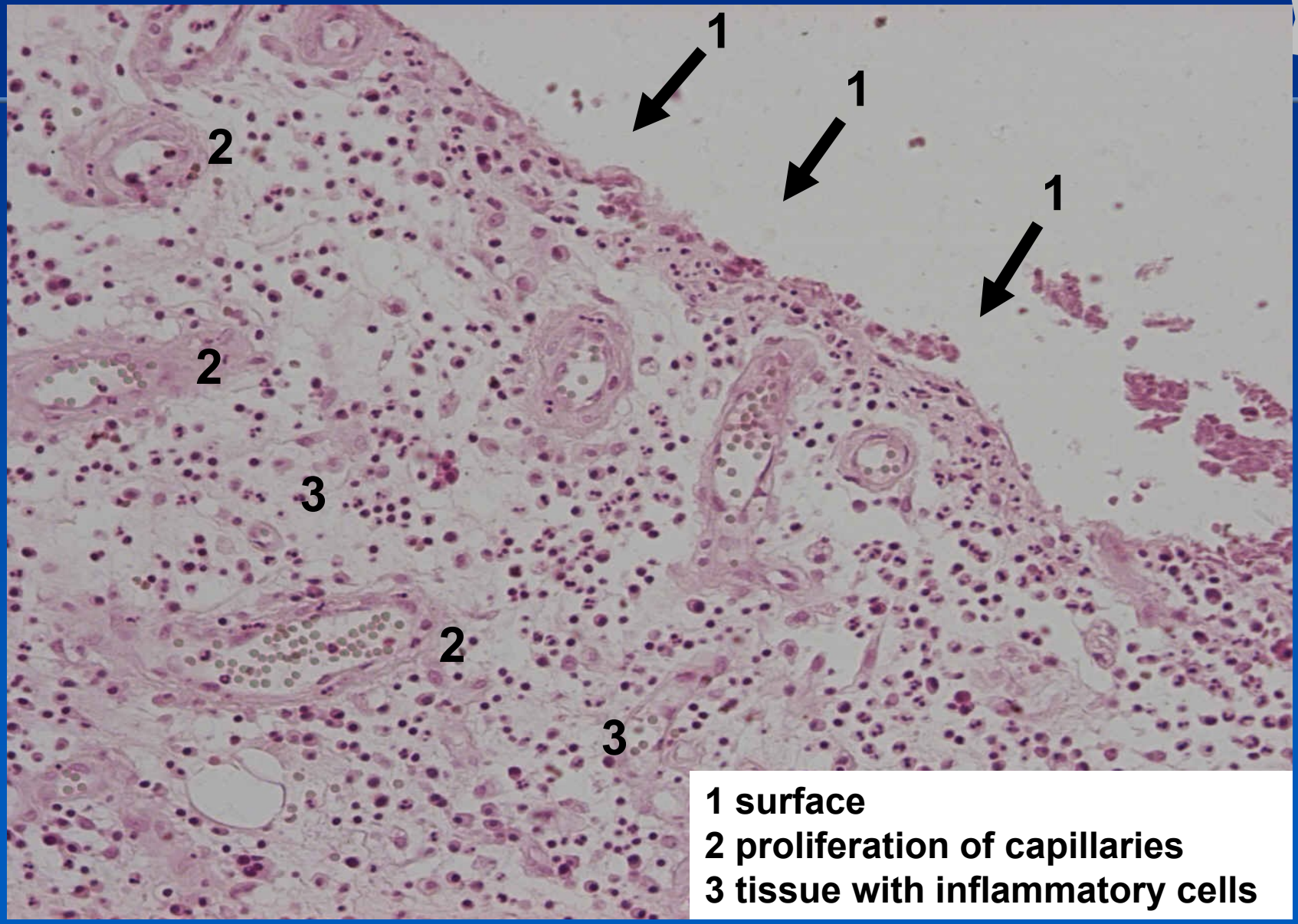
- prolonged duration
- tissue injury + inflammatory reaction + repair
- Causes: persistent infection, immune mediated inflammatory reaction, prolonged exposure to harmful agents (toxin)

# Granulation tissue



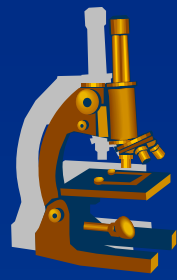
- Major repair instrument
- In:
  - *wound, fracture, ulcer, necrosis healing; thrombus, haematoma  organisation*
- Gross:
  - *soft red tissue, granular surface (capillary loops)*
- Micro:
  - *fibrin fibers*
  - *inflammatory reaction*
  - *fibroblasts, myofibroblasts*
  - *starting collagen fibers  production*
  - *proliferating capillaries – angiogenesis*
  - *later intercellular matrix + tissue remodeling, retraction – scar formation*

# Granulation tissue – inflammatory cells




1 surface
2 proliferation of capillaries
3 tissue with inflammatory cells

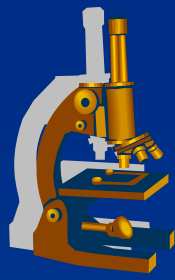
# Granulomatous inflammation



- distinctive pattern of chronic inflammation
- historical classification:
  - ⇨ *„non-specific“ infl.*
    - common general microscopic picture, i.e. purulent infl.
  - ⇨ *specific“*
    - micro typical for a specific cause

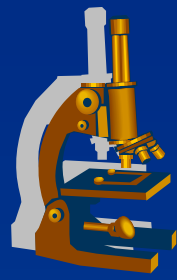
- aggregated macrophages unable to destroy cause → transformation into epithelioid and multinuclear cells → granuloma
- delayed type hypersensitivity (T-cells, macrophages, sometimes eosinophils)
- foreign body granuloma x immune granuloma

# Granulomatous inflammation



- **causes of granulomatous disease:**
  - ⇨ specific infections
    - mycobacteria (e.g. Tuberculosis, leprosy, atypical mycobacteria), many types of fungi, parasites…)
  - ⇨ foreign bodies (undigestible)
    - endogenous (keratin, necrotic bone, cholesterol crystals, urate …)
    - exogenous (e.g. suture material, silica, talc, asbestos,…)
  - ⇨ chemicals and drugs
    - beryllium, sulphonamides
  - ⇨ unknown ? - pathologic hypersensitive reaction to some common antigenes (combination of inborn and external factors)
    - Crohn´s disease, sarcoidosis, Wegener‘s granulomatosis
  - ⇨ stromal and lymph node reaction in some tumors (Hodgkin‘s malignant lymphoma)

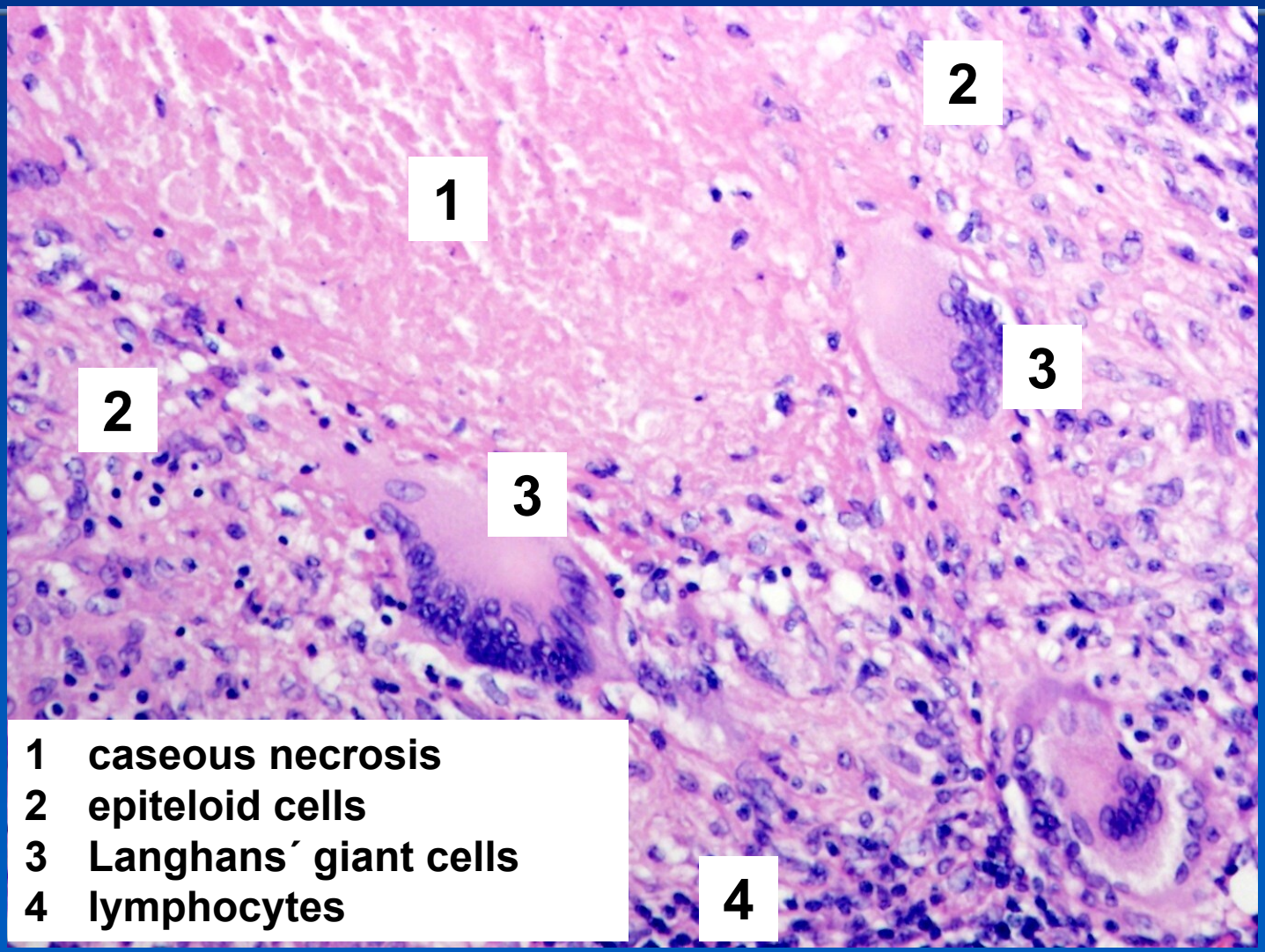
# Tuberculosis



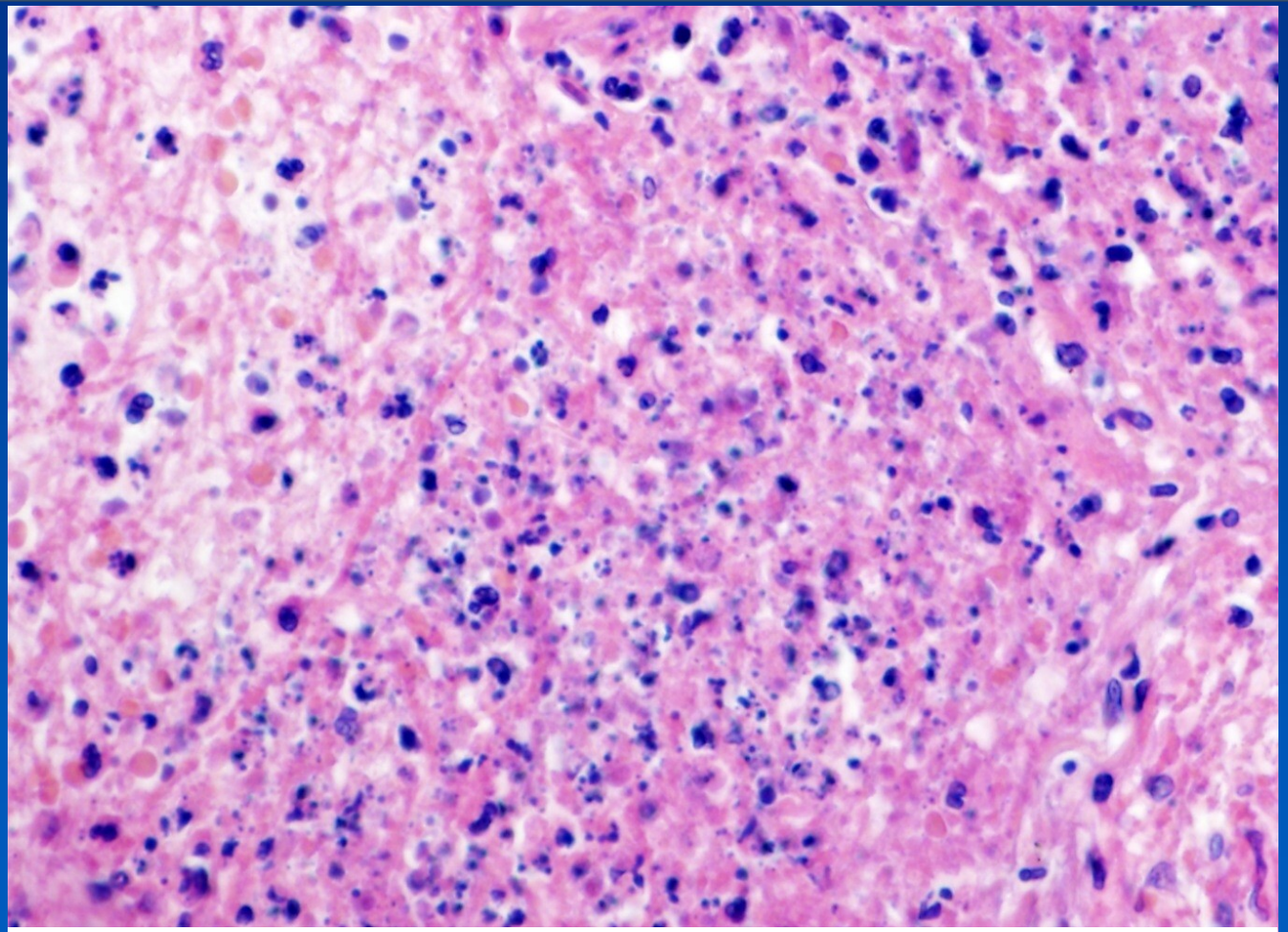
- **etiology**
  - *Mycobacterium tuberculosis*
    - Ziehl-Neelsen staining, acid-resistant bacteria , culture  or PCR detection

- **tuberculous granuloma - basic morphology:**
  - central caseous necrosis (basophilic nuclear fragments)
  - epithelioid macrophages
  - multinucleated Langhans‘ giant cells (fusion of macrophages)
  - rim of T-cells

# Tuberculous granuloma

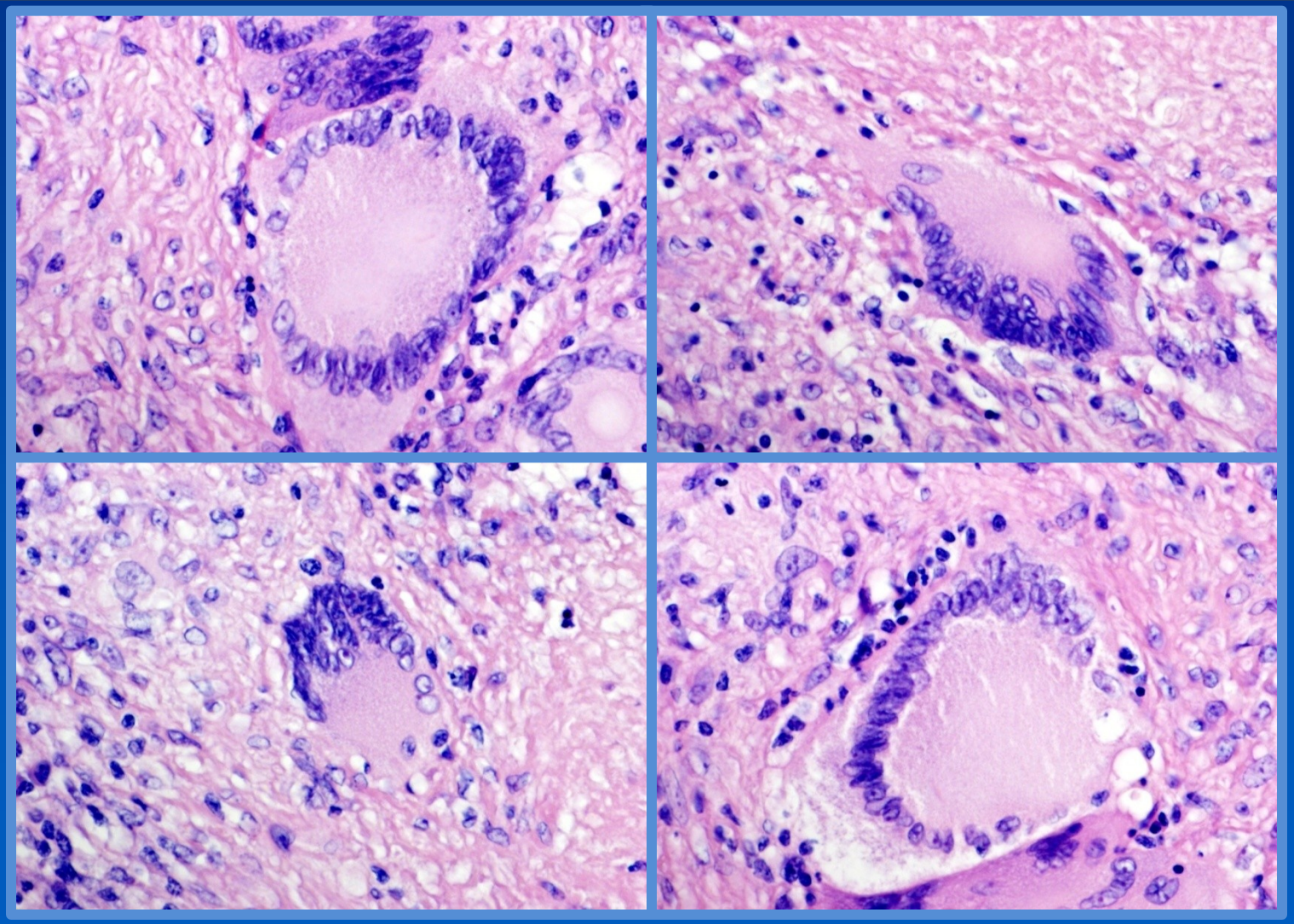


# caseous necrosis

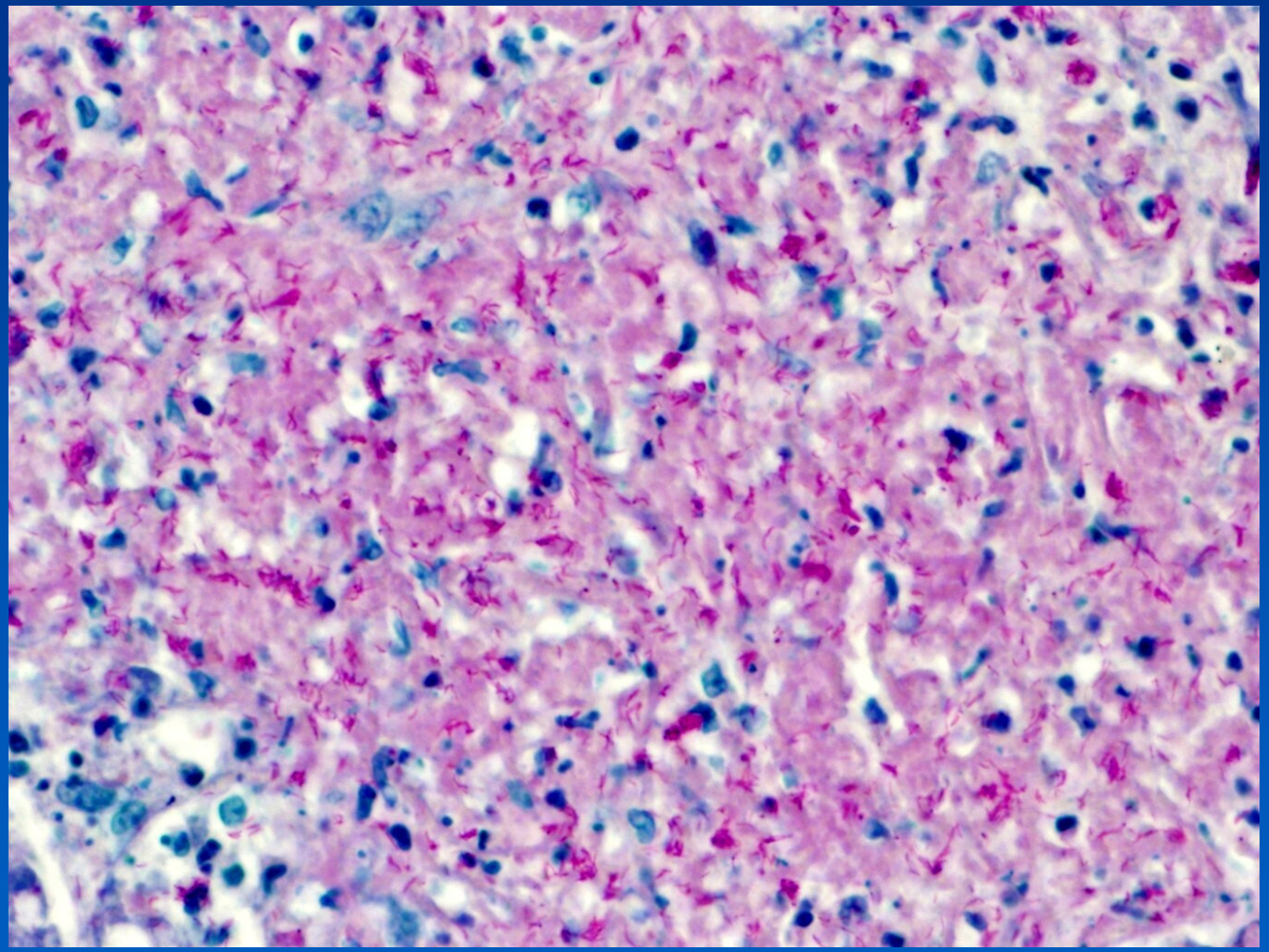


HE staining shows amorphous eosinophilic area stoppled by haematoxyphilic nuclear debris

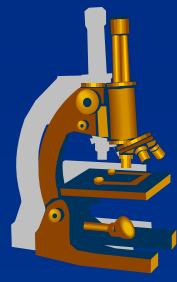
# Langhans´ giant cell



# Ziehl-Neelsen staining, acid-resistant bacteria

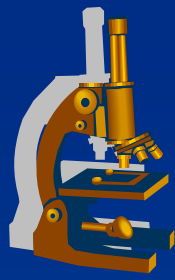


# TB - morphology



- TB exudate – serofibrinous exudate + macrophages with M.tbc – Orth cells
- TB granuloma (tubercle) - proliferative form
- caseification
- colliquation
- calcification

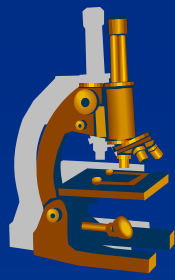
# Tuberculosis



- **Primary tuberculosis**
  - lungs usually first site of contact (GIT, skin)
  - Ghon complex – focus of primary infection , similar granulomas in lymph nodes draining the affected portion of lung
  - primary lession usually organise -> fibrocalcific nodule (tubercle bacilli may be still present) x complications

- **Secondary tuberculosis:** in previously sensitized host
  - mostly caused by reactivation of old primary infection (event. reinfection)
  - in lung - apical foci + cavitation, porogennous spread
  - isolated organ tb (renal, adrenal, meningeal, osteomyelitis, salpingitis
  - progression -> organism virulence x host sensitivity

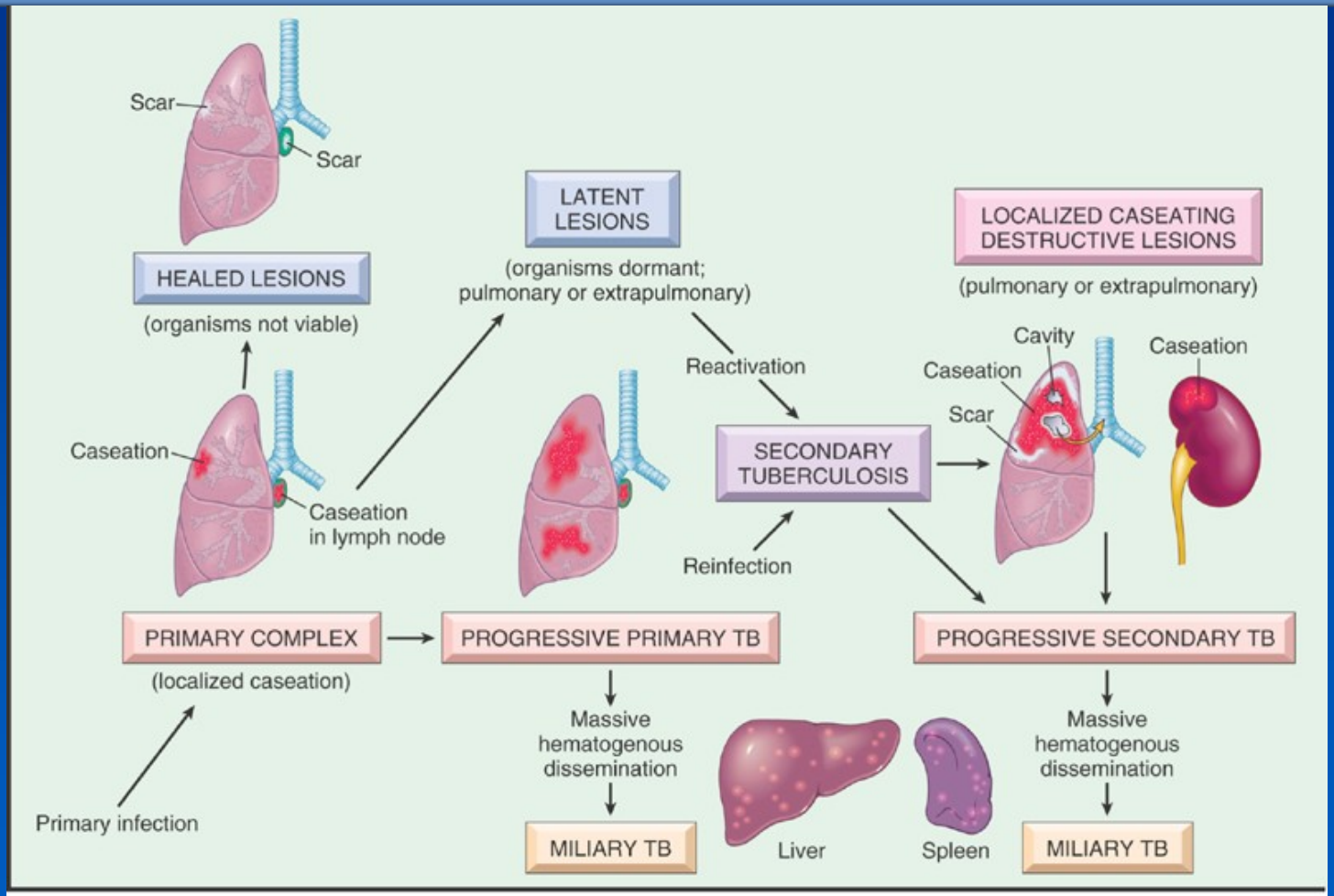
# Tuberculosis

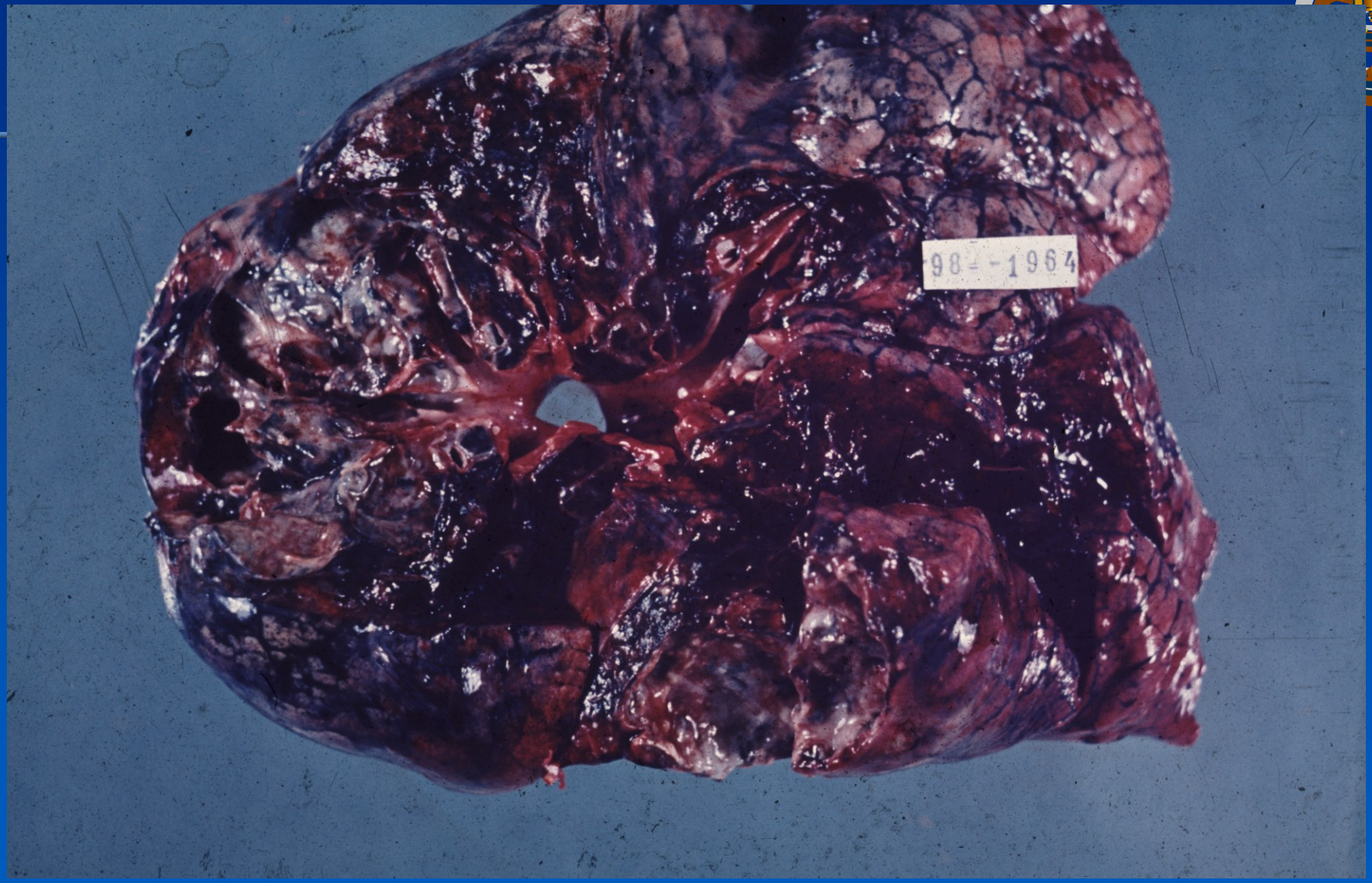


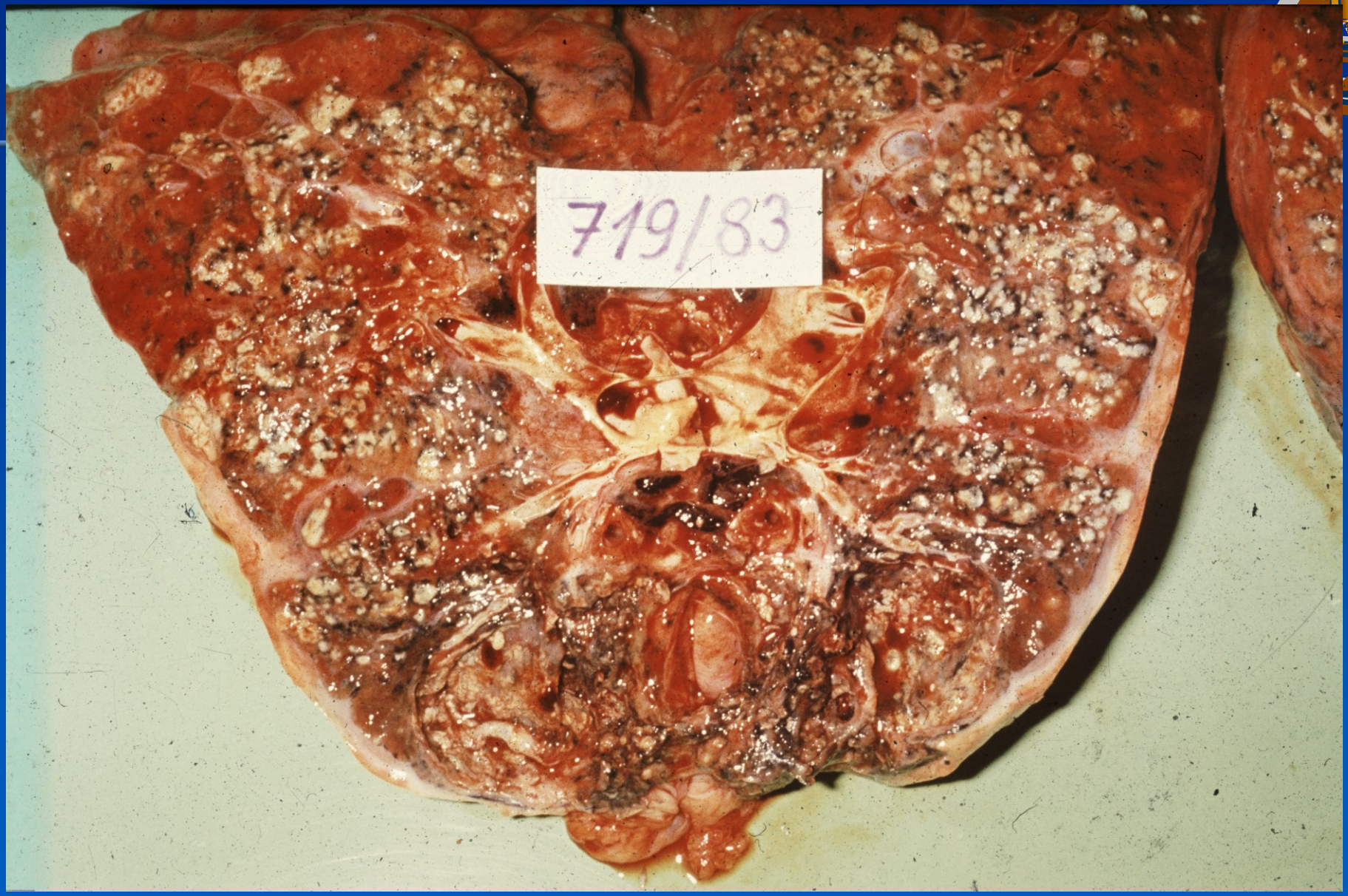
- **miliary (disseminated) tuberculosis**
  - ⇨ may be consequence of either primary or secondary tb
  - ⇨ hematogenous dissemination -> numerous small granulomas in many organs (lungs, meninges, kidneys, bone marrow, liver, …
  - ⇨ serious condition (untreated nearly 100% fatal)

**Complications:**

- ⇨ vessel arosion + rupture – hemoptysis / hemoptoe
- ⇨ spine deformities (heart + lung function problems)
- ⇨ secondary amyloidosis
- ⇨ infertility
- ⇨ …




98 - 1964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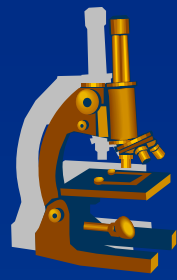
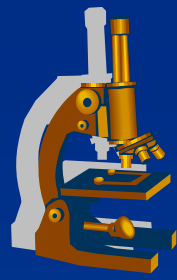
# Sarcoidosis



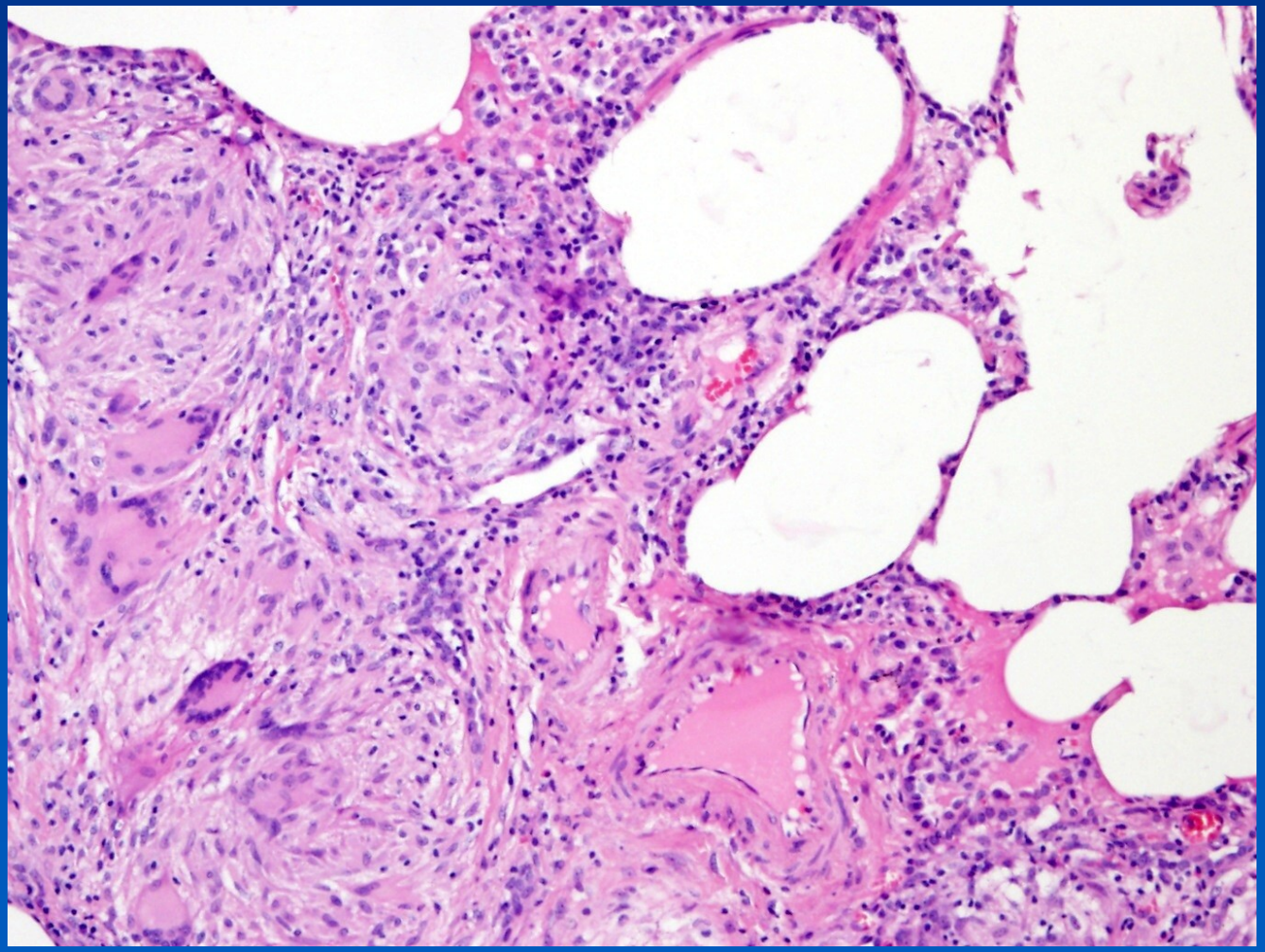
- systemic chronic granulomatous inflammatory disease, direct etiology unknown (disordered immune regulation in genetically predisposed hosts exposed to certain environmental agents), ↑ CD4+ T-cells
- mostly in mediastinal LN, lung, skin, eye; any localisation possible
- regular small „tuberculoid“ granulomas without caseous necrosis (asteroid inclusions, Schaumann‘s inclusions in Langerhans‘ cells) → x TBC (→ biopsy, dg. per exclusionem)

# Sarcoidosis

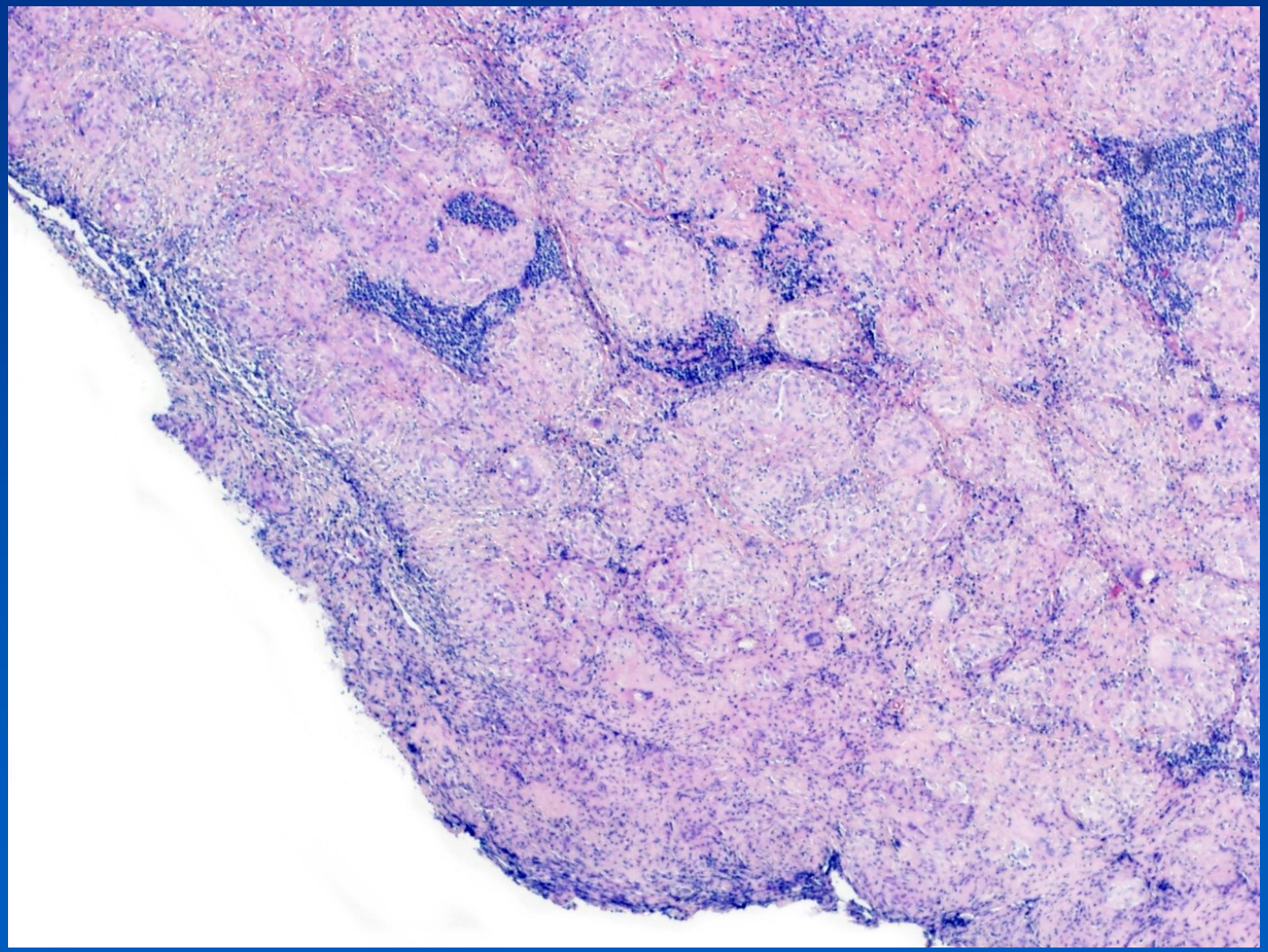


- clinically:
  - may be asymptomatic
  - chest X-ray – bilateral lymphadenopathy
  - ↑ IgG, Ca2+, angiotensin converting enzyme (ACE) in serum
  - slow progression or variable remission + healing
  - 10% mortality (lung fibrosis, cor pulmonale)
  - 20% lung or ocular dysfunction
  - treatment: ***corticosteroids***

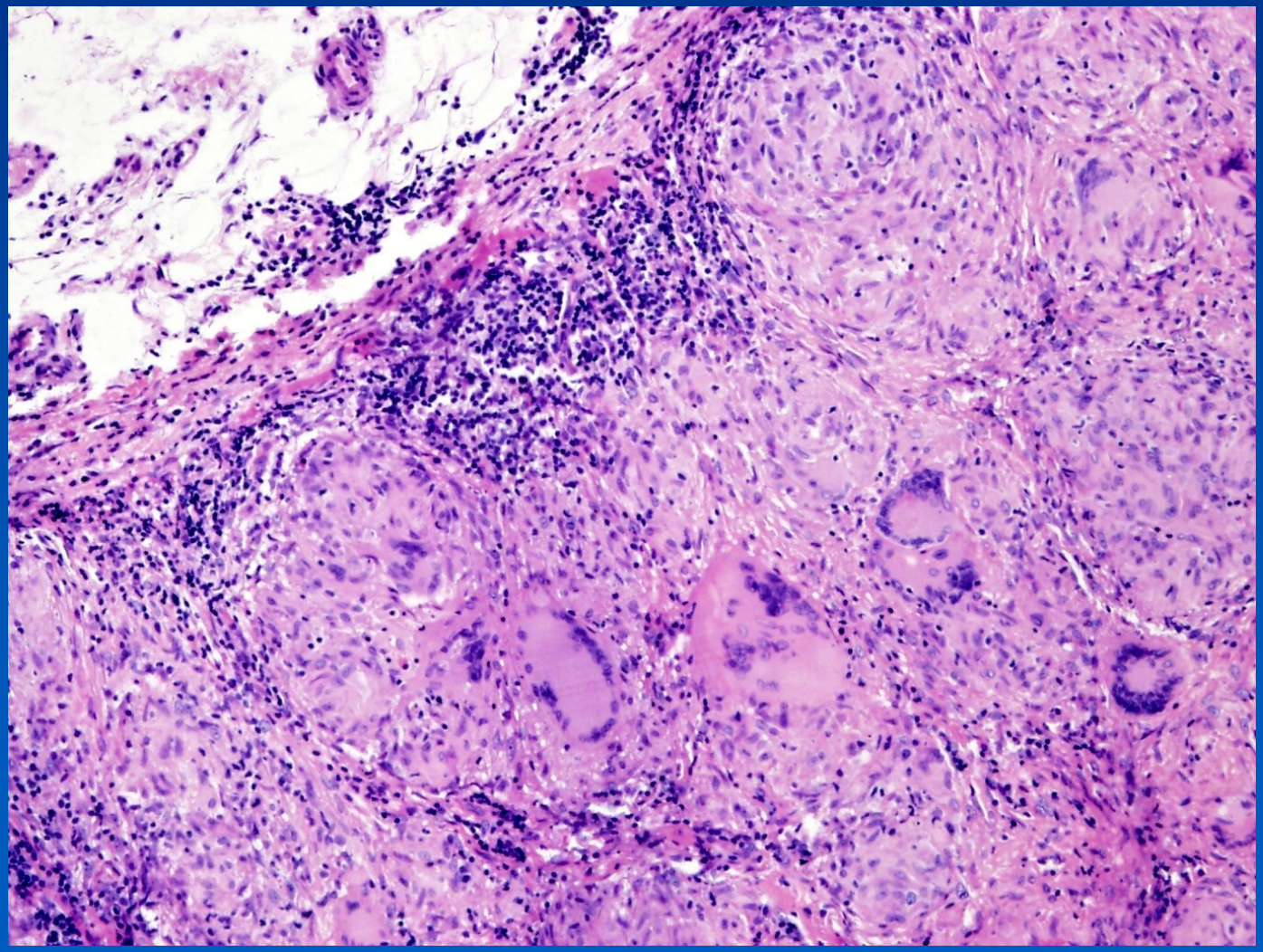
# lung sarcoidosis



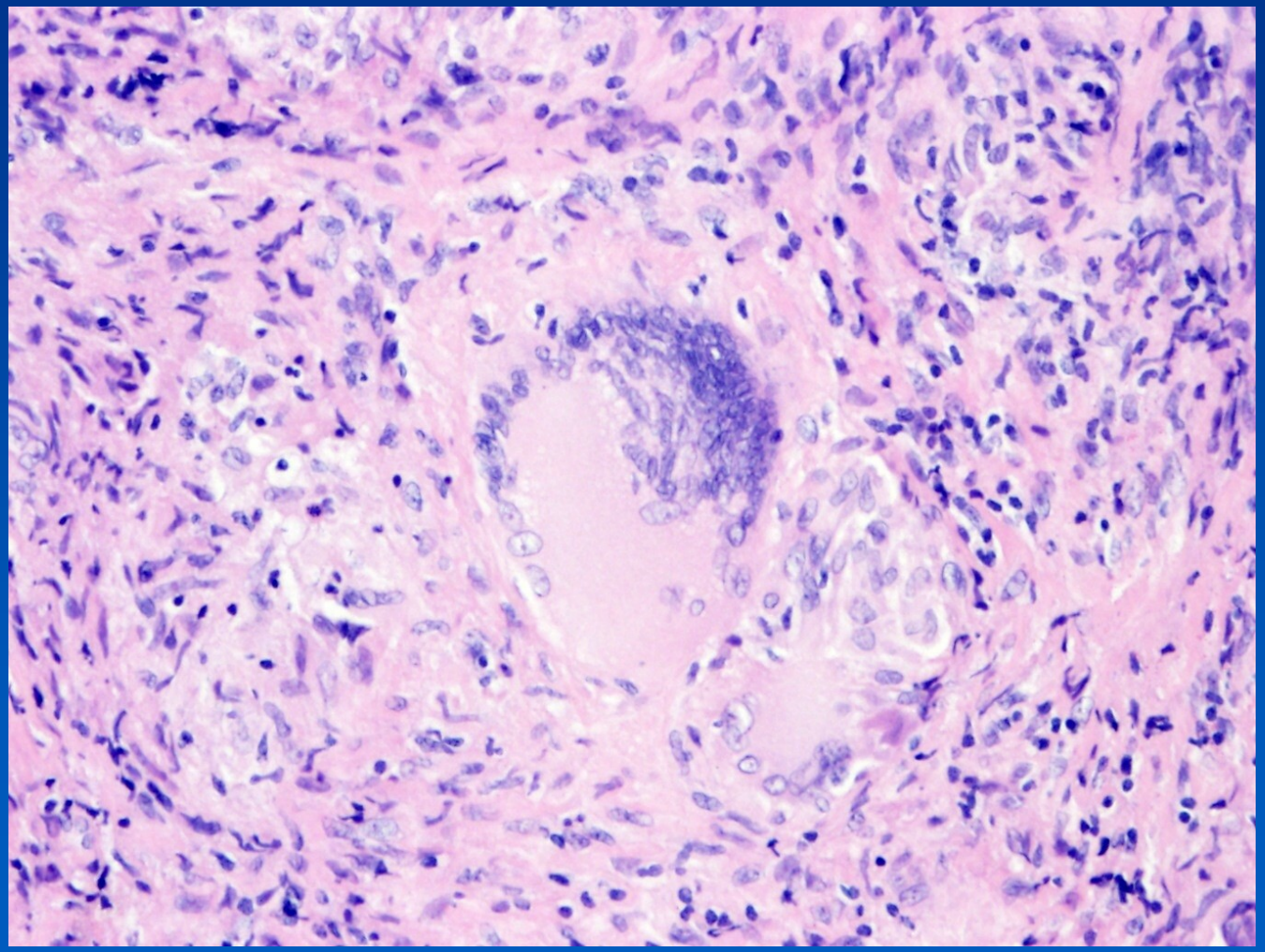
# lymph node sarcoidosis



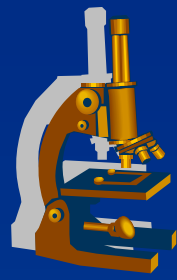
# lymph node sarcoidosis



# lymph node sarcoidosis



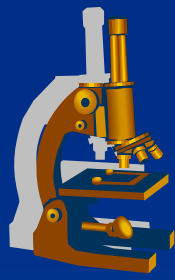
# syphilis (lues)



- *Treponema pallidum* – spirochaete

- forms:
  - ⇨ ***acquired*** *(mostly STD) – 3 stages*
  - ⇨ ***congenital*** *(transplacental transmission)*
    - **late abortion or stillbirth**
    - **infantile liver and lung fibrosis, osteochondritis**
    - **childhood – keratitis, deafness, teeth anomalies**

# syphilis (lues) - acquired



## ⇨ *primary chancre*

- typically acquired by direct sexual contact
- primary chancre (skin lession) appears in the entry site 3 wks after contact
- *Primary chancre - single, firm, painless, non-itchy skin ulceration with a clean base and sharp borders between 0.3 and 3.0 cm in size, serous exudate + treponemata*
- associated with unilateral or bilateral inguinal lymphadenitis
- without treatment heals in a few weeks (3-6) -> atrophic scars

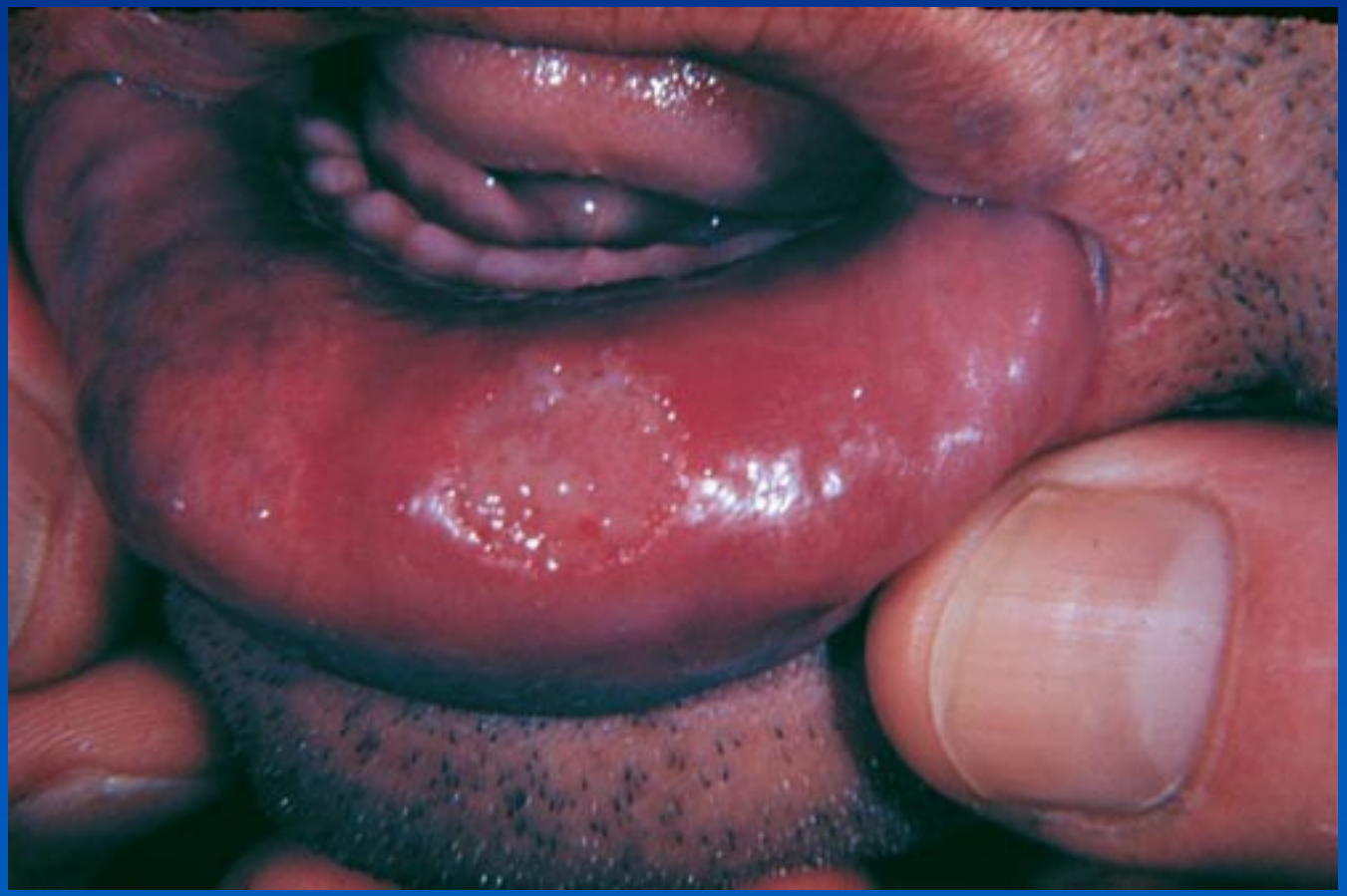
## ⇨ *secondary*

- early generalisation – transient skin and mucosal rash, generalised lymphadenitis in many cases, non-specific + gen. signs (fever, sore throat, weight loss, …), numerous plasma cells in infiltrate in condylomata lata on moist skin, erosion on mucosa

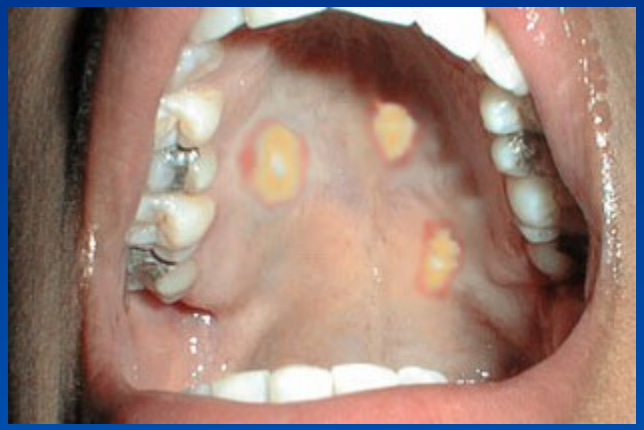
## ⇨ *tertiary*

- specific changes,  8 – 25 years after primary infection,
- symptoms according to localisation of gummata (cerebral cortical atrophy, progressive paralysis, aortic aneurysm)
- gumma: mm-cm, tuberculoid granuloma without complete caseous necrosis (rubbery consistency)

# Syphilis – primary

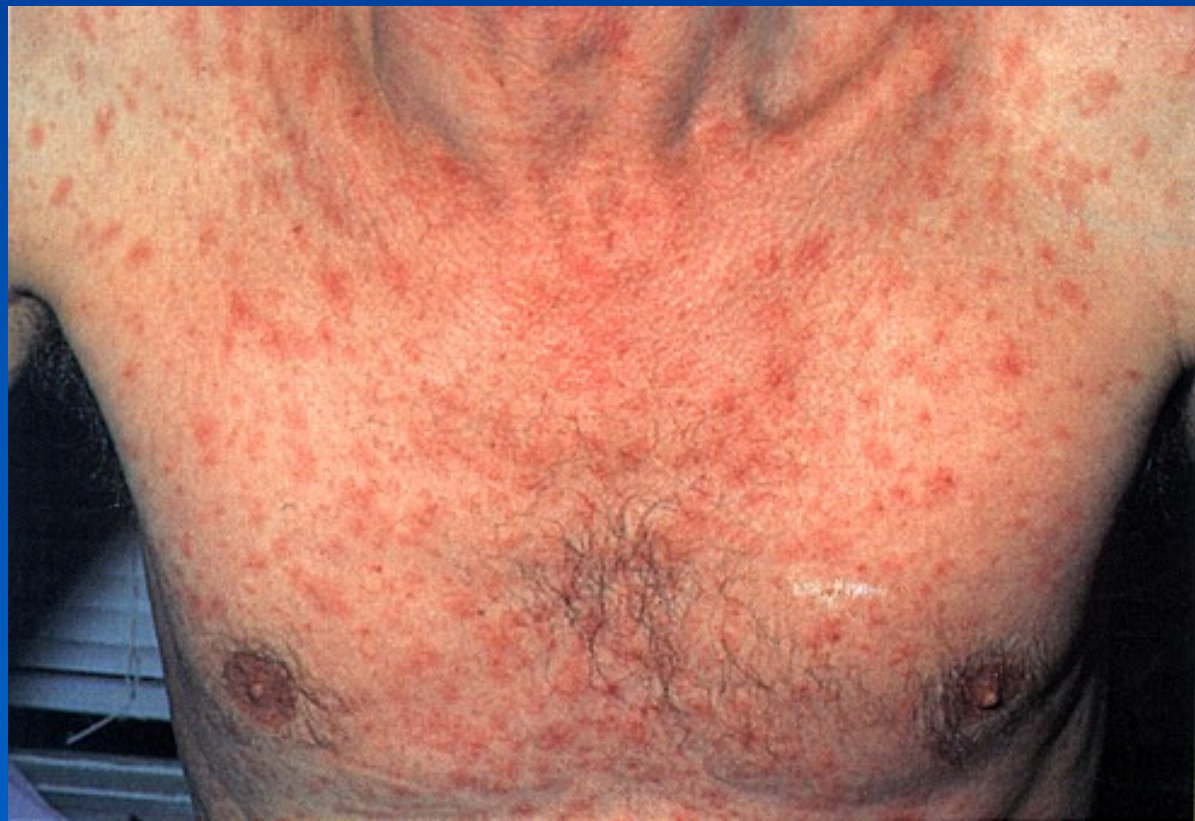


# *Syphilis - secondary*



**Condylomata lata**

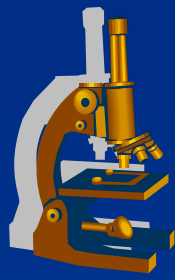
**Syphilitic rash**



# *Treponema pallidum*

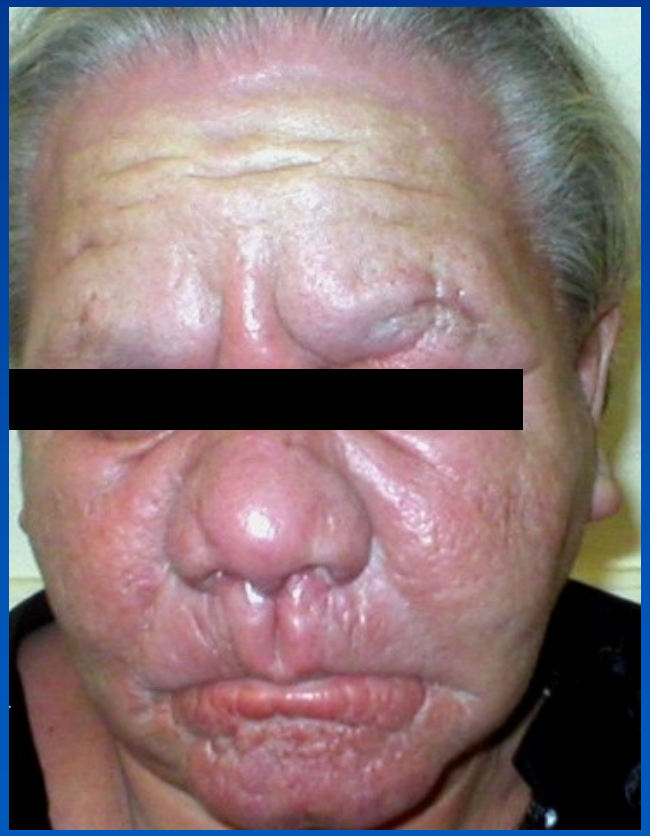
***(spirochetes visualized by silver staining)***

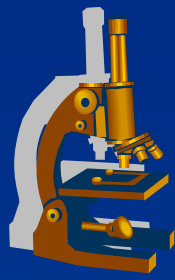
# Leprosy



- *Mycobacterium leprae*
  - in developed countries very rare, usually imported
- *formy:*
  - **tuberculoid form**
    - vigorous imunological $T_H1$ reaction -> granulomas without caseous necrosis in the skin, perineural – ulcers, paralysis, atrophy
  - **lepromatous form**
    - multiple and diffuse infiltrates in the skin (facies leontina), eyes (blindness), lymph nodes, spleen
    - foamy macrophages + mycobacteria
    - often progresive (anergic host)

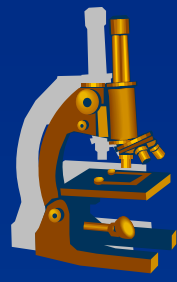
# Leprosy – facies leontina





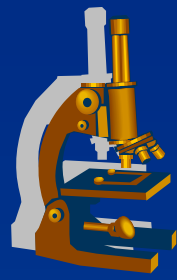
# PROGRESSIVE CHANGES

# Progressive changes



- **healing of tissue defects**
  - ⇨ *regeneration*
  - ⇨ *repair*
    - regeneration and repair often in combination
- **tissue adaptation to the changed conditions**
  - ⇨ *hypertrophy*
  - ⇨ *hyperplasia*
  - ⇨ *metaplasia*

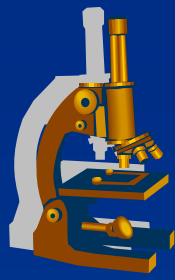
# REGENERATION



- **replacement by identical tissue (morphology, function)**

- **according to regenerative ability:**
  - ⇨ ***labile cells***
    - epithelial cells of skin, gut,…, bone marrow,…,
    - permanent regeneration from stem cells (rapid „turn-over time“)
  - ⇨ ***stable***
    - liver, kidney (proximal tubule epithelial cells), smooth muscle
    - regeneration on demand in tissue loss
  - ⇨ ***permanent (postmitotic)***
    - neurons, cardiac muscle cells
    - mostly no complete functional regeneration

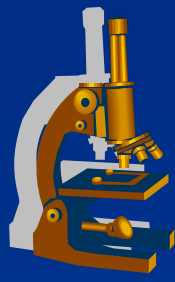
# REPAIR



- replacement of lost tissue usually by granulation tissue → fibrotic scar

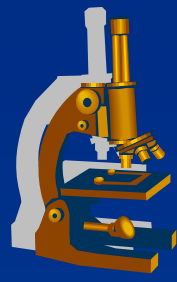
- may affect the function of the organ
  - ⇨ *scar after myocardial infarction*
  - ⇨ *lung fibrosis, cirhosis,…*

# Chronic hepatitis



- > 6 months
- causes:
  - ⇨viral hepatitis HBV , HCV, HDV, (HEV, HGV)
  - ⇨non-alcoholic fatty liver disease
  - ⇨ toxic (alcohol, drugs)
  - ⇨ autoimmune (antibodies antinuclear, x smooth muscle, x microsomal)
  - ⇨inborn metabolic defects (Wilson disease, haemochromatosis, alfa-1-antitrypsin deficiency, etc.)
- gross: enlargement, tougher consistency, rougher surface
- combination of damage, fibrosis, irregular hyperplasia of hepatocytes
- progression to nodular transformation - cirrhosis

# Chronic hepatitis



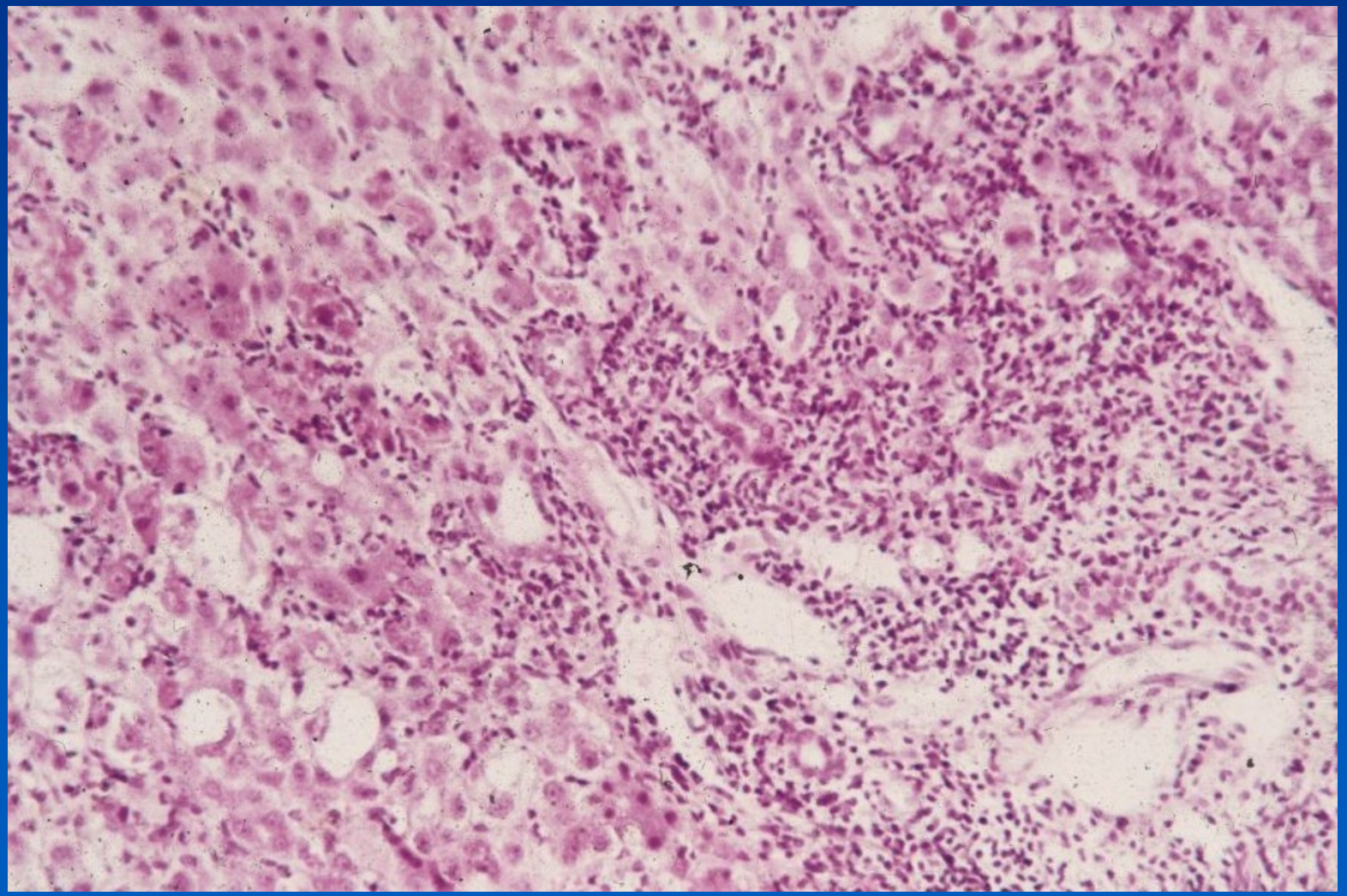
Disease activity (grade):

- interface activity (periportal necrosis)
- portal inflammatory infiltrate
- intralobular necroinflammatory activity

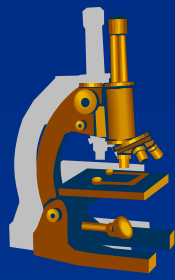
**Extent of fibrosis (stage):**

- fibrotic septa
- bridging
- nodule formation
- cirrhosis

# Chronic hepatitis



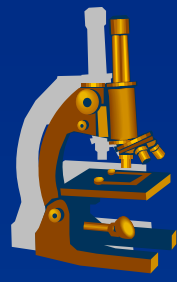
# *Cirrhosis*



- Etiology:
  - ⇨ *massive acute necrosis*
  - ⇨ *chronic hepatitis*
  - ⇨ *biliary diseases*
    - inborn (atresia),
    - acquired: autoimmune (primary biliary cirrhosis, prim. sclerosing cholangitis), sec. biliary cirrhosis (chronic obstruction)
  - ⇨ *cryptogenic cirrhosis*

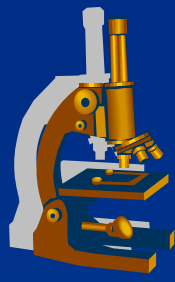
- Gross: tough, usually diminished size
  - ⇨ *micronodular*
  - ⇨ *macronodular*

# Cirrhosis



- diffuse parenchymal injury + consequent fibrosis (bridging septa)
- nodular transformation (hepatocyte regeneration x failure of architectectural reconstruction), persisting regressive changes
- reorganisation of vascular architecture
- changes of intrahepatic biliary tract, incl. ductular hyperplasia

# Complications of cirrhosis



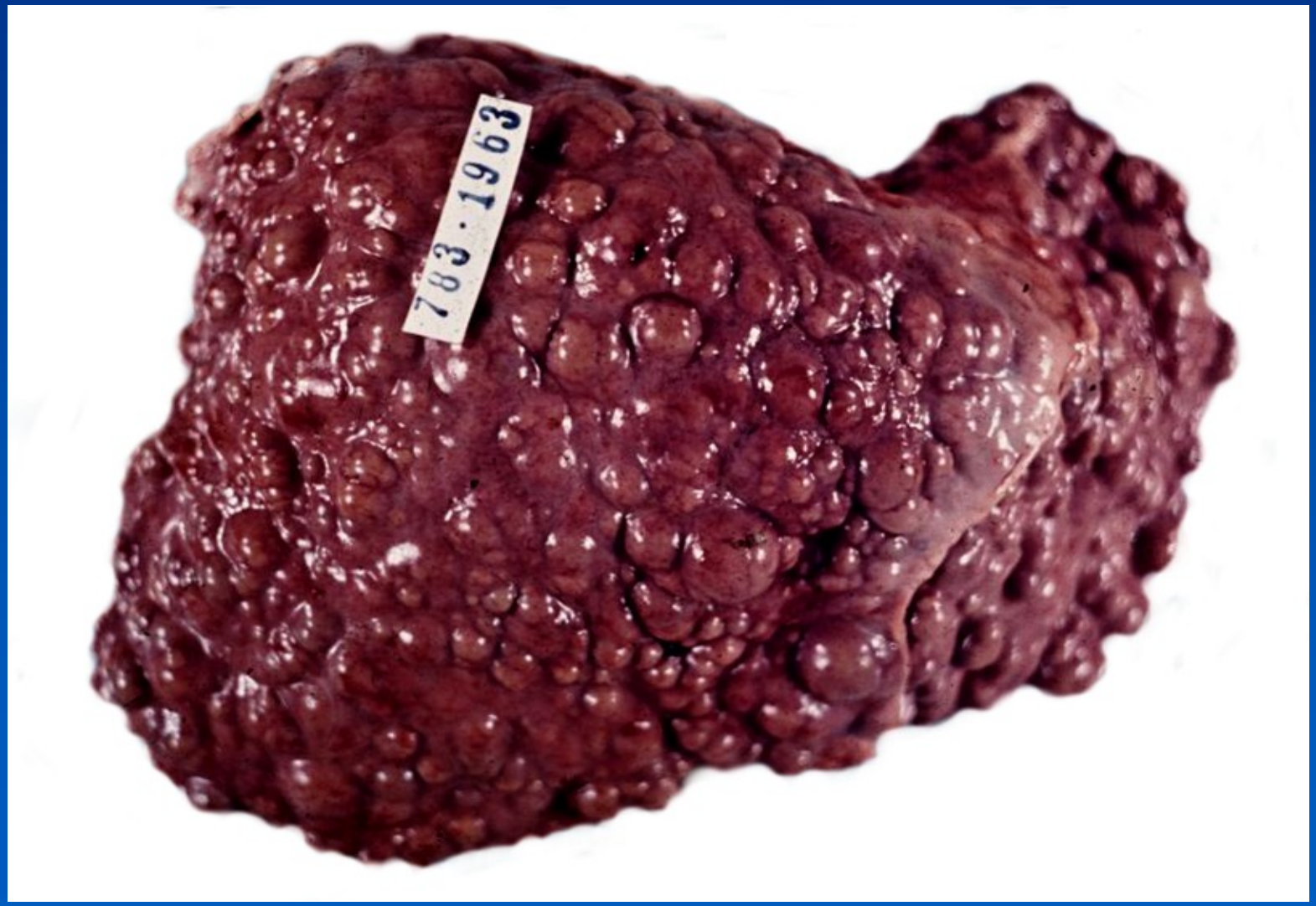
- liver failure: inadequate synthesis, inadequate detoxication, insufficient Kupffer cell function

- portal hypertesion: splenomegaly, intestinal venous congestion (! infarsation, inflammation)

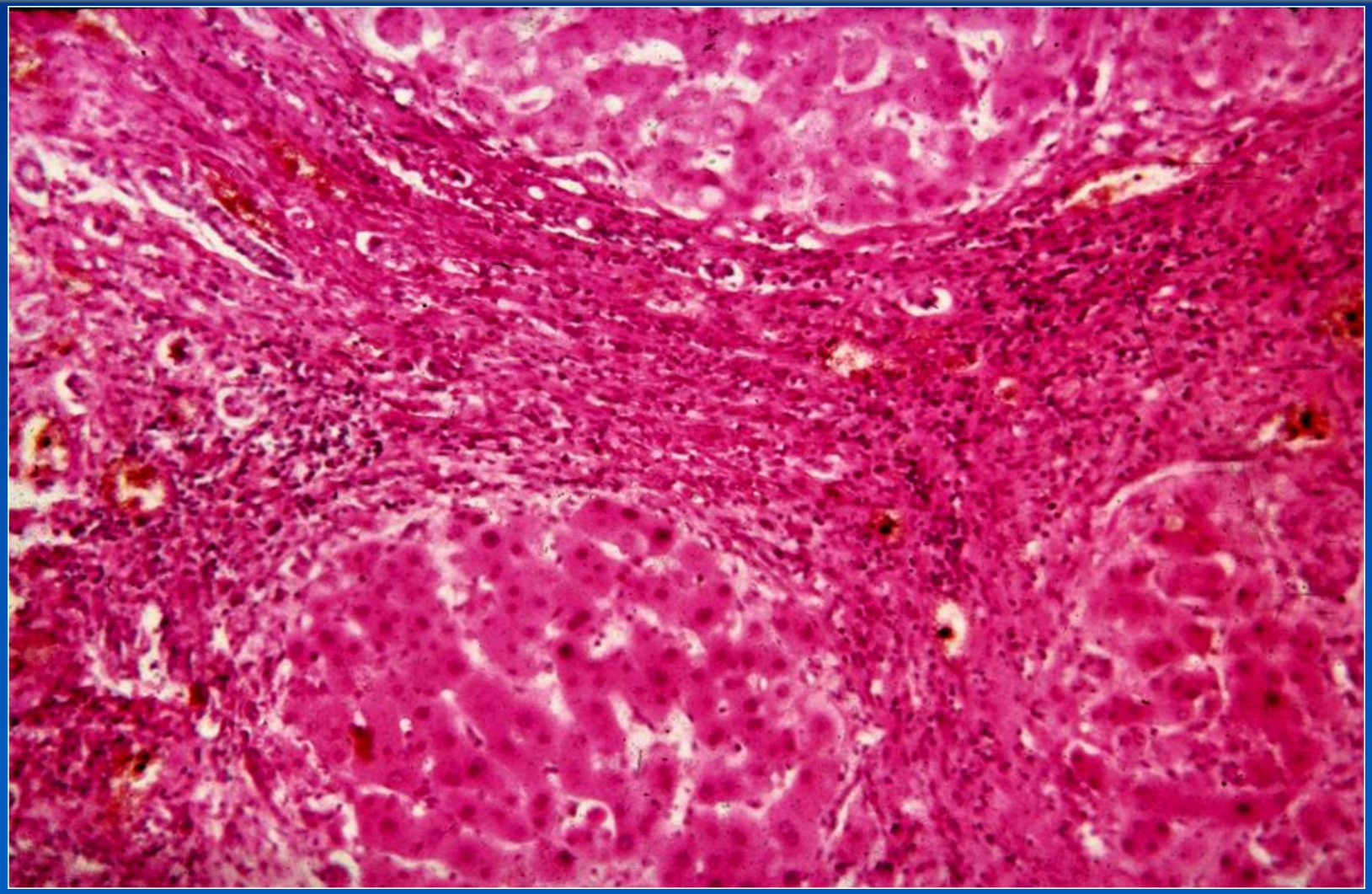
  ascites (! peritonitis), portocaval anastomoses

- carcinoma (usually hepatocellular)

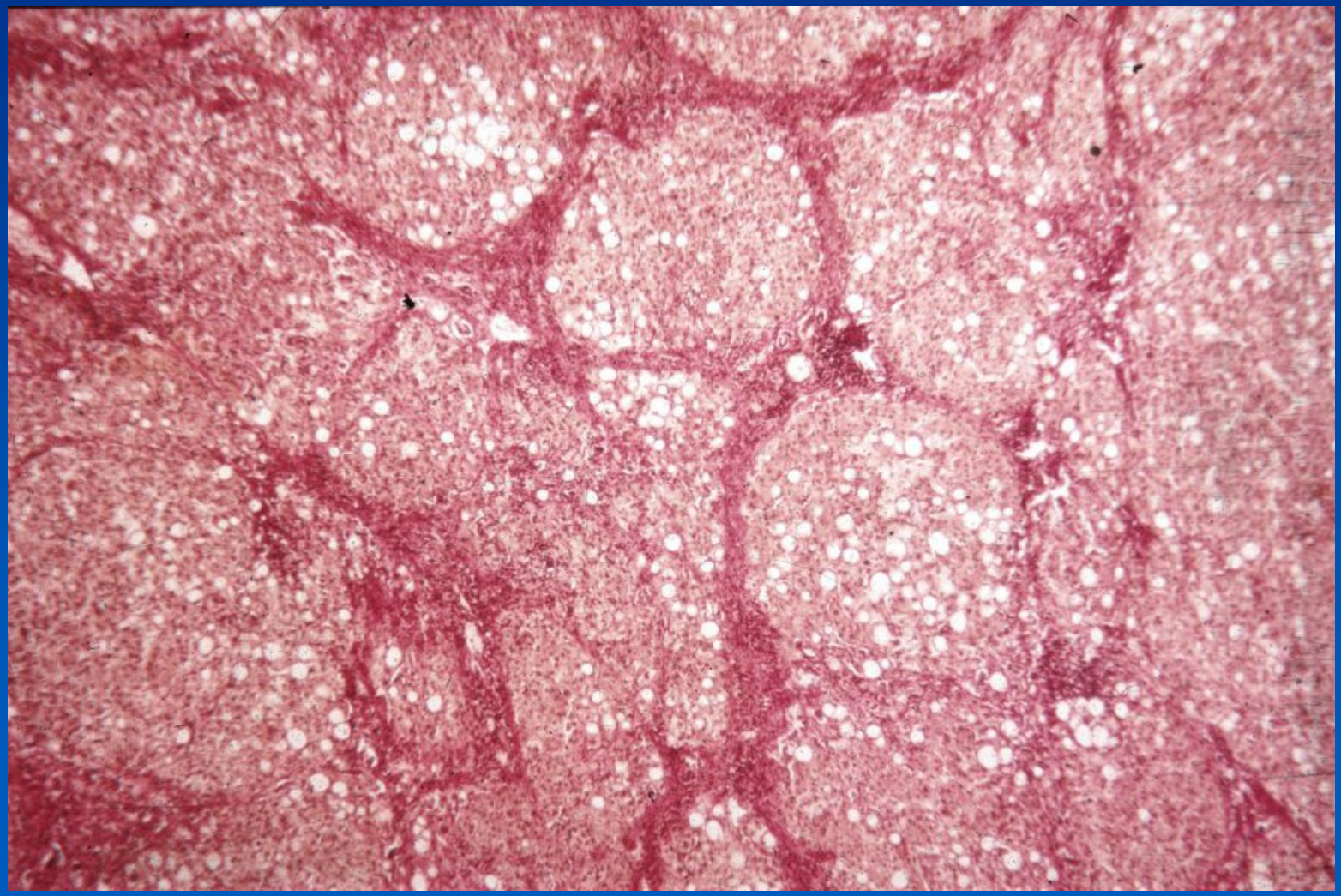
# Cirrhosis – nodular transformation



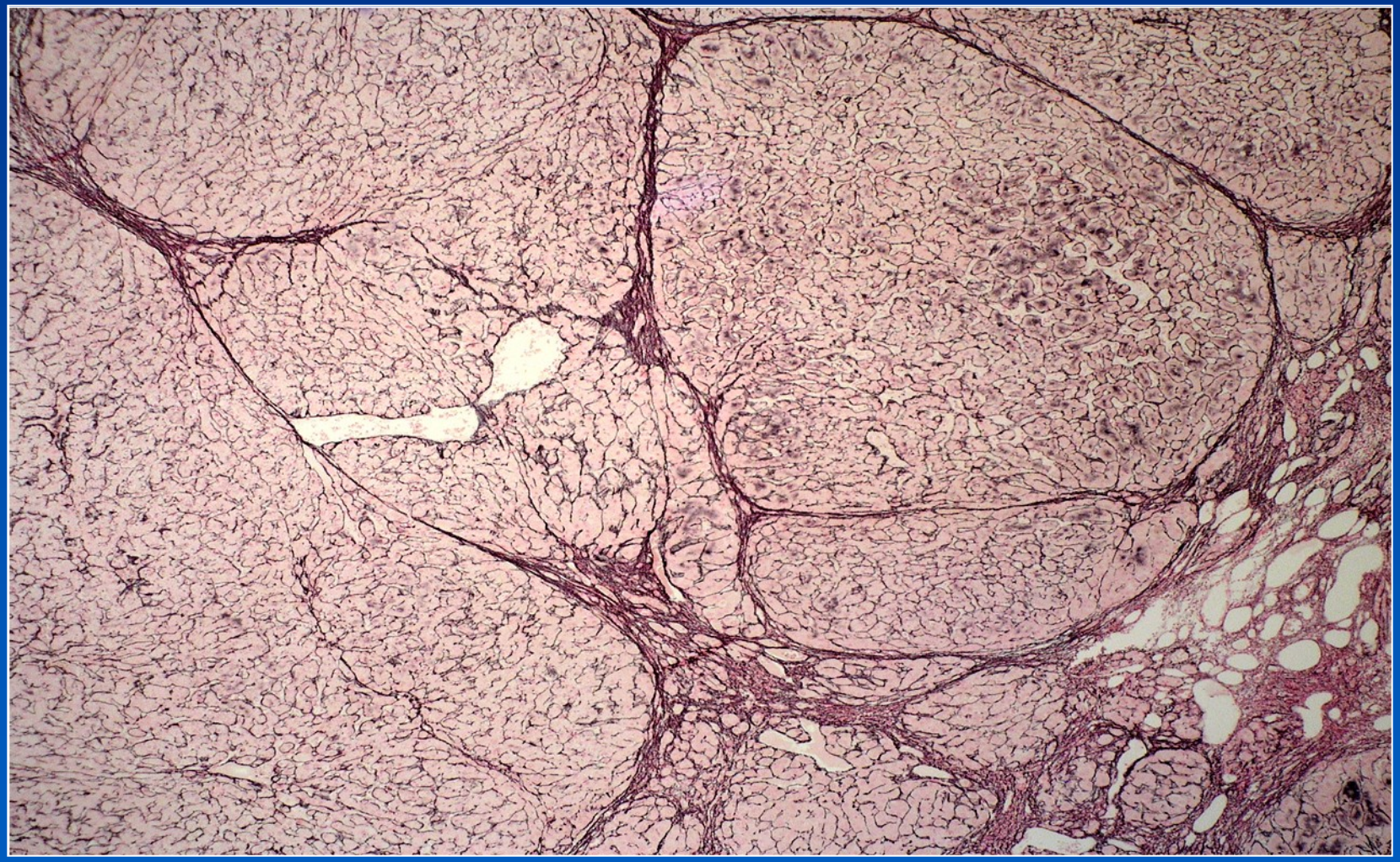
# Cirrhosis – nodular transformation, chronic hepatitis, cholestasis



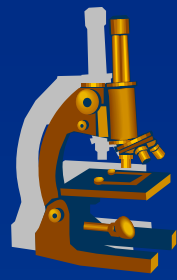
# Cirrhosis



# Cirrhosis

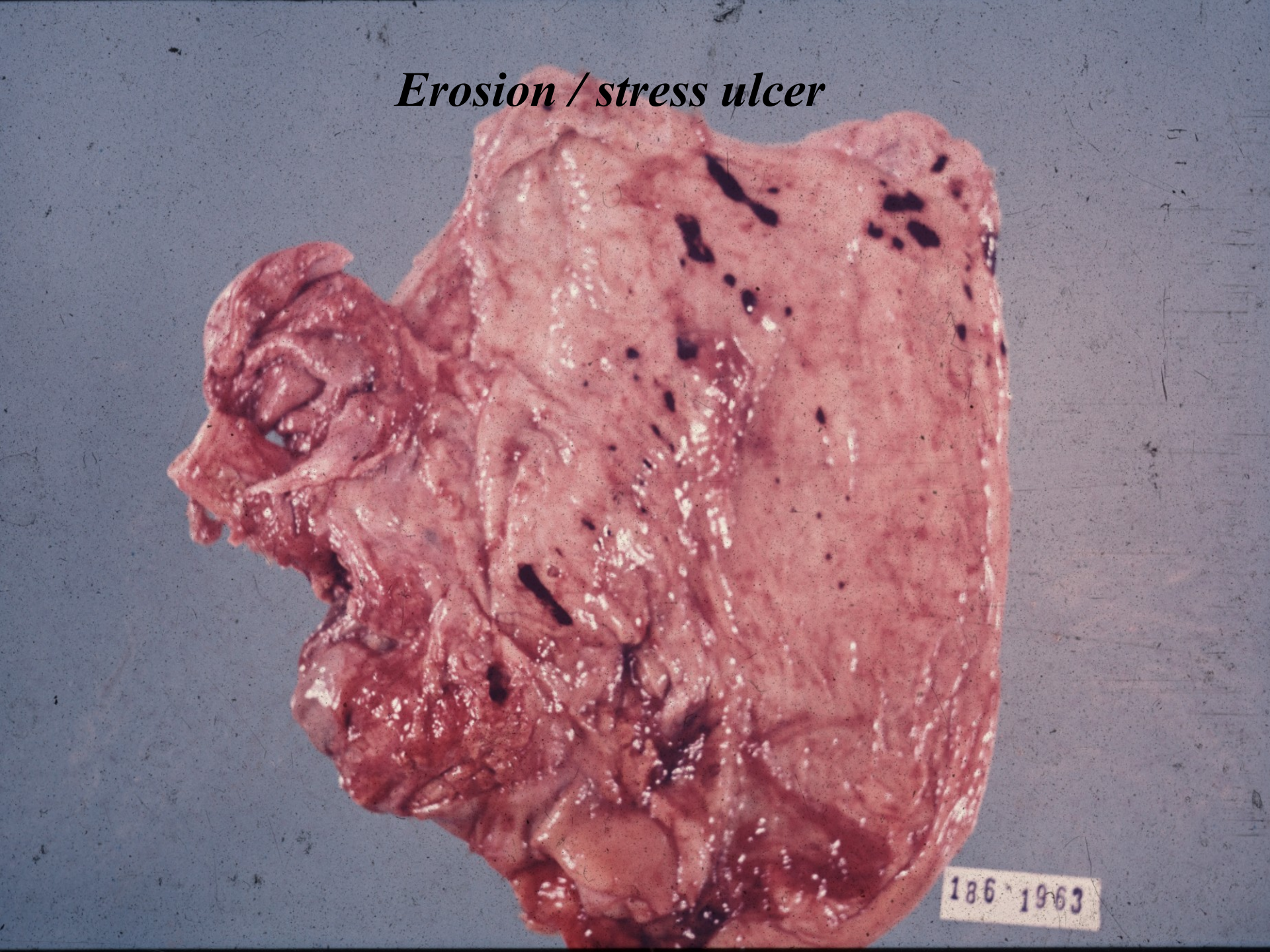


# Stomach erosions



- NSAIDs + other drugs, alcohol, vomiting, stress, burns, infection, raised intracranial pressure
- antrum and body, multiple
- microcirculation disorder, capillary rupture, acid hypersecretion
- < 3 mm
- limited by m. mucosae !!!
- healing by regeneration

# *Erosion / stress ulcer*



# Chronic peptic ulcer

- chronic, usually solitary lesion in GIT parts exposed to acid and peptic juices, commonly at mucosal junction
- extends through m. mucosae into submucosa or deeper
- bulbus duodeni, stomach antrum, GE junction, stomic junction, Meckel diverticulum
- imbalance between mucosal defence and damage by gastric juices/bile, drugs, ischaemia (stress)
- H. pylori (100% in duodenal ulcers, cca 70% in gastric ulcers), but only 10-20% of infected develop ulcer


FIG. 37.—The main sites of "peptic" ulcers.

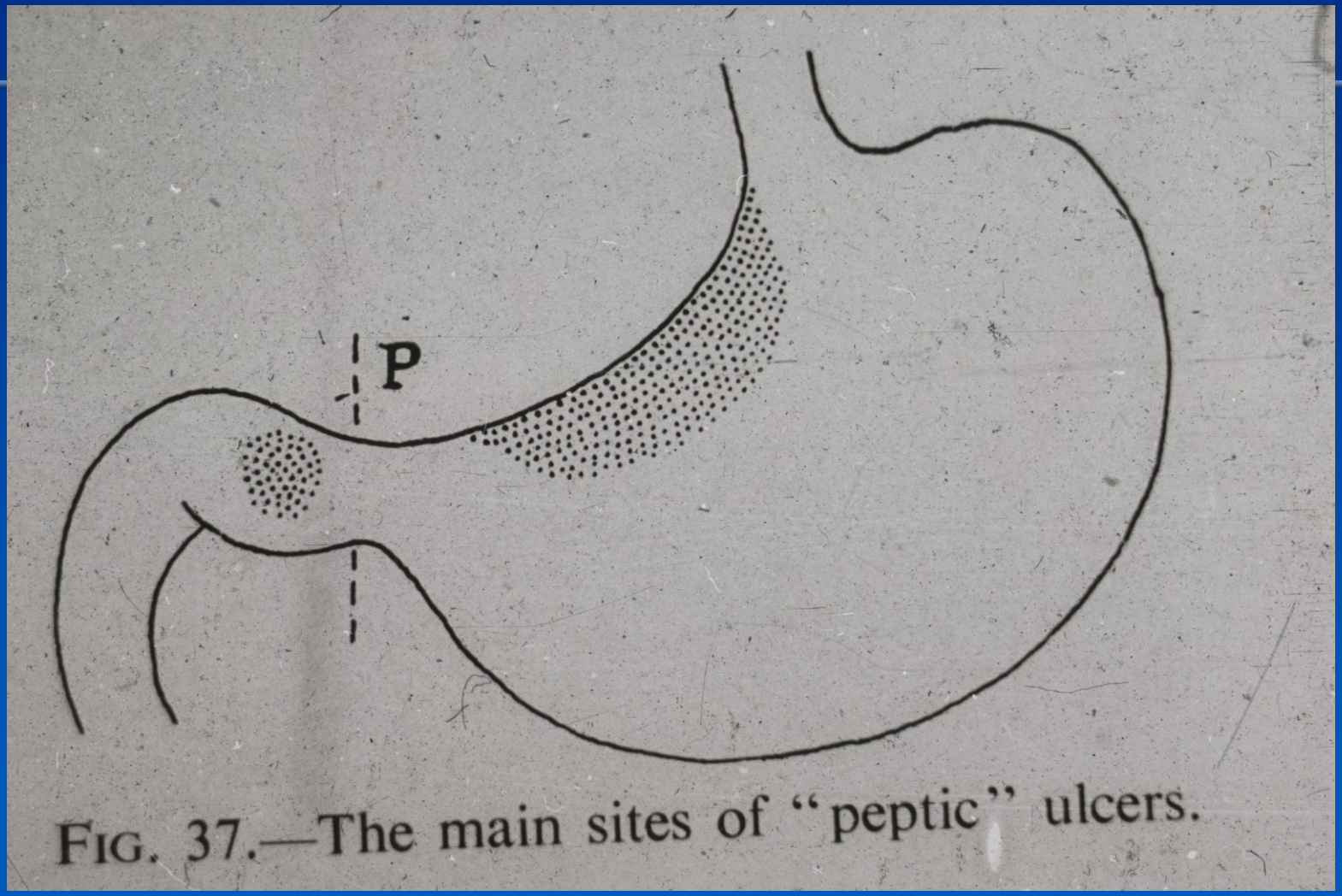
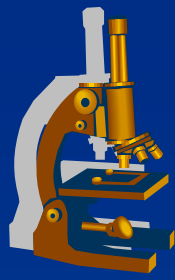


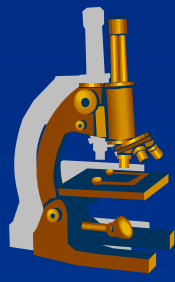

FIG. 37.—The main sites of "peptic" ulcers.

# Chronic peptic ulcer



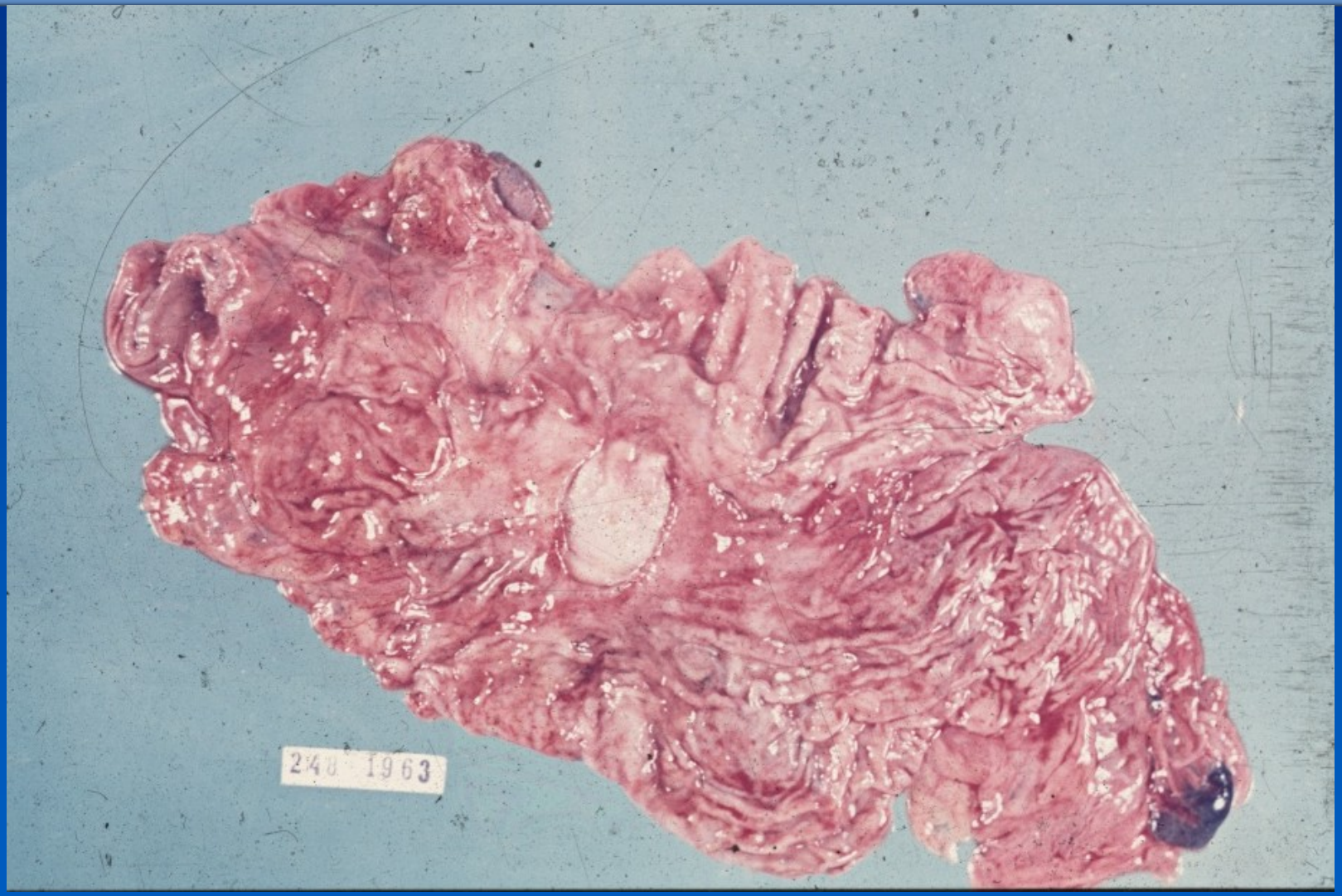
- gross: starts as sharply demarcated defect, 4 – 40 mm, straight walls, haemorrhagic base
- later overhanging mucosa, sometimes slightly elevated borders, smooth base, scarring
- histology: in active ulcer 4 layers
  - ⇨ cell debris and fibrinoid necrosis
  - ⇨ mixed inflammatory infiltrate
  - ⇨ granulation tissue
  - ⇨ fibrotic scar

# *complications*

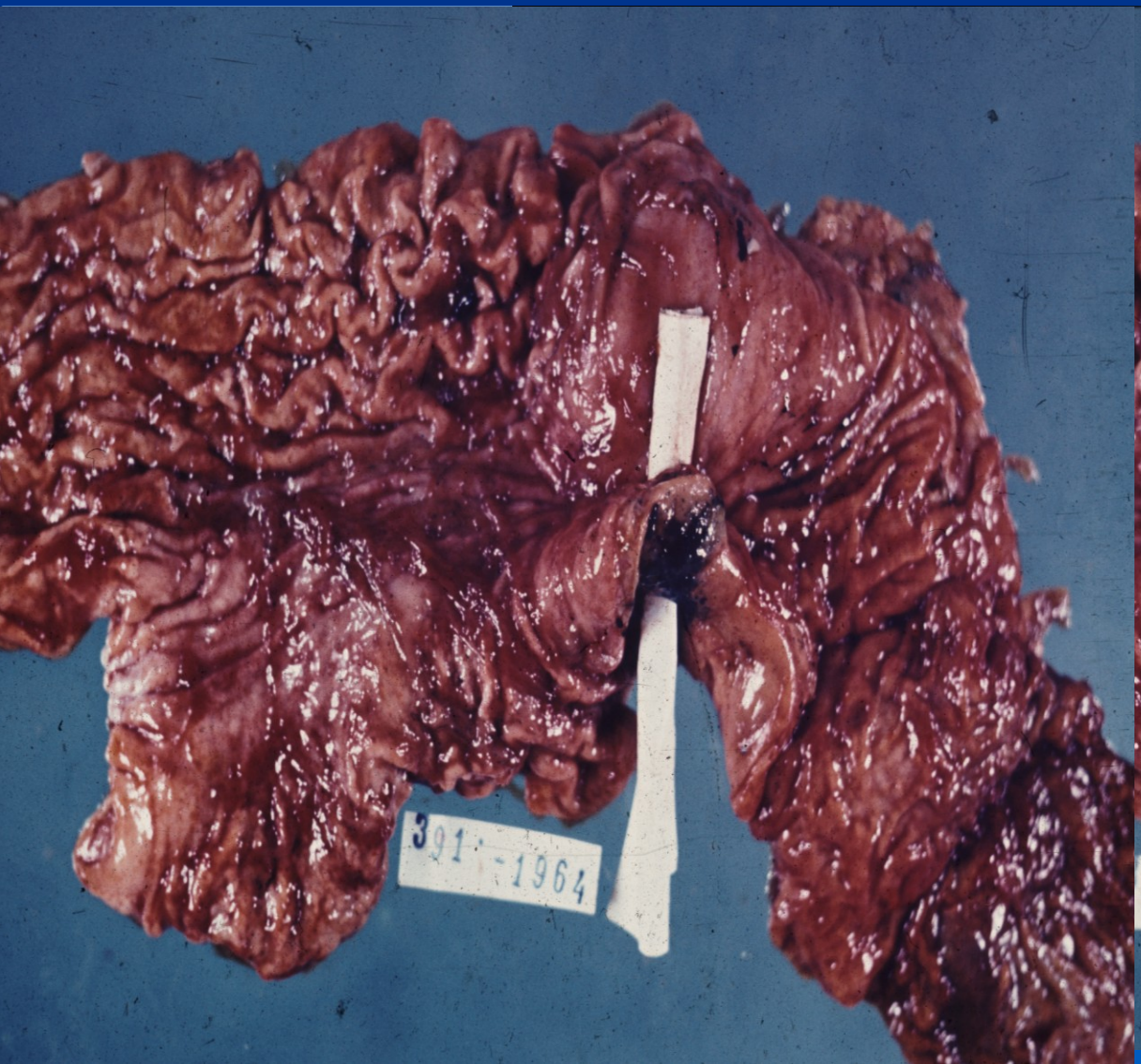


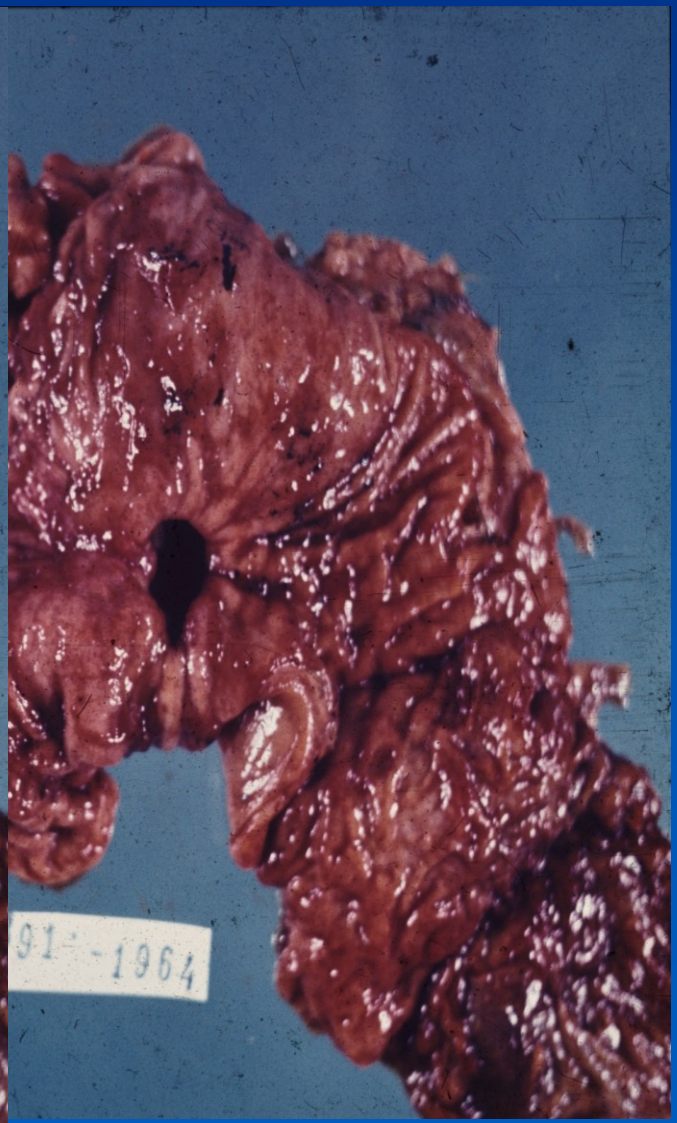
- haemorrhage (overt, occult, anaemia)
- perforation, shock, peritonitis
- penetration into adjacent organs
- scarring, stenosis
- malignant transformation (stomach)

# Chronic peptic ulcer

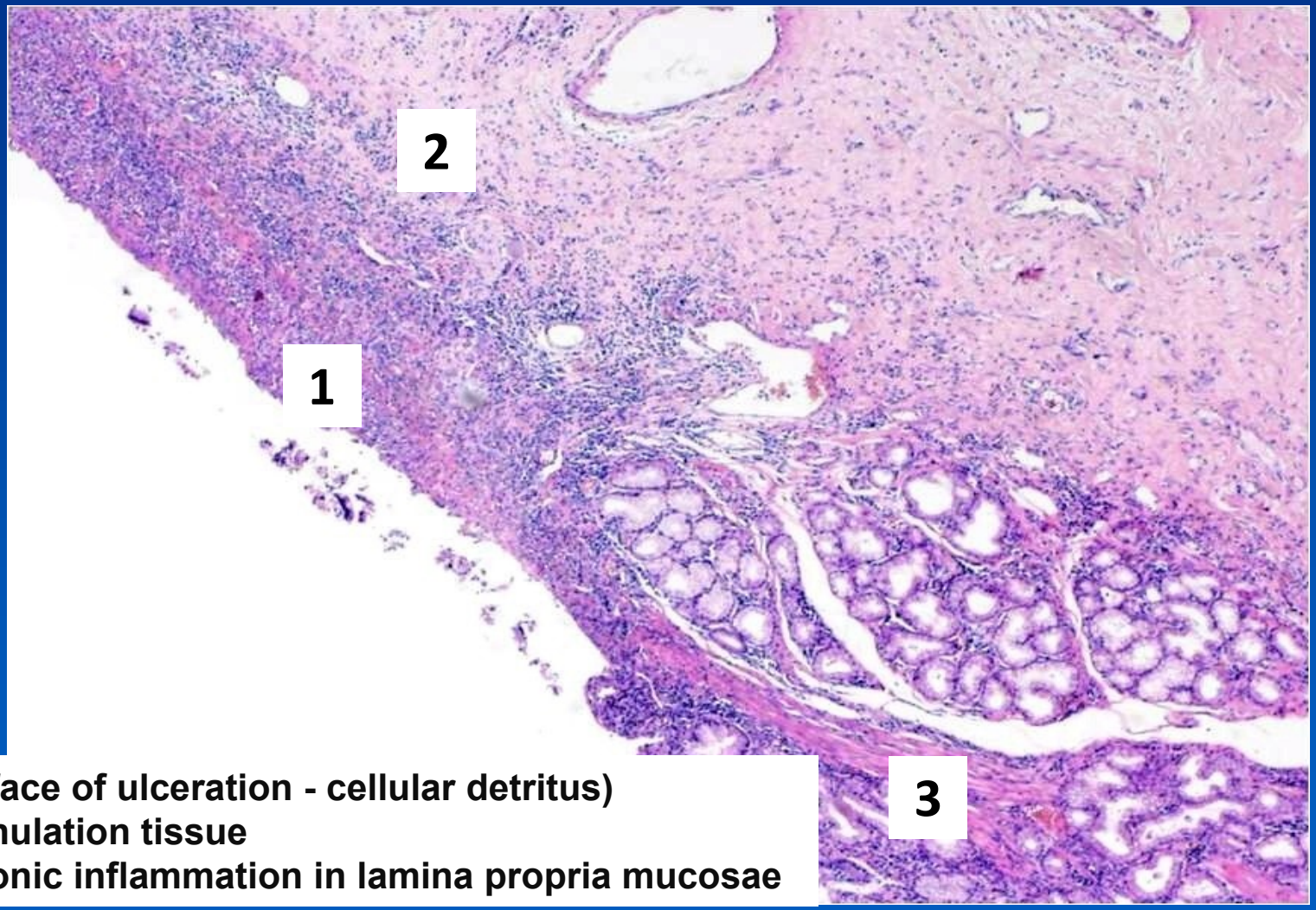


# Perforated duodenal ulcer



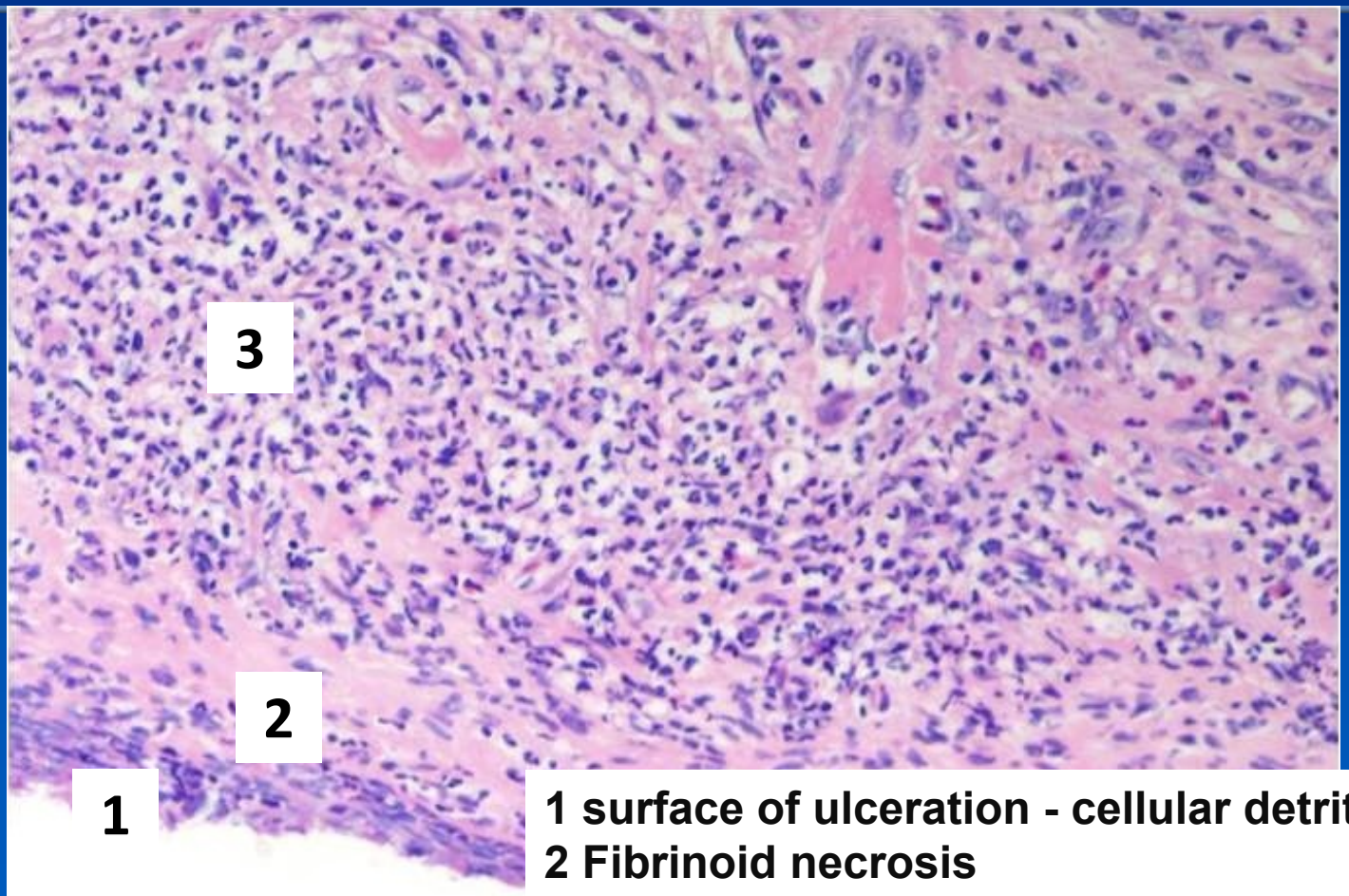



# Chronic peptic ulcer - duodenum



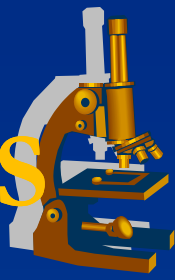

1 surface of ulceration - cellular detritus)
2 granulation tissue
3 chronic inflammation in lamina propria mucosae

# Chronic peptic ulcer - duodenum



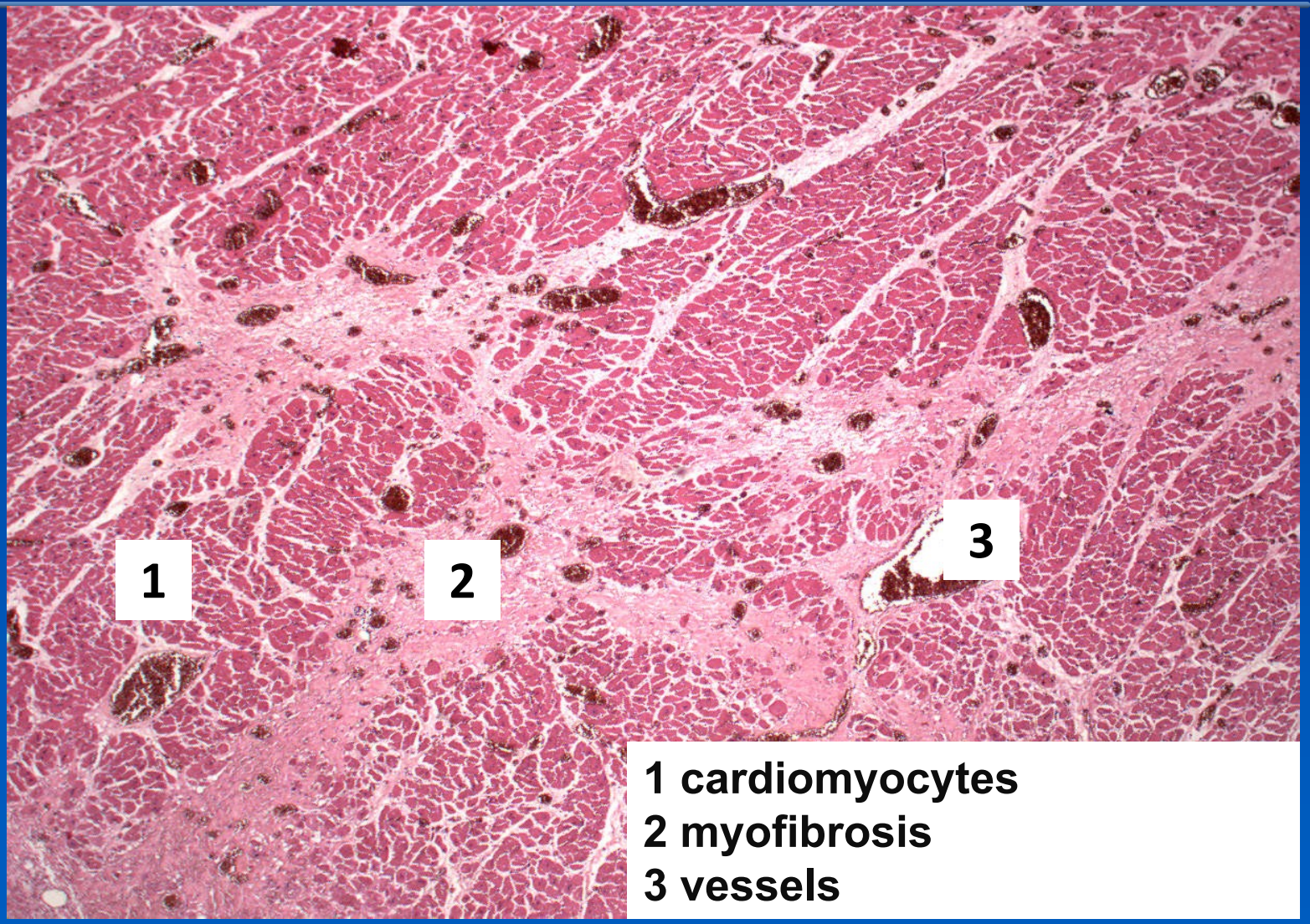

1 surface of ulceration - cellular detritus)
2 Fibrinoid necrosis
3 granulation tissue with mixed inflammatory infiltrate

# MYOFIBROSIS DISPERSA CORDIS

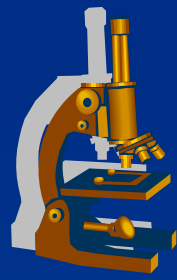


- Repeated multiple microinfarcts/myomalatia of cardiomyocytes („angina pectoris“)
- Repair by granulation tissue, scarring
- Disperse scars – small whitish foci in myocardium

# MYOFIBROSIS DISPERSA CORDIS

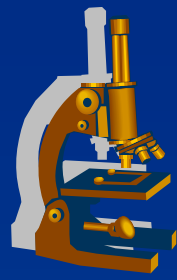


# Hyperplasia



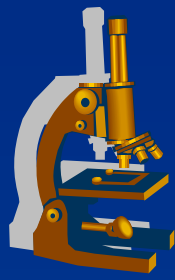
- increase in cell number by cell division → tissue/organ enlargement
- physiological: hormonal, compensatory
  - ⇨ Hyperplasia of breast tissue (in puberty, pregnancy, lactation)
- pathological: excess of hormones / growth factors, still under control (autonomous exceptions rare)
  - ⇨ Benign prostatic hyperplasia
  - ⇨ Endometrial hyperplasia
  - ⇨ Thyroid hyperplasia (goiter)

# BENIGN PROSTATIC HYPERPLASIA

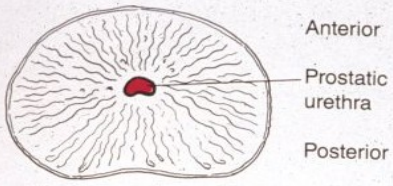


- common in older men, high incidence > 60 yrs
- adenomyomatous hyperplasia
  - *stromal (smooth muscle, fibrotic tissue)*
  - *+ glandular, alternating with atrophy, cystic and regressive changes*
  - *!!! two cellular layers – outer myoepithelial, inner secretory !!!*
- gross: enlarged, nodular, tougher
- main changes in central (periurethral) region

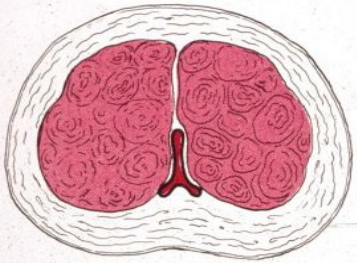
# BENIGN PROSTATIC HYPERPLASIA



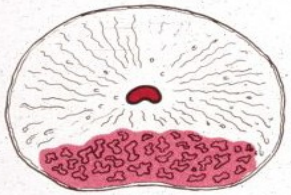
- Outcome:
  - *partial → complete urethra obstruction -> urinary residuum, risk of infection (+ ascending – pyelonephritis)*
  - *bladder trabecular hypertrophy*
  - *hydronephrosis*
- Benign, but setting for possible preneoplastic changes
- Th: surgery, drugs




NORMAL PROSTATE



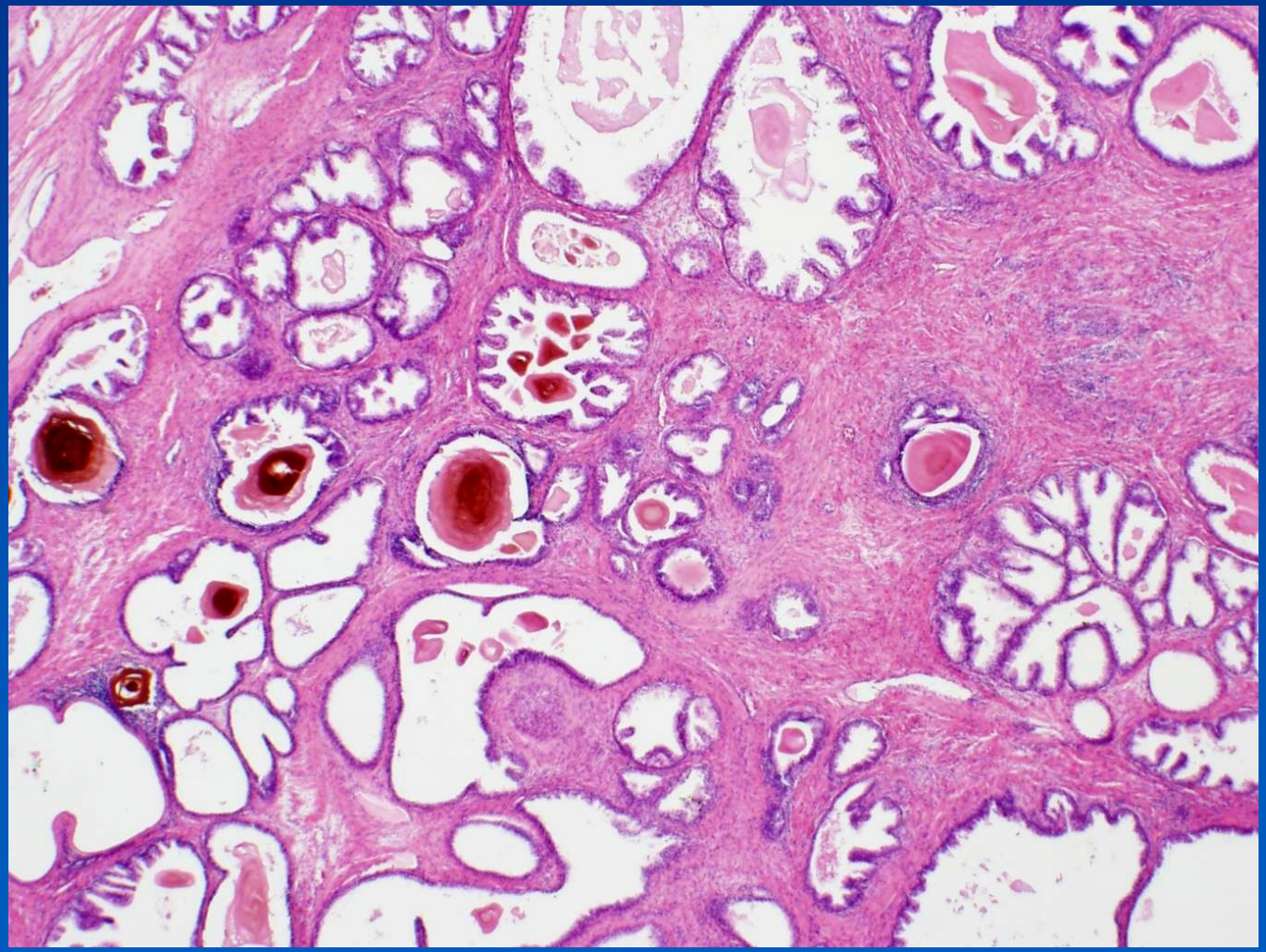
NODULAR PROSTATIC HYPERPLASIA



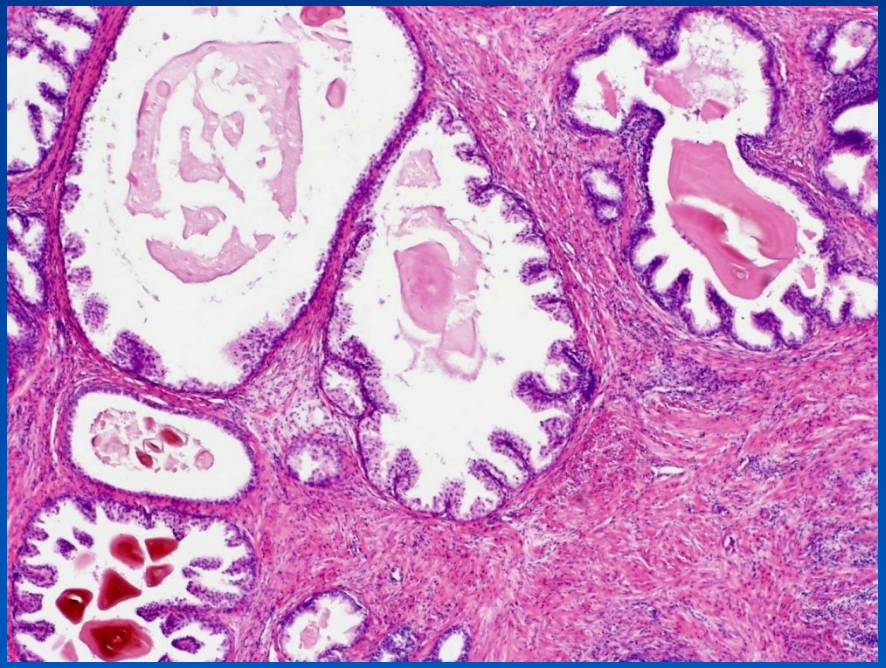
CARCINOMA OF PROSTATE

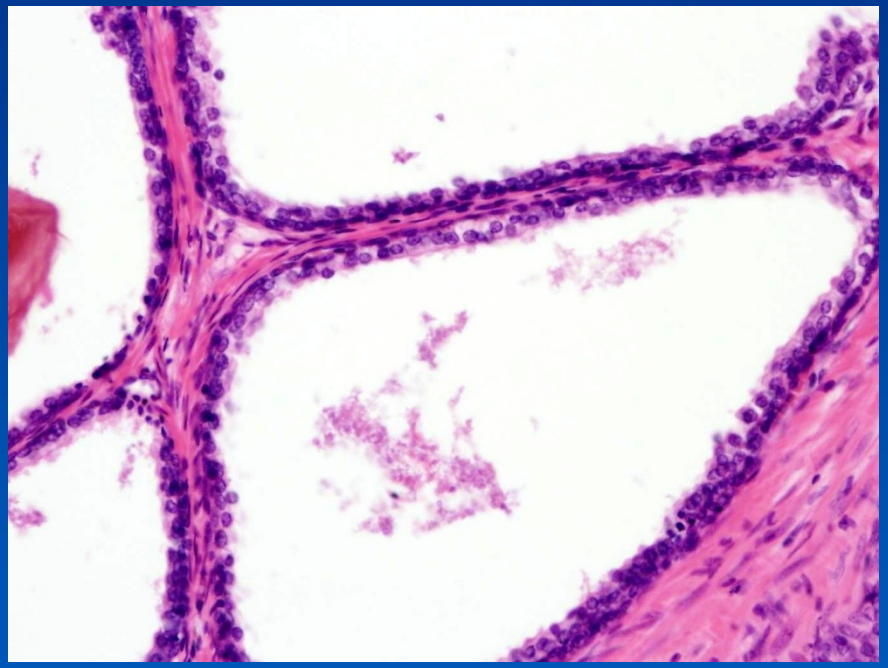
FIGURE 17-35
Normal prostate, nodular hyperplasia, and adenocarcinoma. In prostatic hyperplasia the nodules distort and compress the urethra and exert pressure on the surrounding normal prostatic tissue. Prostatic carcinoma usually arises from peripheral glands, in which case it does not compress the urethra.

# BENIGN PROSTATIC HYPERPLASIA

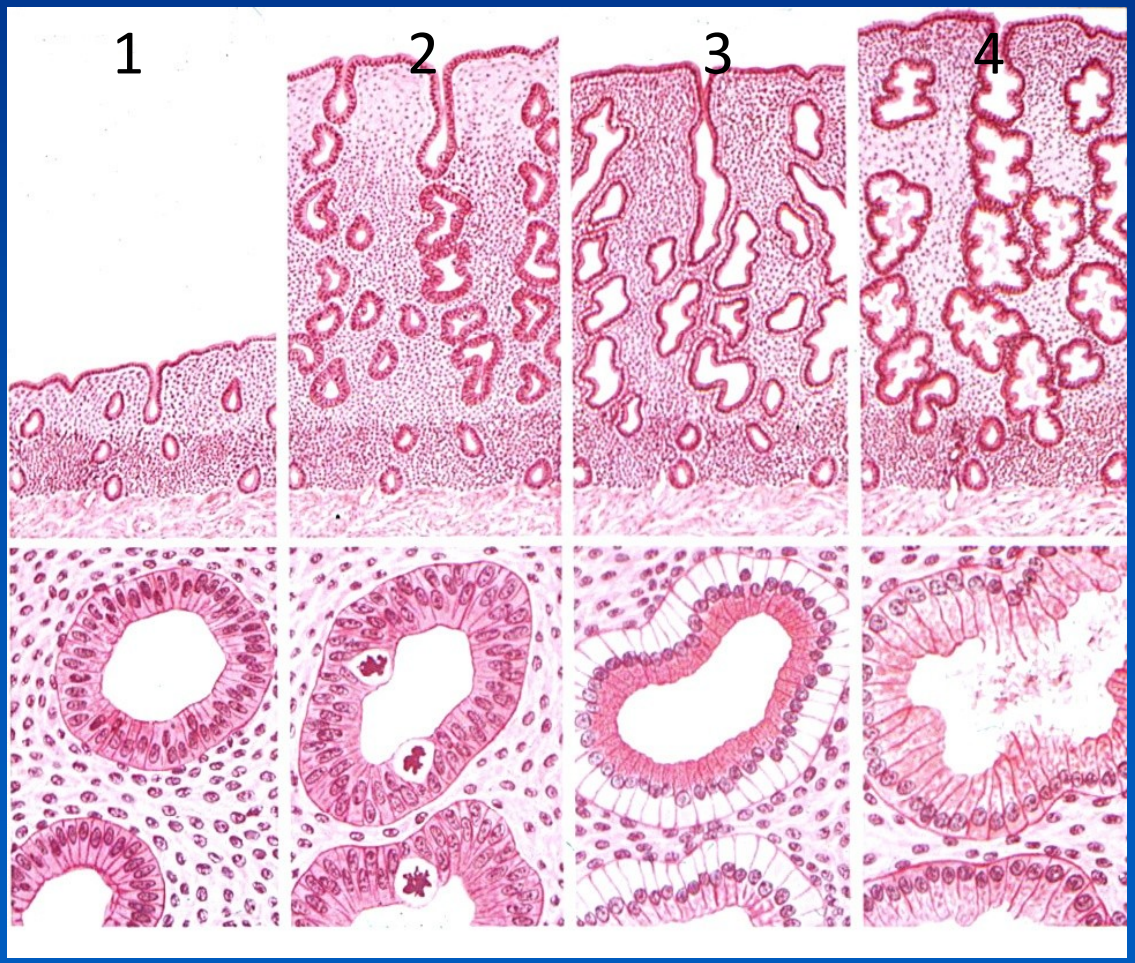


# BENIGN PROSTATIC HYPERPLASIA



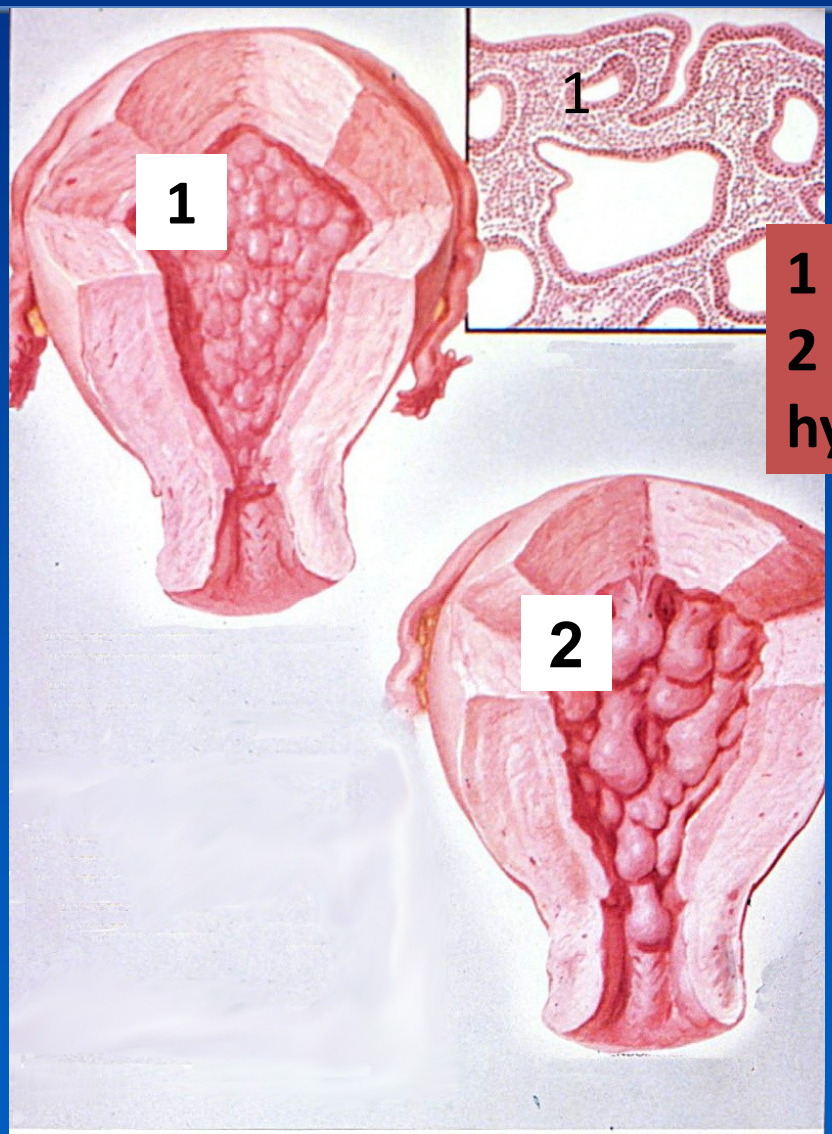


# Endometrium, menstrual cycle



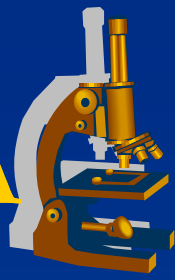

1 early proliferative
2 late proliferative
3 early secretory
4 mid/late secretory

# Hyperplastic endometrium




**1 endometrial hyperplasia**
**2 Polypous endometrial hyperplasia**

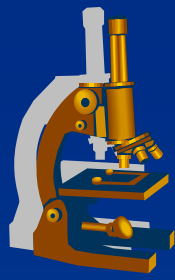
# ENDOMETRIAL HYPERPLASIA



- **Gross**: *thicker mucosa (USG)*

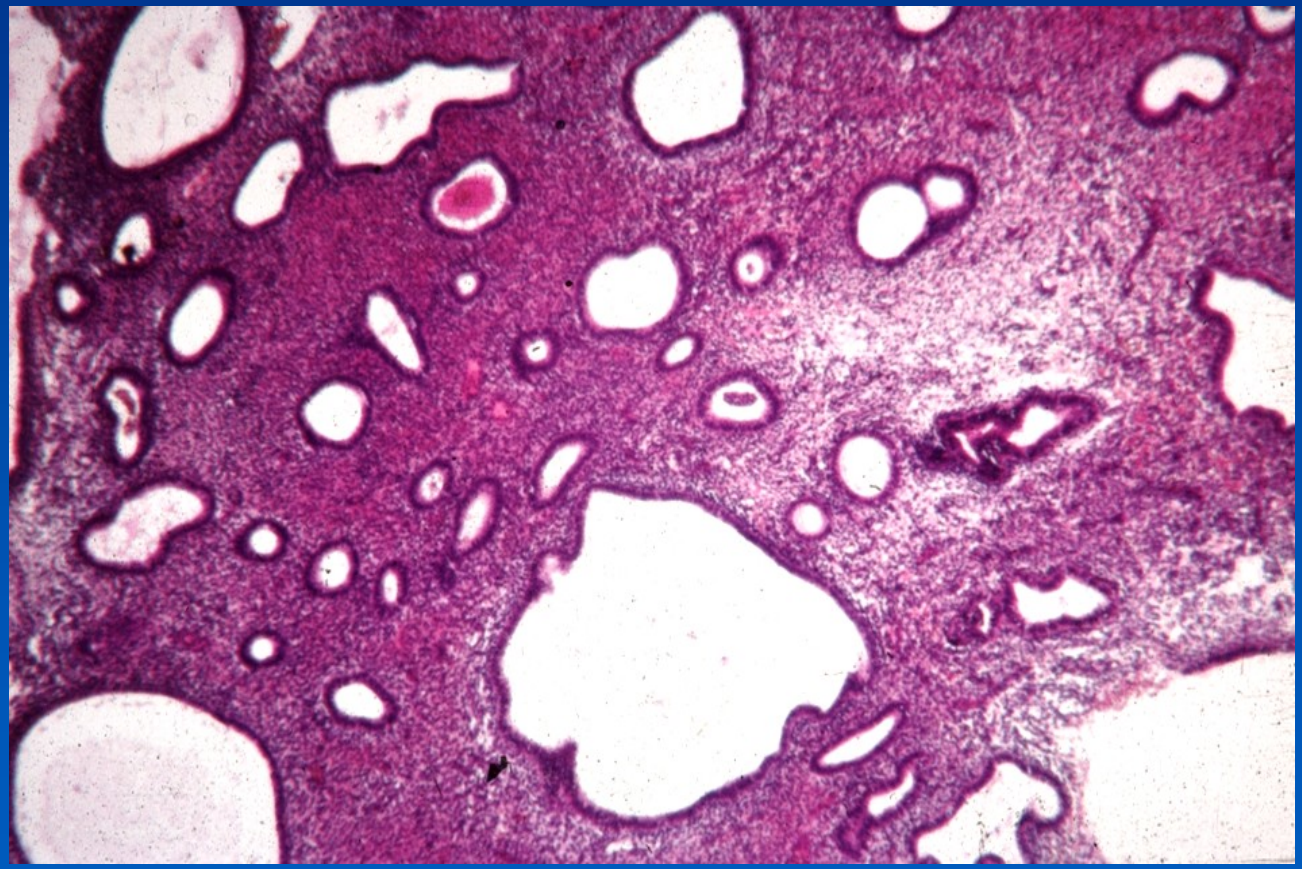
- Micro:
  - ⇨ *both glandular and stromal proliferation*
  - ⇨ *glands more numerous (norm 1:1)*
  - ⇨ *architectonics simple (cystic dilatation) or complex*
  - ⇨ *proliferative epithelium (basal nuclei, possible stratification)*
  - ⇨ *ATYPIA: nuclear enlargement, hyperchromasia, distinctive nucleoli, mitotic activity, anisokaryosis.*

# Classification of endometrial hyperplasia

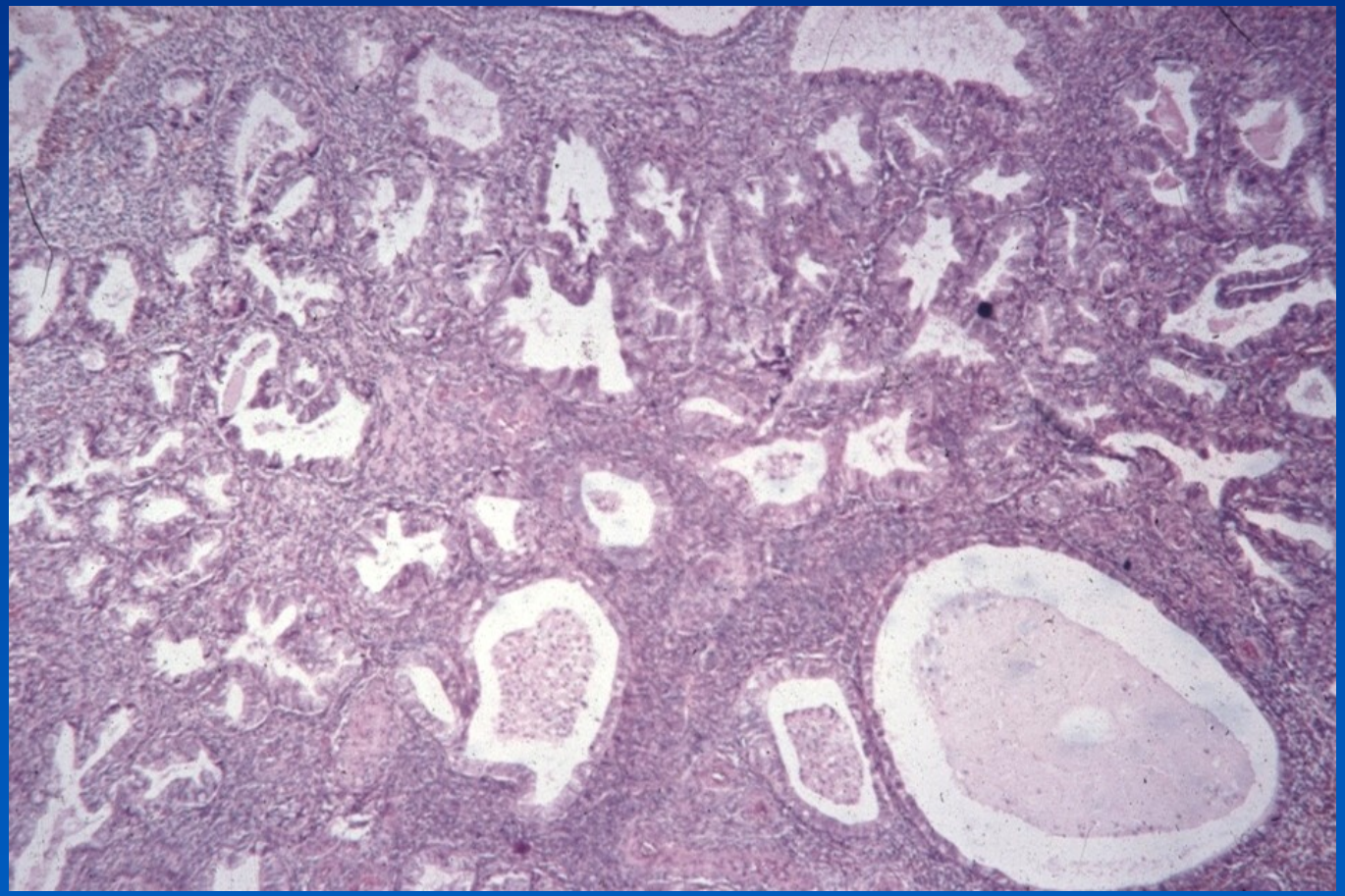


- Simple
  - *cystic glandular dilatation*
  - *increased glandular + stromal cellularity*
  - *no atypias*
- Complex
  - *major architectural change – infoldings*
  - *lower amount of stroma – crowding*
- Atypical (simple or complex)
  - *specify architecture: simple or complex + cellular atypia*
  - *endometrial intraepithelial neoplasia*

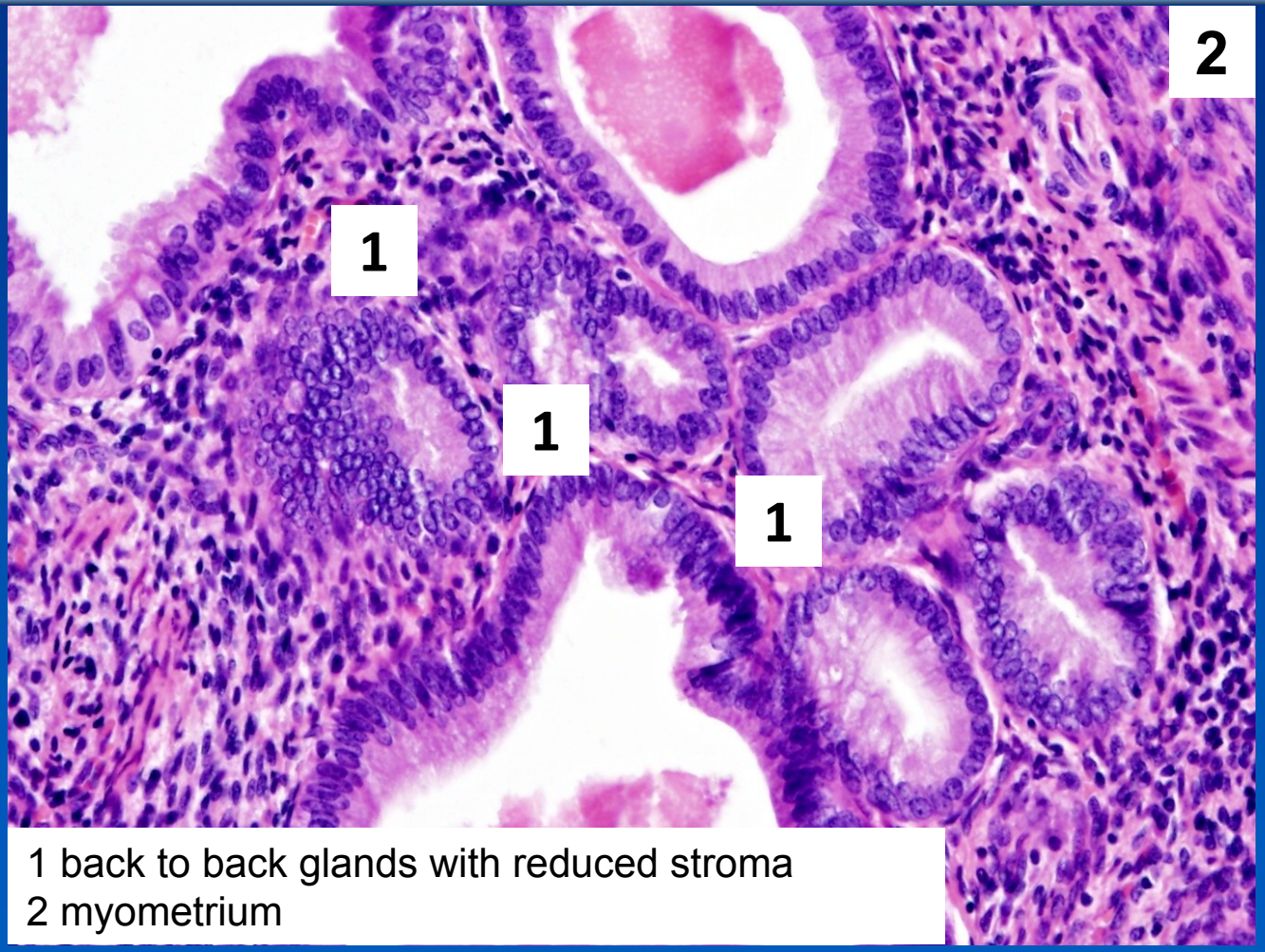
# Simple hyperplasia



# *Complex hyperplasia*

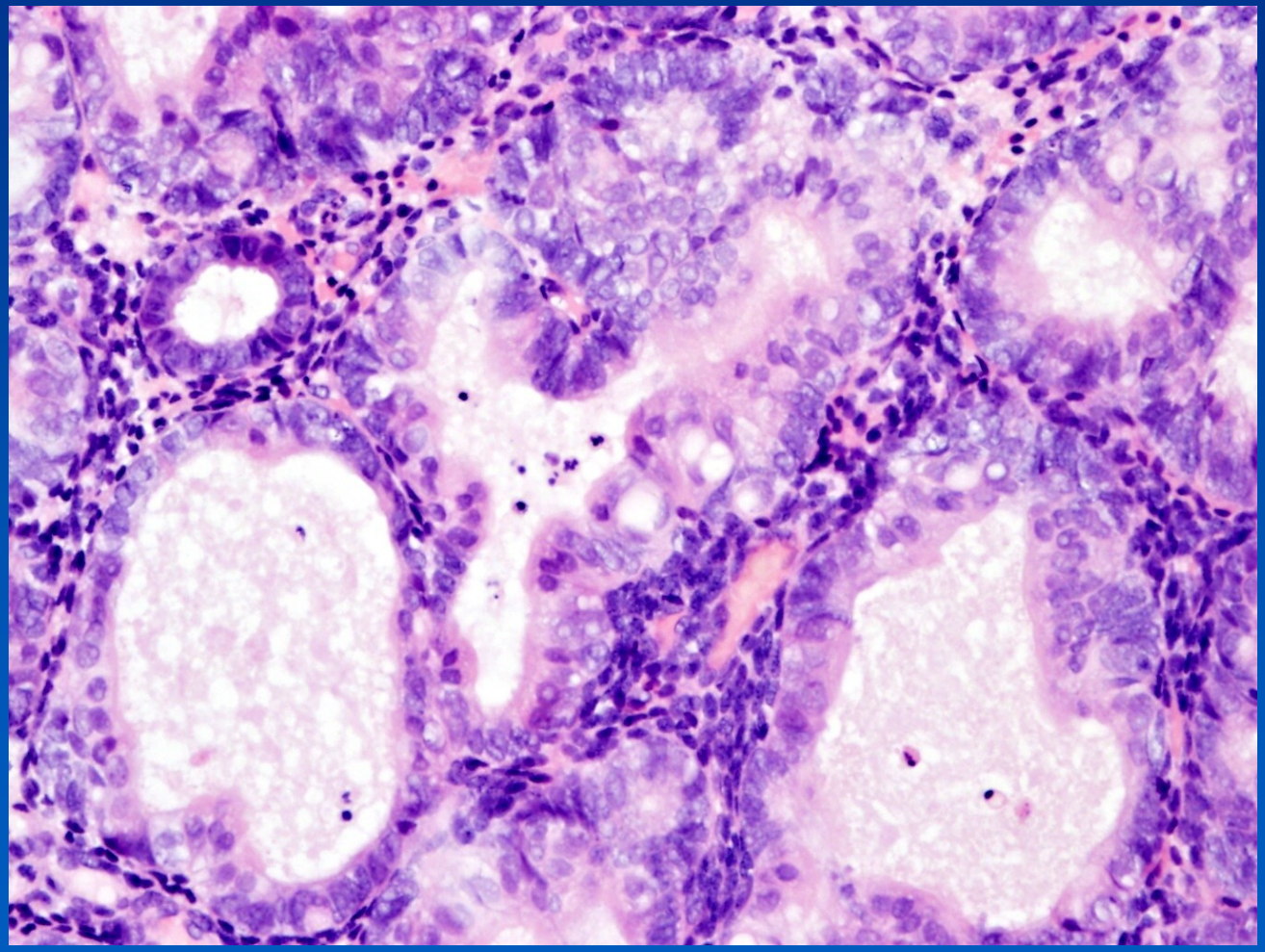


# complex hyperplasia without atypia

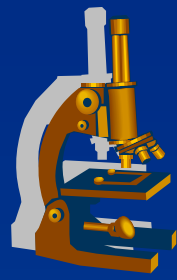



1 back to back glands with reduced stroma
2 myometrium

# Complex hyperplasia with atypia

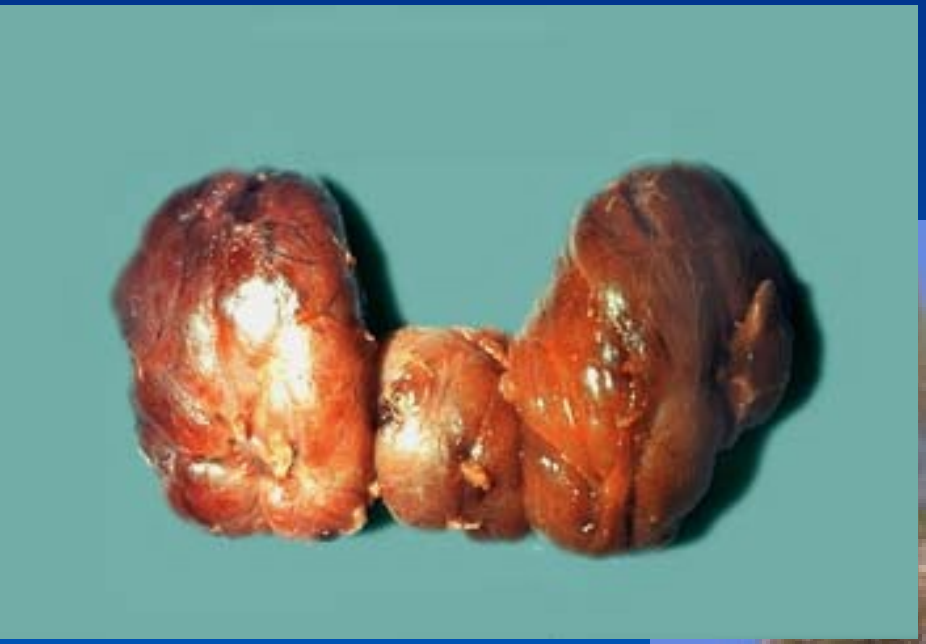


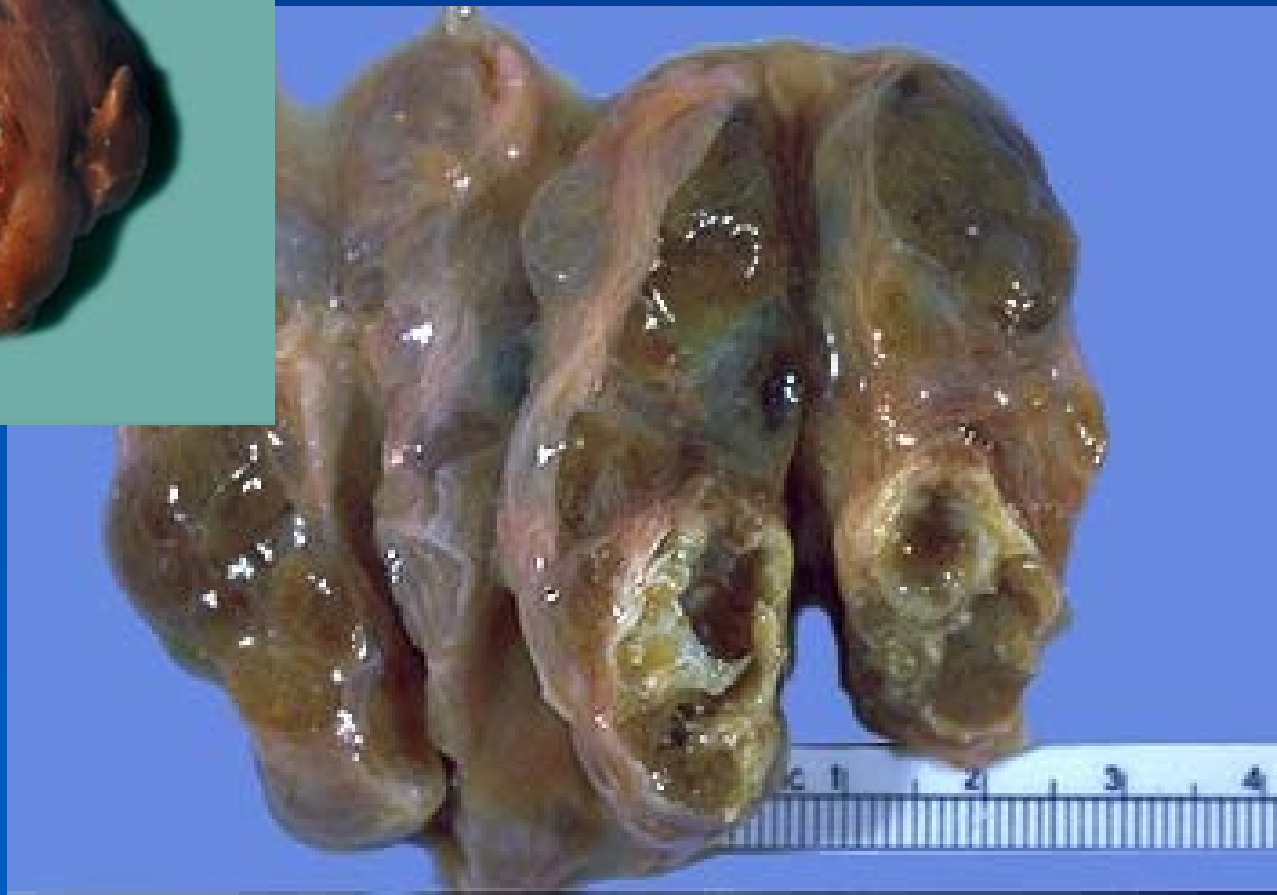
# Thyroid hyperplasia



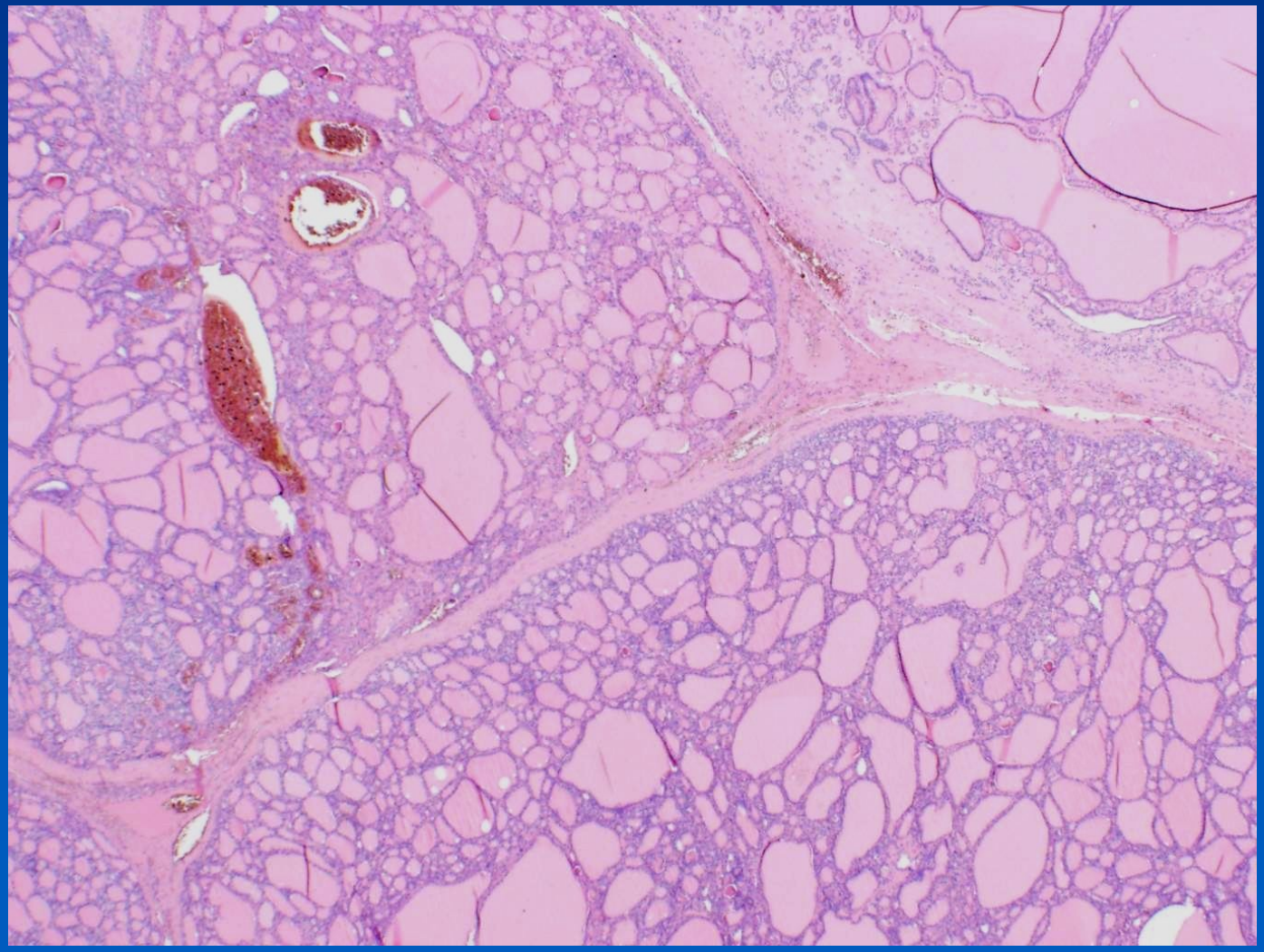
- Goiter
  - ⇨ ***diffuse***
    - simple – nontoxic
    - Graves disease – autoimmune,
    - diff. hyperplasia

- Nodular goiter
  - ⇨***activation of hypothalamic-pituitary-thyroidal axis (iodine defficiency)***
  - ⇨ ***hyperplastic phase, colloid transformation – involution***
  - ⇨***mixture of  dilated follicles, regressive fibrosis, bleeding, calcification***

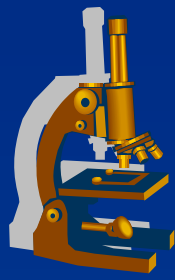




# Thyroid hyperplasia nodular goiter

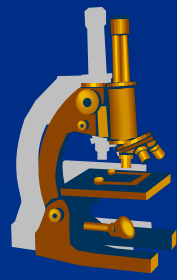


# Graves‘ disease



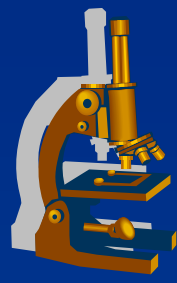
- Hyperplastic thyroid → hyperthyroidism
- Graves‘ (Basedow) disease
  - *organ-specific AI,*
  - *autoantibodies bind on TSH receptor – long-acting thyroid stimulator (LATS)*
- Gross – *enlarged, firm, red*
- Micro – *follicular hyperplasia, papillary, colloid reduction, stromal hyperaemia*

# Hypertrophy



- **increase in cell size without cell division - ↑** production of cellular proteins
- **physiogical:**
  - ⇨ ***muscle hypertrophy*** *(response to increased workload)*
  - ⇨ *hormone-induced (pregnant uterus)*
- **pathological conditions:**
  - ⇨ ***myocardial hypertrophy*** *– essential hypertension, valvular disease (aortal, mitral stenosis, etc)*
  - ⇨ *arterial wall hypertrophy in hypertension*

# Metaplasia



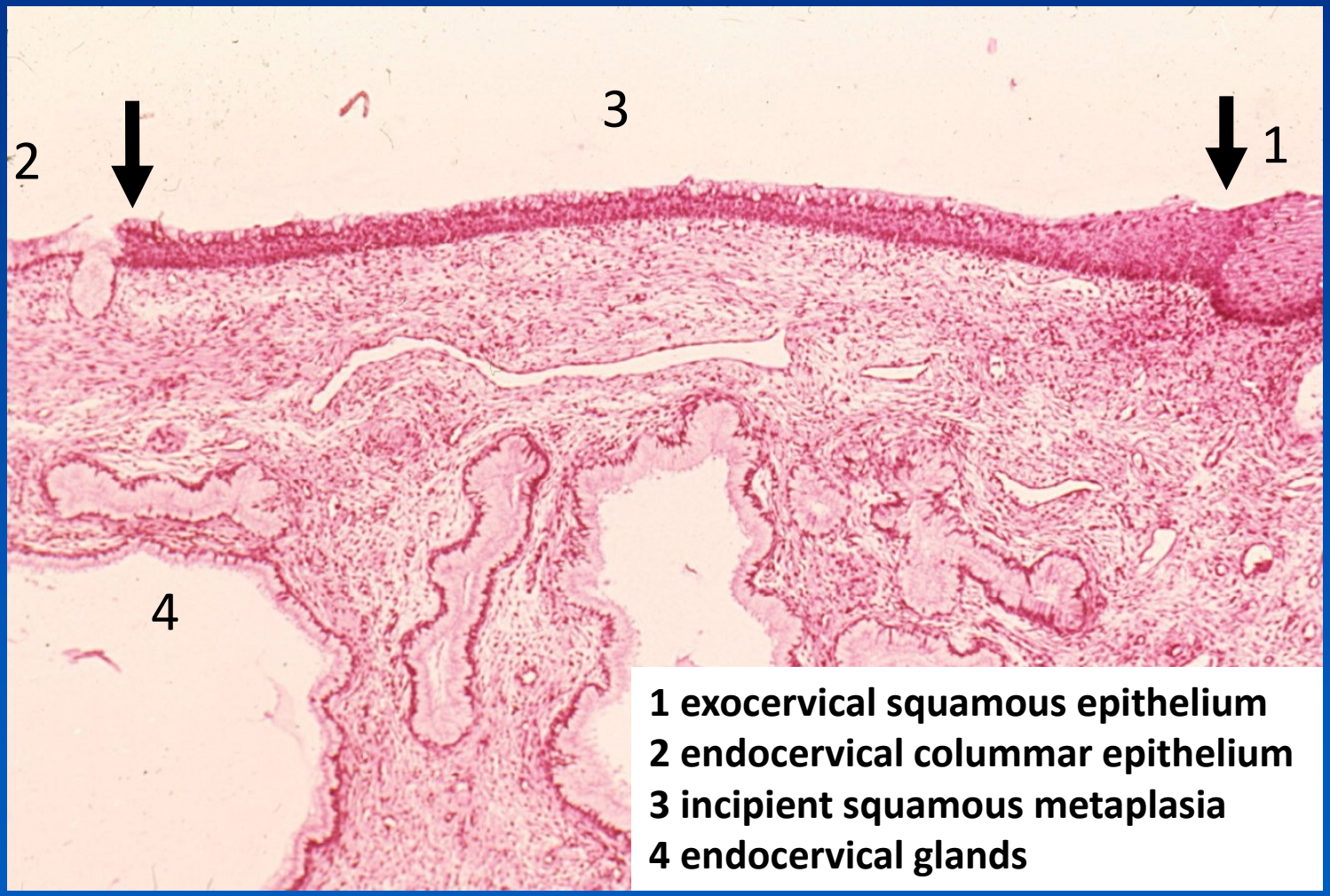
- reversible replacement of one mature diffrerentiated cell type by another via stem cells (adaptive substitution under stress conditions)
- exxagerated differentiation (non-keratinizing squamous epithelium into keratinizing, cartilage ossification, …)
- (rarely direct transformation of a cell by de-differentiation followed by different differentiation)
- epithelial or mesenchymal cells
- may undergo further indirect transformation to neoplasia via dysplasia

- chronic cell injury – smoking, reflux of gastric acid to oesophagus, etc.

⇨ **squamous metaplasia (columnar → squamous)**
- bronchial epithelium – smokers
- endocervical mucosa

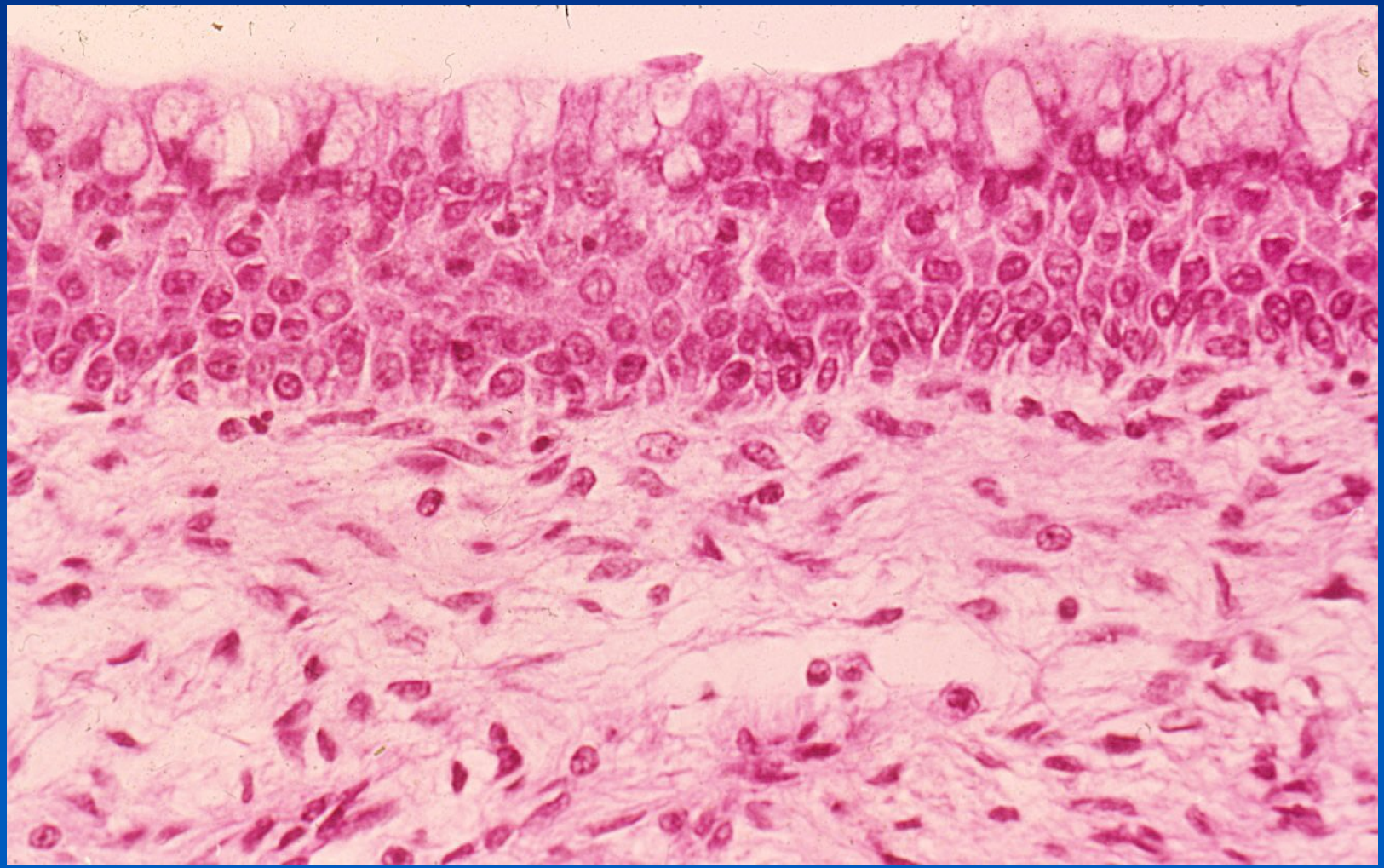
⇨ **interstinal metaplasia**
- Barret´s oesophagus in reflux, gastric mucosa in chronic gastritis

# Incipient squamous metaplasia of endocervical columnar epithelium

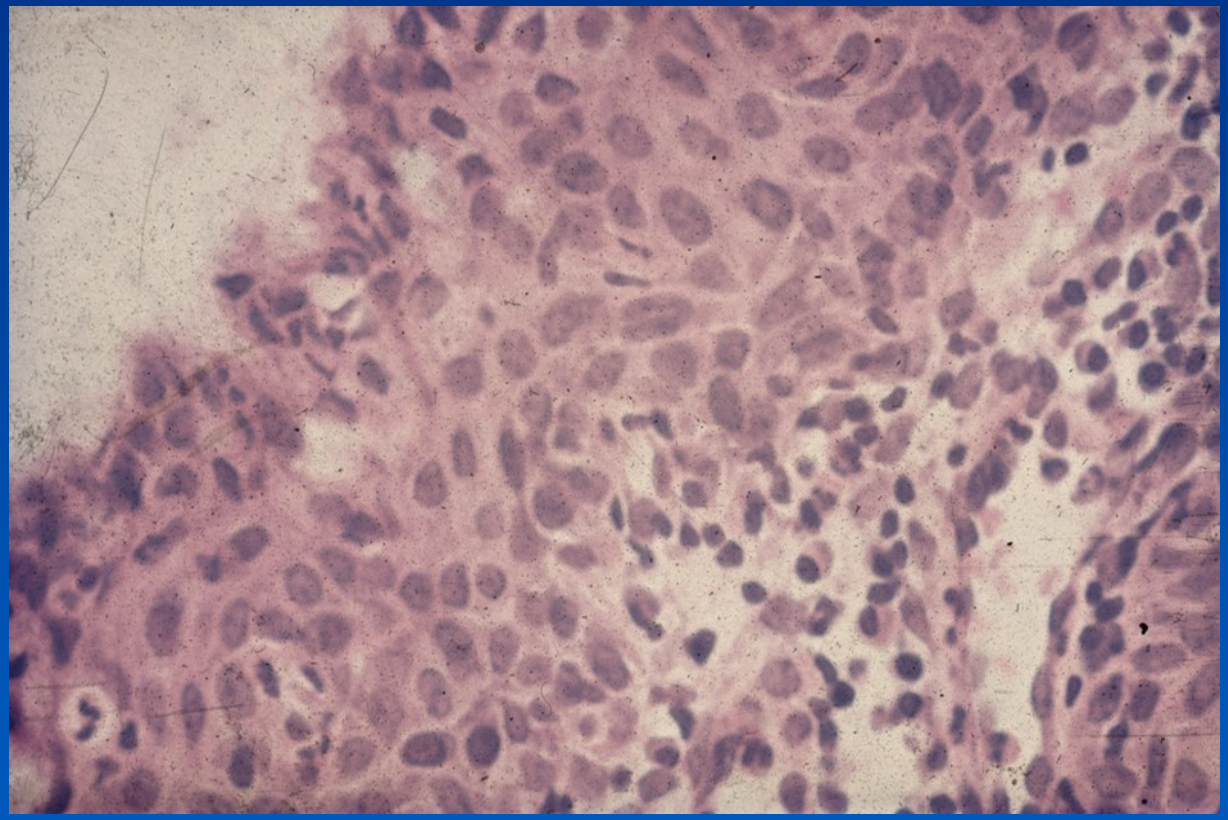



1 exocervical squamous epithelium
2 endocervical columnar epithelium
3 incipient squamous metaplasia
4 endocervical glands

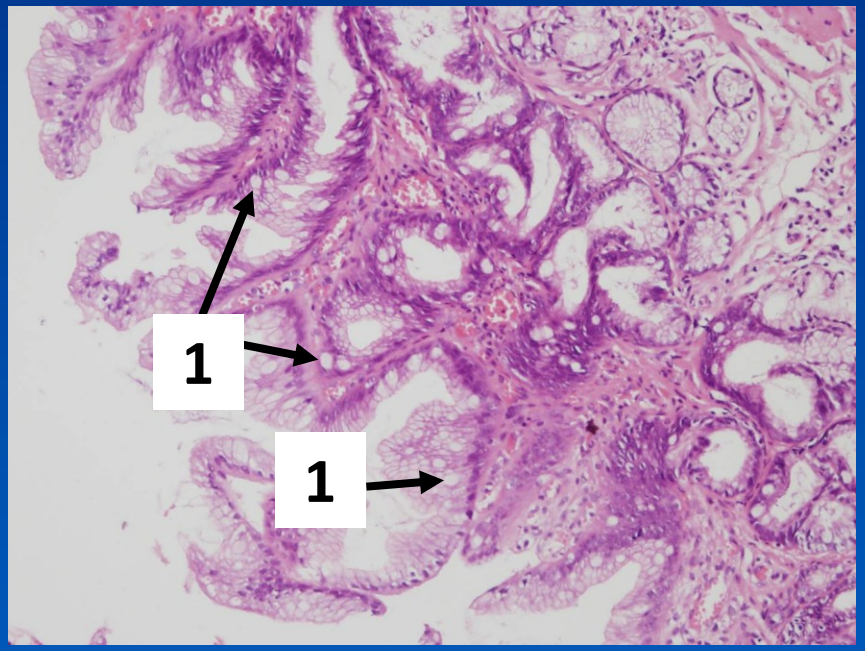
# Incipient squamous metaplasia of endocervical columnar epithelium

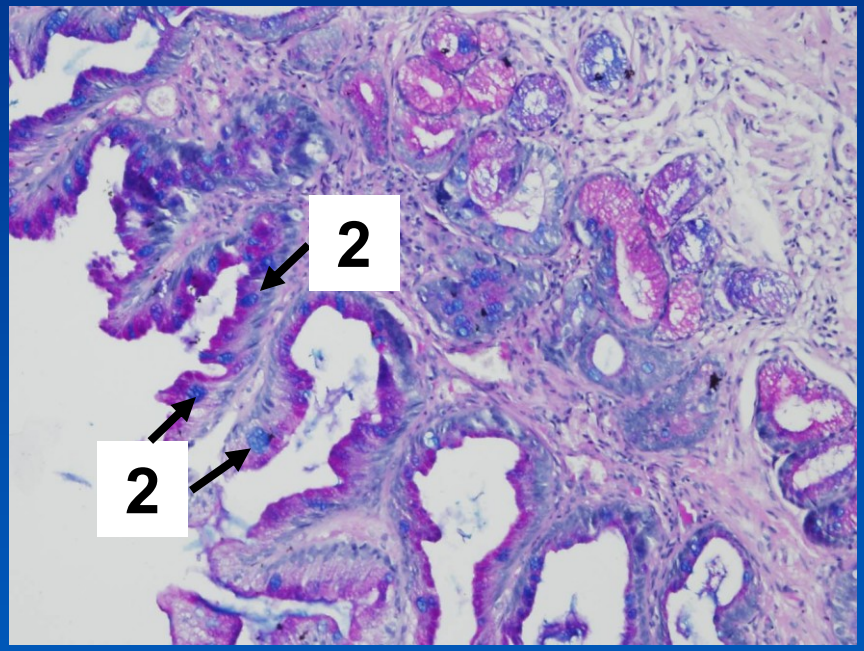


# Immature sq. metaplasia



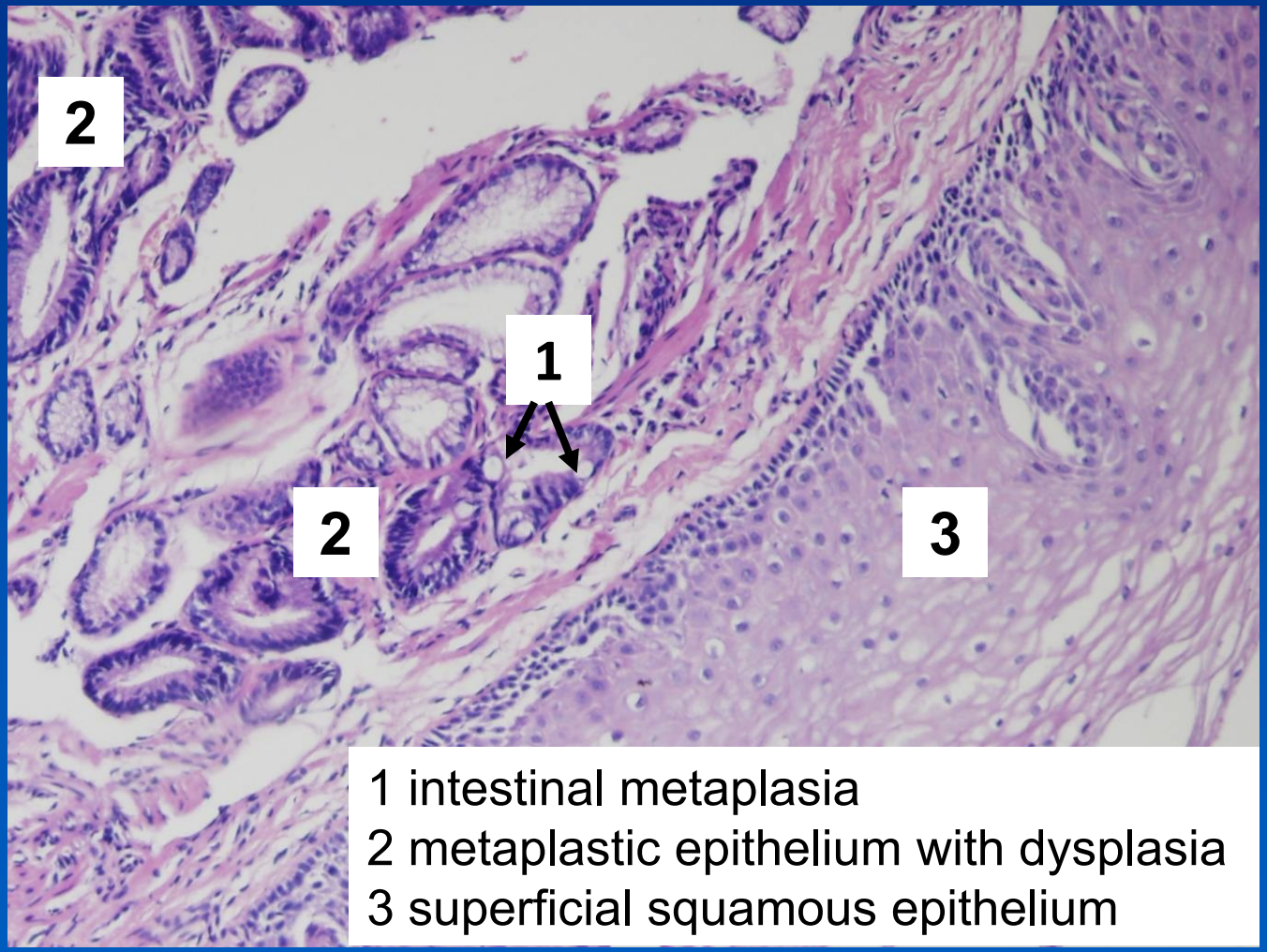
# Barrett´s oesophagus



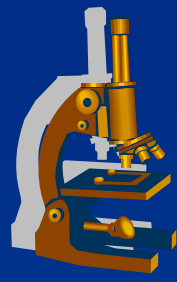

1 intestinal metaplasia (goblet cells)
2 PAS staining – acid mucin substances detection in metaplastic cells

# Barrett´s oesophagus



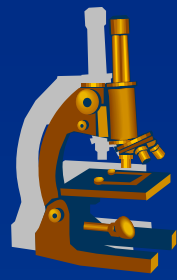

1 intestinal metaplasia
2 metaplastic epithelium with dysplasia
3 superficial squamous epithelium

# Tumour-like lesion



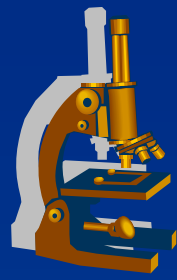
- a nonneoplastic demarcated growing focal lesion that resembles a true neoplasm (by naked eye or microscopy)
  - ⇨ ***progresive changes***
  - ⇨ ***cysts, pseudocysts***
  - ⇨ ***chronic inflammation (inflammatory pseudotumor)***
  - ⇨ ***embryonal development changes (hamartoma, choristoma)***

# Tumour-like lesion
# Progressive changes



- **Sometimes a preneoplastic change**
- **hyperplasia, hypertrophy, hyperregeneration**
  - ⇨ e.g. nodular hyperplasia
    - nodular goiter,
    - benign prostatic hyperplasia, etc.
  - ⇨ pseudoepiteliomatous hyperplasia epithelial hyperplasia associated with chronic irritation and inflammatory response
    - e.g. squamous epithelium in the border of varicose ulcer

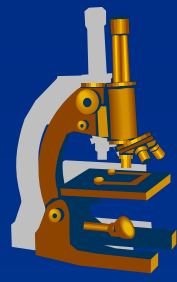
# Tumour-like lesion
## Cysts, pseudocysts



- cyst – pathological cavity lined by epithelium, usually fluid-filled

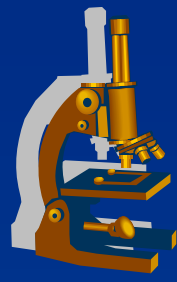
- pseudocysts lack epithelial / endothelial / mesothelial lining cells
  - ⇨ e.g. pancreatic pseudocyst, postmalatic pseudocyst

# Tumour-like lesion
## Cysts, pseudocysts



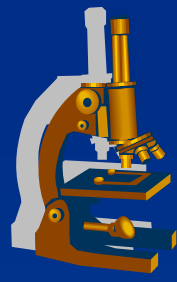
- **common types of cysts:**
  - ⇨ congenital – due to embryonal deffect
    - branchial, thyroglossal, familial polycystic disease
  - ⇨ retention – epidermoid, pilar cysts of the skin
  - ⇨ implantation – as a result of surgical or accidental implantation of epidermis
  - ⇨ parasitic – hydatid cysts due to Echinococcus
  - ⇨ neoplastic - true tumors– e.g. cystadenoma, cystadenocarcinoma

# Tumour-like lesion
## Cysts, pseudocysts



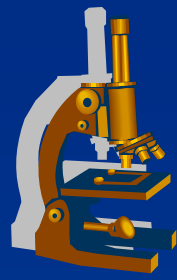
- solitary x multiple / polycystosis
- according to content (serous, mucinous, sebaceous, colloid, hemorrhagic, …)

# Tumour-like lesion
# Chronic inflammation



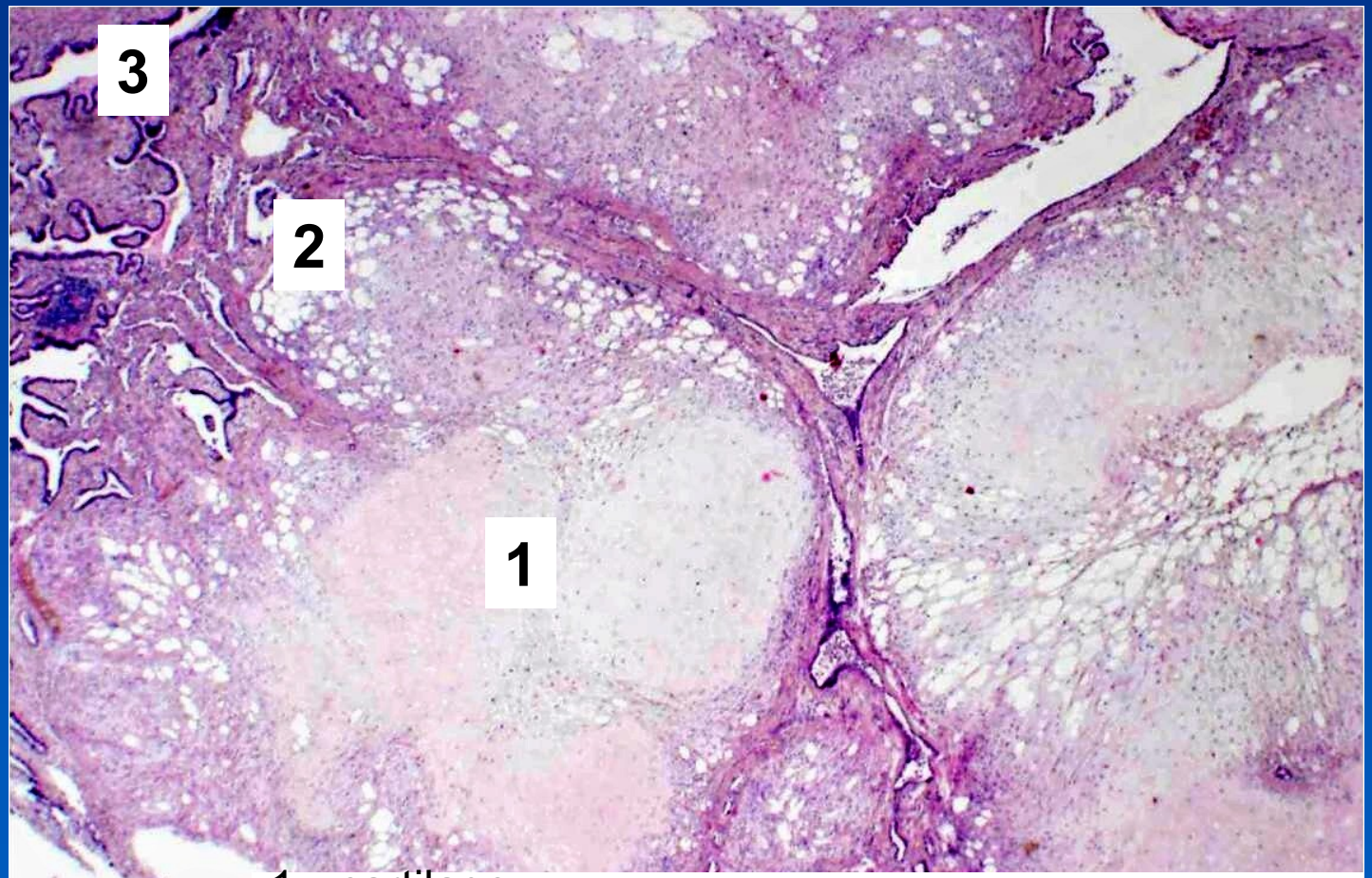
- part of a repair process (suture granuloma)
- relapsing/chronic purulent inflammation (pelvic inflammatory disease, actinomycosis)
- xanthoma (accentuated macrophagic reaction, yellow color)
- inflammatory polyp/hyperplasia

# Tumour-like lesion
# Embryonal maldevelopment



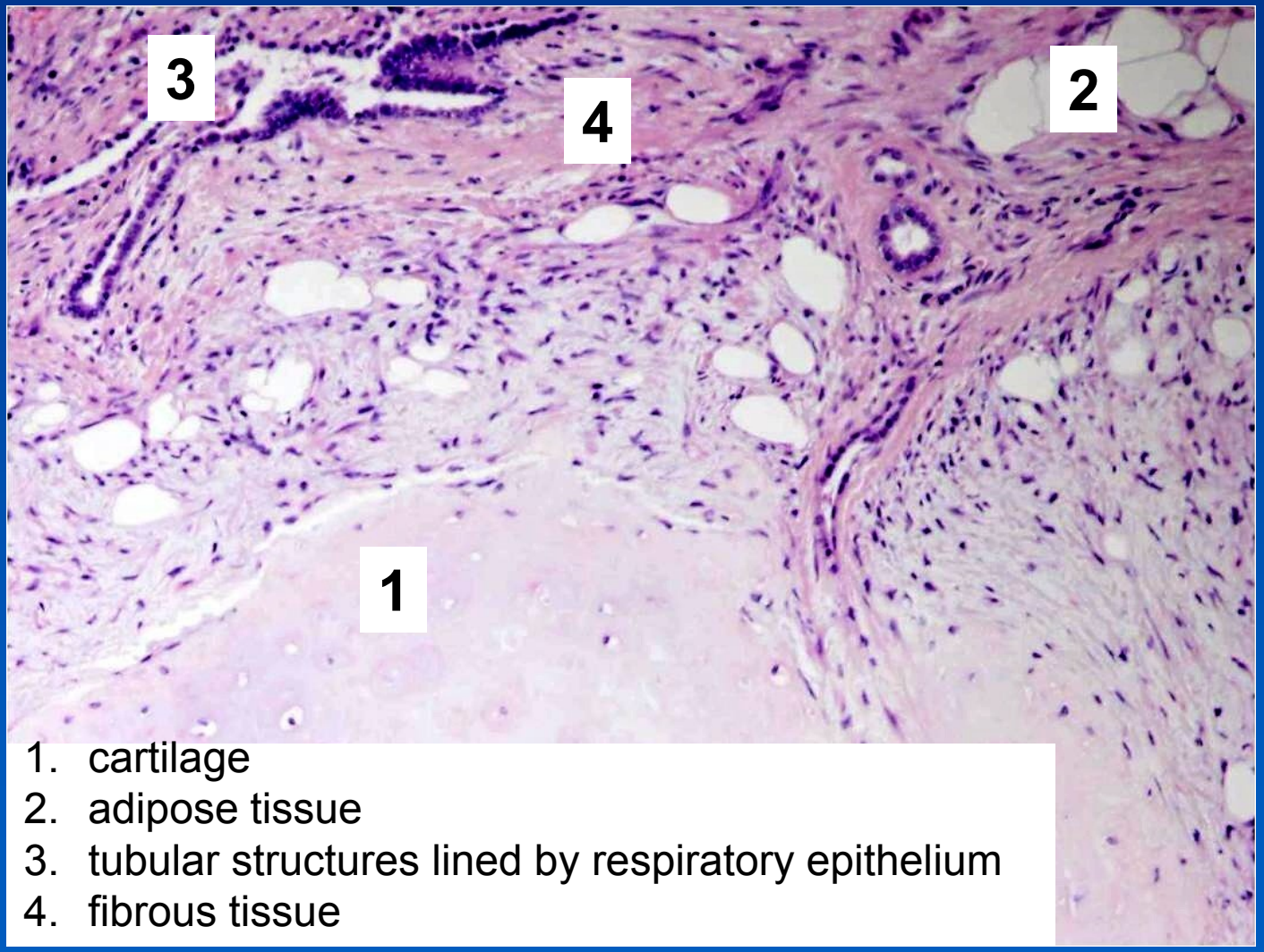
- **choristoma**
  - mass of histologically normal tissue that is present in an abnormal location – heterotopic tissue rest
  - adrenal choristoma in kidney, etc.
- **hamartoma**
  - benign  malformation consisting of an disorganized abnormal mixture of mature indigenous cells and tissues
  - chondrohamartoma of lung (possibly a true tumor) , etc.

# chondrohamartoma of lung

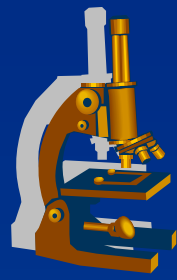



1. cartilage
2. adipose tissue
3. tubular structures lined by respiratory epithelium

# chondrohamartoma of lung

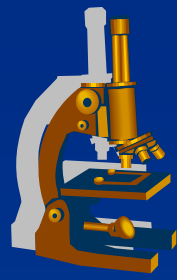



1. cartilage
2. adipose tissue
3. tubular structures lined by respiratory epithelium
4. fibrous tissue



# *General oncology*

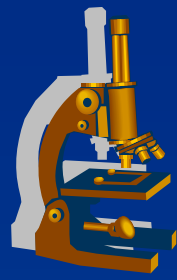
# General oncology



- tumour
  - lesion with persistent autonomous abnormal growth / unregulated cell division

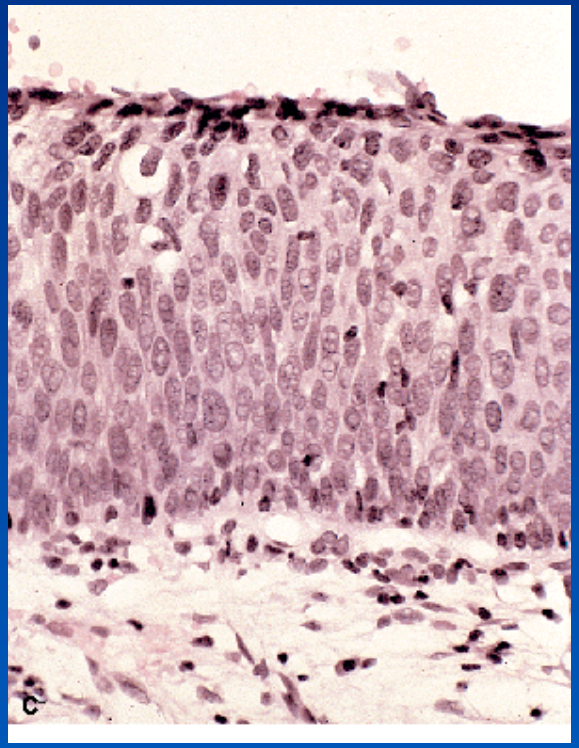
- tumour structure:
  - parenchyma (neoplastic cells)
  - stroma (connective tissue - support and nutrition) – inadequate stroma → possible regressive changes

# General oncology

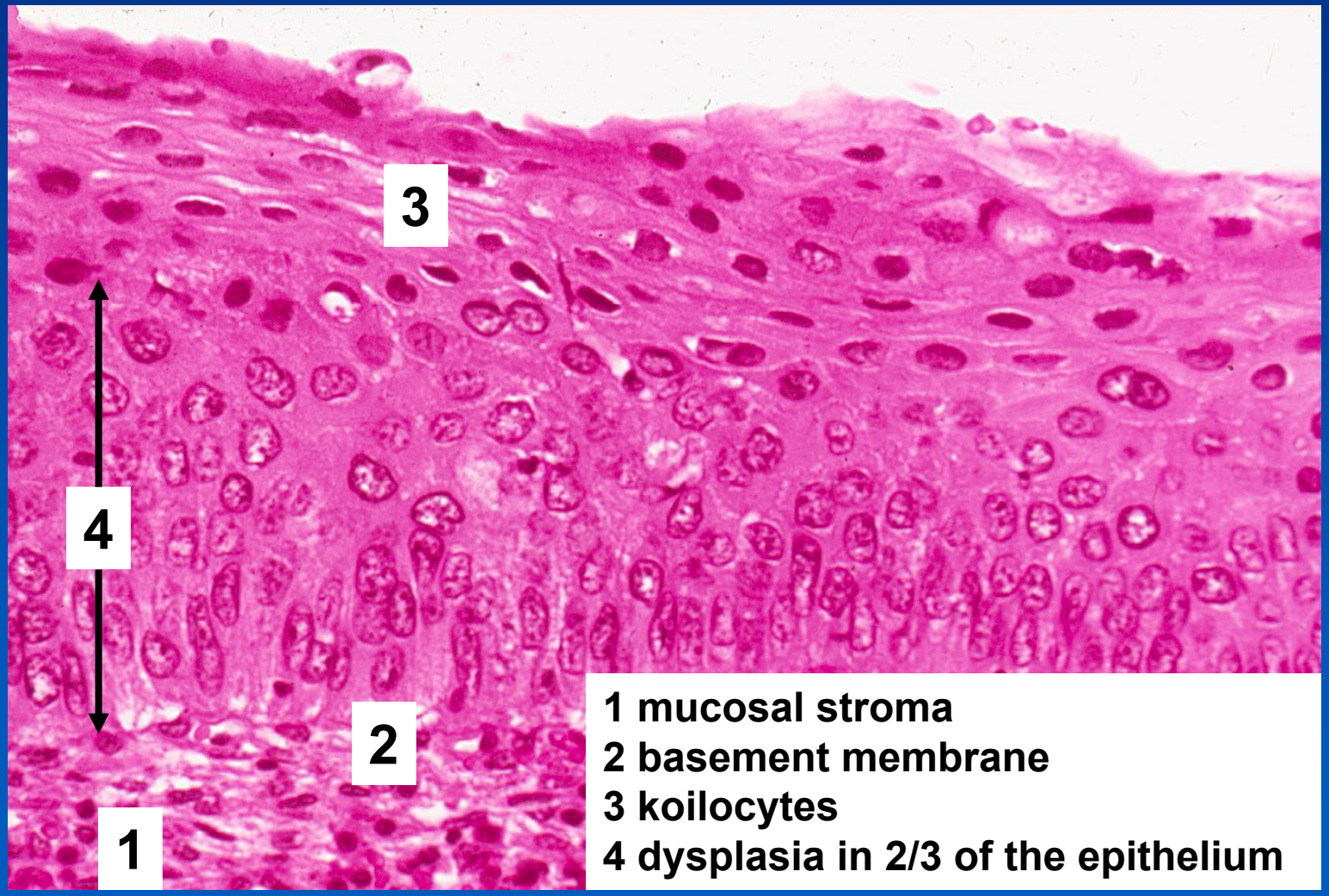


- **epithelial dysplasia = premalignant condition**
  - ⇨ *micro:*
    - **loss of normal maturation/differentiation**
    - **cellular atypia**
      - cellular pleomorphism, ↑ N/C ratio, hyperchromatism
    - changes in the structural arrangement of cells in the epithelium
  - ⇨ *classification:*
    - **Low-grade (mild) x high-grade (moderate/severe) dysplasia**
  - ⇨ *may be caused by chronic inflammation, irritation (physical or chemical injury), carcinogenic agents (HPV)*
  - ⇨ *may be reversible in early stages (low-grade dysplasia), high-grade dysplasia has a higher risk of progression to carcinoma in situ or invasive carcinoma*

# *Cervical dysplasia*
# *High-grade CIN (CIN II)*

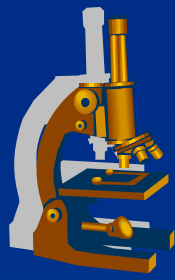


# *Cervical dysplasia*
# *High-grade CIN (CIN II)*




1 mucosal stroma
2 basement membrane
3 koilocytes
4 dysplasia in 2/3 of the epithelium

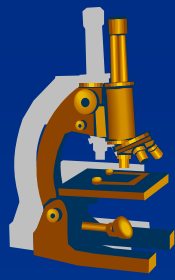
# General oncology



- **anaplasia**
  - *loss of cell differentiation*
  - *morphology of anaplastic tumors may mimic immature/embryonal tissue*

- **carcinoma in situ**
  - *localized epithelial neoplasm with all the cellular features of malignancy, but without invasion through epithelial basement membrane*
  - *often together with dysplasia in the group (concept) of intraepithelial neoplasia (named after localisation – CIN, PIN, VIN, PanIN, etc.)*

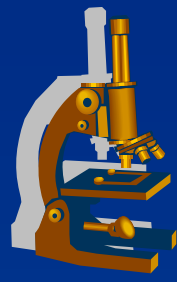
# General oncology



- **invasive carcinoma**
  - *the final step in the process of carcinogenesis*
  - *invasion of tumor cells through the basement membrane*
  - *metastatic potential*

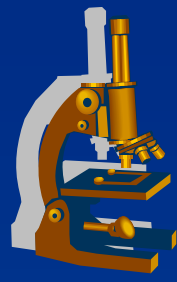
- **desmoplasia / desmoplastic stromal reaction**
  - *proliferation of connective tissue, stromal response to neoplastic process.*

# General oncology
# Carcinogenesis



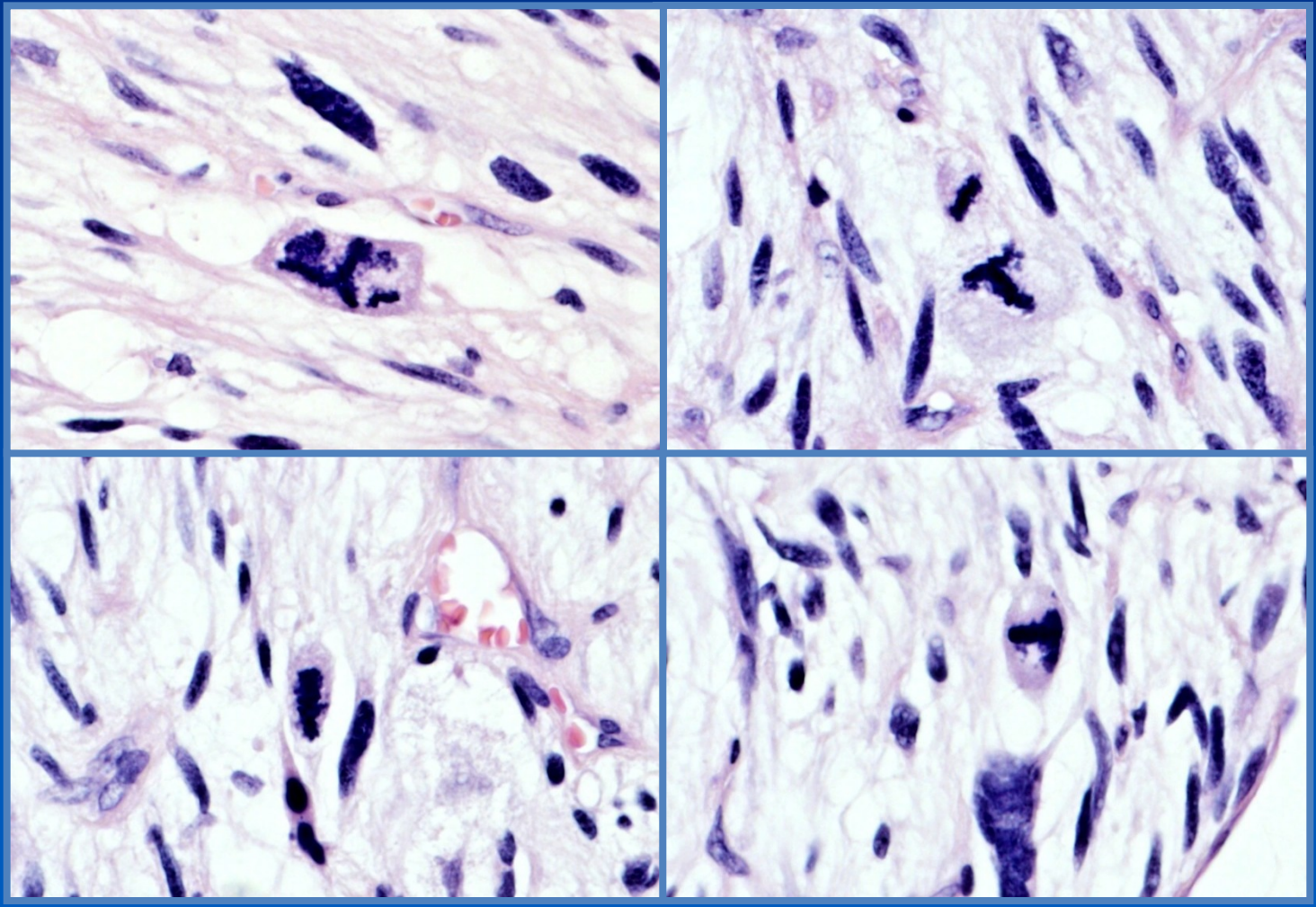
- **Multifactorial, complex**
  - ⇨ ***external factors***
    - ionising, non-ionising radiation
    - **carcinogens** (tobacco smoke, aflatoxins, nitrosamines)
    - **oncogennic viruses** (HPV, EBV, HTLV-1, HSV-8), bacteria (Helicobacter)
  - ⇨***endogennous factors - hereditary***
    - **approx. 15% of malignancies due to genetic factors**
    - inherited tumor risk – breast/ovary carcinoma by mutation ***BRCA1*** či ***BRCA2****; familial polyposis coli,* *neurofibromatosis, retinoblastoma,* ***Li-Fraumeni syndrome***

# General oncology
# signs of malignancy

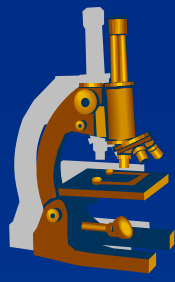


- CYTOLOGIC CHANGES (ATYPIA) :
  - *cytologic and/or nuclear pleomorphism, anisokaryosis, anisocytosis*
  - *nuclear enlargement*
  - *increased nucleocytoplasmatic index (N/C)*
  - *nuclear hyperchromasia*
  - *irregular chromatin texture*
  - *irregular shape of the nuclear membrane (grooves)*
  - *increased mitotic activity*
  - *atypical mitoses (tripolar, multi-center, asymmetrical)*
  - *sometimes multinucleated cells*

# Atypical mitosis (tripolar)

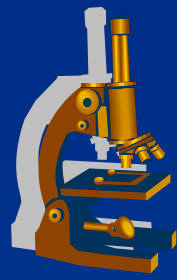


# Principal characteristics of benign and malignant tumors



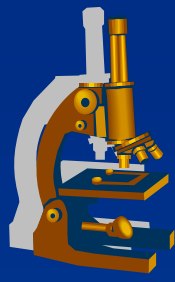
| | benign | malignant |
|---|---|---|
| **Histological resemblance to normal tissue** | Good | Variable, often poor |
| **Mitotic activity** | Low | High + atypical |
| **Grow rate** | Slow | Relatively rapid |
| **Nuclear morphology** | Often normal | Usually hyperchromatic |
| **Border** | Often circumscribed or encapsulated | Often poorly defined or irregular |
| **Necrosis** | Rare | Common |
| **Invasion** | No | Yes (often) |
| **Metastases** | Never | Frequent |

# Nomenclature of tumours



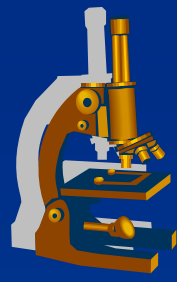
- All have the suffix „-oma“
- Benign epithelial tumor: papilloma, adenoma
- Benign connective tissue have a prefix denoting the cell of origin (fibr- , leiomyo-, hemangio -, lipo - ,…)
- Malignant epithelial tumors are carcinomas
- Malignant connective tissue tumors are sarcomas

# Examples of tumour nomenclature



| Type | Benign | Malignant |
|---|---|---|
| **Epithelial**<br>Squamous cell<br>Glandular | Squamous cell papilloma<br>Adenoma | Squamous cell carcinoma<br>Adenocarcinoma |
| **Mesenchymal**<br>Smooth muscle<br>Addipose tissue<br>Blood vessels | Leiomyoma<br>Lipoma<br>Angioma | Leiomyosarcoma<br>Liposarcoma<br>Angiosarcoma |

# TUMOUR DIAGNOSIS



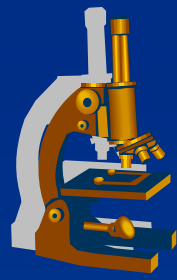
## 1. MICROSCOPIC

⇨ *+ event. IHC, electron microscopy, molecular biology, genetics*

## 2. TUMOUR TYPE (histogenetic)

- epithelial,
- mesenchymal
- neuroectodermal
- germinal
- mixed
- (choriocarcinoma)
- (mesothelial)

# TUMOUR DIAGNOSIS



## 3. GRADING

- ⇨ histologic grade of malignancy » possible biologic behaviour
- ⇨ G1 – G4 well differentiated - undifferentiated

## 4. STAGING

- ⇨ stage according TNM classification
- ⇨ *T* *N* *M*

**tumor node metastasis**

# diagnostic algorithm

clinical signs
clinical examination

cancer suspicion

yes

no

diagnostic imaging techniques
(x-ray, CT, MRI,...USG,...)

no

suspected cancer

yes

benign tumor, pseudotumor

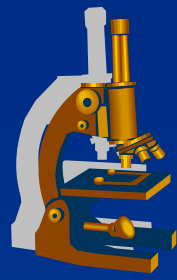
Cancer staging → therapy

exploratory biopsy

typing, grading, staging

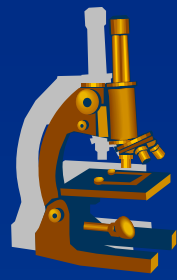
malignant tumor

# *Tumor code*



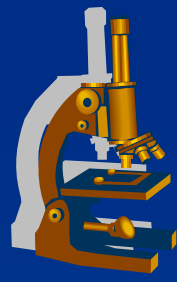
- WHO International Classification of Diseases for Oncology (ICD-O):
  - ⇨ ***numerical classification and coding system by topography and morphology***
- TNM Classification of Malignant Tumors (UICC), AJCC Cancer Staging Manual:
  - ⇨ ***coding system of tumor stage***
- WHO Classification of Tumours, Pathology and Genetics:
  - ⇨ ***histologic classification by organ system***

# *Tumor code*



- Topography (localization) C00.0 – C80.9 (lip – unknown primary localization)
- Subdivision: C34 lung
  - C34.0 main bronchus
  - C34.1 upper lobe
  - …

# *Tumor code*



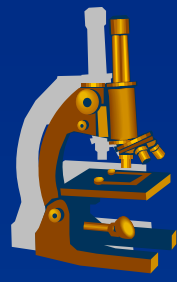
Morphology (histology): digital

- 4 digits – basic histogenetic structure

  8070 – tumor of squamous cell

  8140 – tumor of glandular cell

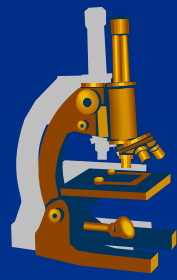
# *Tumor code*



Morphology (histology): digital

- 5. digit – biologic behaviour
  - /0 benign (incl. low grade dysplasia)
  - /1 uncertain, intermediate biologic behaviour, low malignant potential
  - /2 high grade dysplasia, carcinoma/melanoma in situ
  - /3 malignant, primary localization
  - /6 malignant, metastasis
  - /9 malignant, unknown if primary or metastatic

# *Tumor code*



Morphology (histology): digital

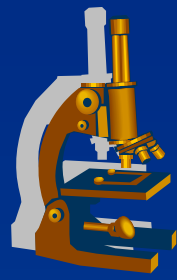
- 6. digit : grading/differentiation of malignant tumors

1 – 4 well – moderate – low – undifferentiated

8140/0 adenoma

8140/31: well differentiated adenocarcinoma in primary localization

# *Tumor code*



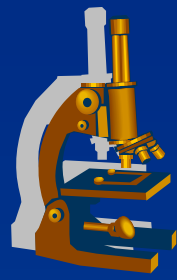
Staging

T size or contiguous extension of the primary tumor

N absence or presence/extent of cancer in the regional draining lymph nodes

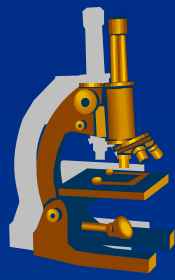
M absence or presence of distant spread or metastasis

# *Tumor code*



- T0 no evidence of primary tumor
- Tis tumor in situ
- T1,T2,T3,T4 increasing size/local extension
- TX primary tumor cannot be assessed
- similarly N0, N1-4, NX
- M0,M1

# *Tumor code*



Example:

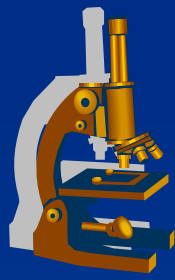
***C16.1***

***M-8140/33***

***pT3,pN3,pM1***

***Poorly differentiated adenocarcinoma of stomach fundus with extension into subserosal connective tissue, metastases in 7 or more LN, with distant metastases***

# *Treatment of tumors*

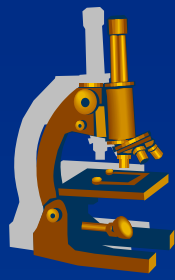


- cancer treatment is striving to reduce (ideally eliminate) all tumor cells
- problems: inoperable tumors, resistance to therapy, toxicity of therapy, late side effects of treatment

- palliative care
  - ***supportive care provided to patients with incurable diseases in order to improve the quality (often not the quantity) of life***

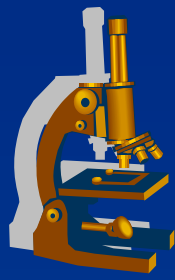
- **prevention is the most effective !!!**

# *Treatment of tumors*



- surgery
  - ***cancer location !!! Mostly solid tumors x leukemia***
  - ***the goal of treatment is usually to remove the tumor with surgery***
- chemotherapy
  - ***are most often used for treating leukemia, lymphoma***
  - ***neoadjuvant therapy***
    - aims to reduce the size or extent of the cancer before using radical treatment intervention)
- radiation
- hormone therapy
  - ***breat carcinoma, prostatic carcinoma,…***
  - ***the histological examination determined the presence of hormone receptors on tumor cells***

# *Treatment of tumors*



- biological therapy
  - ⇨ ***type of treatment that works with your immune system***
    ***X chemotherapy attacks the cancer cells directly***
  - ⇨ ***cytokines (IFNα, IFNγ, IL-2), monoclonal antibodies***

- gene therapy in the future ???