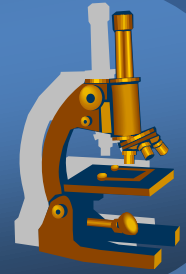


# *Systemic Pathology*



***CARDIOVASCULAR  
system***

# ATHEROSCLEROSIS



- disease of large and medium-sizes arteries with lipid deposition into intima
- **active inflammatory process**
- **endogenous risk factors, mostly noninfluenceables :**
  - **age, MxF** (estrogen?), *familiar factors (f. hypercholesterolemia), hereditary homocysteinemia*
- **exogenous risk factors:**
  - **hyperlipidemia** (LDL) ←←← *hypothyreosis, nephrotic sy;*
  - **hypertension, diabetes mellitus, life style** *smoking (nicotine, CO), sedentary life, food + obesity; ↑CRP*

# Atherosclerosis - pathogenesis



## 1. Endothelial injury

- *mechanic* ( $\uparrow$ BP, turbulence)
- *endotoxins, immune complexes, exogenous toxins (cig. smoke),  $\uparrow$  cholesterol*

*$\uparrow$  expression of cell adhesion molecules,  $\uparrow$  permeability,  $\uparrow$  thrombogenicity*

## 2. Lipoprotein insudation (LDL) – **oxidation** in intima

## 3. Inflammation

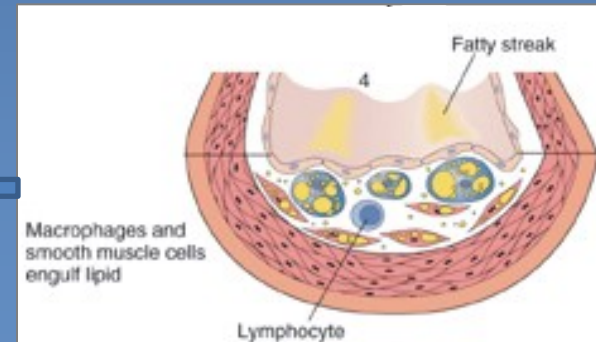
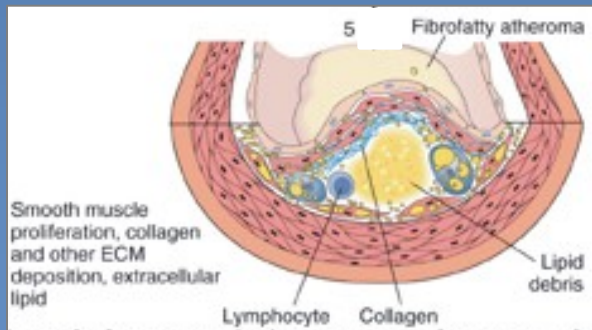
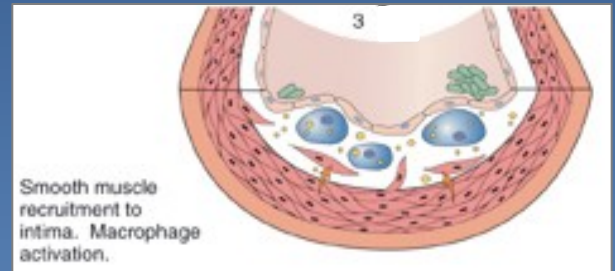
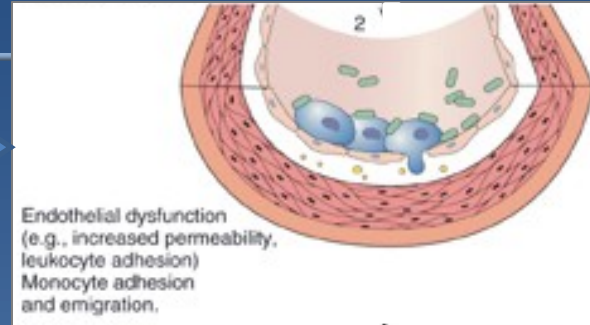
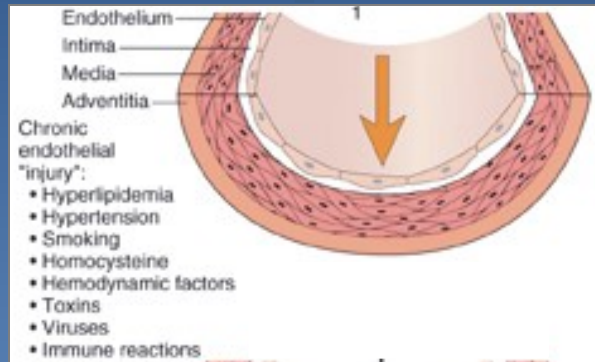
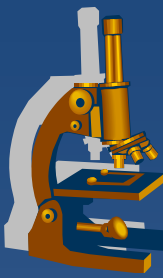
- *blood monocytes ( $\rightarrow$ foam cells), T-cells, platelets, smooth muscle cells*

## 4. Repair - proliferation of myointimal cells

- *synthesis of collagen, elastin, proteoglycans  $\rightarrow$  **fibrotic plaque**, + lipid accumulation - **atheromatous plaque***

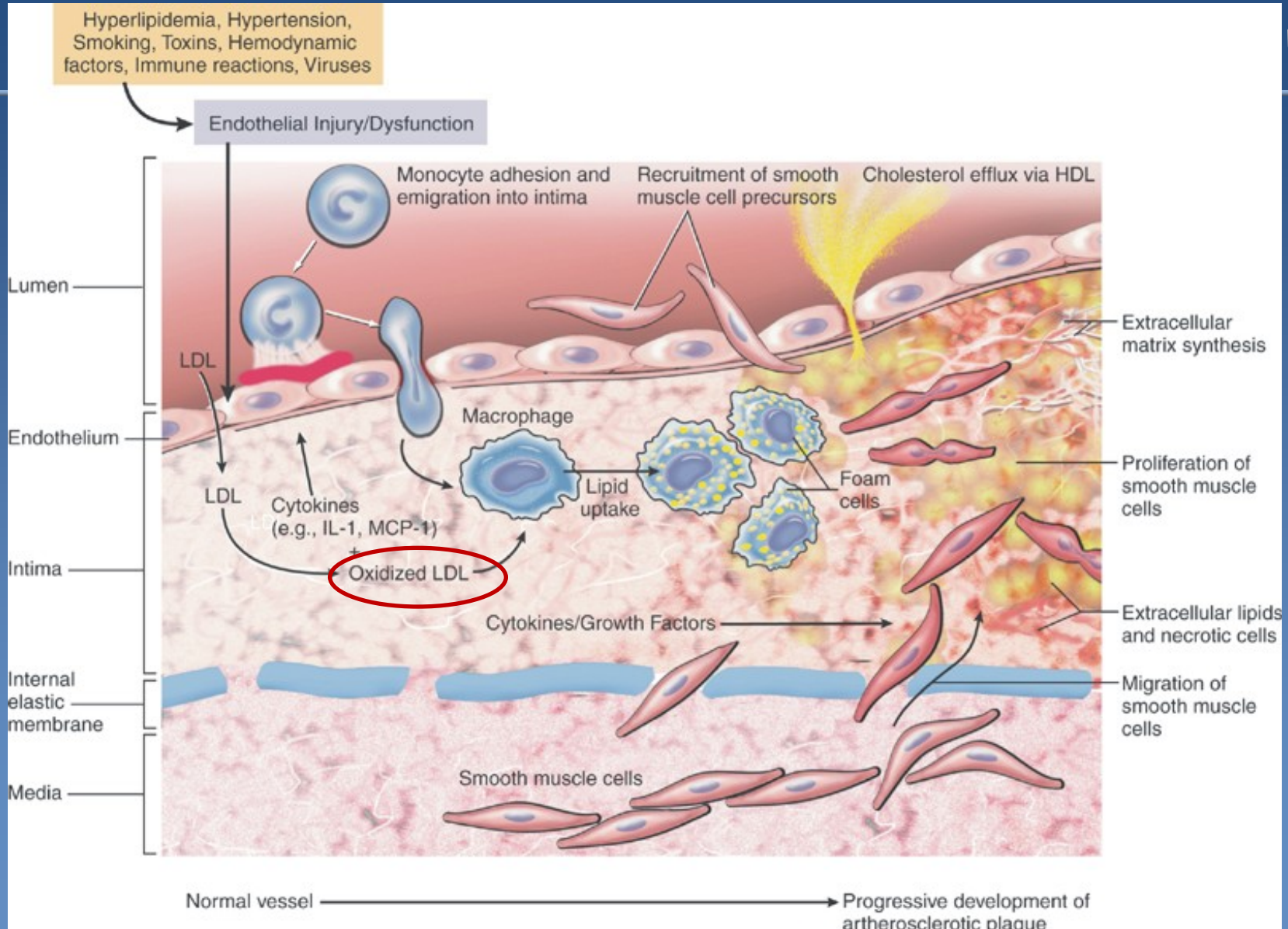
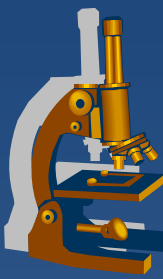
*stable plaque under repeated inflammation turns into unstable plaque – fibrous cap + endothelium rupture - thrombus*

# Atherosclerosis - pathogenesis





# atherosclerosis – cell interactions in an atheromatous plaque



# *Atherosclerosis*

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- ✘ fatty streak
- ✘ fibrotic plaque
- ✘ atheromatous plaque
- ✘ complicated atheromatous plaque  
(ulceration, calcification, thrombosis)

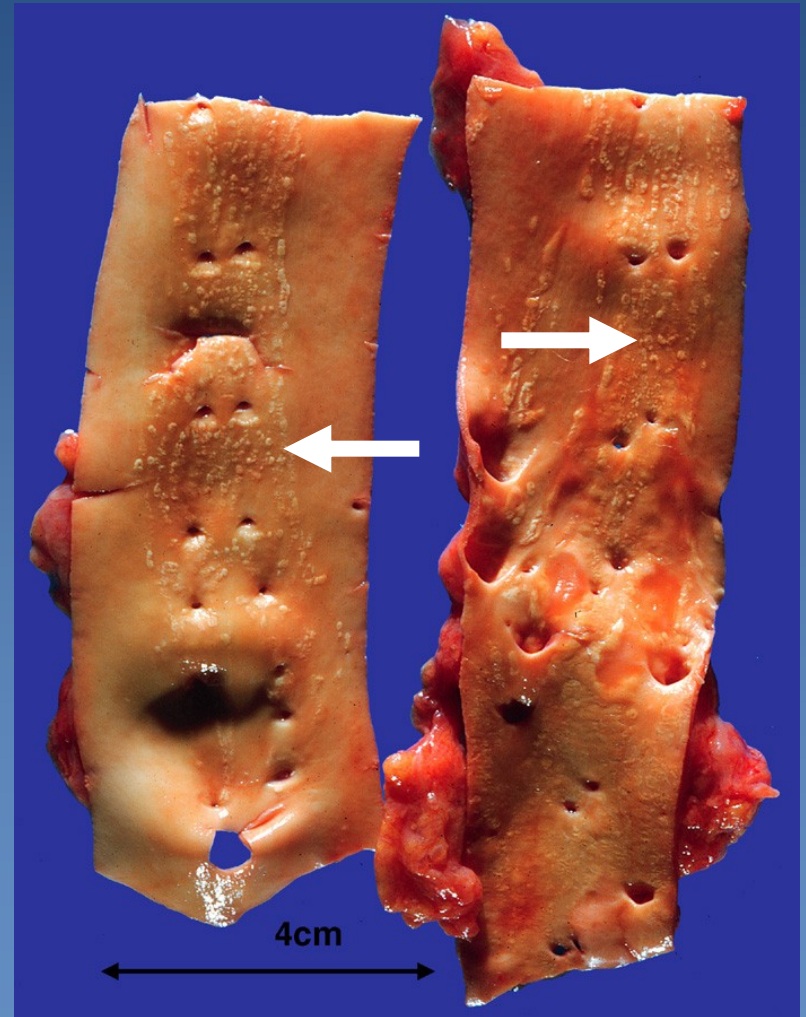
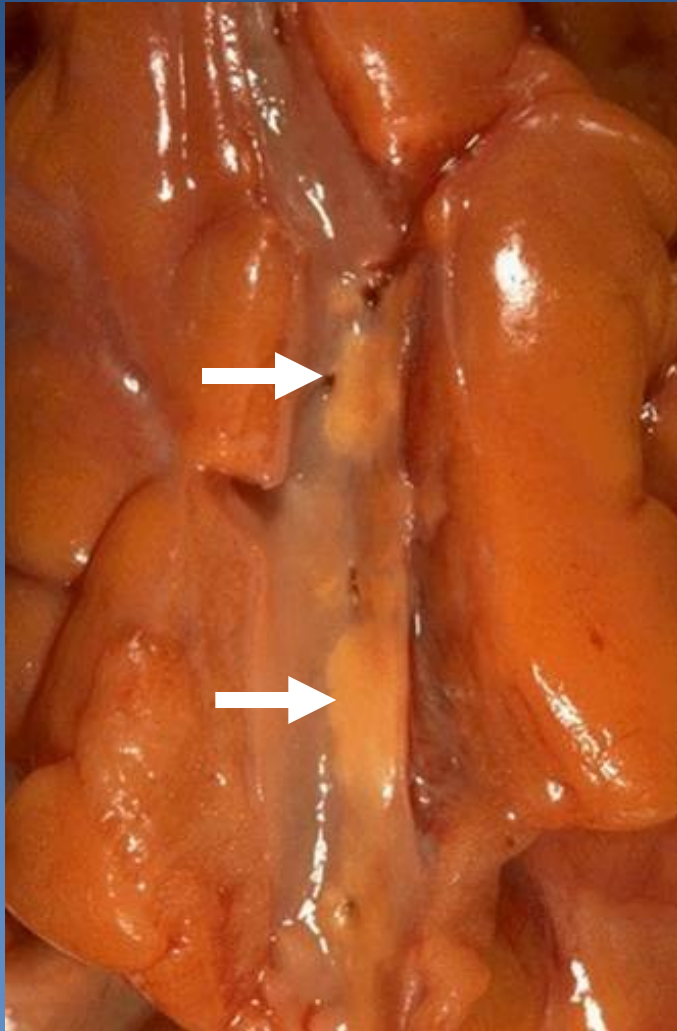
# *Atherosclerosis*



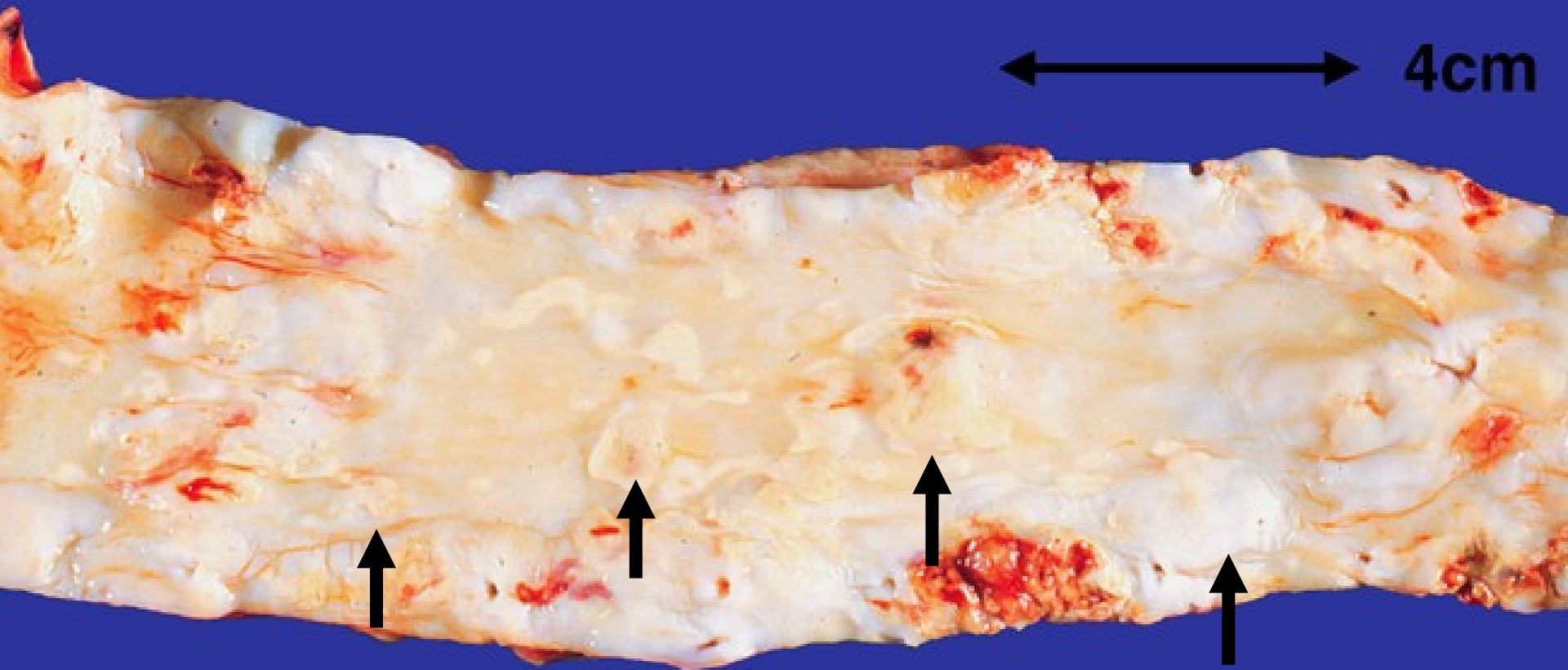
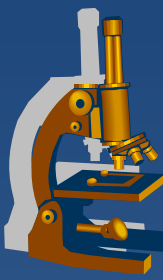
SEQUELS: arterial occlusion in situ

- ✘ chronic (→ hypoxia, atrophy)
- ✘ acute (→ ischemia, infarction, encephalomalatia)
- ✘ embolism (thrombus, plaque material)
- ✘ weakening of arterial wall (aneurysm), risk of rupture
- ✘ bleeding (from plaque, fissured wall)
- ✘ calcification (hypertensive factor)

# *Atherosclerosis- fatty streak*

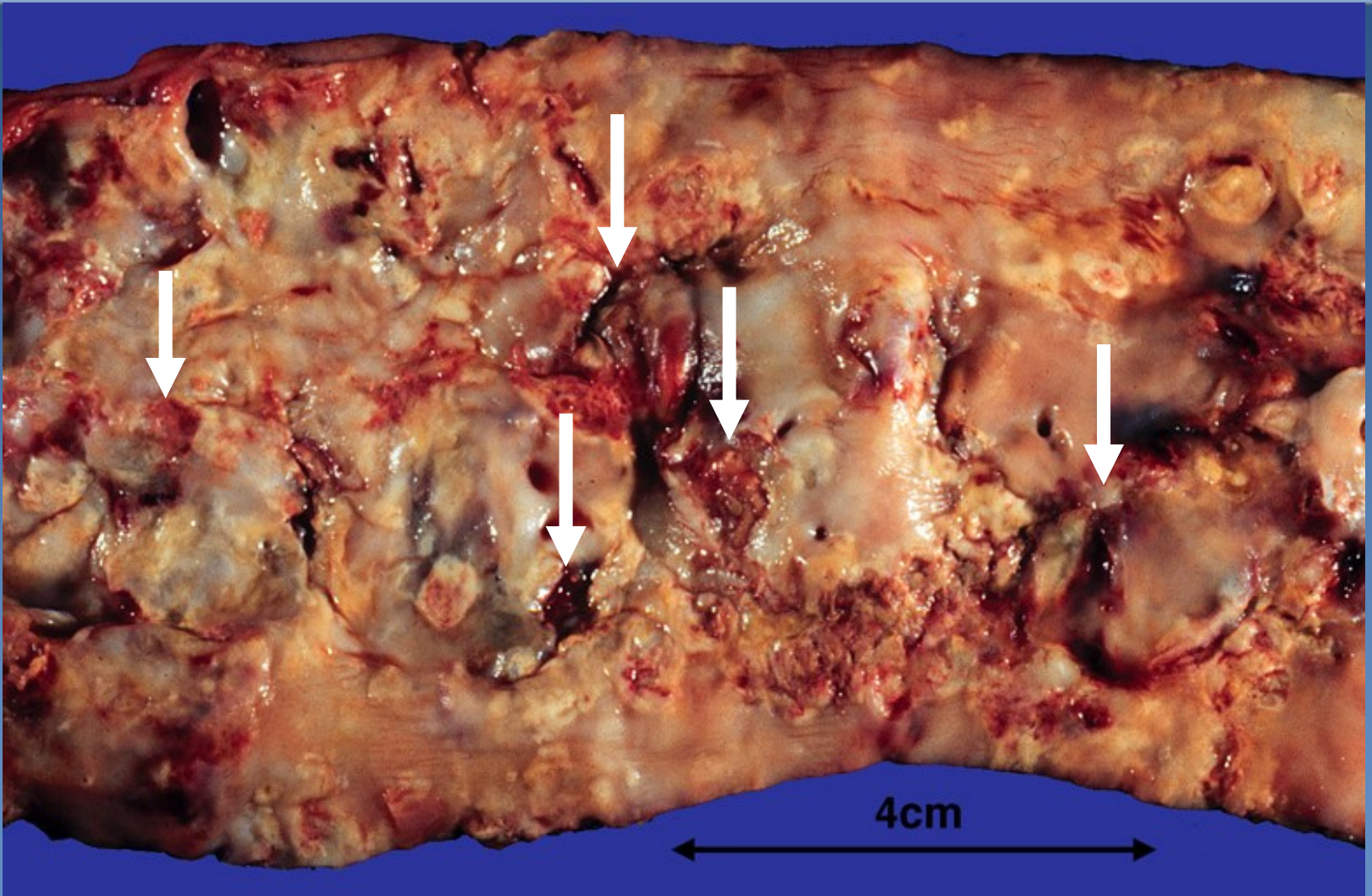
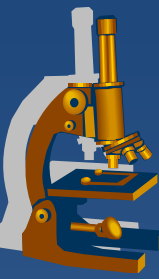


# ***Atherosclerosis - fibrous and atheromatous plaques***



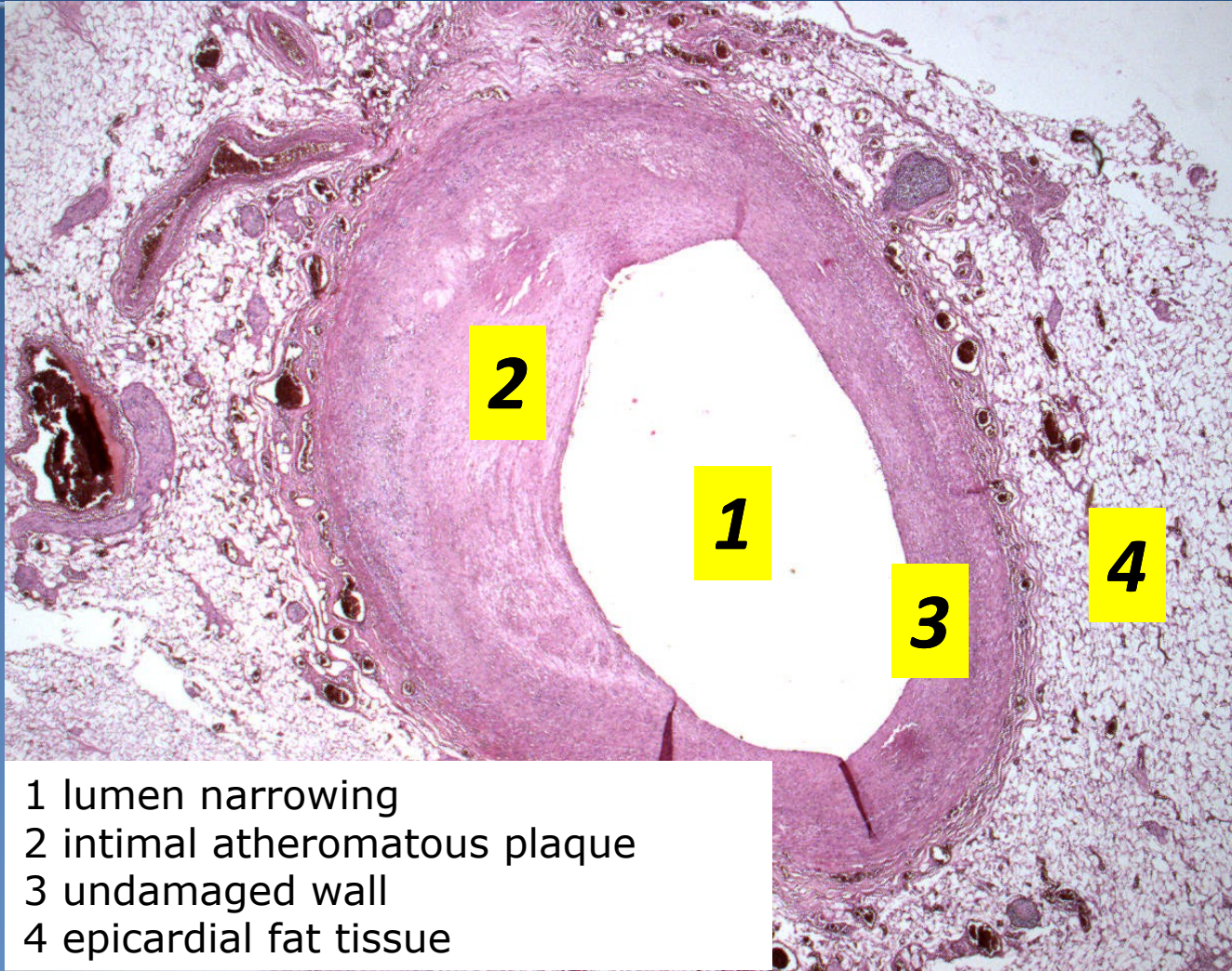


# *Atherosclerosis- plaque ulceration, mural thrombosis*





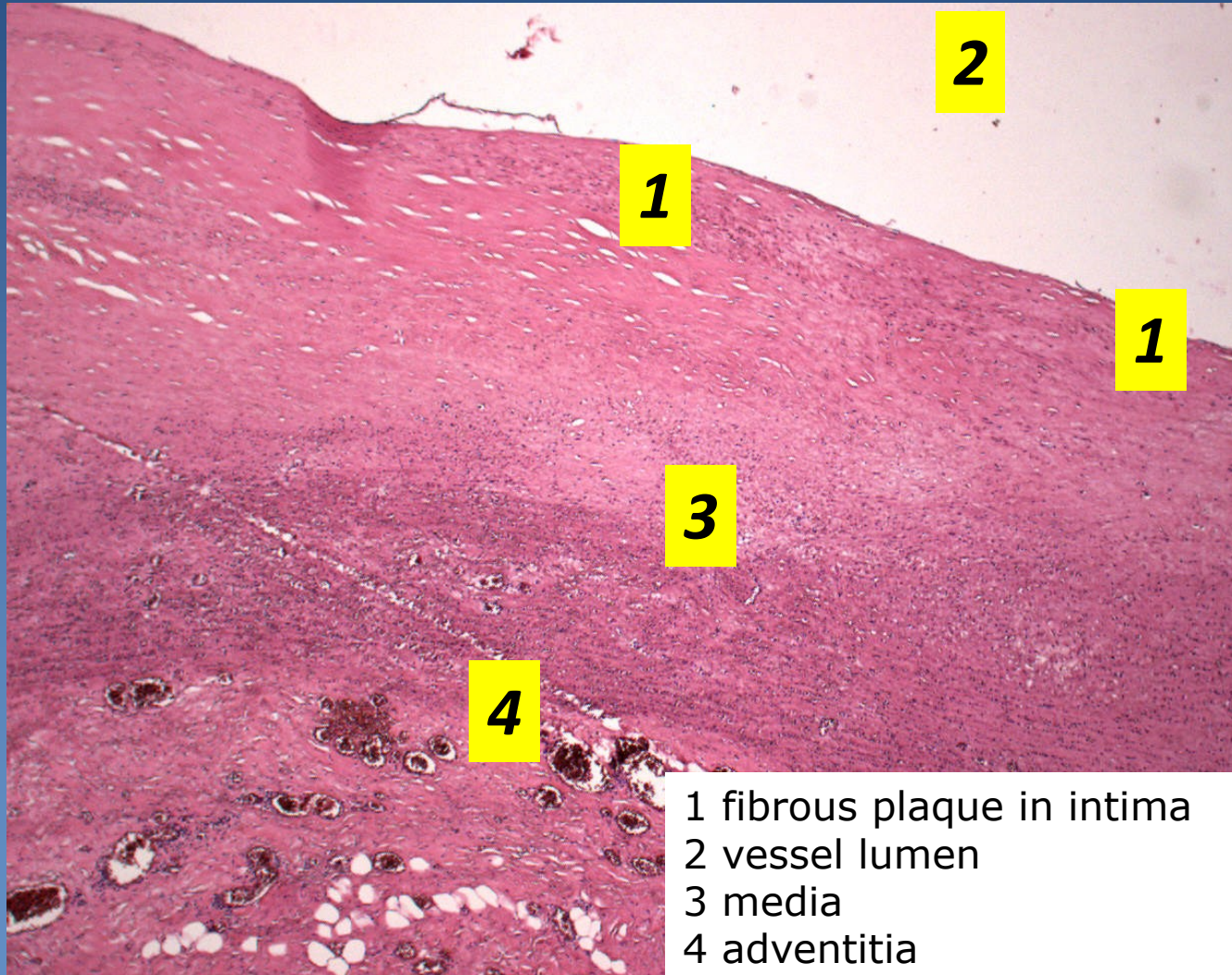
# *Atherosclerosis- coronary artery*



- 1 lumen narrowing
- 2 intimal atheromatous plaque
- 3 undamaged wall
- 4 epicardial fat tissue

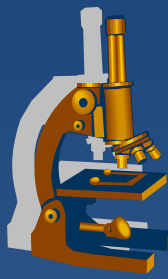


# *Atherosclerosis – fibrous plaque*

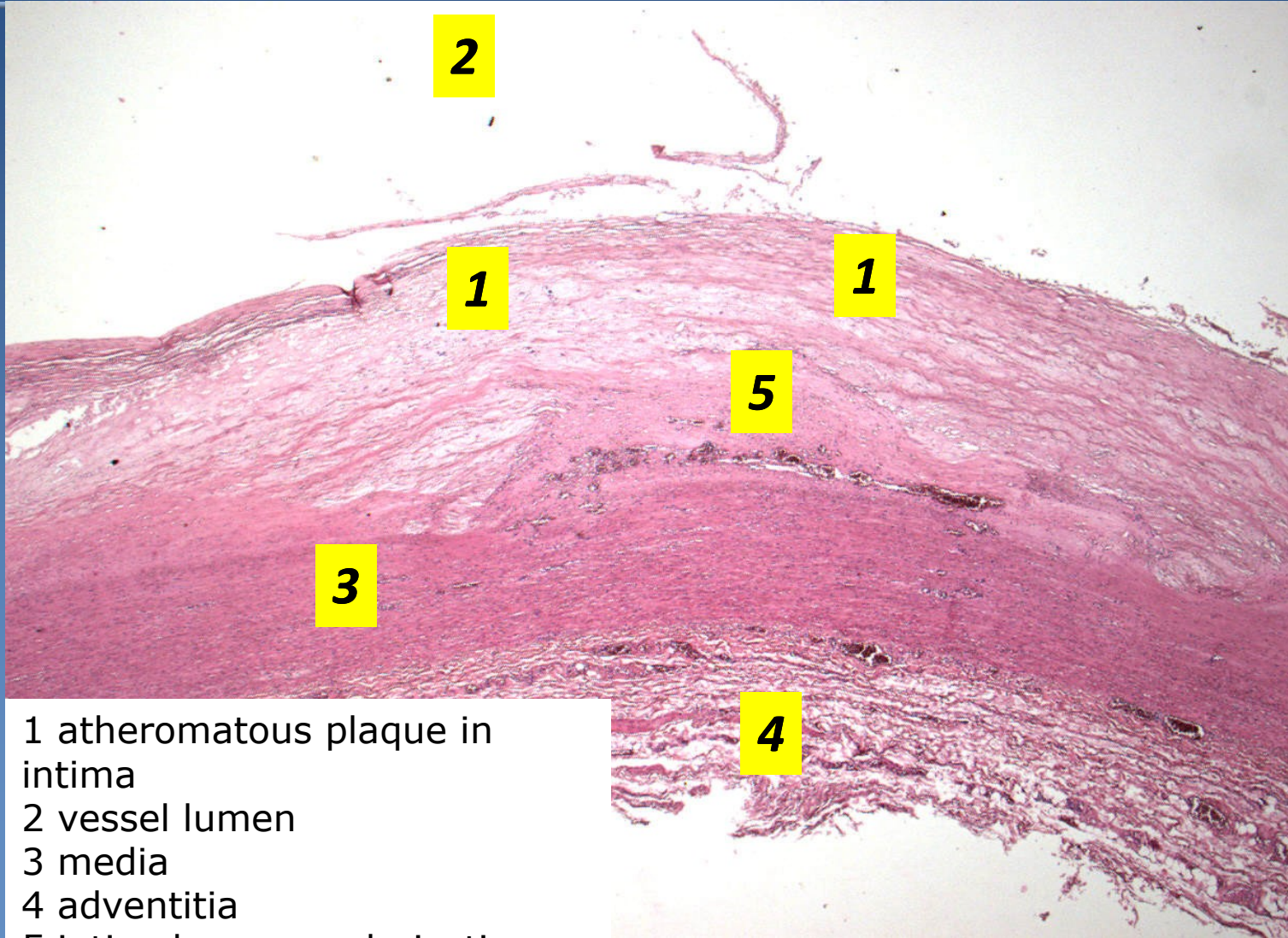


- 1 fibrous plaque in intima
- 2 vessel lumen
- 3 media
- 4 adventitia





# *Atherosclerosis - atheromatous plaque*

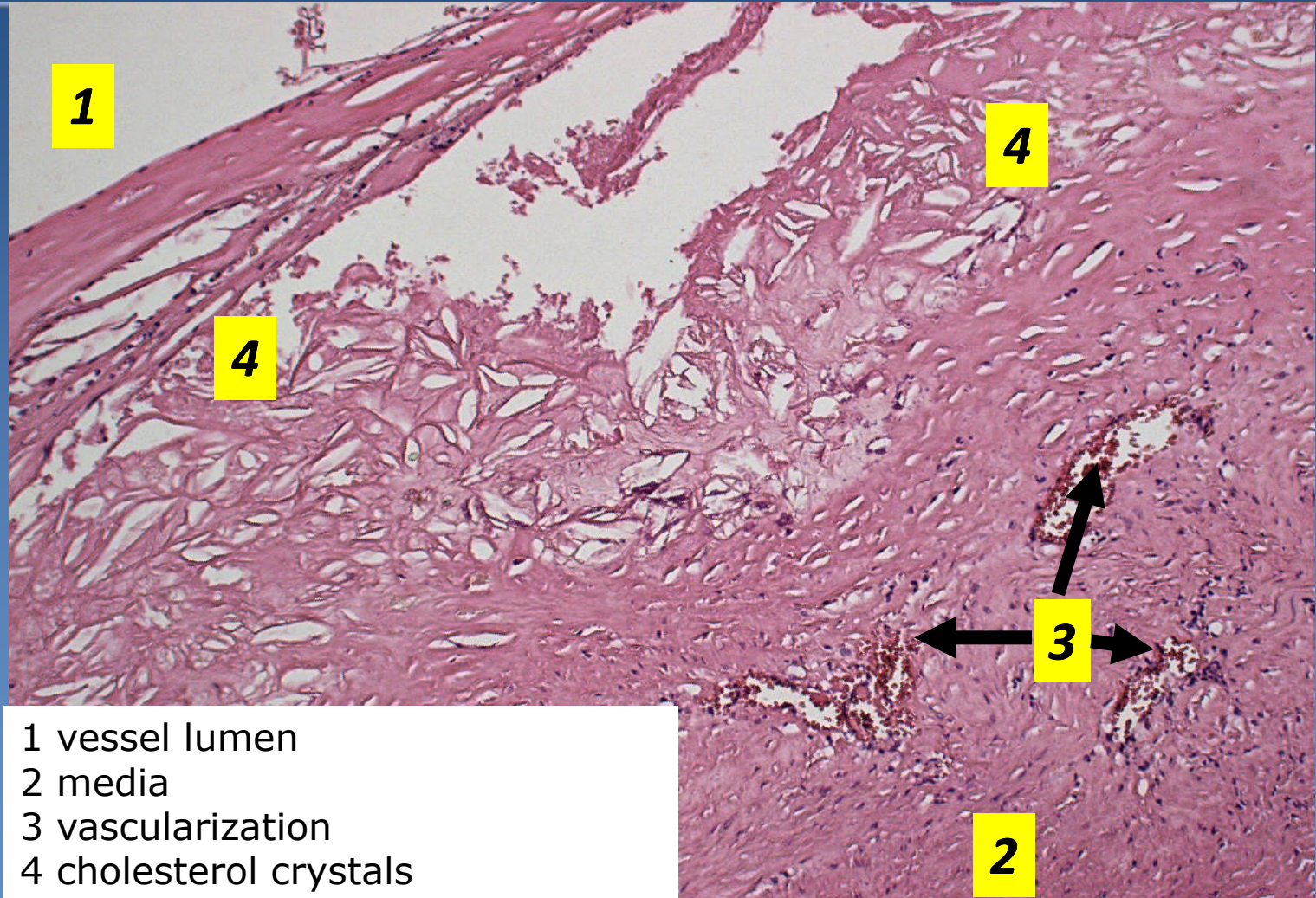


- 1 atheromatous plaque in intima
- 2 vessel lumen
- 3 media
- 4 adventitia
- 5 intimal neovascularization





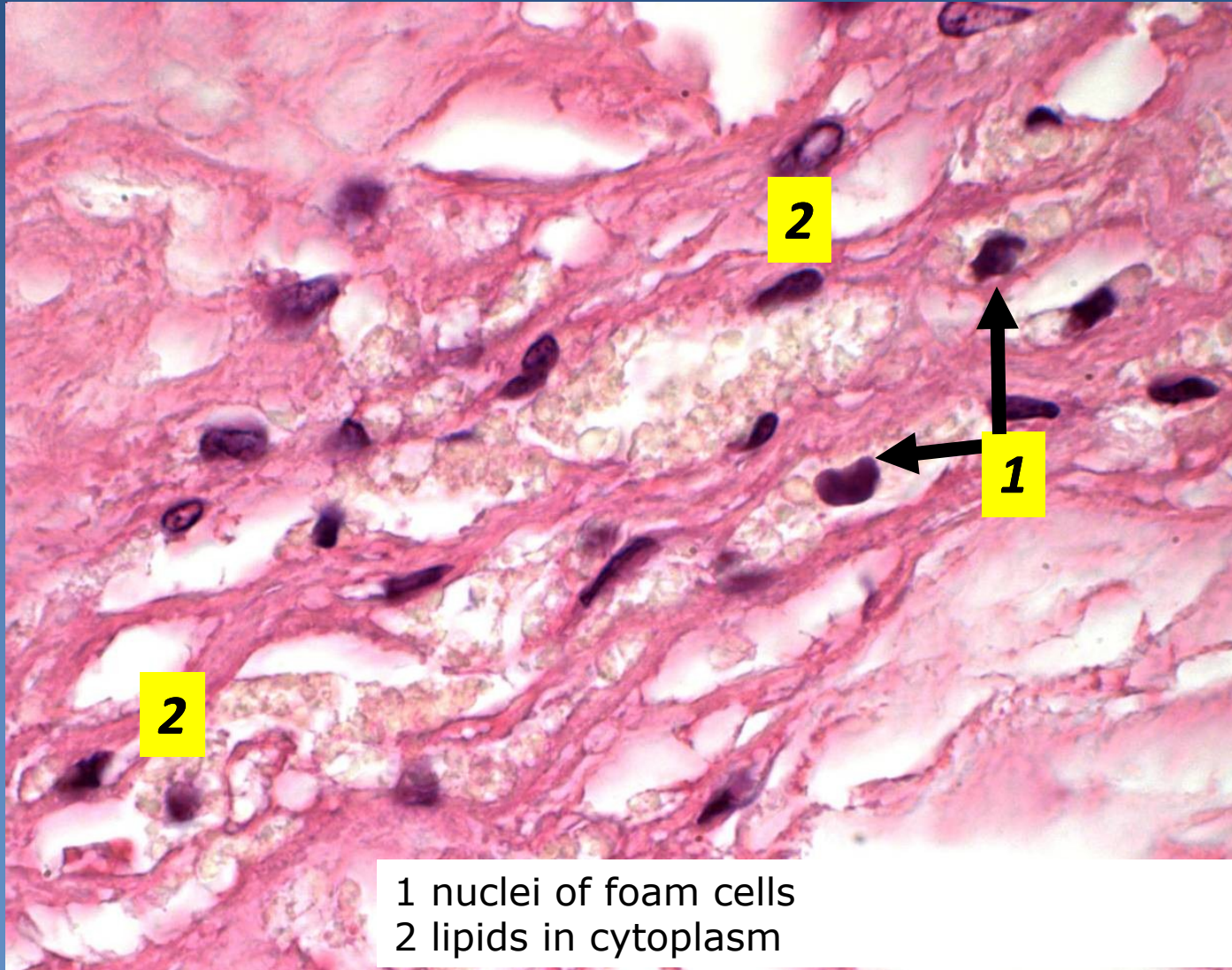
# *Atherosclerosis - atheromatous plaque, intimal neovascularization*



- 1 vessel lumen
- 2 media
- 3 vascularization
- 4 cholesterol crystals

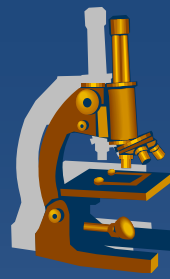


# *Atherosclerosis – foam cells in atheromatous plaque*

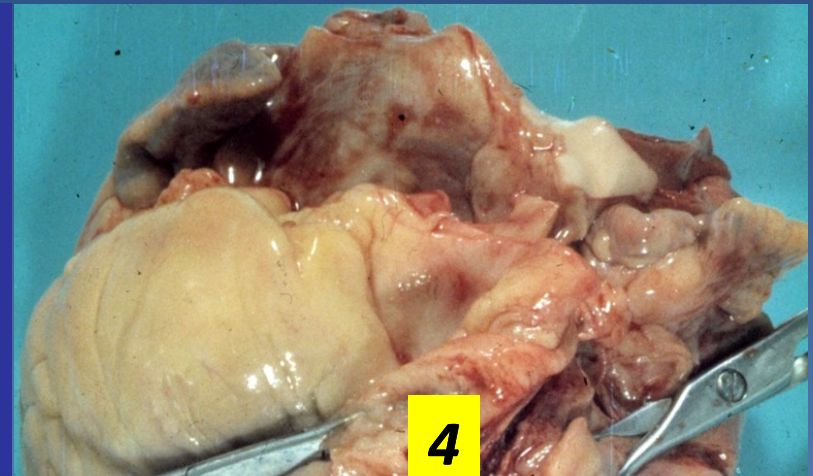
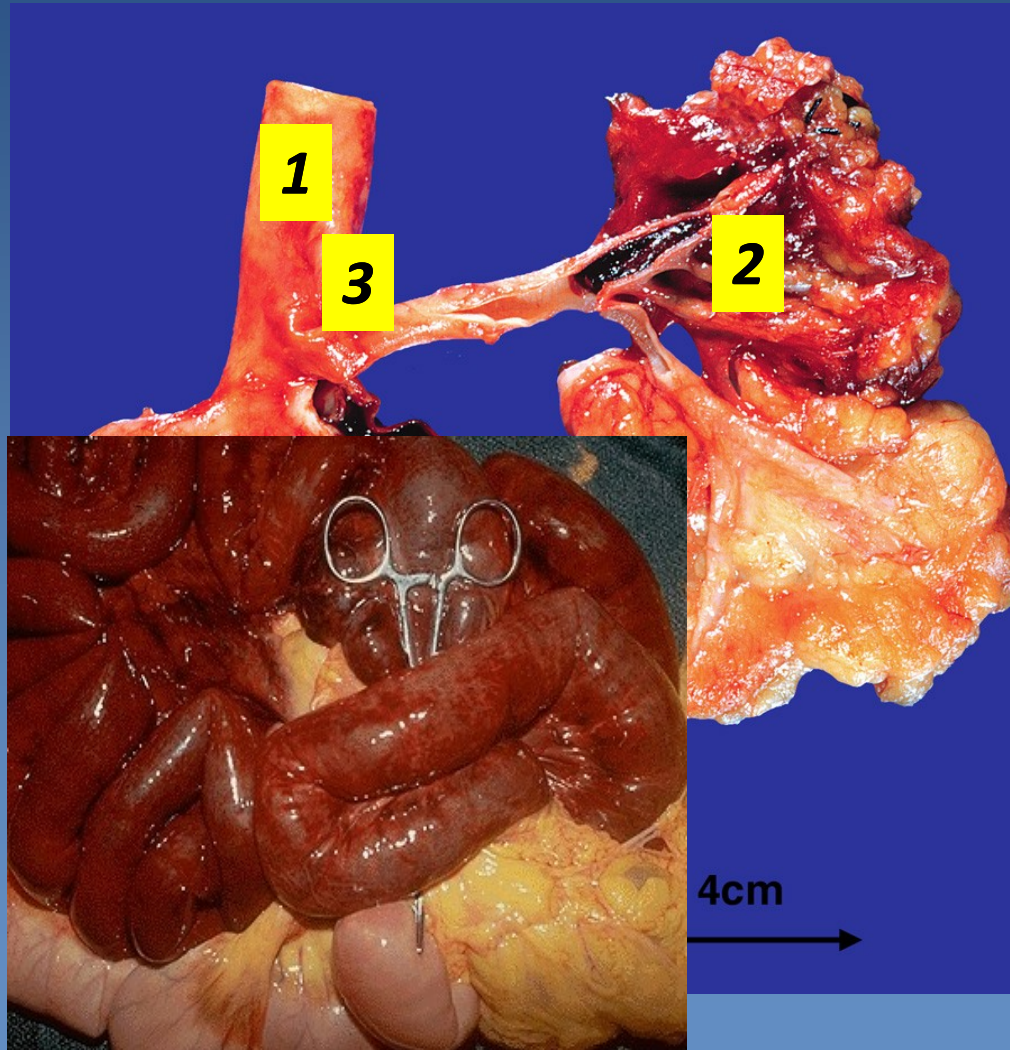


1 nuclei of foam cells  
2 lipids in cytoplasm

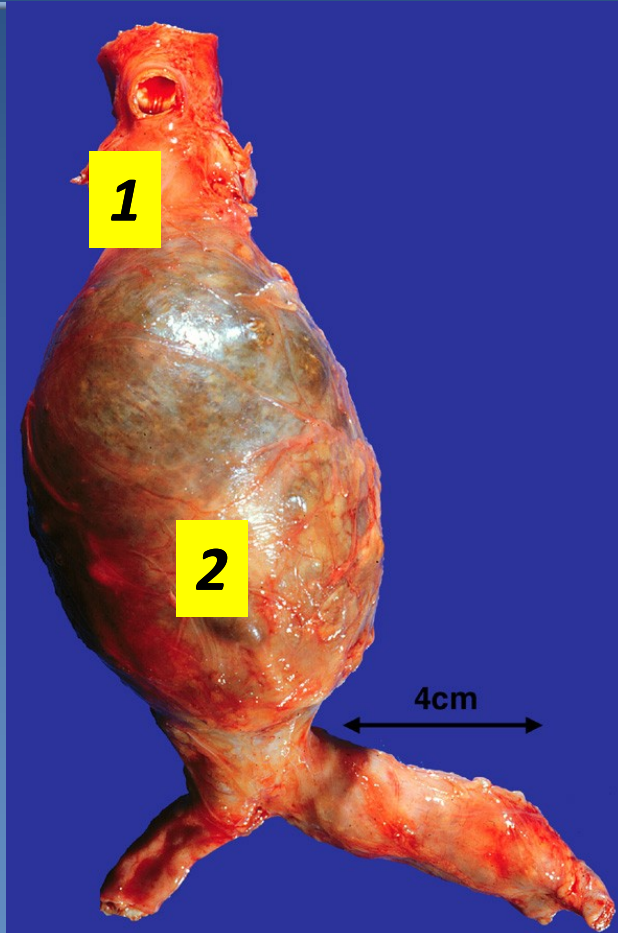




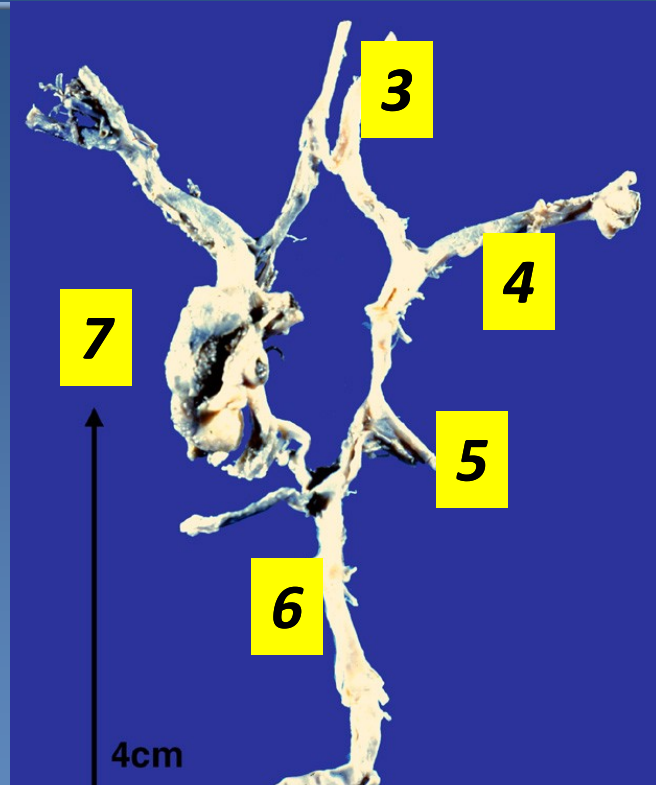
# *Atherosclerosis - complications thrombosis/thrombembolia*



# Atherosclerosis - complications - aneurysm



1 abdominal aorta  
2 aneurysm



3 a. cerebri anterior  
4 a. cerebri media  
5 a. cerebri posterior  
6 a. basilaris  
7 aneurysm

# Arteriosclerosis

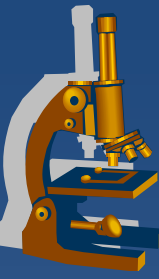


- ✗ in muscular arteries
- ✗ smooth muscle hypertrophy
- ✗ intimal fibrosis
- ✗ collagenisation of elastic membrane
- ✗ hyalinisation (hyaline a.)

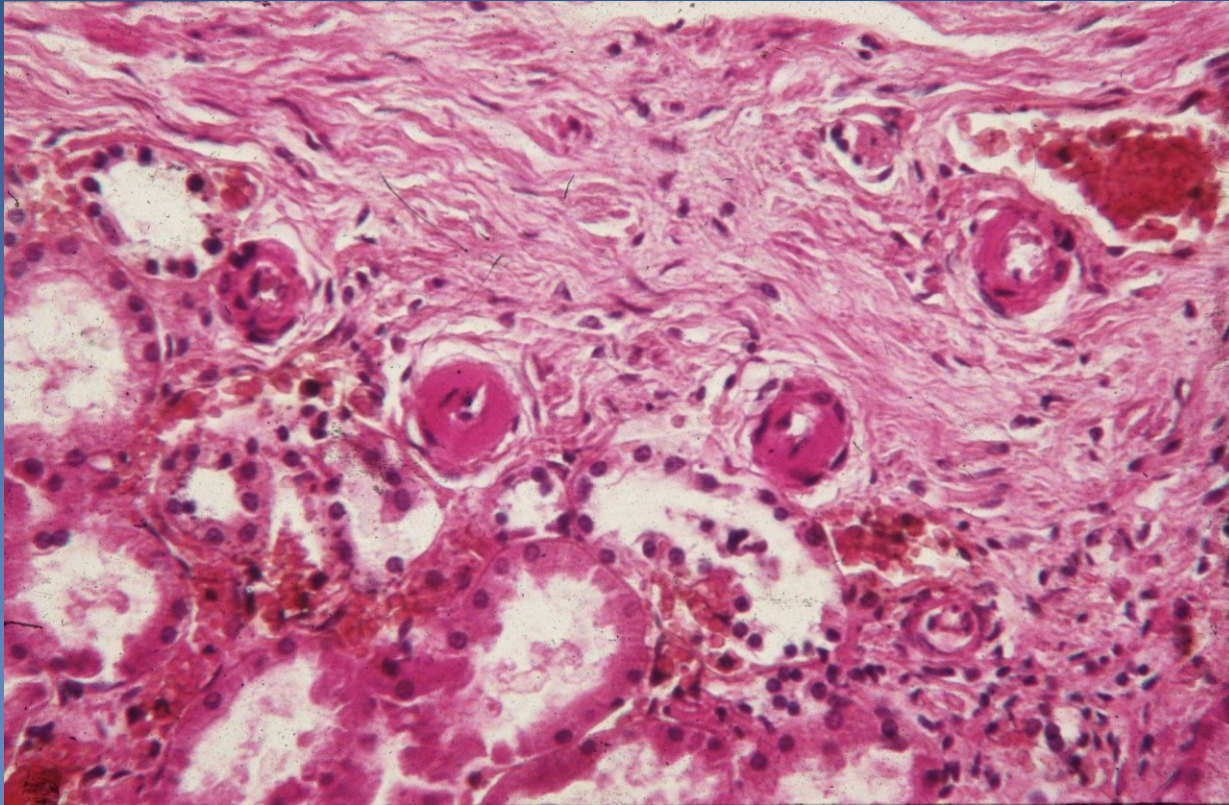
age and/or hypertension related changes

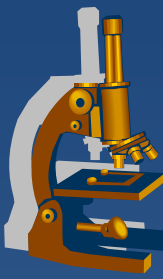
→ nephrosclerosis, cerebral ischemia, ...





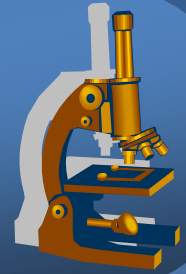
# *Hyaline arteriolosclerosis*





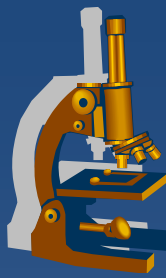
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# *Cardiac pathology*





# Morphology



- ✗ pericardial sac – cca 30ml clear yellowish fluid
- ✗ **male = 300 – 350 g**,
  - *hypertrophy > 400g*
- ✗ **myocardium:**
  - RV 3 – 4 mm
  - LV 12 – 15 mm
- ✗ **foramen ovale**
  - *closed x opened → paradoxical embolia*



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# ***Congenital cardiovascular disease***

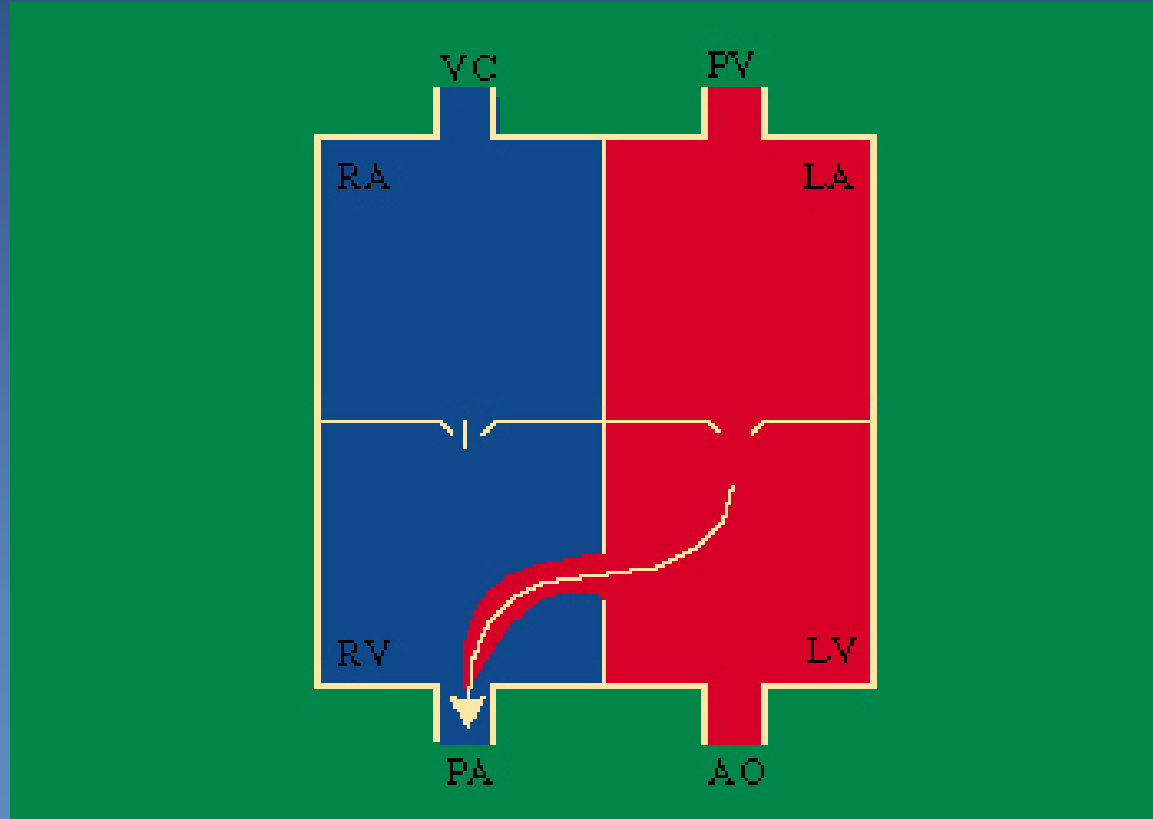
# *Pathological shunts*



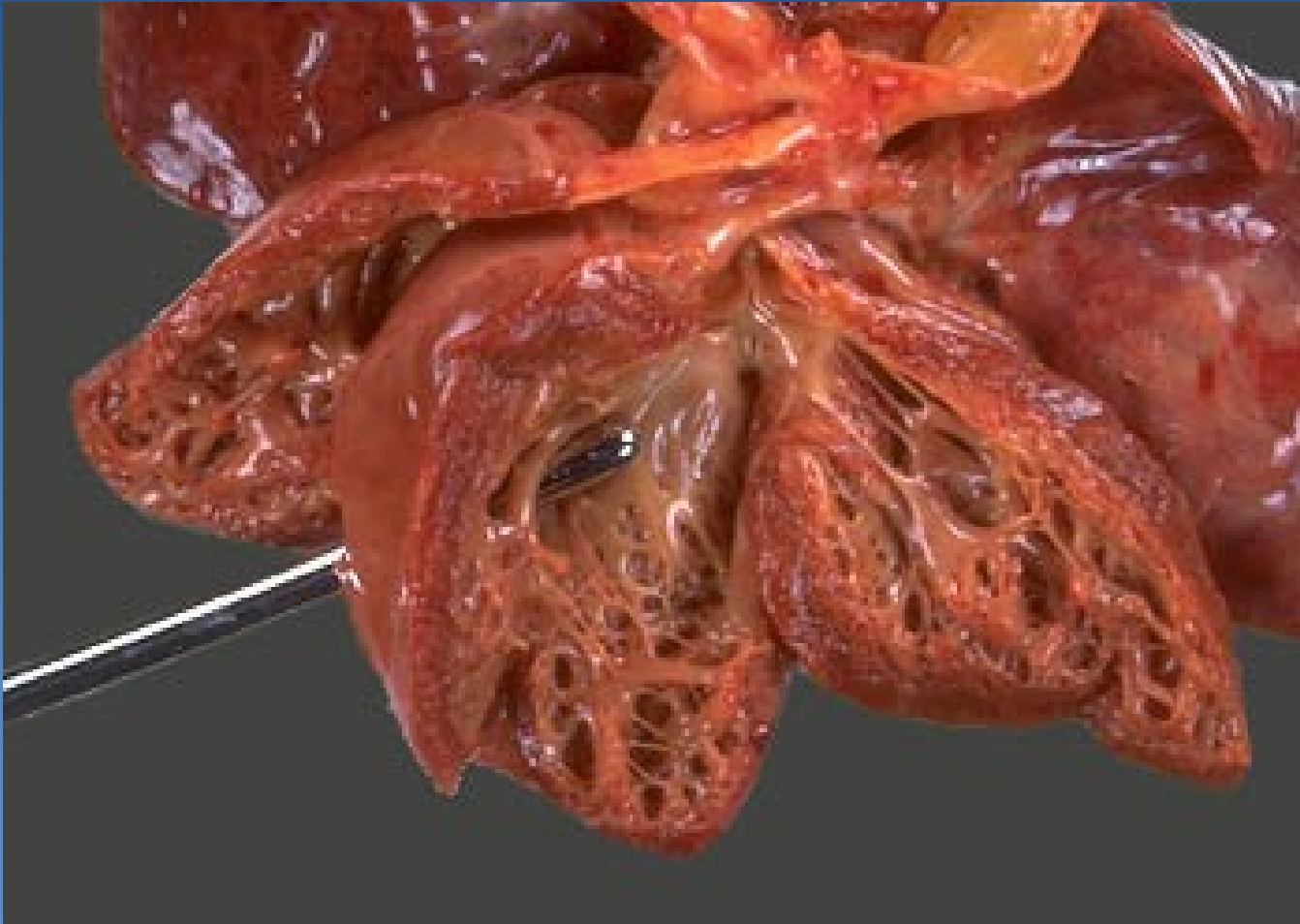
- x atrial septal defect
- x ventricular septal defect
- x patent ductus arteriosus

Initially left-to right shunts, i.e. non-cyanotic,  
later (in heart defects) right ventricular  
hypertrophy – reverse shunt, cyanotic  
defect

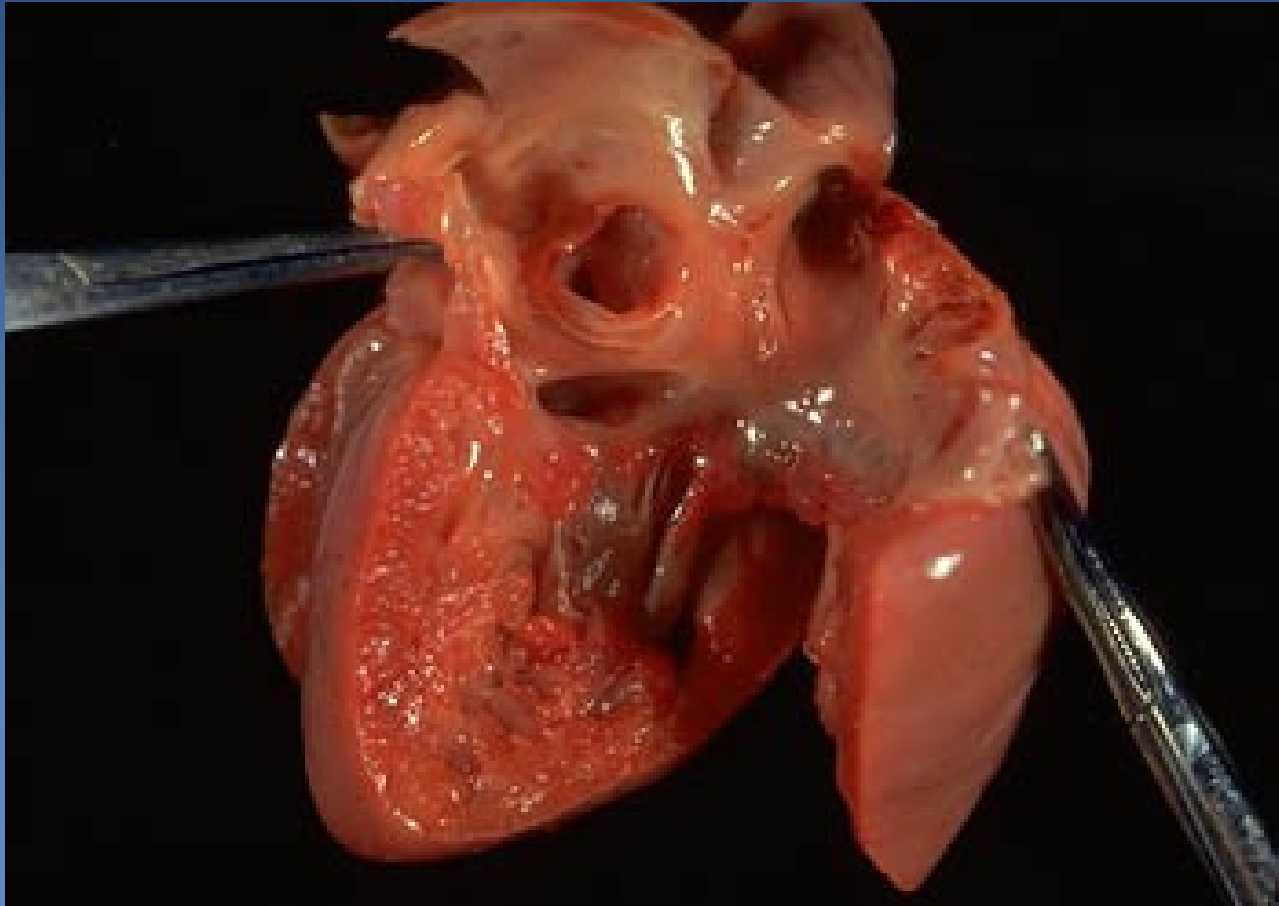
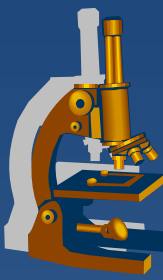
# *Ventricular septal defect*



# *Ventricular septal defect*



# *Atrial septal defect*



# ***Congenital stenosis***

---



- x** coarctation of the aorta – congenital constriction
- x** valvular stenosis

Hypertrophy, hypertension and dilatation ahead of stenotic part. Collateral circulation, if possible.

# *Coarctation of the aorta*

---



- ✗ Aortic constriction
- ✗ with patent duct. arteriosus (pre- or postductal)
- ✗ with closed duct. arteriosus

Congestive heart failure,  
bacterial endocarditis,  
intracerebral haemorrhage



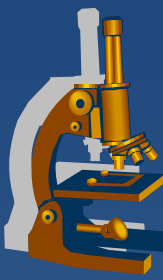
# *Complex congenital heart disease*

---

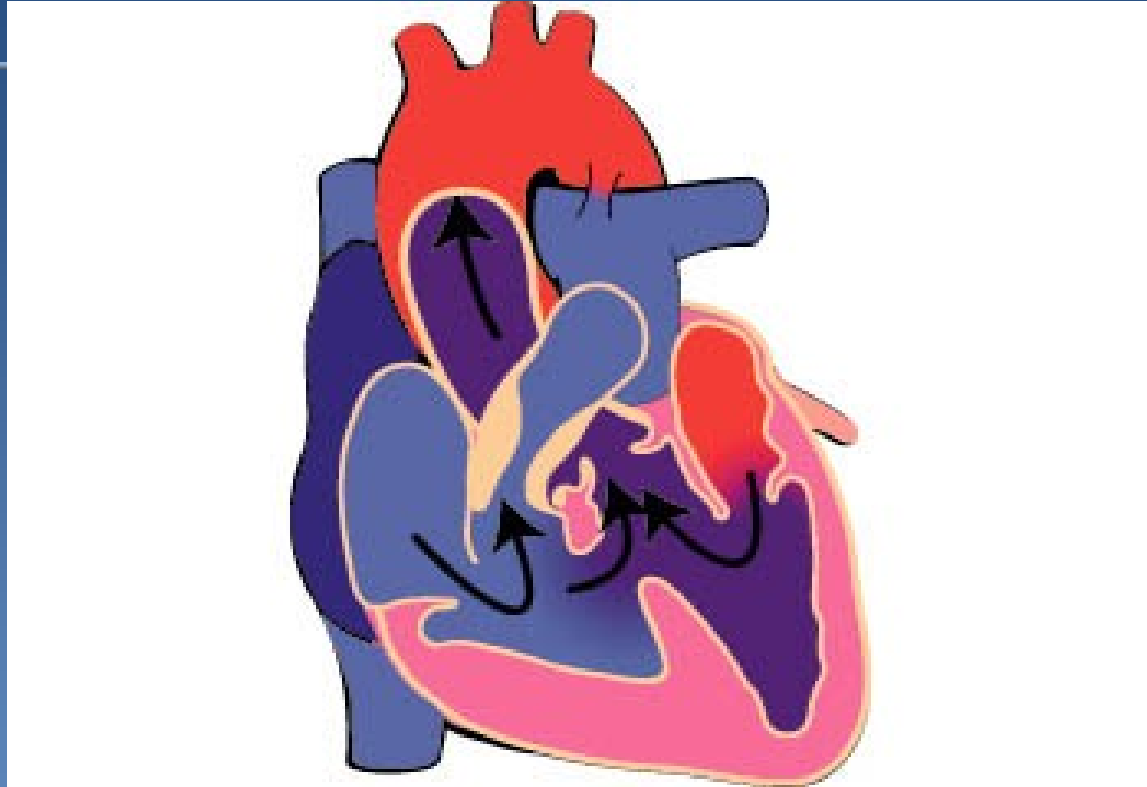


- ✘ Fallot's tetralogy
- ✘ transposition of the great arteries

Combination of malformations, i. e.  
hypoplasia, shunting or incorrect  
connection, stenosis, etc.



# *Fallot's tetralogy*



ventricular septal defect with dilated overriding aorta,  
stenosis of the pulmonary valve,  
right ventricular hypertrophy

# Pericardial pathology



## 1) Pericardial effusion

- transudate in congestive heart failure or hypoproteinemia, slow (up to 500ml – pericardial dilatation)

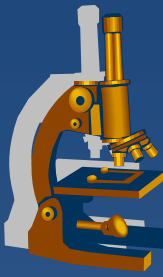
## 2) haemopericardium

– wall rupture in MI or aortic root dissection → **fatal cardiac tamponade**

*diastolic filling restriction*

# Pericardial pathology

---



## 3) Inflammatory exudate in pericarditis:

### **a) non-infectious**

– pericarditis epistenocardiaca, uremic, post-operative, SLE, Dressler sy (post-MI autoimmune)

### **b) infectious**

– *haematogenous, direct spread, lymphogenous; variable agents*

# ***Acute fibrinous pericarditis***



- ✘ Gross: yellow-greyish superficial coating – granular layer, villi - cor villosum, hirsutum;
- ✘ Micro: mesh of thin eosinophilic strands, commonly + inflammatory infiltrate
- ✘ Healing: may be complicated. Fibrinolysis x organisation by granulation tissue → adhesions, dystrophic calcification.

# *Acute fibrinous pericarditis*

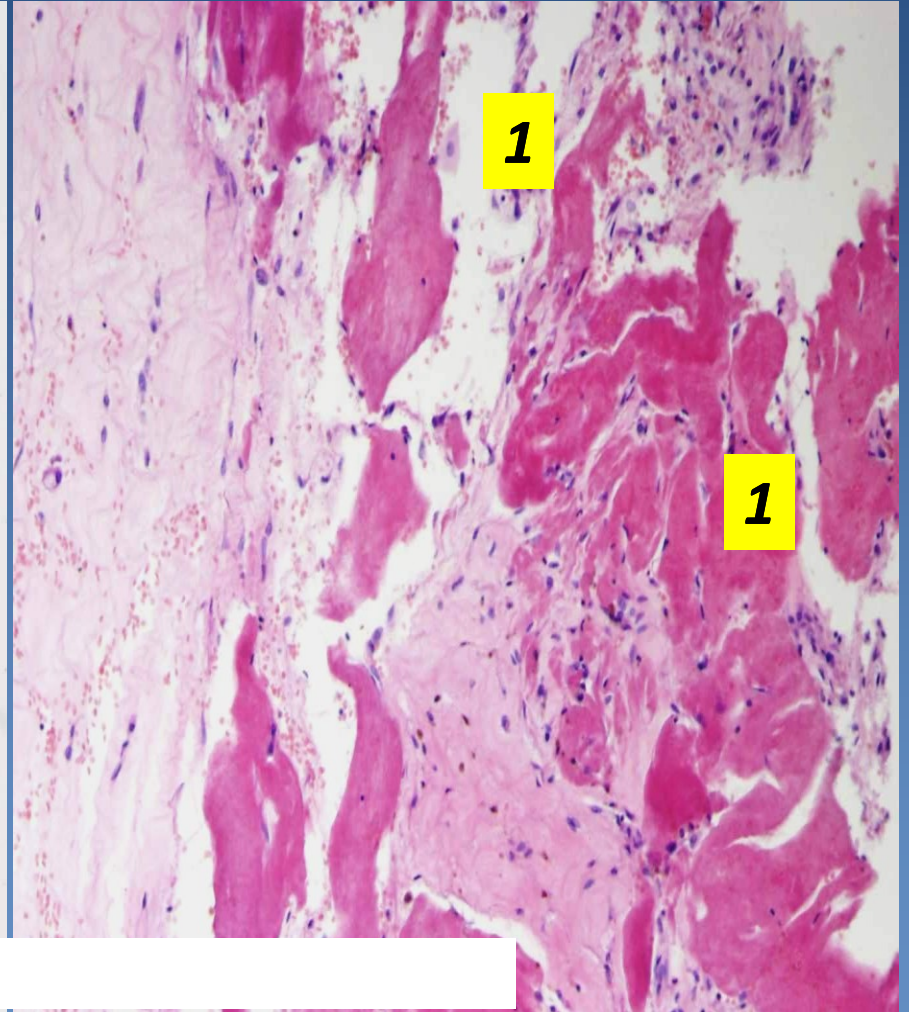




# *fibrinous pericarditis*



1 fibrinous exudate



# *Systemic hypertension*

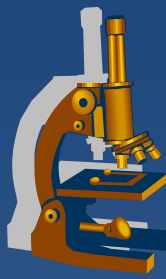
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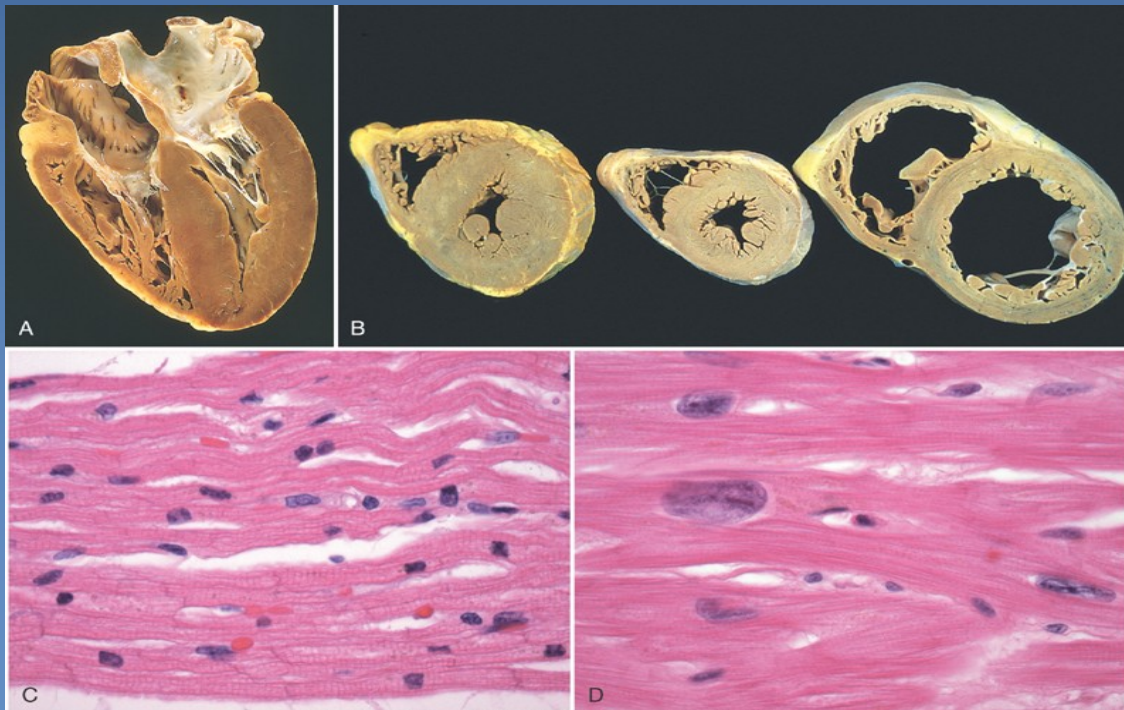
- ✘ Primary (essential) h.
- ✘ Secondary h. (renal, endocrine hyperfunction, aortic coarctation, drug induced)



# Systemic hypertension and heart



- × 90–95% essential , risk factor for AS
- × **work overload** → LV adaptation to ↑ peripheral resistance = **cor hypertonicum** (concentric LV hypertrophy) → limited compensatory mechanisms → **cor hypertonicum decompensatum** (dilatation of hypertrophic LV)
- × → heart insufficiency ← relative coronary incompetence

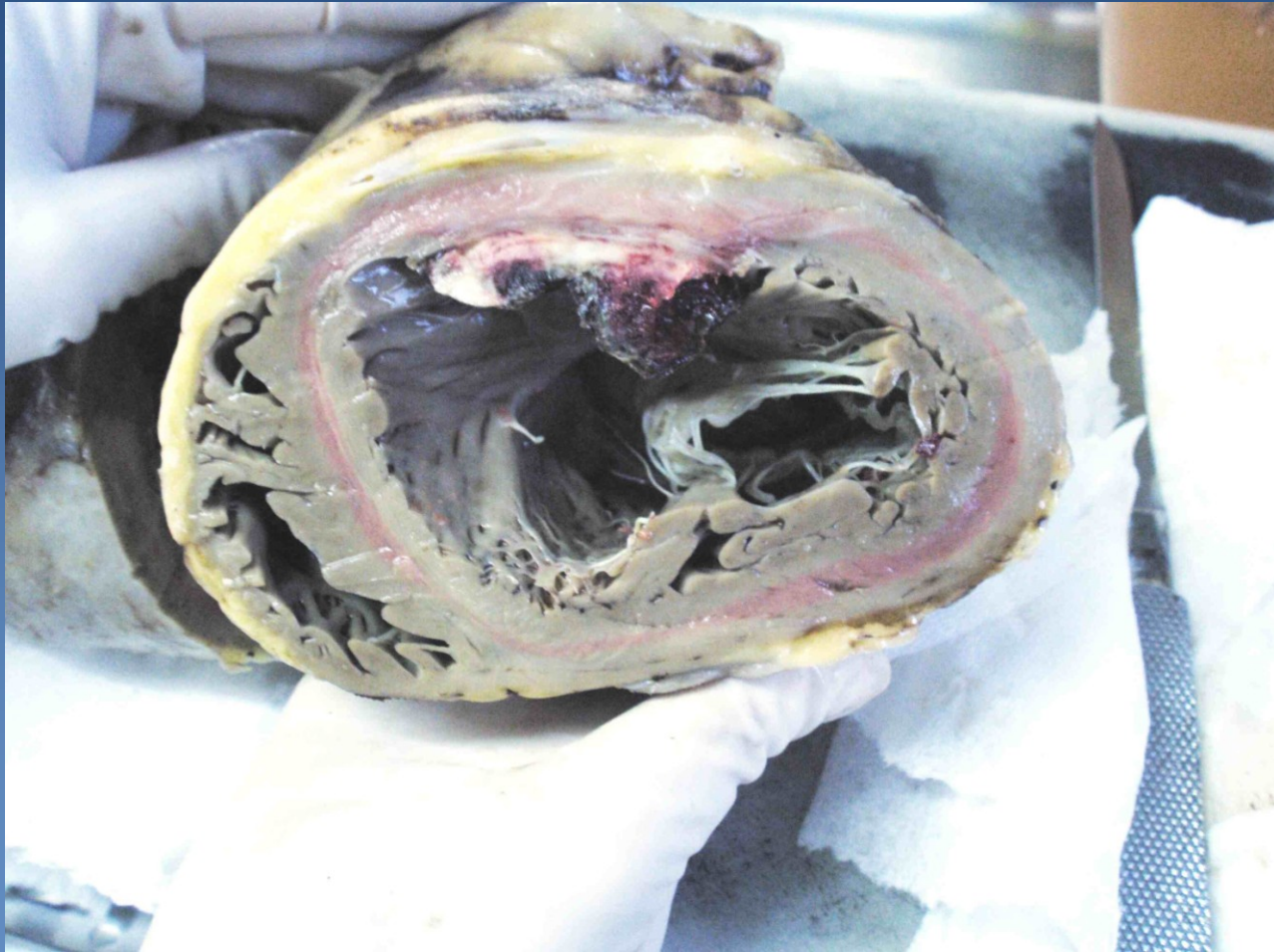


# *Cor hypertonicum*





# *LV hypertrophy*



# *Heart failure*

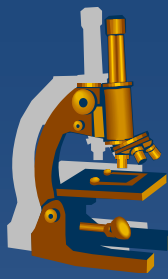


- ✘ heart unable to pump blood at a rate sufficient for metabolic demands of the tissues
- ✘ systolic dysfunction - ↓ myocardial contractile function (ischemic injury, pressure or volume overload – valvular disease, hypertension, cardiomyopathy)
- ✘ diastolic dysfunction - inability to dilatate sufficiently (massive LV hypertrophy, myofibrosis, amyloidosis)
- ✘ cardiac – extracardial pathologic changes

# Cardial changes



- × **disproportion between heart function and peripheral vascular resistance**
- × differ according rapidity of development:
  - **sudden** → acute dilatation
  - **chronic** → adaptation → → →  
*myocardial hypertrophy (↑ nutritional demands) +/- ventricular dilatation  
(enhanced contractility – Frank-Starling mechanism), + activation of  
neurohumoral systems (norepinephrin, renin-angiotensin sy, atrial natriuretic peptide*



# Extracardial changes

---

- × **venous congestion** – e.g. liver (-> *hepar moschatum*)
- × **induration** – fibroproduction (liver, spleen, kidney)
- × **oedema** –
- × **cyanosis** – visible on acral parts

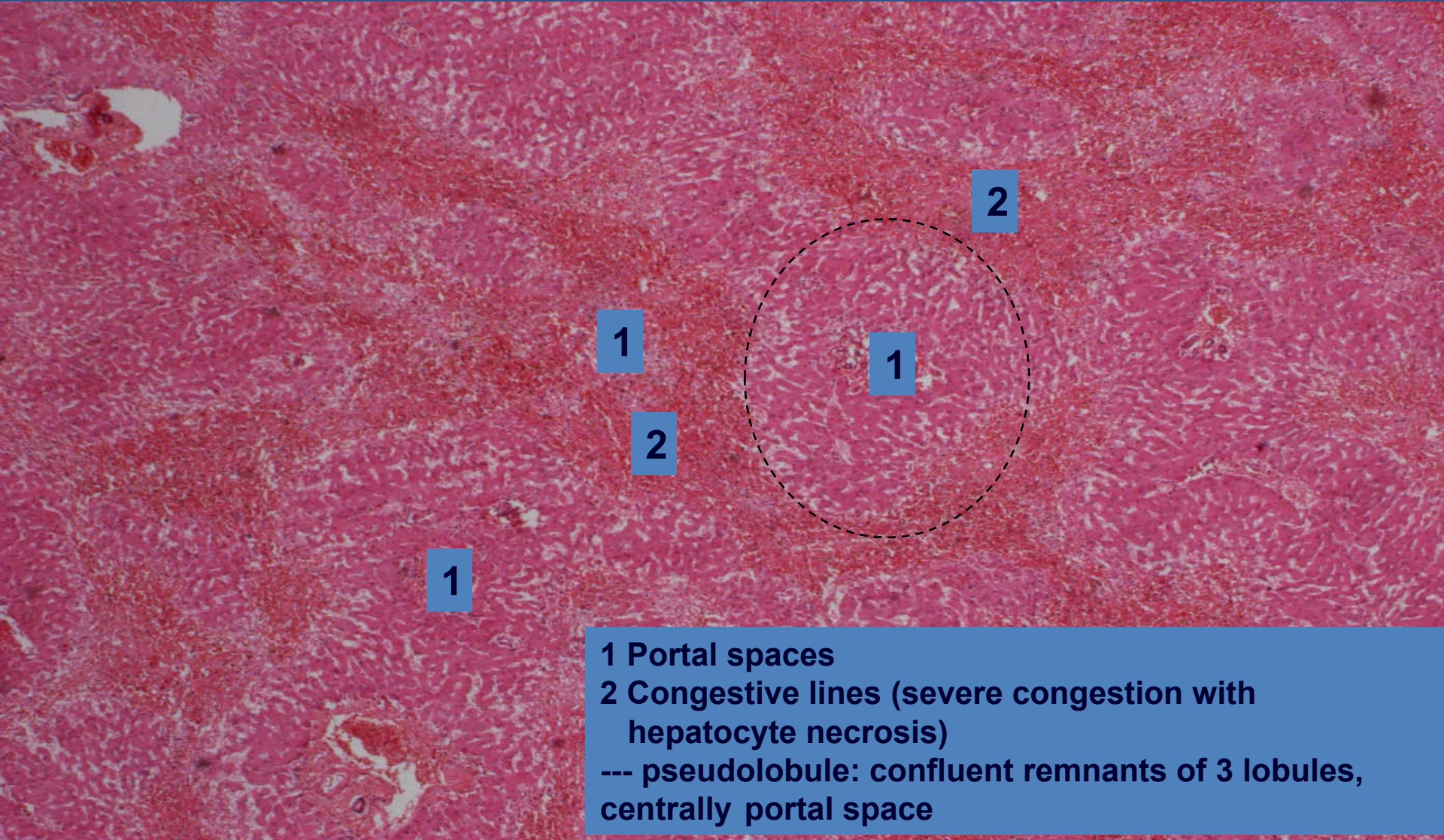


***Chronic venous congestion  
(nutmeg liver - hepar moschatum)***





# Hepatic venous congestion



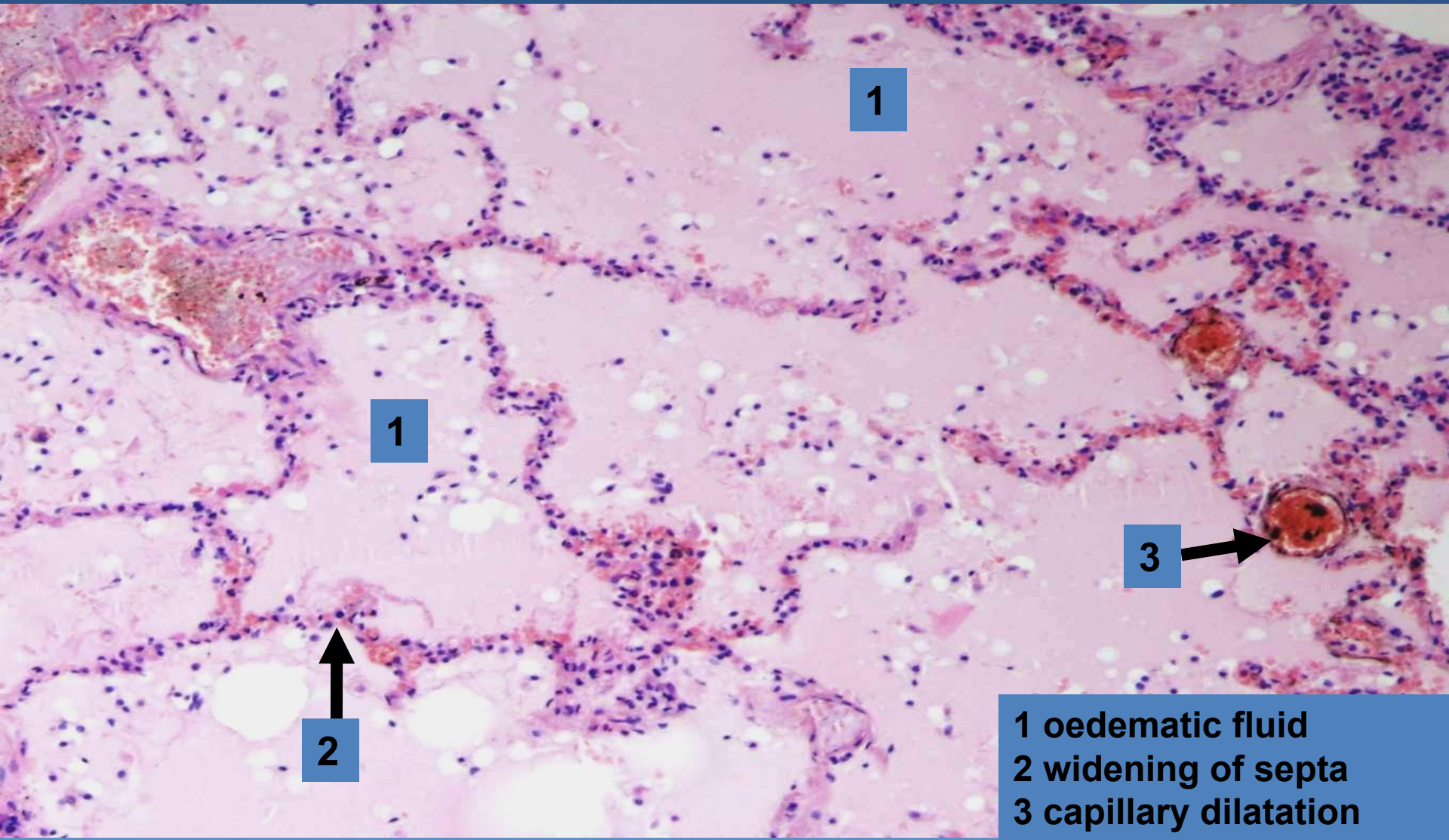
1 Portal spaces

2 Congestive lines (severe congestion with hepatocyte necrosis)

--- pseudolobule: confluent remnants of 3 lobules, centrally portal space



# *Pulmonary oedema*



1

1

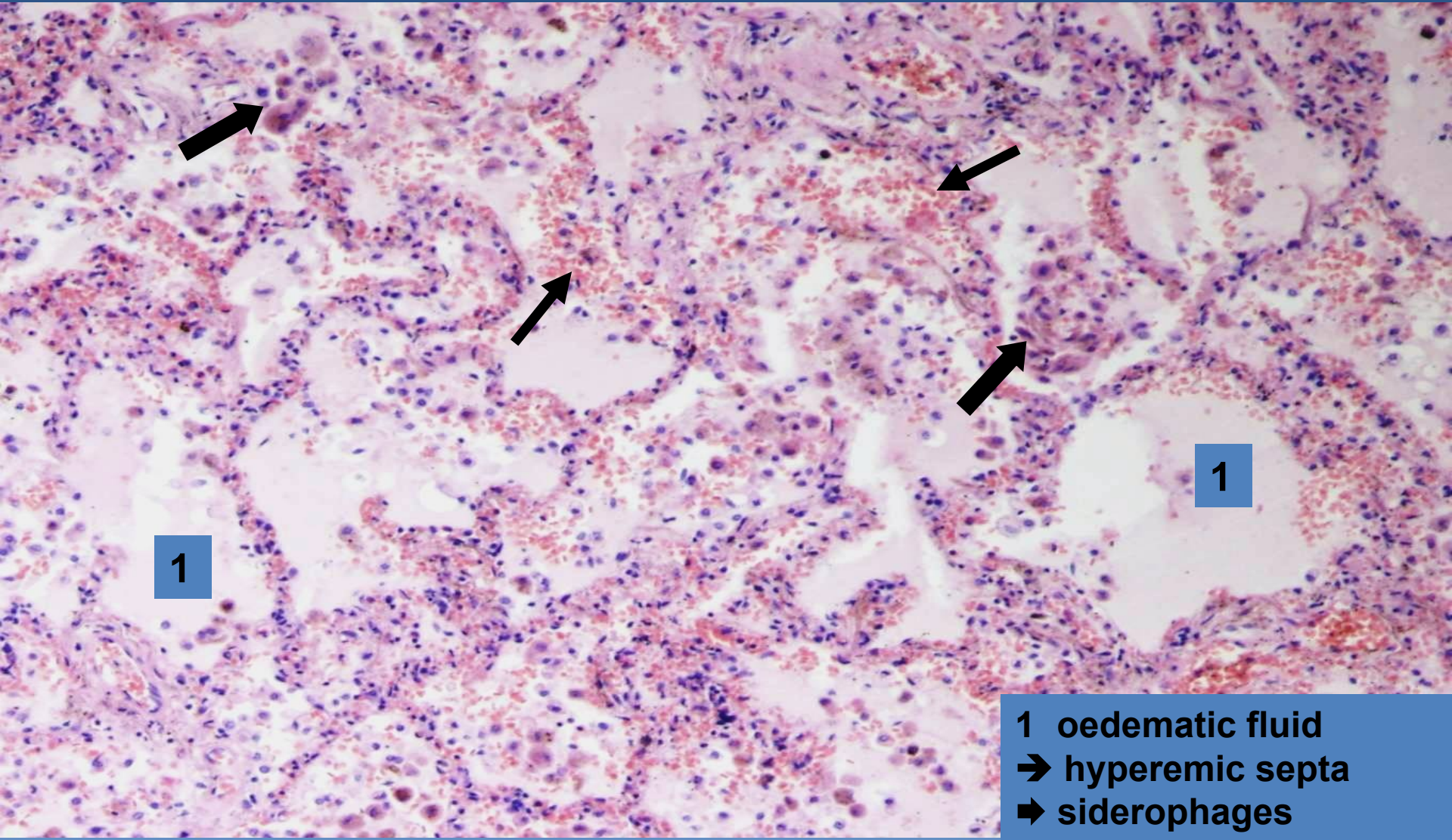
3

2

1 oedematous fluid  
2 widening of septa  
3 capillary dilatation



# *Chronic pulmonary venous congestion*



- 1 oedematous fluid
- hyperemic septa
- siderophages

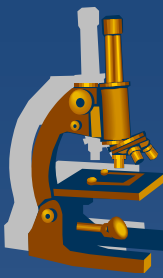


# *Ischemic heart disease (IHD)*



- ✘ group of pathophysiologically related syndromes resulting from **myocardial ischemia** (hypoxia or anoxia, ↓ nutrients, ↓ removal of metabolites)
- ✘ imbalance between the demand and supply by coronary arteries.
- ✘ important factor – coronary AS
- ✘ forms:
  - ⇒ *angina pectoris*
  - ⇒ *myocardial infarction (MI)*
  - ⇒ *chronic IHD with heart failure*
  - ⇒ *sudden cardiac death*

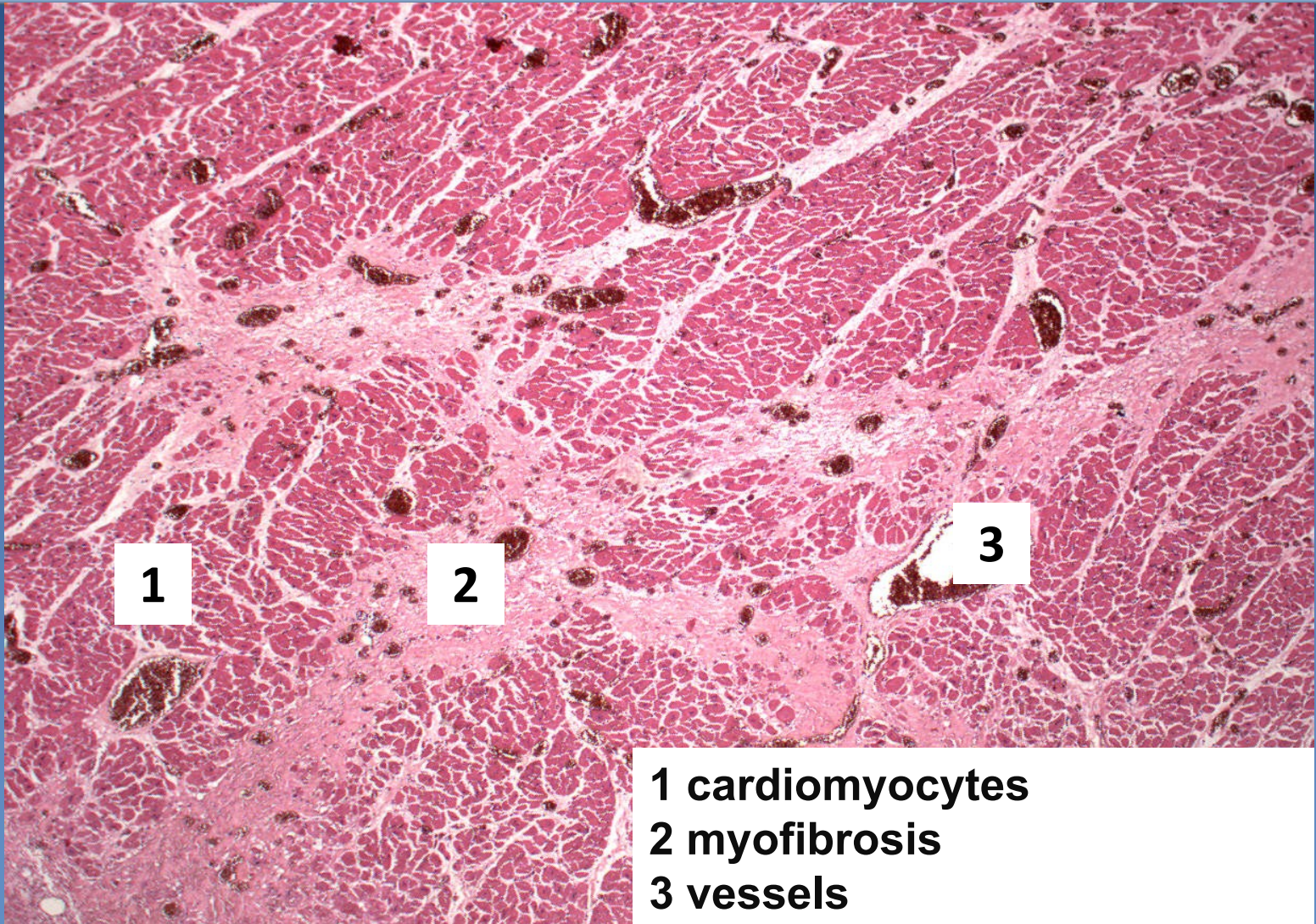
# ***Ischemic heart disease (IHD)***



## **x Morphology of myocardial ischemia:**

- ⇒ *myofibrosis*
- ⇒ *myomalatia (= partial necrosis – cardiomyocytes only)*
- ⇒ *myocardial infarction: transmural/subendocardial (complete coagulative necrosis incl. interstitium)*

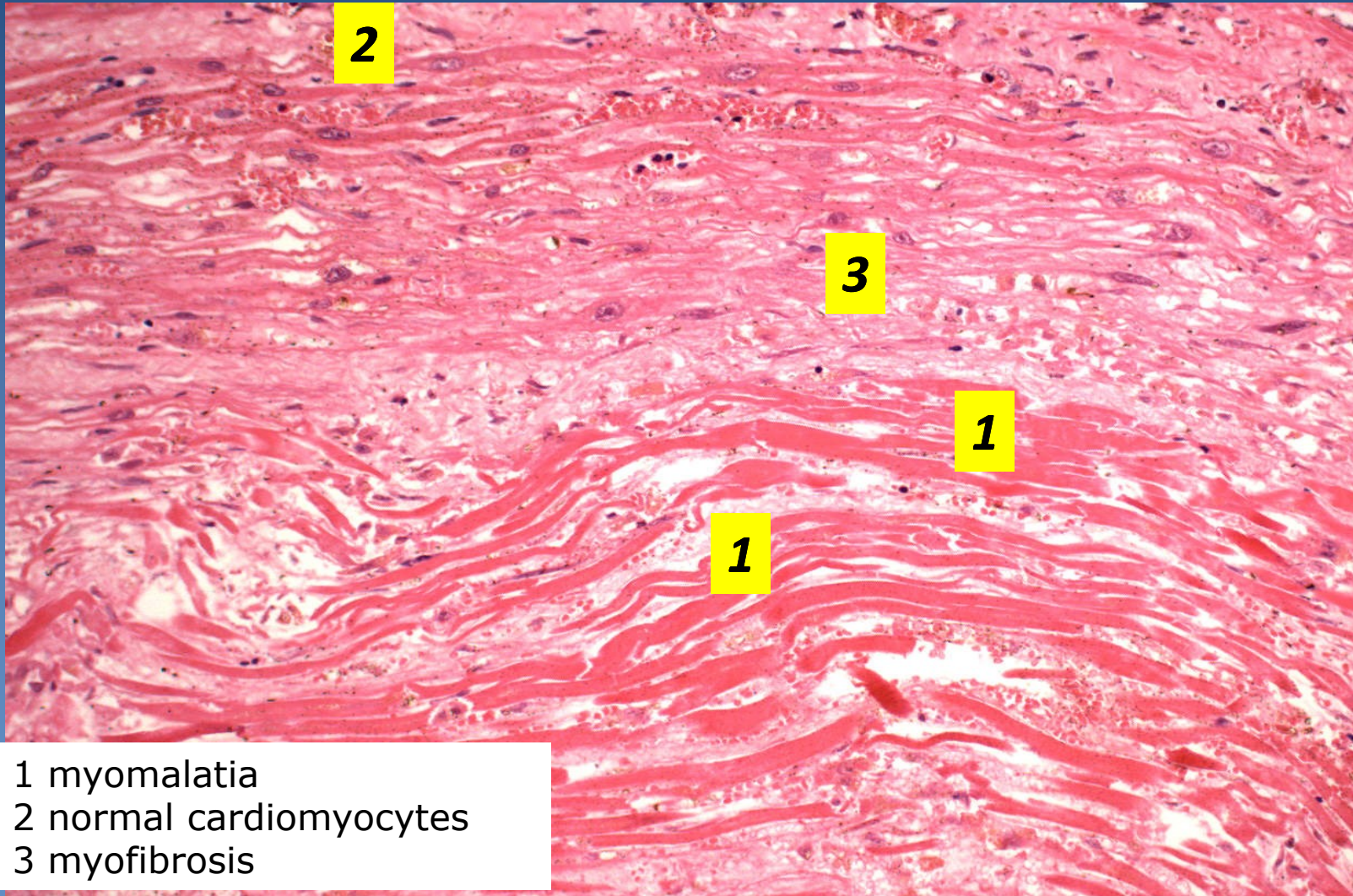
# Myofibrosis



- 1 cardiomyocytes
- 2 myofibrosis
- 3 vessels



# Myomalatia



- 1 myomalatia
- 2 normal cardiomyocytes
- 3 myofibrosis



# Pathogenesis of IHD

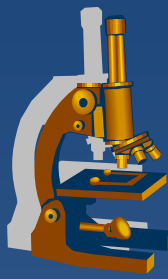


## 1) AS of coronary aa.

- commonly at a. branching
- fixed obstruction by plaque (fibrous, atheromatic)
- acute plaque change (rupture, erosion, haemorrhage, thrombosis)
- 75% stenosis – ischemia during  $\uparrow$  workload – stable angina pectoris
- 90% stenosis – ischemia even at rest – unstable angina - preinfarction

## 2) non-atherosclerotic

- coronary emboli – endocarditis, atrial fibrillation, mural thr., paradoxical e.
- coronary vasospasm
- aortic dissection
- coronary vasculitis
- congenital coronary aa. defects
  - hematologic disorders, amyloidosis, shock, etc.



# Angina pectoris (AP)

× **transient myocardial ischemia** → chest pain !!!

## 1. stable (typical)

- due to increased workload, duration  $\leq 15$  min, relieved by rest or nitroglycerin
- no myocardial necrosis
- subendocardial LV myocardium

## 2. unstable

- increasing frequency / duration of pain attack, even at rest
- plaque disruption + mural thrombosis, possible vasospasm
- preinfarction angina

## 3. variant (Prinzmetal) angina

- mostly unrelated to physical activity, coronary vasospasm - vasodilatative therapy

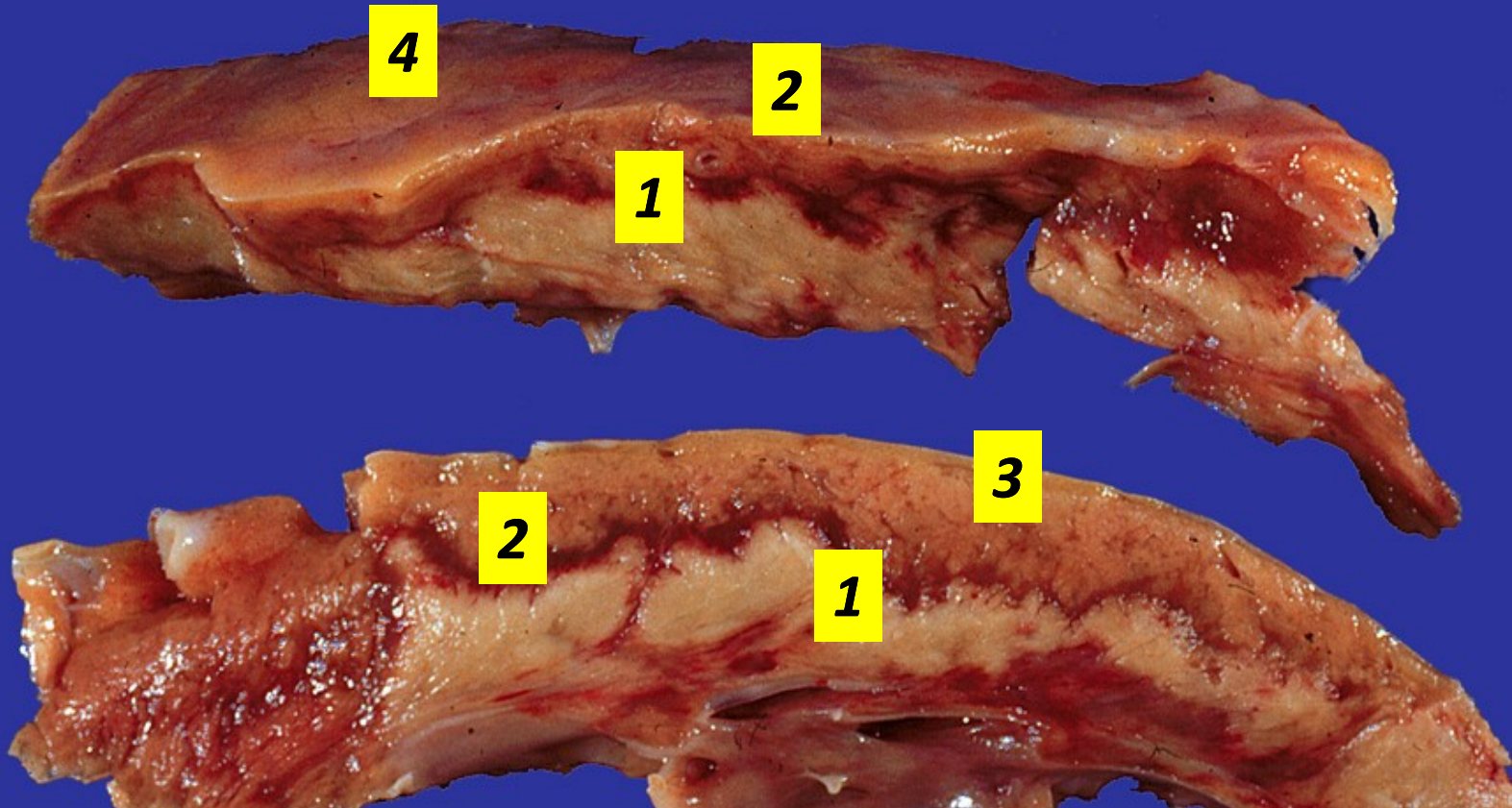
# *Myocardial infarction*



ischaemic coagulative necrosis

- ✗ **Causes:** usually coronary thrombosis, complicated atheromatic plaque, event. embolism, spasm, inflammation. Rarely systemic causes.
- ✗ **Gross:** evolution; first signs (red, softer) after 12 hrs., 2-3 days established infarction (yellowish, haemorrhagic rim), weeks – formation of firm white fibrotic scar
- ✗ **Micro:** necrotic cells more red, loss of nuclei and striation. Neutrophils, later macrophages in stroma, reparation by granulation tissue, scar

# Myocardial infarction



1 subendocardial coagulative necrosis 2 hyperemic rim 3 normal myocardium 4 epicardium



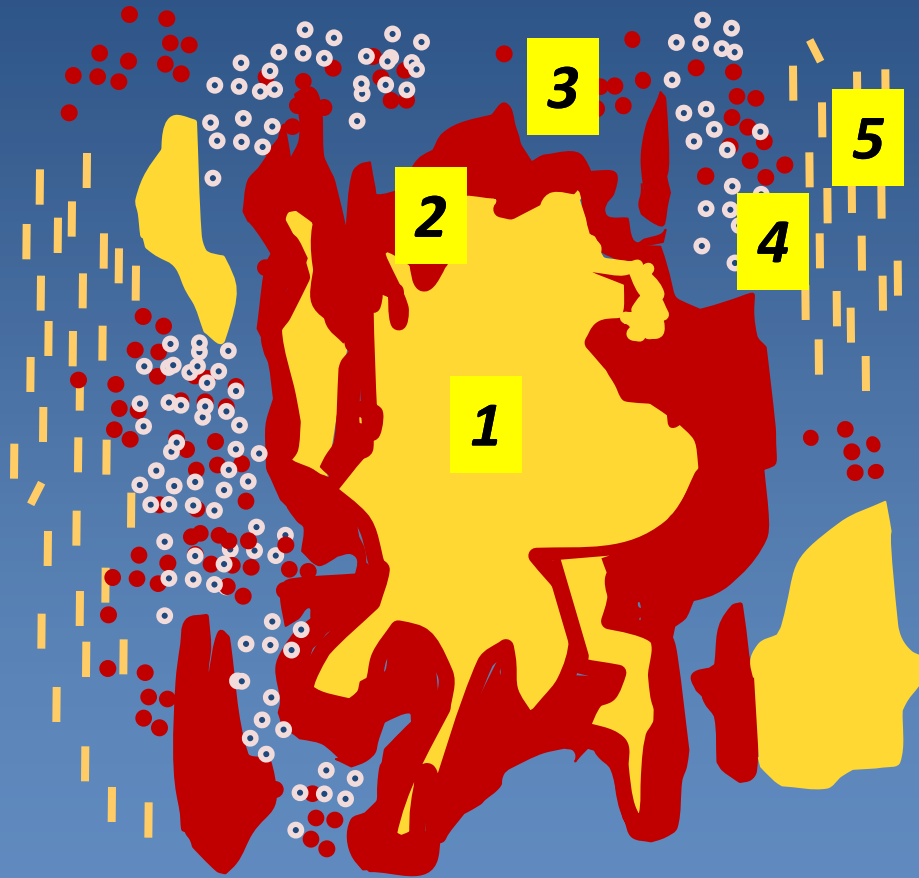
# *Myocardial infarction*








## Micro:

- ✘ 12-24 hr: edema, hypereosinophilia of necrotic cells, pyknosis
- ✘ 1-3 days: neutrophils, loss of nuclei
- ✘ 3-7 days: macrophages at the border, desintegration of myofibers
- ✘ 1-2 wk: repair by granulation tissue,
- ✘ cca 2 mo: scar

# Microscopic changes in developed MI



- 1 coagulative necrosis 
- 2 myomalacia 
- 3 hyperemic rim 
- 4 neutrophils 
- 5 regressive changes 

# Myocardial infarction

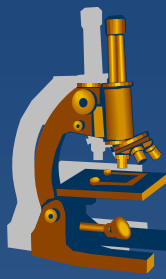


- × **transmural (QIM, STEMI) - + ST elevation on ECG**

- $\geq \frac{3}{4}$  of wall thickness, breadth  $>25$  mm
- complete coronary artery obstruction  
emergency angioplasty/stenting

- × **non-transmural (subendocardial, Non-STEMI)**

- internal  $\frac{1}{4}$  až  $\frac{1}{2}$  of LV wall
- collateral blood flow, incomplete obstruction, shorter ischemia



# MI complications

- 1. sudden death (arrhythmia)**
- 2. cardiogenic shock (contractile dysfunction)**
- 3. pericarditis epistenocardiaca**  
*-> sero-fibrinous inflammation*
- 4. mural thrombosis**  
*-> embolism into systemic circulation (-> brain, kidney, intestine, spleen infarction)*
- 5. ventricular aneurysm**  
*-> acute – risk of rupture, thrombosis; chronic – LV insufficiency*
- 6. cardiac rupture**  
*-> free wall, septum, : tamponade / acute heart failure*
- 7. papillary muscle rupture**  
*-> valvular incompetence → acute heart failure*



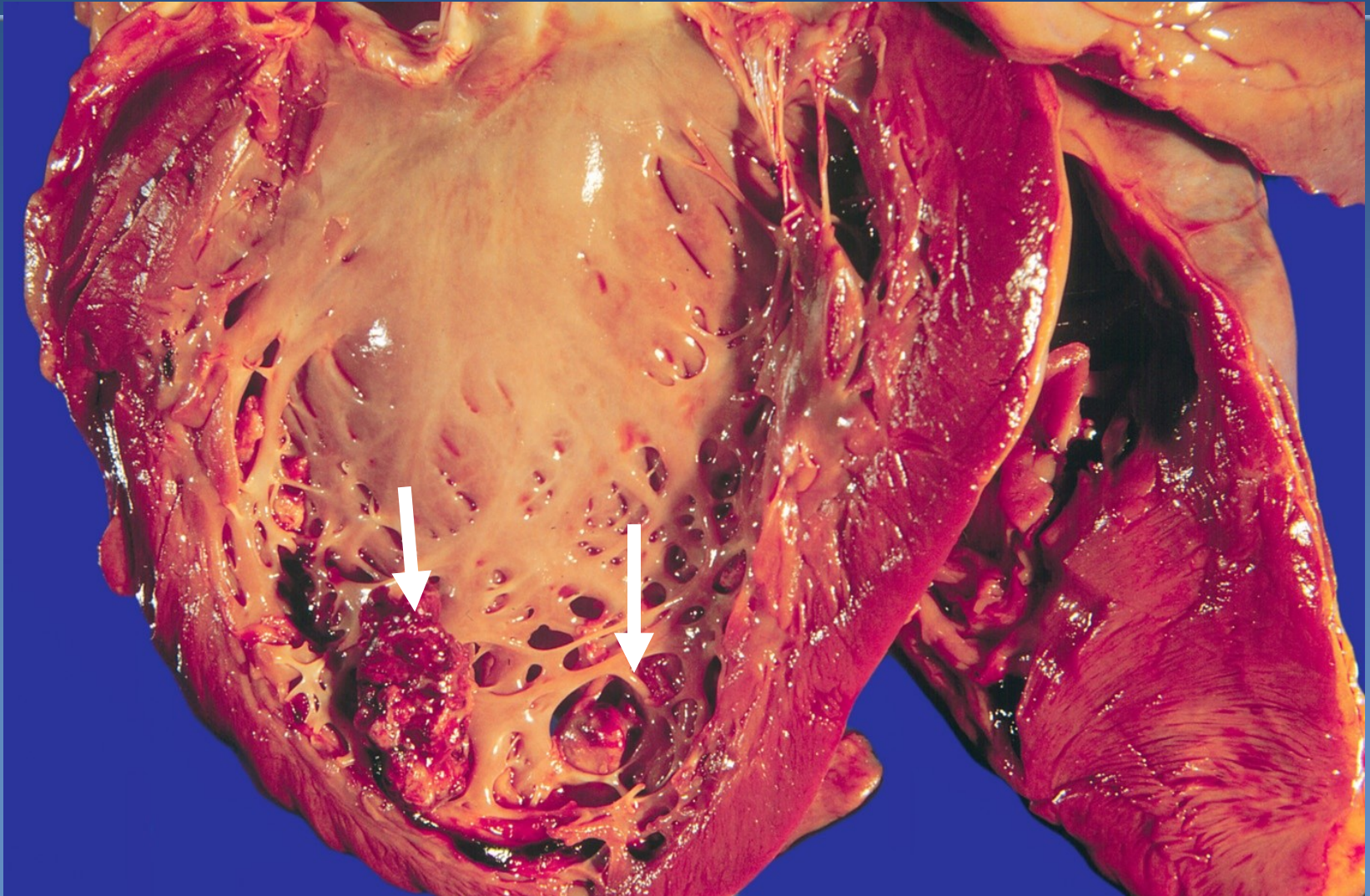
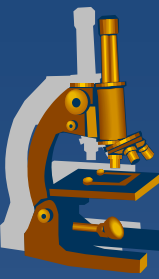
# ***MI complications***

---

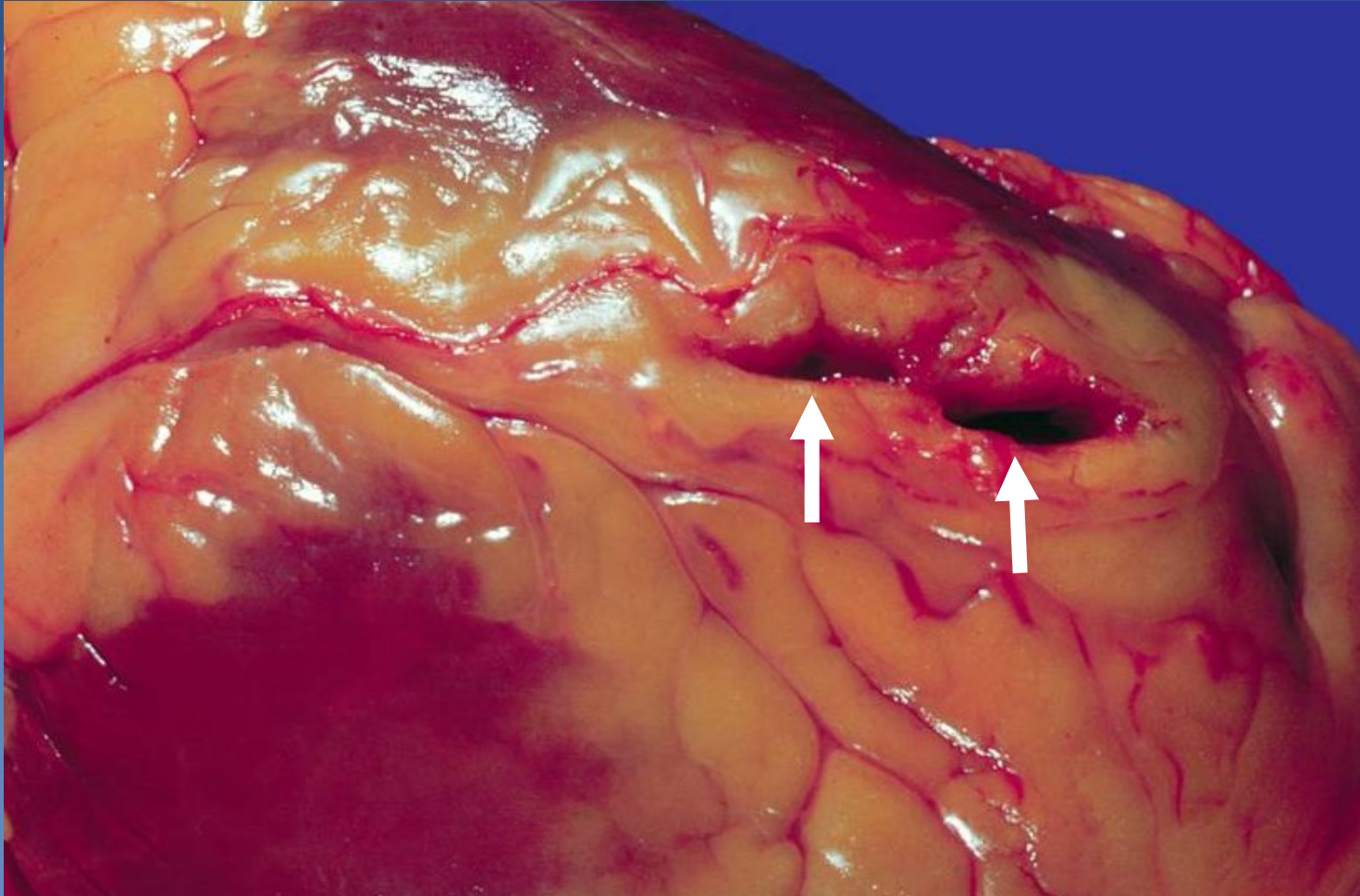


- x** persistent pain – extension of infarct
- x** Dressler's syndrome – autoimmune; chest pain, fever, effusion during weeks – months
- x** progressive late heart failure - IHD

# ***MI – mural thrombosis***

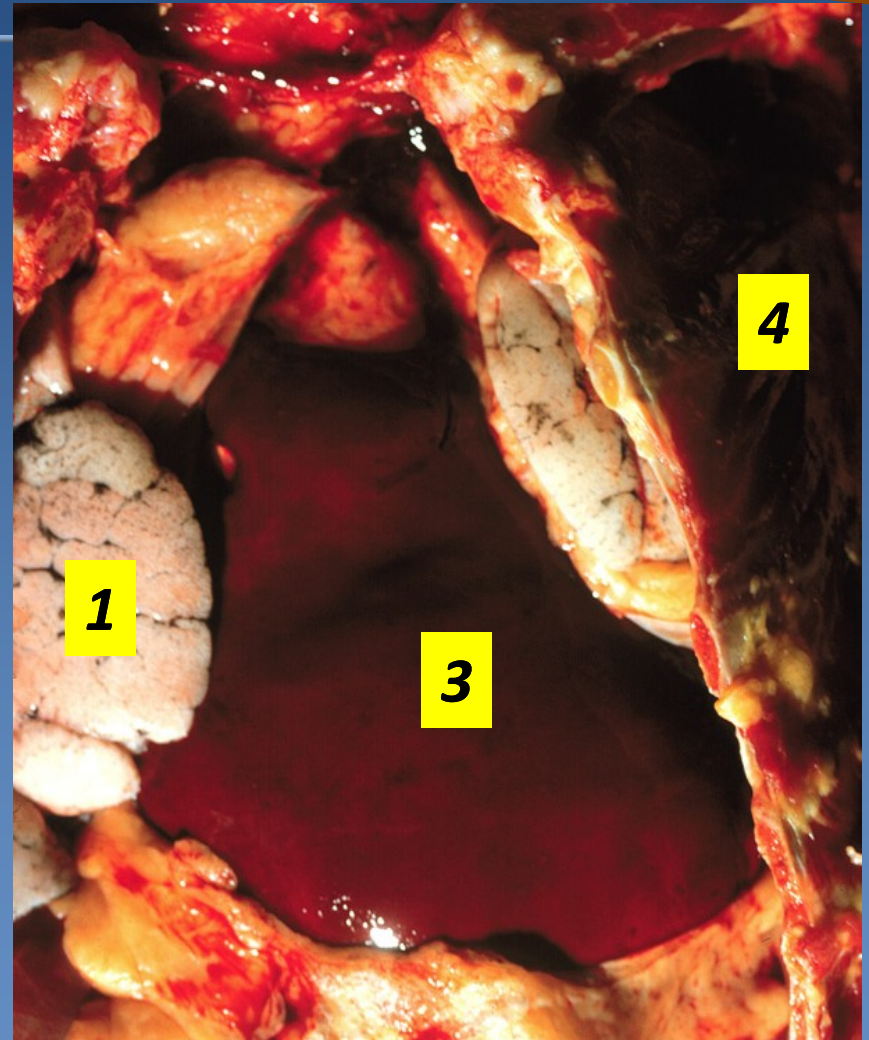
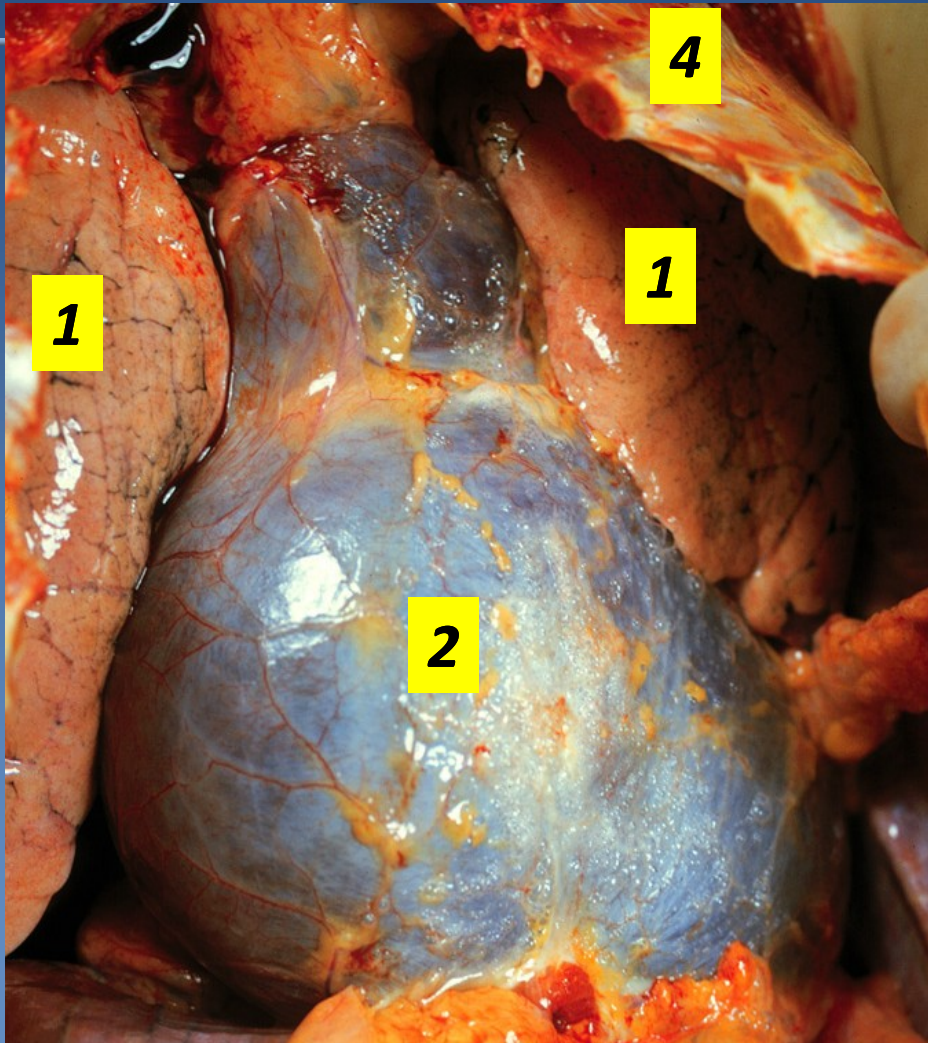
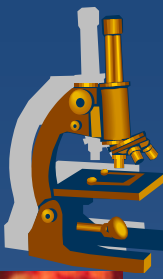


# *Mi – rupture*



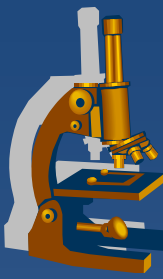


# *MI – rupture, tamponade*

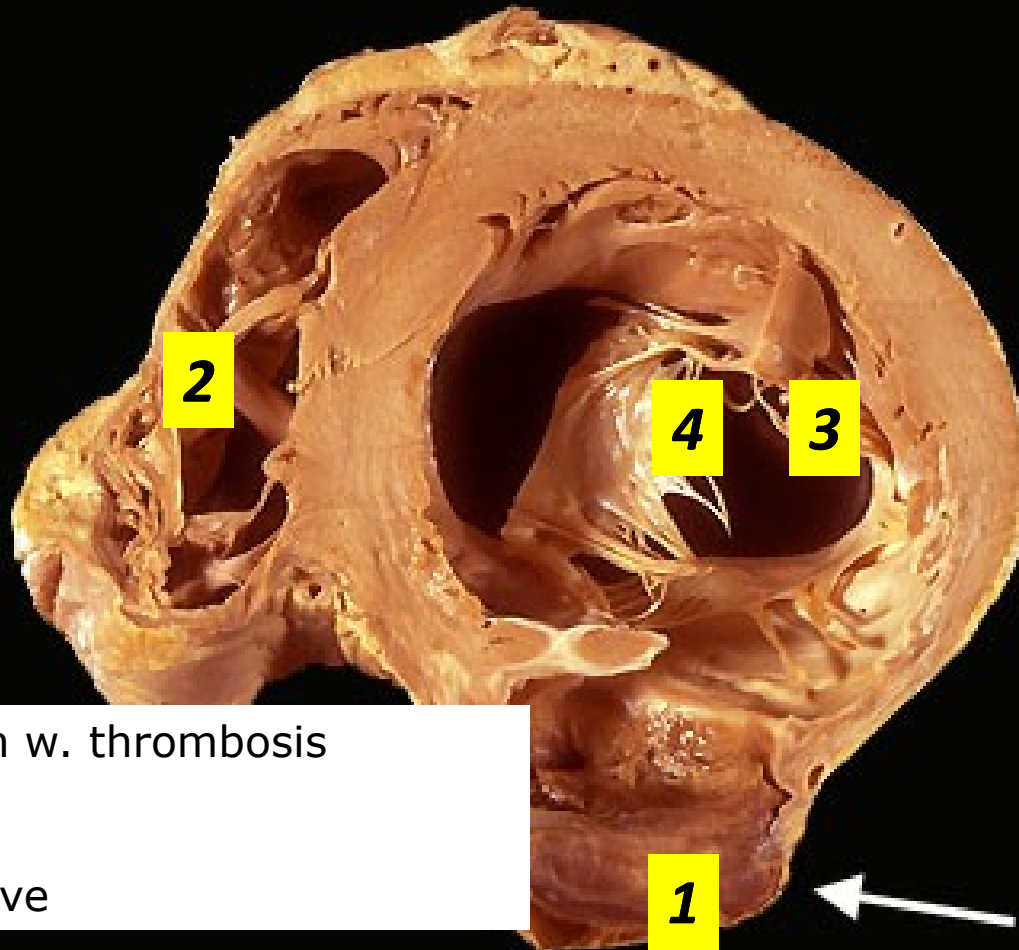


**1 lung    2 pericardial sac    3 blood coagulum    4 thoracic wall**





# *MI – LV aneurysm*



- 1 aneurysm w. thrombosis
- 2 RV
- 3 LV
- 4 mitral valve

# ***Chronic ischemic heart disease (IHD)***

---



- ✘ angina pectoris or MI in anamnesis
- ✘ progressive heart failure due to ischemic myocardial damage → LV failure → congestive RV failure
- ✘ heart hypertrophy + dilatation, myofibrosis and/or post-MI scars
- ✘ multiple coronary arteries with significant AS stenosis
- ✘ imminent risk of MI, sudden cardiac death due to arrhythmia, heart failure

# ***Sudden cardiac death***



= unexpected death from cardiac causes, without preexisting symptoms or within 1 hr of the onset of symptoms

✗ most commonly due to lethal arrhythmia (ventricular fibrillation, asystole)

✗ sudden collapse without signs of acute MI

✗ other causes:

⇒ *dissecting/ruptured aortic aneurysm*

⇒ *pulmonary thromboembolism*

⇒ *massive intracerebral haemorrhage*

⇒ *heritable conditions incl. anatomic, electrical – channelopathies*

# Myocarditis

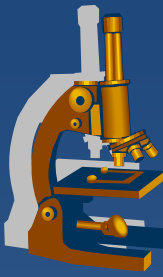


- ✗ myokardial inflammatory damage without ischemia
  
- ✗ **gross:**
  - ⇒ *cardiac dilatation, flabby, mottled myocardium*
  
- ✗ **micro:**
  - ⇒ *inflammatory infiltrate (according etiology) + cardiomyocyte regressive changes incl. necrosis*
  
- ✗ **etiology:**
  - ⇒ viruses, rickettsia, chlamydia, bacteria (diphtheria, sepsis), fungi, protozoa (toxoplasmosis), helminths (trichinosis)
  - ⇒ immune-mediated (*drug hypersensitivity, postviral, rheumatic fever, rejection*)
  - ⇒ *ionising radiation*
  - ⇒ unknown (*giant-cell myocarditis*)



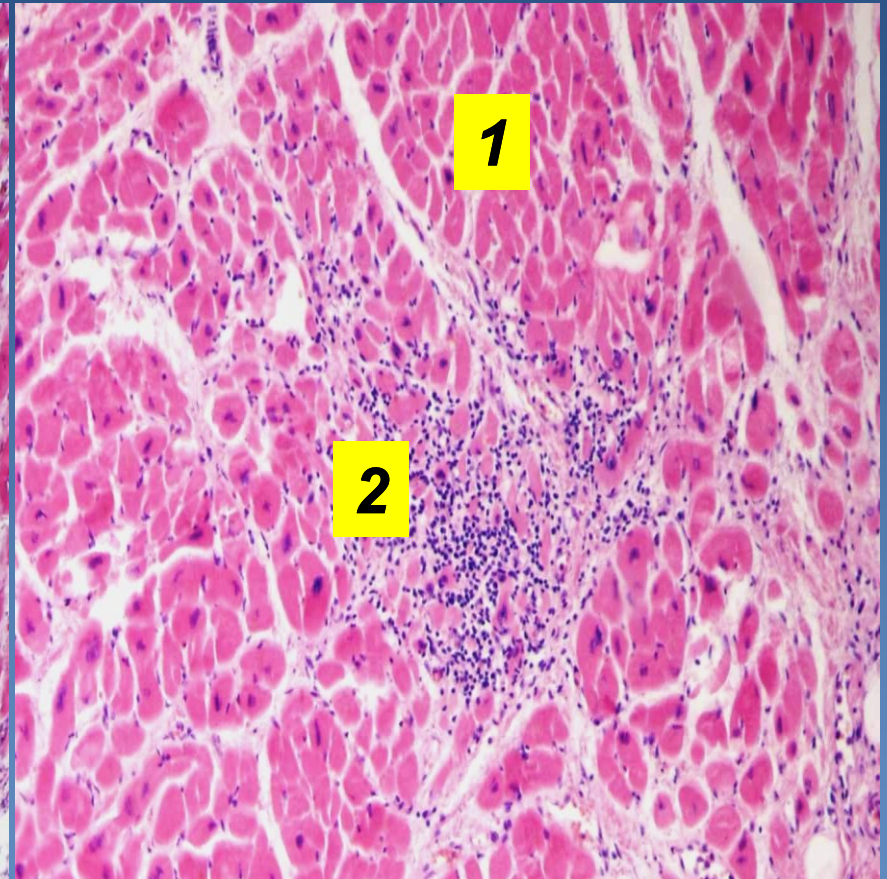
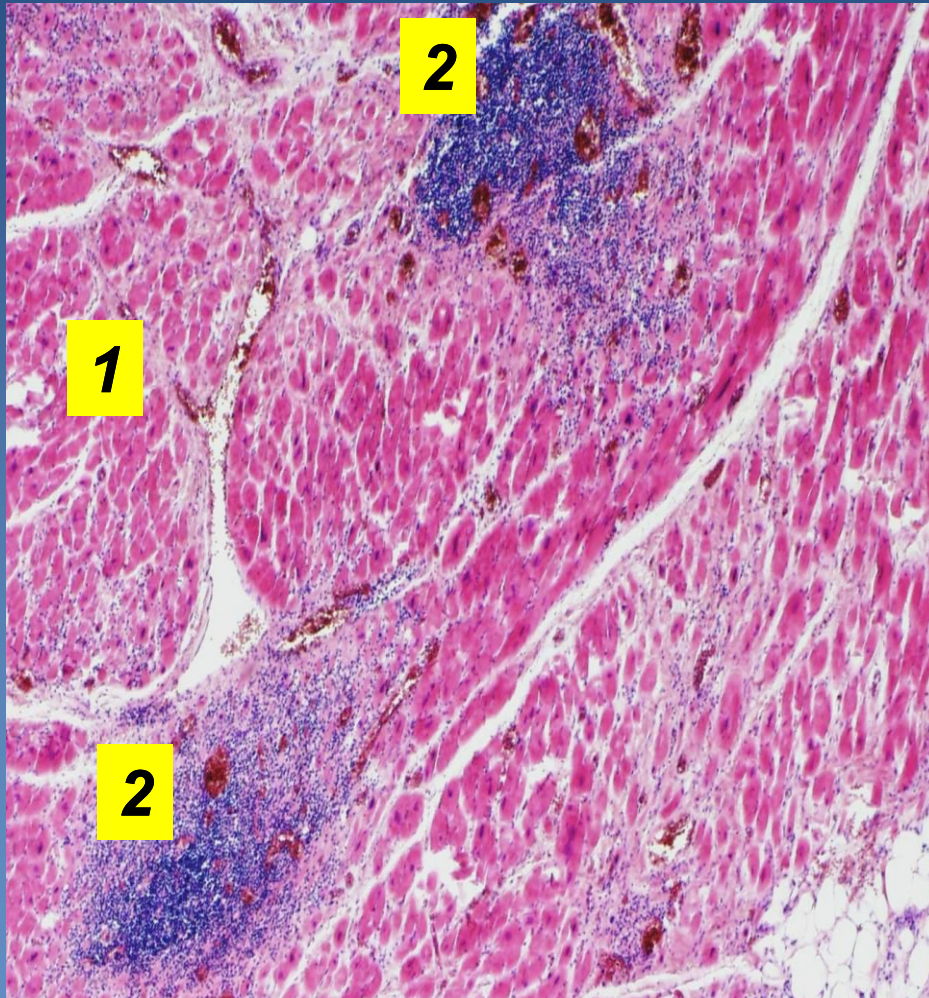
# *Viral myocarditis*

---



- ✗ *Coxsackie, parvovirus B19, influenza, EBV, CMV, HIV*
- ✗ inflammatory infiltrate: T-cells mostly
- ✗ after acute attack commonly autoimmune-mediated cardiomyocytes destruction and fibrosis → dilated cardiomyopathy

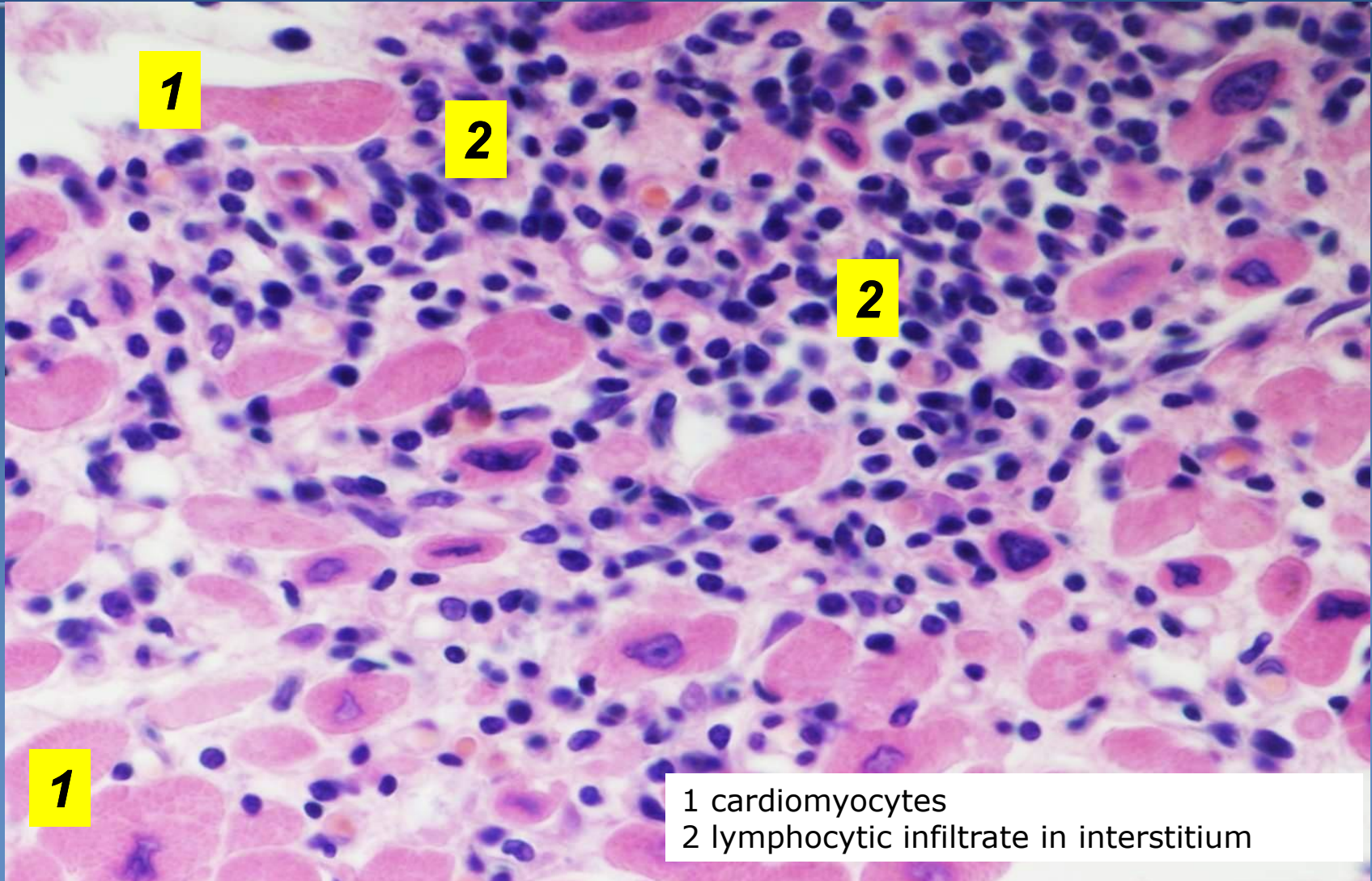
# *Viral myocarditis*



1 cardiomyocytes  
2 lymphocytic infiltrate in interstitium



# *Viral myocarditis*



1

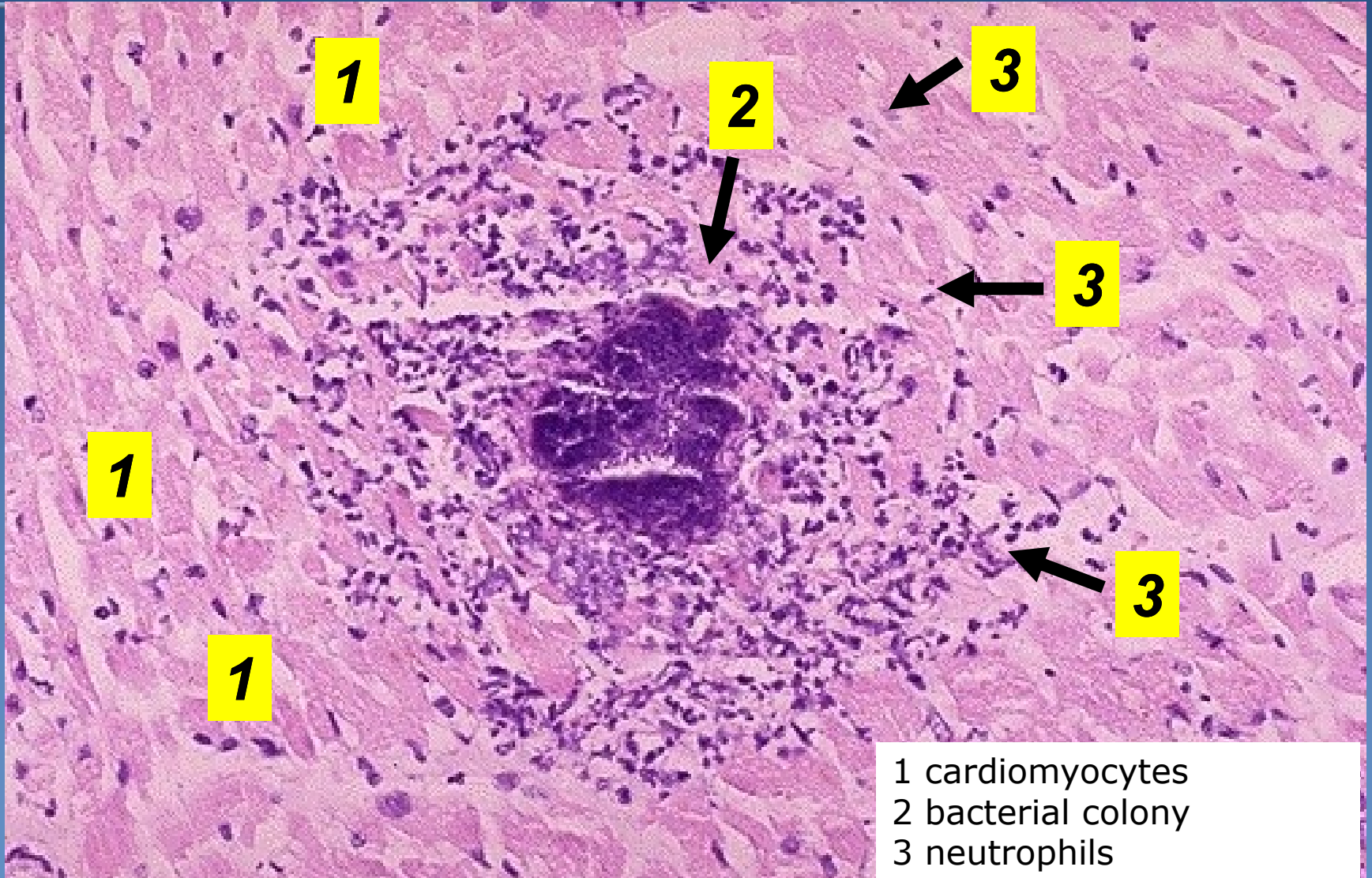
1

2

2

1 cardiomyocytes  
2 lymphocytic infiltrate in interstitium

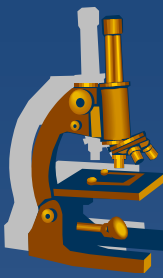
# *Septic myocarditis*



1 cardiomyocytes  
2 bacterial colony  
3 neutrophils



# Cardiomyopathies



= heart disease due to myocardial abnormality, with heart dysfunction  
diagnosis after exclusion of IHD, valvular disease, congenital d. or hypertension

## ✗ heterogenous group of disorders:

### ⇒ dilated (DCM)

– dilatation + hypertrophy, ↓ LV contraction, possible mural thrombosis; 20–50% genetic (AD);  
*alcoholic, peripartum, myocarditis...*

### ⇒ hypertrophic (HCM)

– massive LV hypertrophy, 100% genetic, diastolic dysfunction, histologic „disarray“

### ⇒ restrictive cardiomyopathy

– diastolic dysfunction, ↓ of compliance - ↓ filling, myocardial stiffness

### ⇒ specific CM

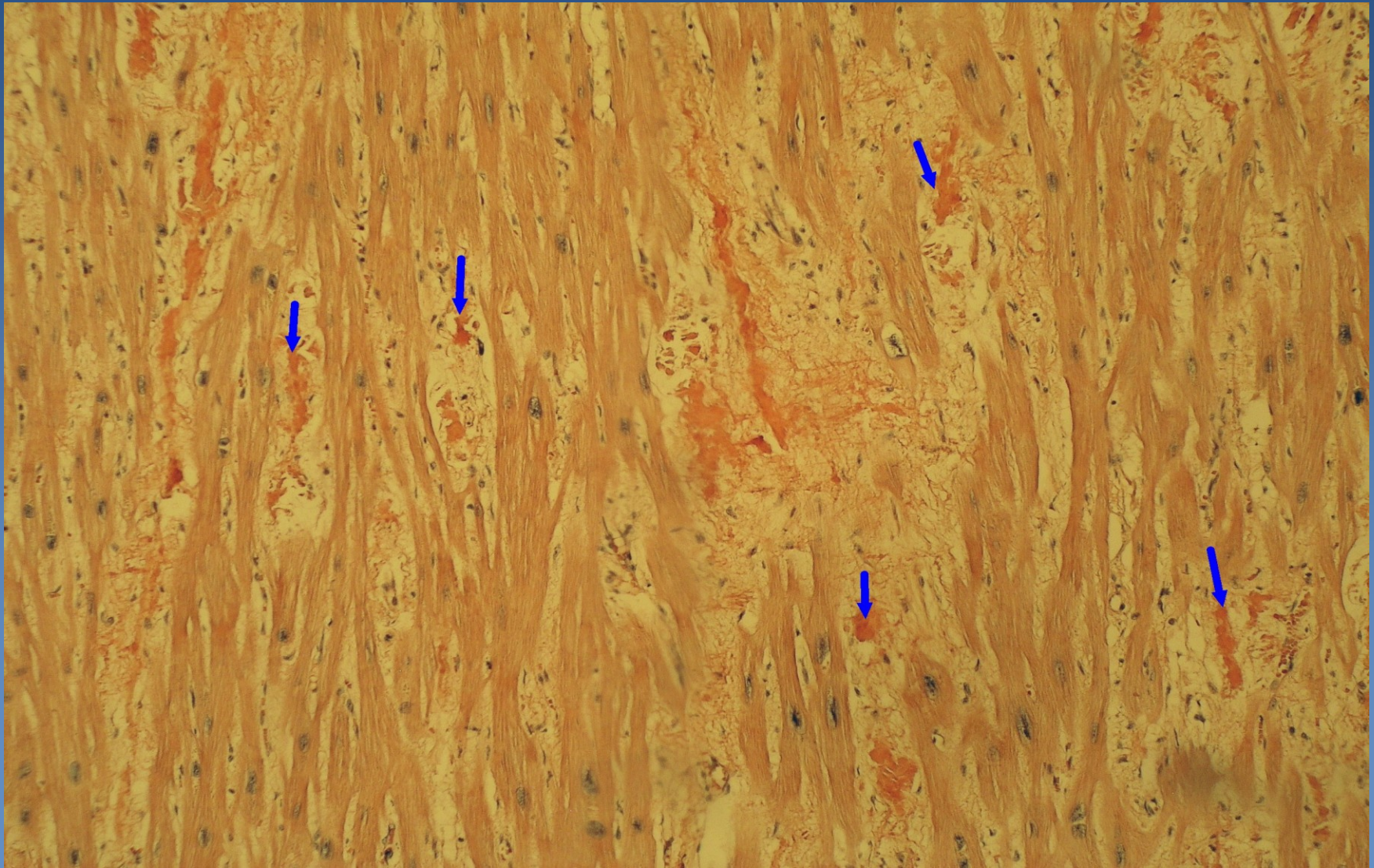
– Duchenne muscle dystrophy, toxic (drugs), endocrine d., metabolic d. (hemochromatosis, amyloidosis, glycogenosis, ...)

# Myocardial amyloidosis



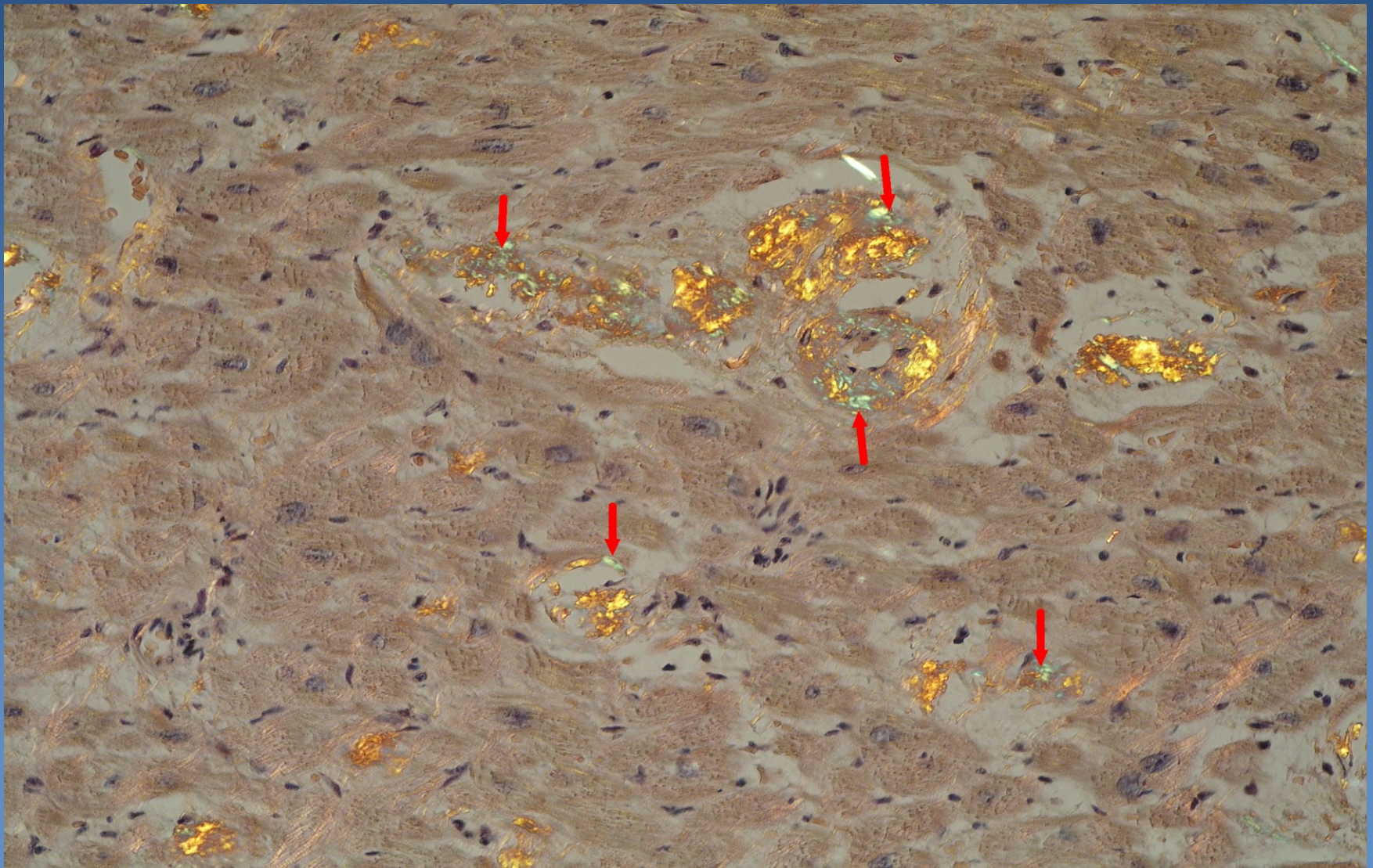
- ✗ local x systemic (mostly AL amyloidosis)
- ✗ senile amyloidosis
  - ⇒ *atrial + ventricles; amyloid protein = prealbumin (transthyretin)*
- ✗ *isolated atrial amyloidosis*
  - ⇒ *amyloid protein = atrial natriuretic peptide*
- ✗ **gross**: consistency normal - firm (rubbery)
- ✗ **micro**: variable amyloid deposits v interstitium and vessels, Congo red + polarization

# *Myocardial amyloidosis*





# *Myocardial amyloidosis*





# *Endocardial / valvular diseases*



- ✘ endocarditis

  - ⇒ *infectious or immune-mediated endocardial inflammation*

- ✘ degenerative diseases

  - ⇒ *calcific aortic (rarely mitral) stenosis, mitral valve prolapse, annular and marginal sclerosis*

- ✘ endocrine diseases

  - ⇒ *carcinoid syndrome*

- ✘ nonbacterial thrombotic endocarditis (in debilitated patients)

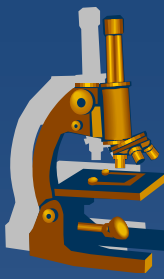
# *Mitral valve prolapse*



# ***Aortic valve calcification***



# Rheumatic fever, rheumatic heart disease



✗ acute non-purulent, **immune-mediated** systemic poststreptococcal inflammation (cross-reactive antibodies)

## ✗ acute stage: **PANCARDITIS**

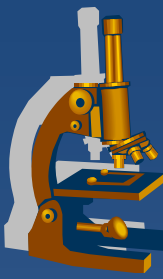
⇒ *fibrinous pericarditis + myocarditis with Aschoff bodies (foci of **fibrinoid necrosis** + inflammatory reaction + verrucous endocarditis (small depositions of fibrin along the closure lines of Ao a Mi valves)*

⇒ *acute endocarditis commonly recurrent*

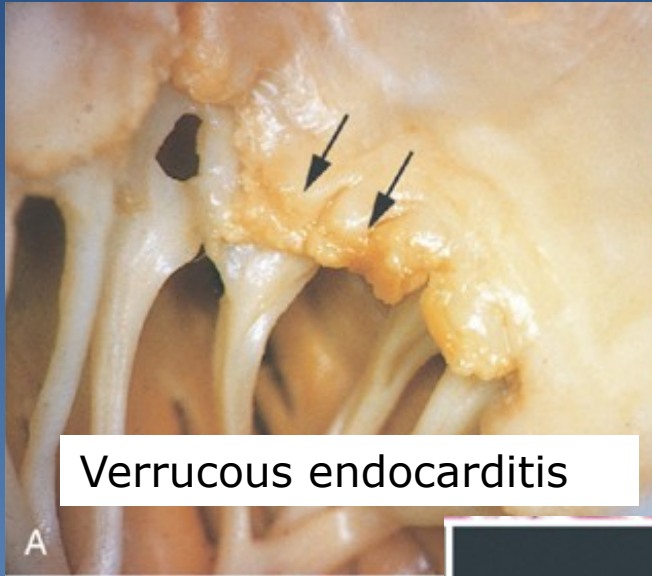
## ✗ chronic stage:

⇒ *diffuse fibrous thickening + distortion, commissural fusion → dystrophic calcification - stenosis + incompetence)*

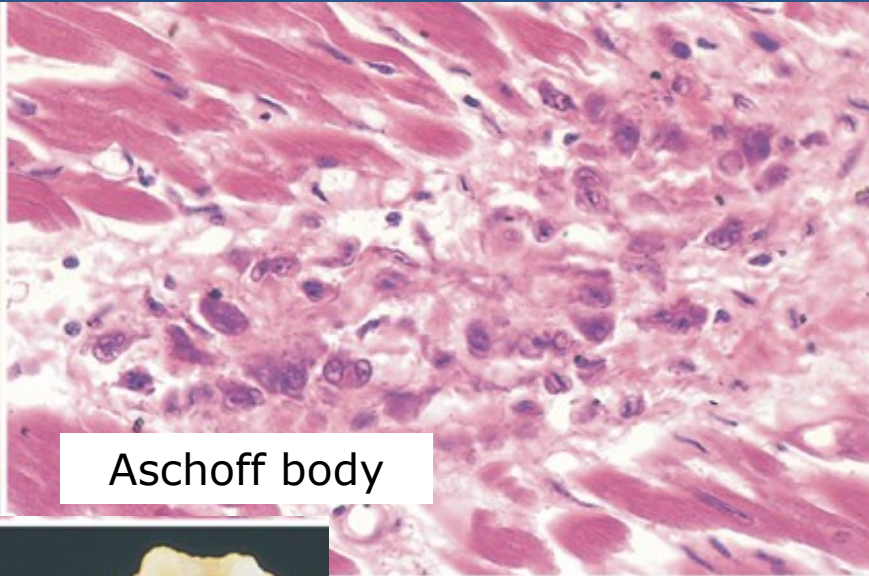




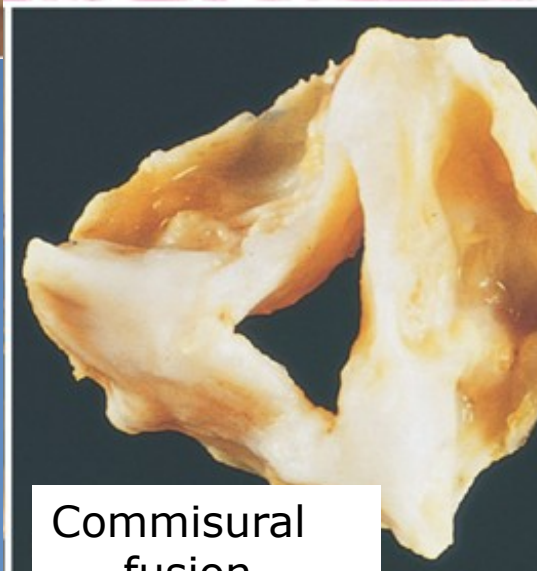
# *rheumatic heart disease*



Verrucous endocarditis



Aschoff body



Commissural fusion

# *Infective endocarditis*



- ✗ commonly by highly virulent microorganisms
  - ⇒ *Strep. pyogenes, Strep. pneumoniae, Staph. aureus, ... ev. fungi*
- ✗ subacute IE – less virulent microorganisms
  - ⇒ *viridans streptococci*
- ✗ predisposition:
  - ⇒ *deformed valve, bioprosthesis, postcatethrization, i.v. drug addicts*
- ✗ bacteremia - endocardial damage by bacteria - trombosis = infective vegetation

# *Infective endocarditis*



✗ **gross:** friable red-brown mass 0,5-2 cm on leaflets or chordae tendinae, valvular damage incl. ulceration

✗ **micro:**

⇒ *fibrin + bacterial colonies + neutrophils (+ granulation tissue)*

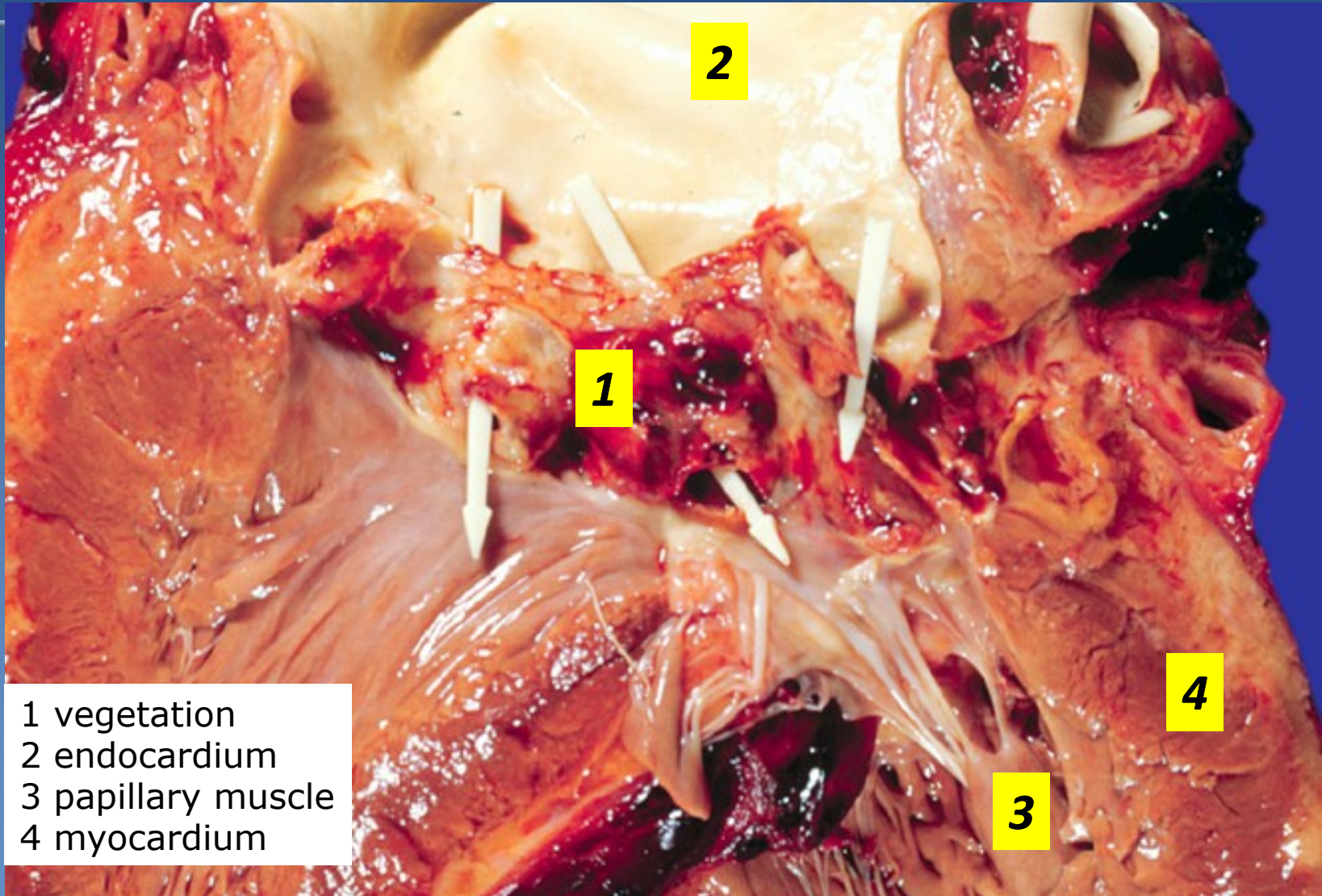
⇒ *Inflammation/ necrosis of the valve tissue*

✗ **complications:**

⇒ *acute: valvular damage, myocarditis + abscess, pyemia, thrombembolism*

⇒ *chronic valvular disease*

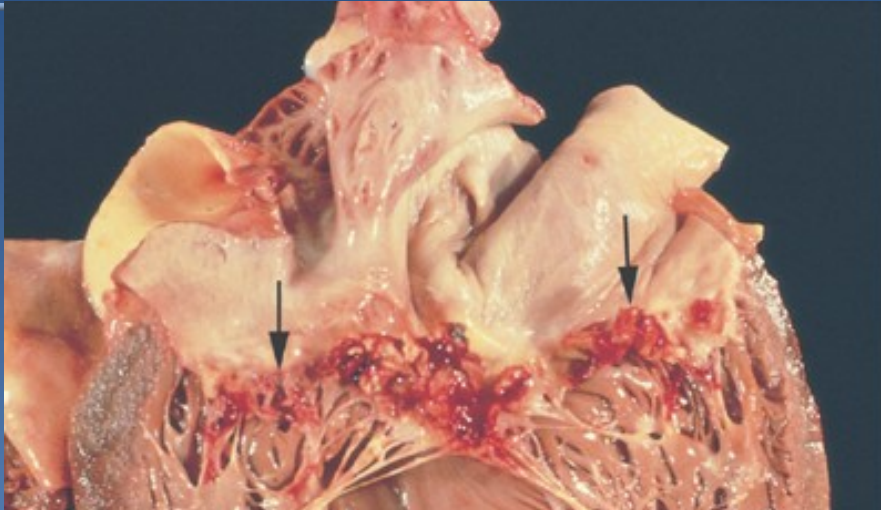
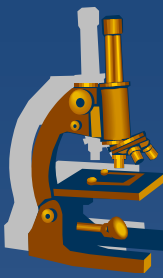
# ***Infective endocarditis- valve destruction***



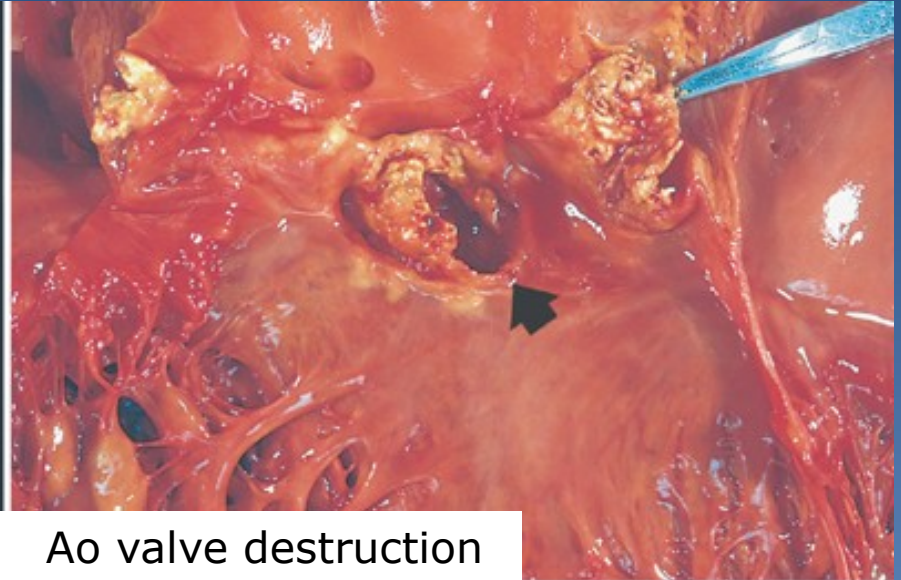
- 1 vegetation
- 2 endocardium
- 3 papillary muscle
- 4 myocardium



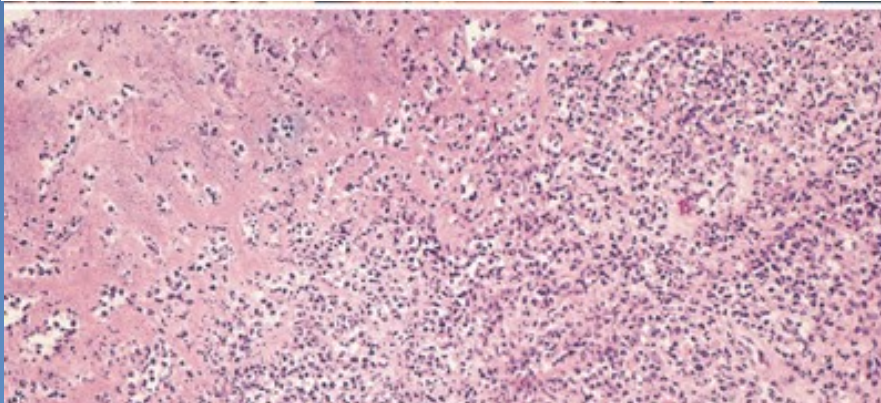
# *Infective endocarditis*



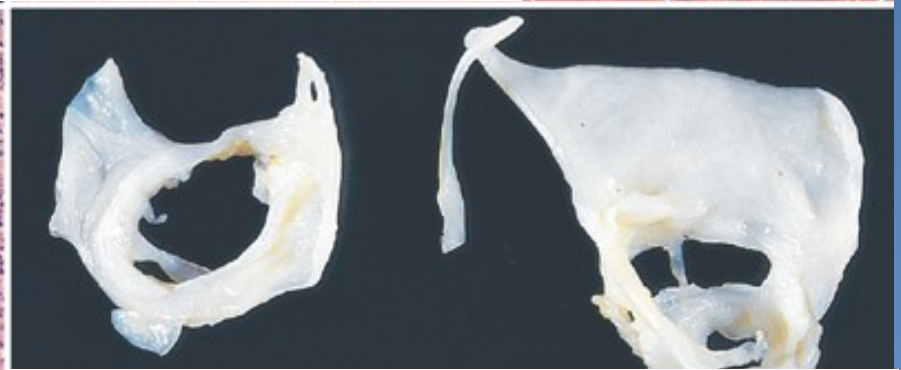
Mi vegetations



Ao valve destruction

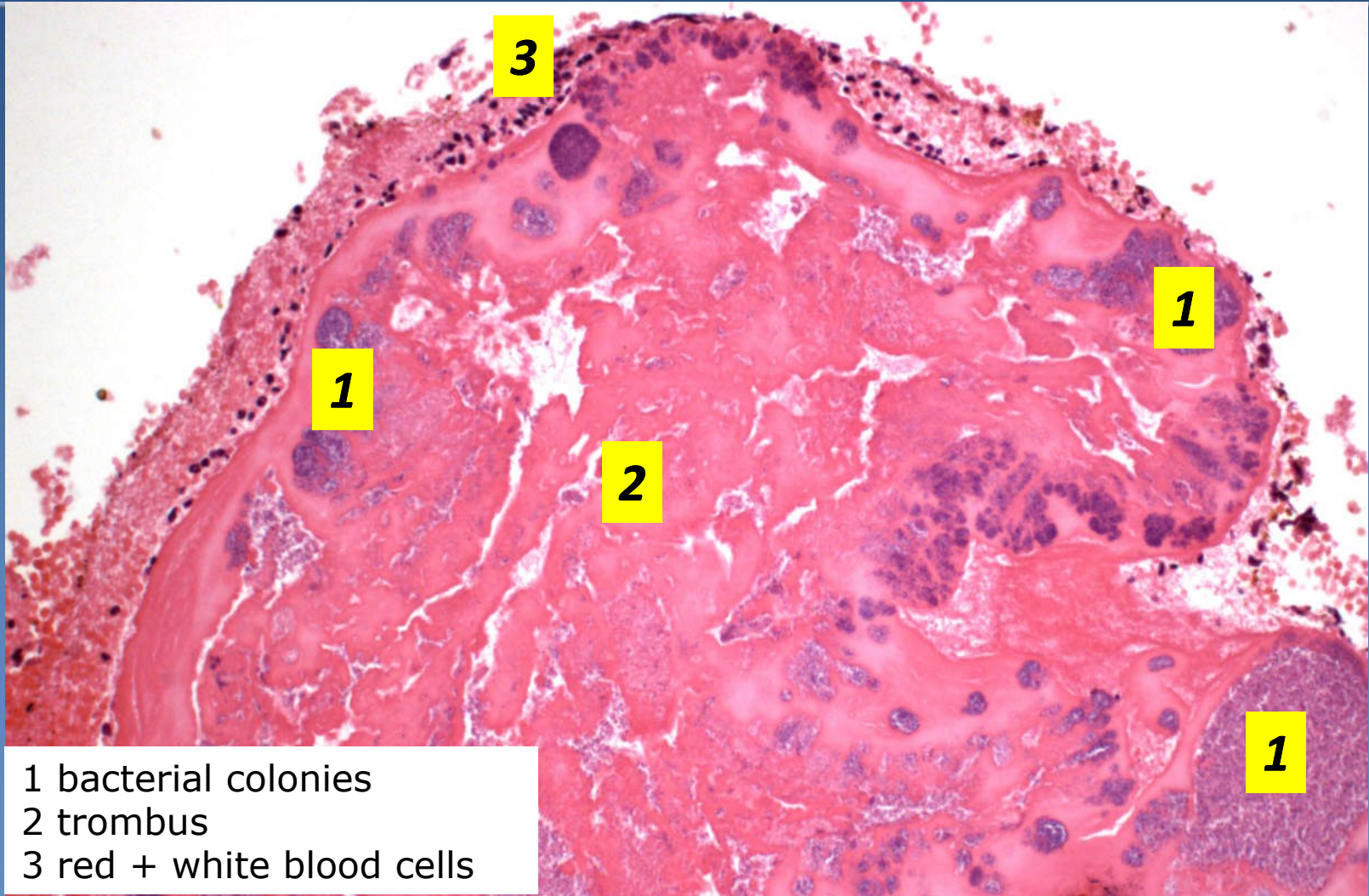


purulent inflammation



IE repair (Mi fenestration without vegetations)

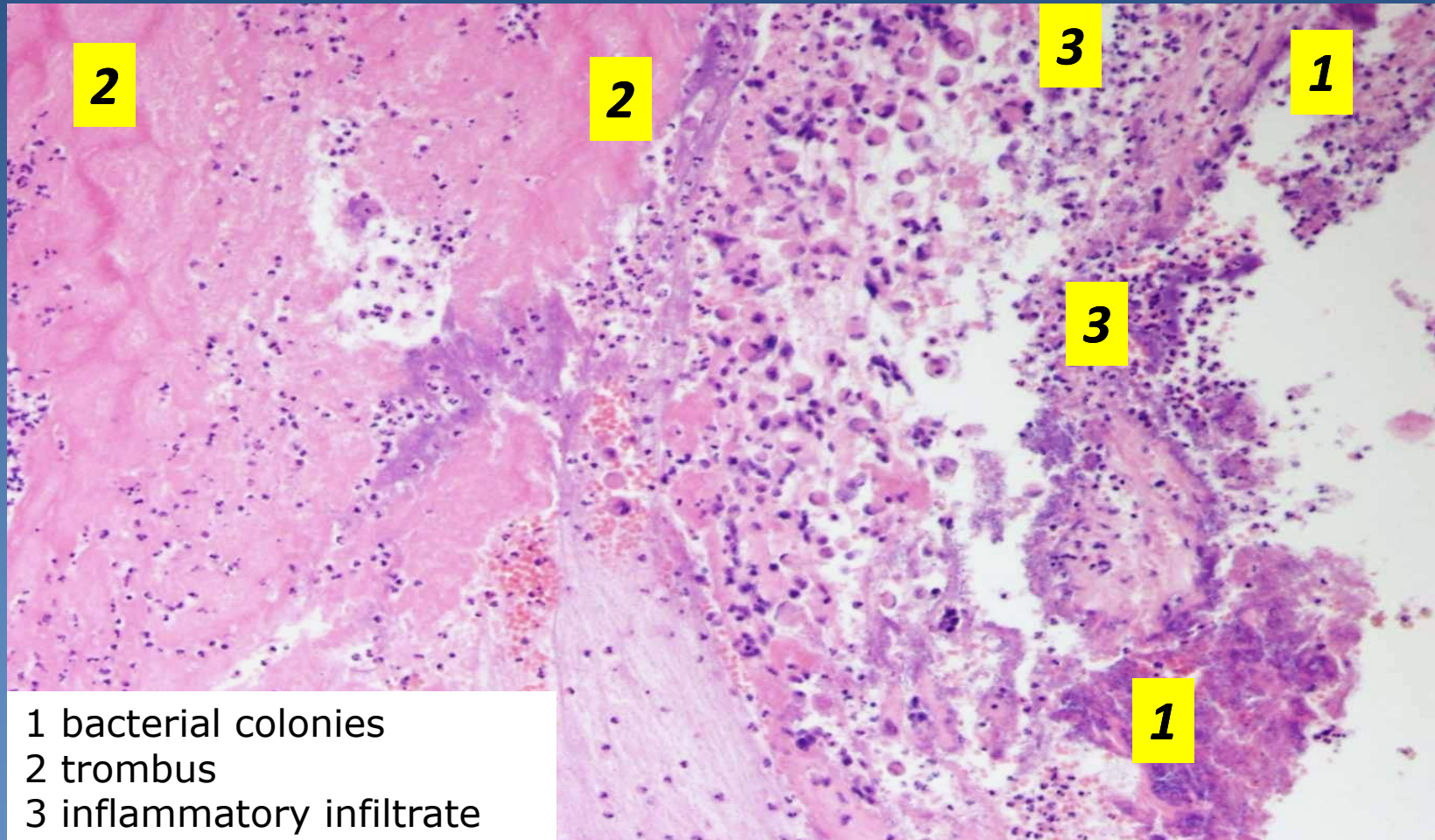
# ***Infective endocarditis - vegetations***



- 1 bacterial colonies
- 2 trombus
- 3 red + white blood cells

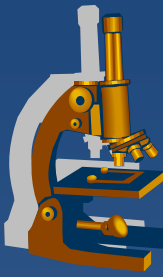


# *Infective endocarditis - vegetations*



- 1 bacterial colonies
- 2 trombus
- 3 inflammatory infiltrate

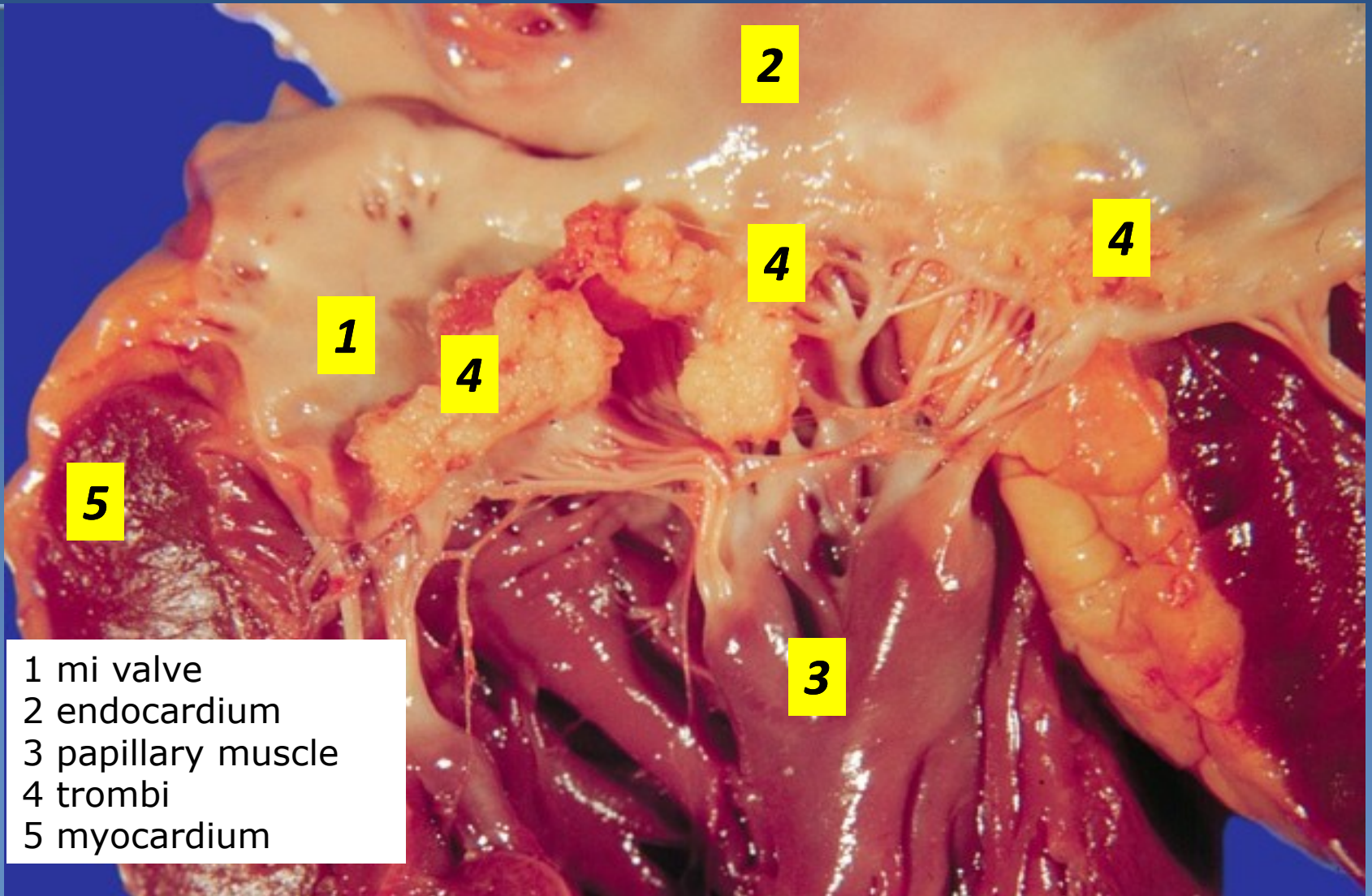
# ***Non-bacterial thrombotic endocarditis***



- ✗ **sterile** vegetations due to **hypercoagulative state**  $\Rightarrow$  concurrent venous thrombosis and lung embolization
- ✗ **in generalized malignancies**, chronic nephropathy with uremia, COPD etc.
- ✗ mostly on **mitral valve** (normal)
- ✗ micro: verrucous vegetations (single or multiple), 1-5 mm, bland thrombi
- ✗ possible source of **emboli**

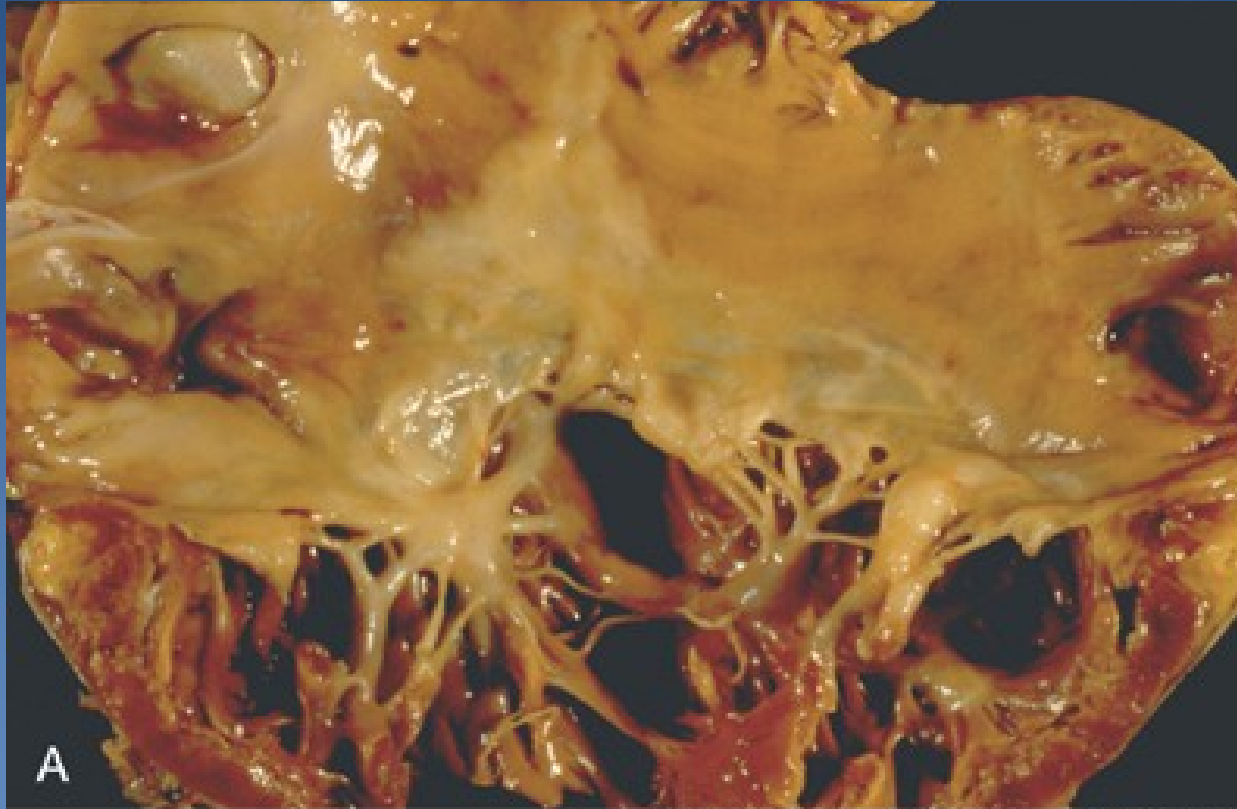


# *Non-bacterial thrombotic endocarditis*

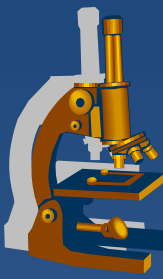


- 1 mi valve
- 2 endocardium
- 3 papillary muscle
- 4 trombi
- 5 myocardium

# *Carcinoid syndrome*

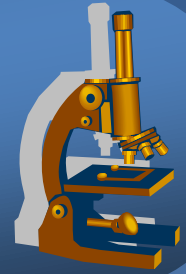


endocardial fibrous plaquelike thickenings – RA, RV



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# *Cardiovascular tumors*

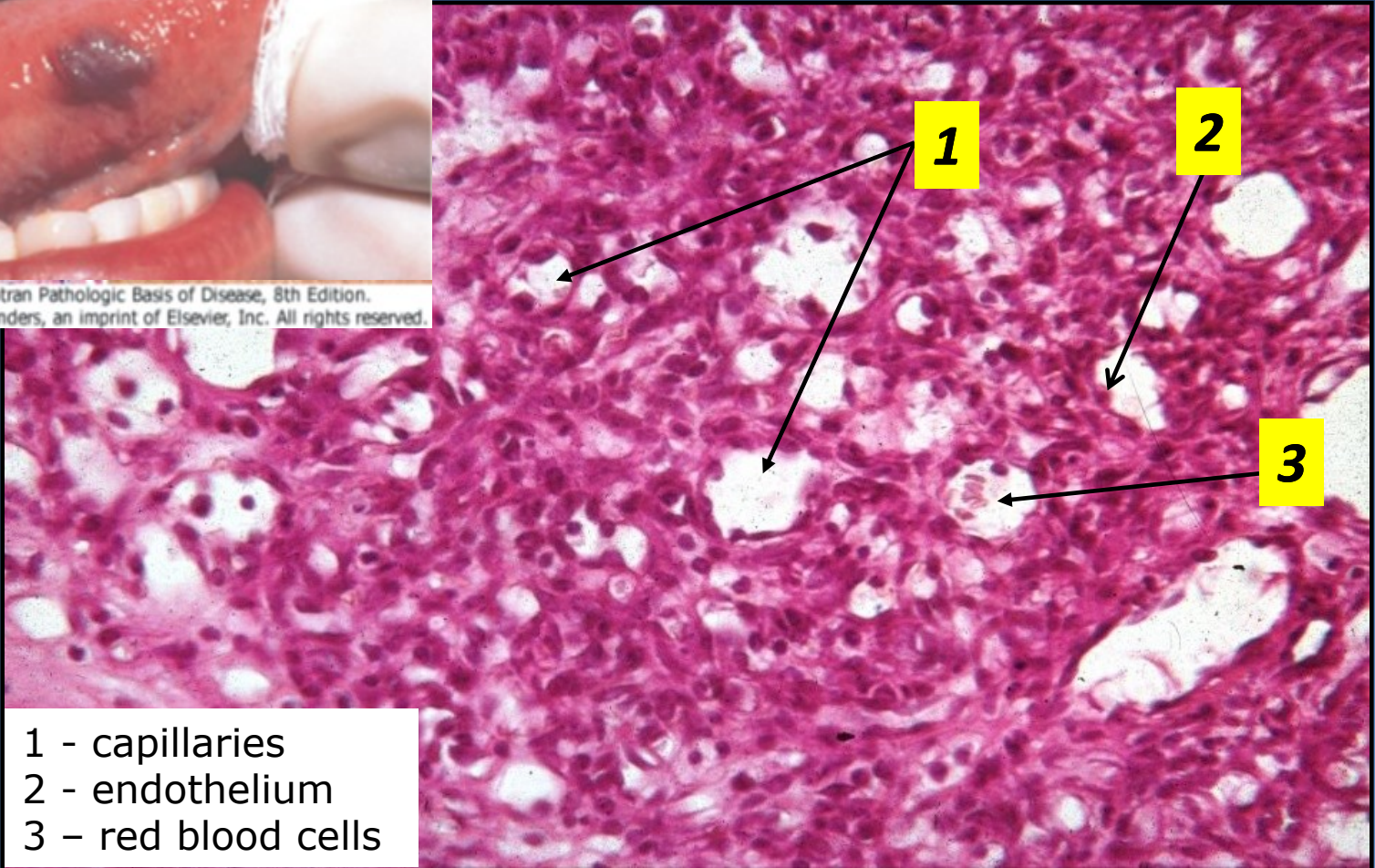




# Capillary hemangioma



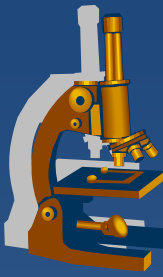
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- 1 - capillaries
- 2 - endothelium
- 3 - red blood cells



# *Cavernous hemangioma*



## **x**gross:

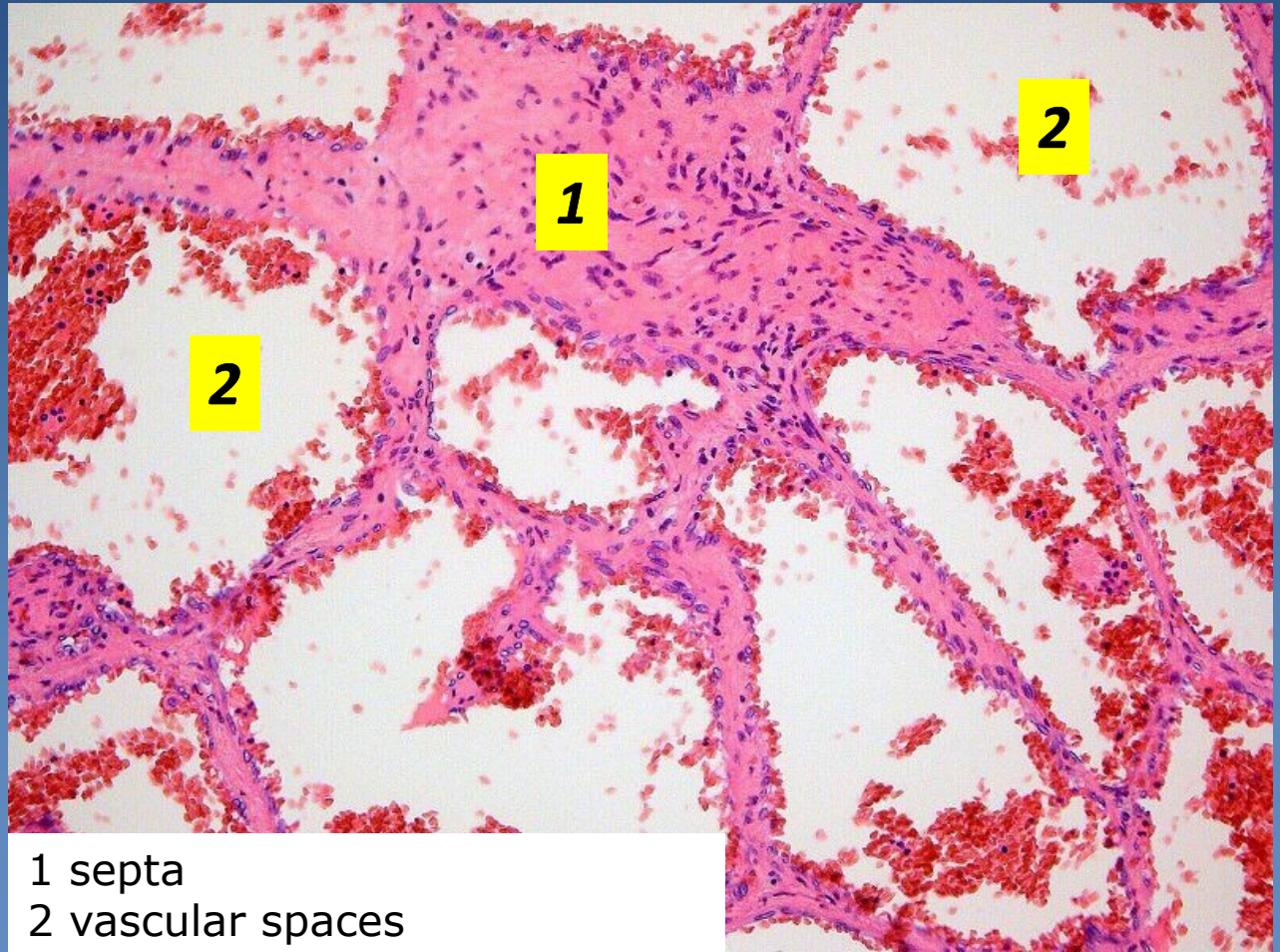
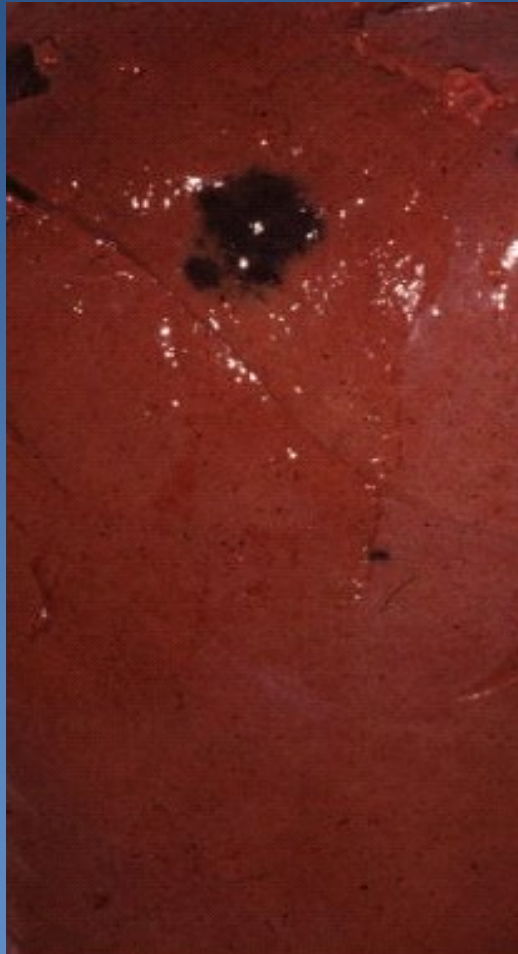
- ⇒ red -blue focus (nodular)
- ⇒ possible large size (-15 cm)
- ⇒ liver, spleen, skin; commonly multiple

## **x**micro:

- ⇒ large blood-filled vascular spaces divided by fibrous septa



# *Cavernous hemangioma*



1 septa  
2 vascular spaces

# *Kaposi sarcoma*



- x classic form** – chronic, in mediterranean or jewish origin, usually (90%) confined to skin
- x endemic** – south-african children, lymphadenopathic, aggressive
- x immunosuppression (transplant) associated** – internal organs in 50%
- x AIDS associated**

# *Kaposi sarcoma*



- ✗ HHV-8, hyperproliferation of endothelial cells, prevention of apoptosis
- ✗ **gross:** red to purple patches – raised plaques – nodules
- ✗ **micro:** irregular blood spaces, plump atypical endothelial cells, + perivascular aggregates of spindle cells

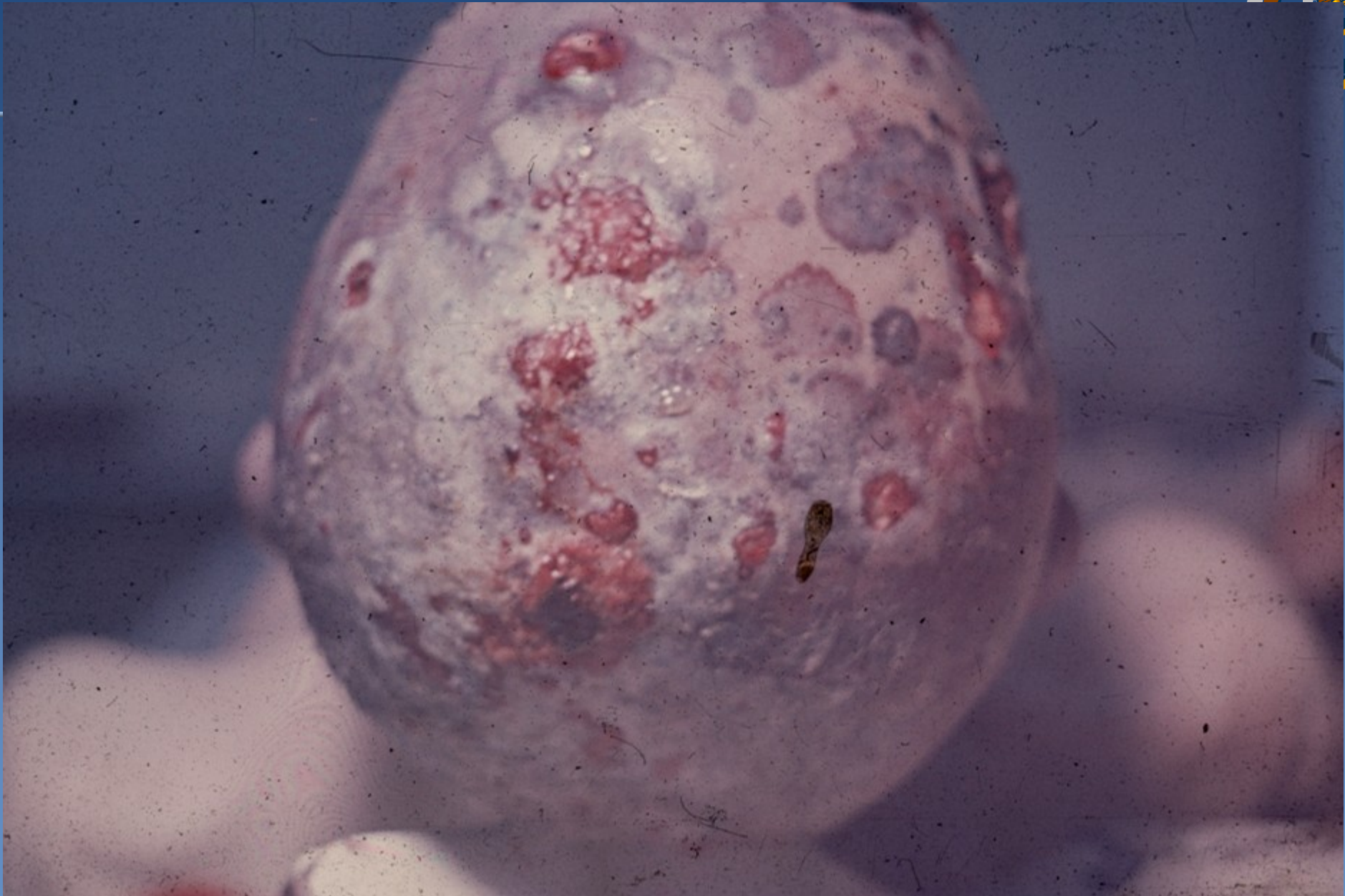


# *Kaposi sarcoma*



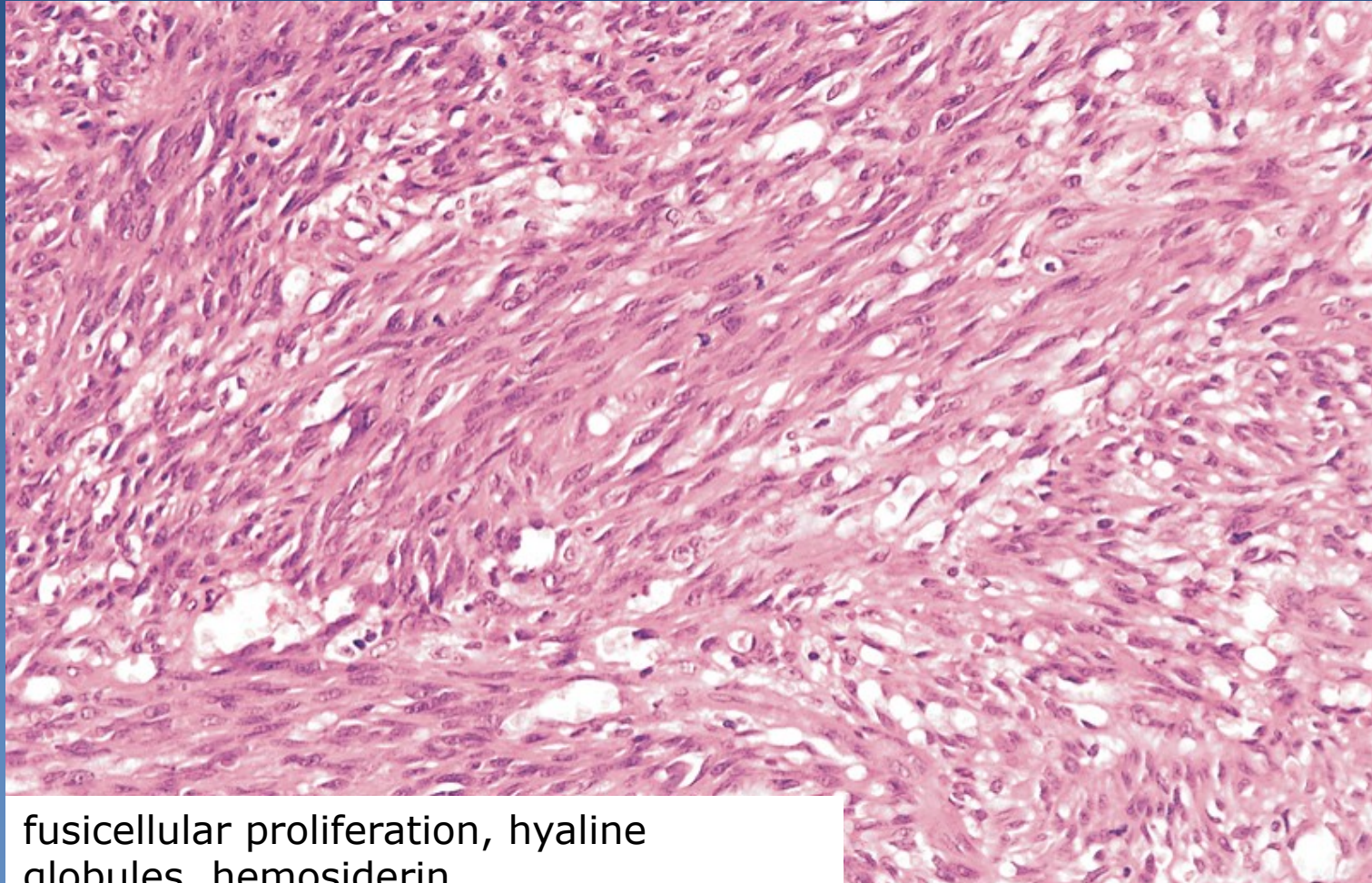
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# *Kaposi sarcoma*





# *Kaposi sarcoma*



fusicellular proliferation, hyaline globules, hemosiderin

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# Heart tumors



- ✗ primary tumors rare, mostly **benign myxomas**
  
- ✗ malignant mesenchymal (sarcomas)
  - ⇒ *leiomyo - , rhabdomyo - , hemangio - , fibrosarcoma*
  
- ✗ secondary tumors
  - ⇒ *20-30 x more common than primary*
  - ⇒ *metastases + infiltrates : lung, breast carcinomas, malignant melanoma, malignant lymphomas and leukemias*
  - ⇒ *direct spread (lung ca, mesothelioma, renal ca)*
  - ⇒ *pericarditis carcinomatosa – hemorrhagic effusion*



# Benign tumors



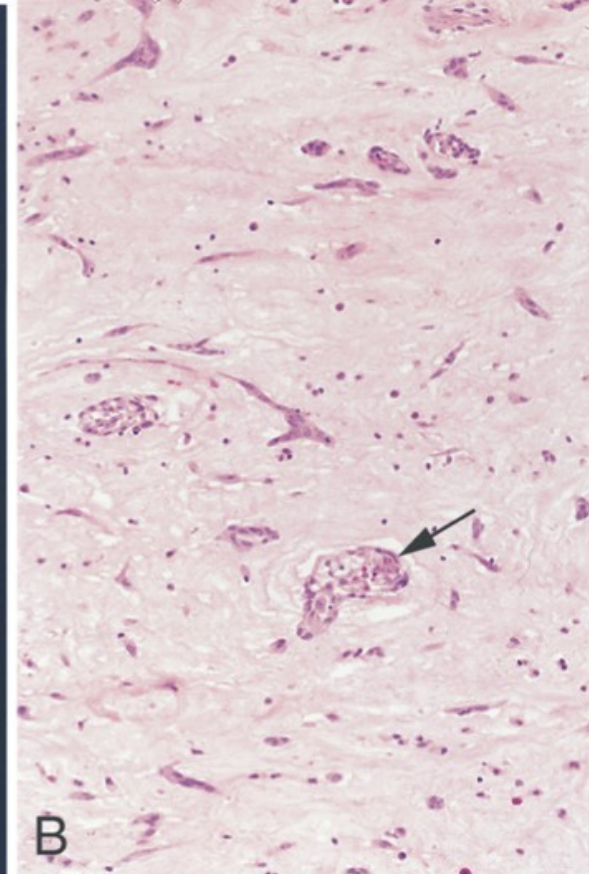
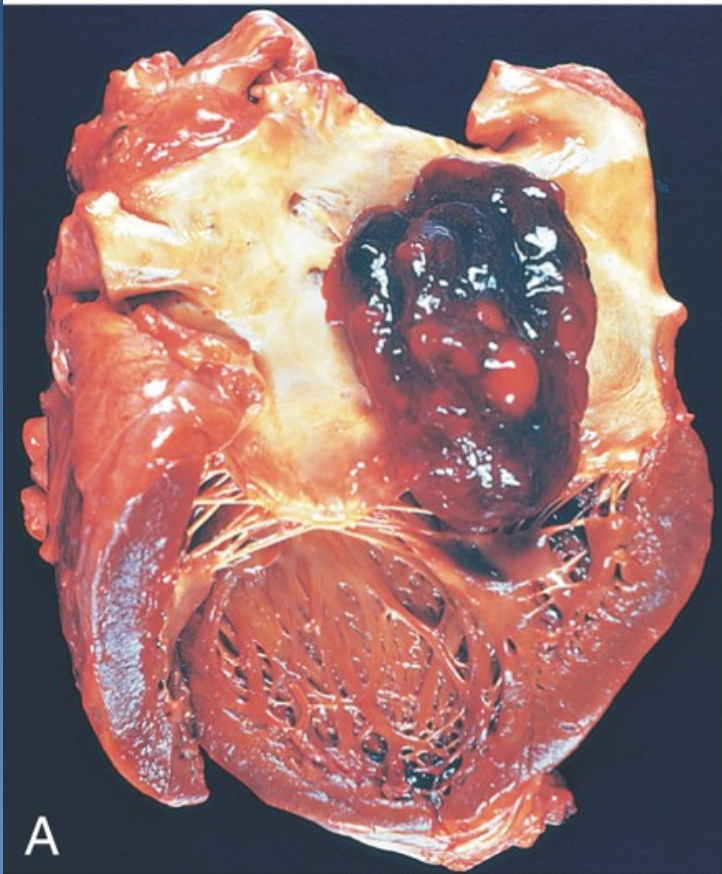
## ✘ Myxoma

- ⇒ *mostly in the left atrium (fossa ovalis on septum)*
- ⇒ *4 – 6 cm, usually single*
- ⇒ *sessile x pedunculated, papillary x villous, soft – gelatinous, regressive changes (haemorrhage, fibrosis)*
- *micro: polygonal (stellate / globular) cells in myxoid matrix (acid mucopolysaccharides)*

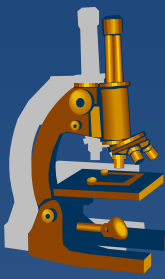
✘ **other: hemangioma, lipoma, rhabdomyoma...**



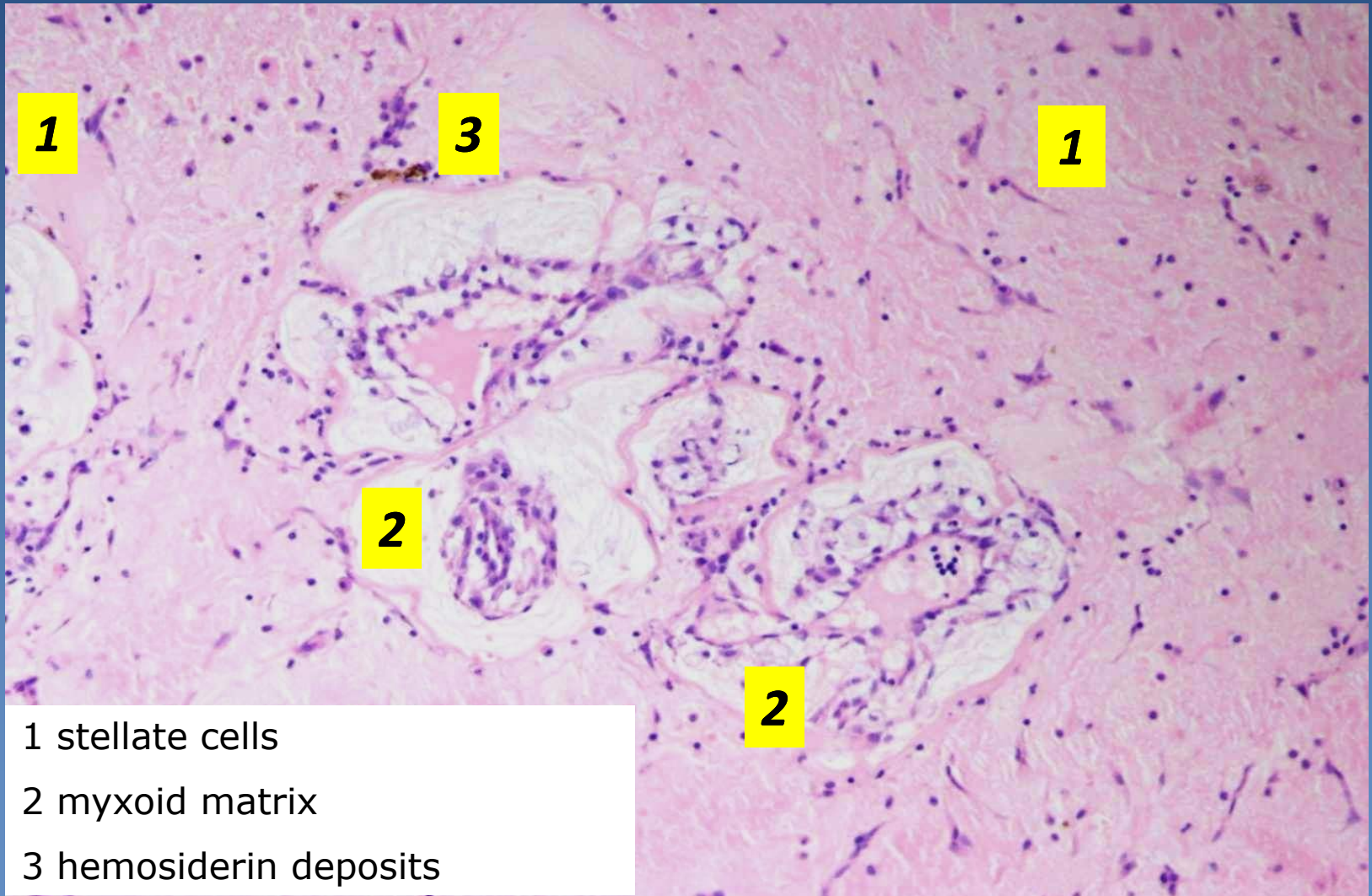
# *LV myxoma*



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# *Myxoma (100x)*

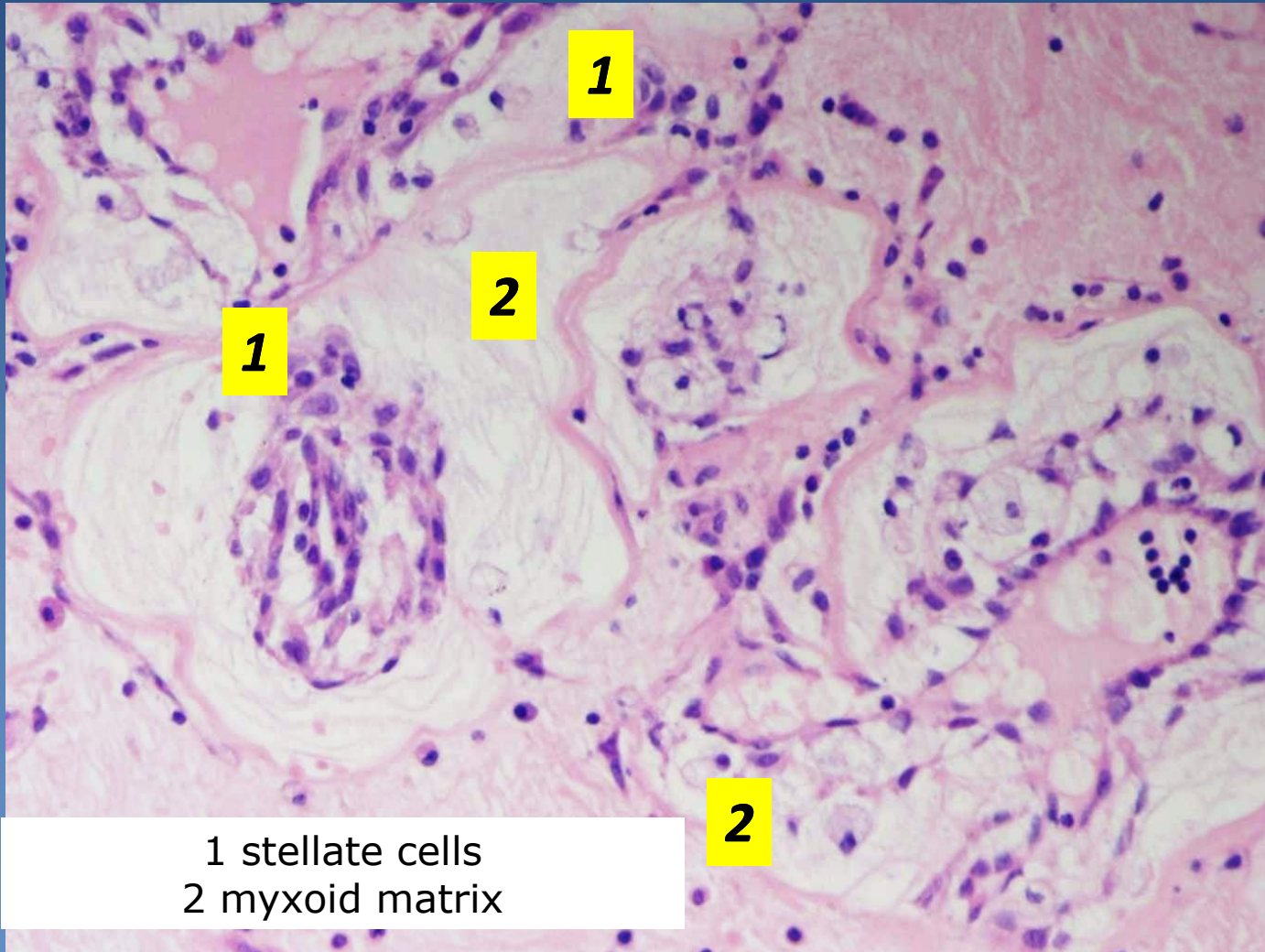


- 1 stellate cells
- 2 myxoid matrix
- 3 hemosiderin deposits

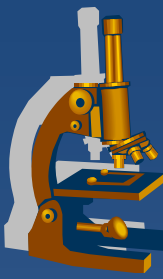




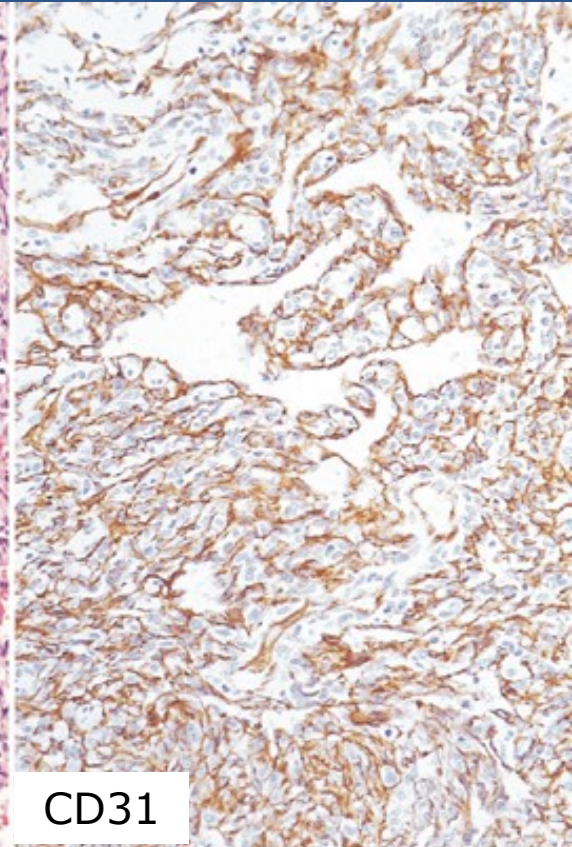
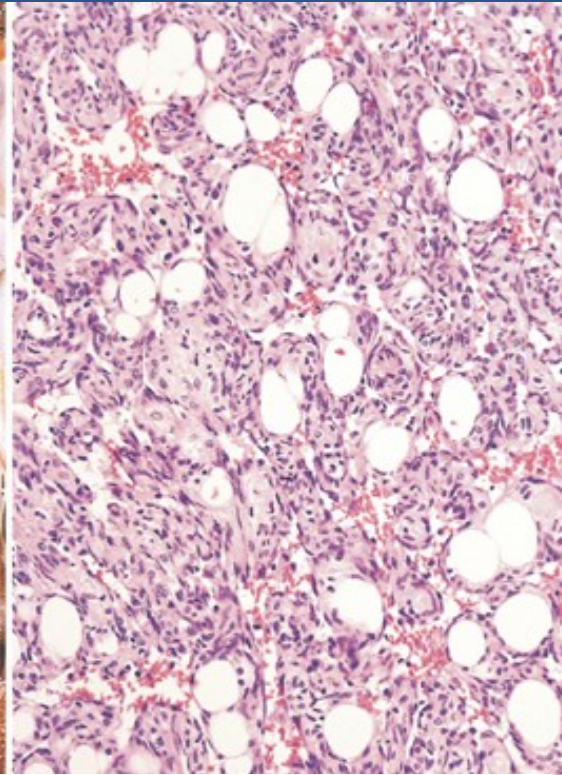
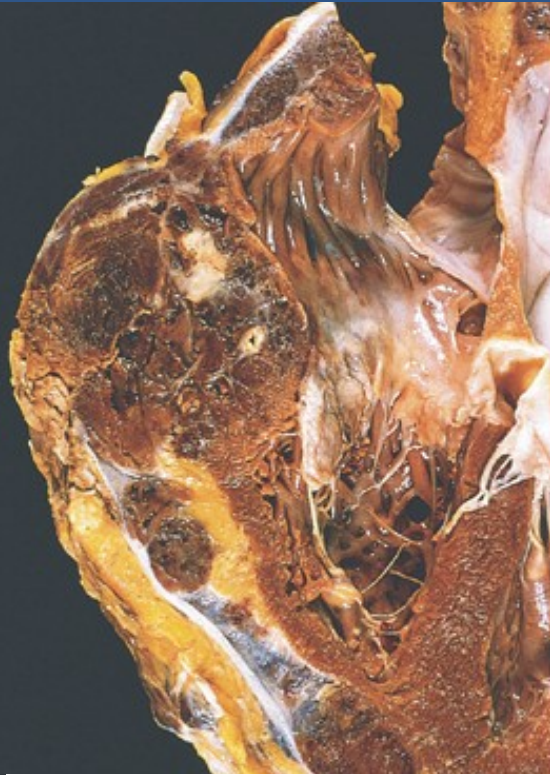
# *Myxoma (400x)*







# Angiosarcoma

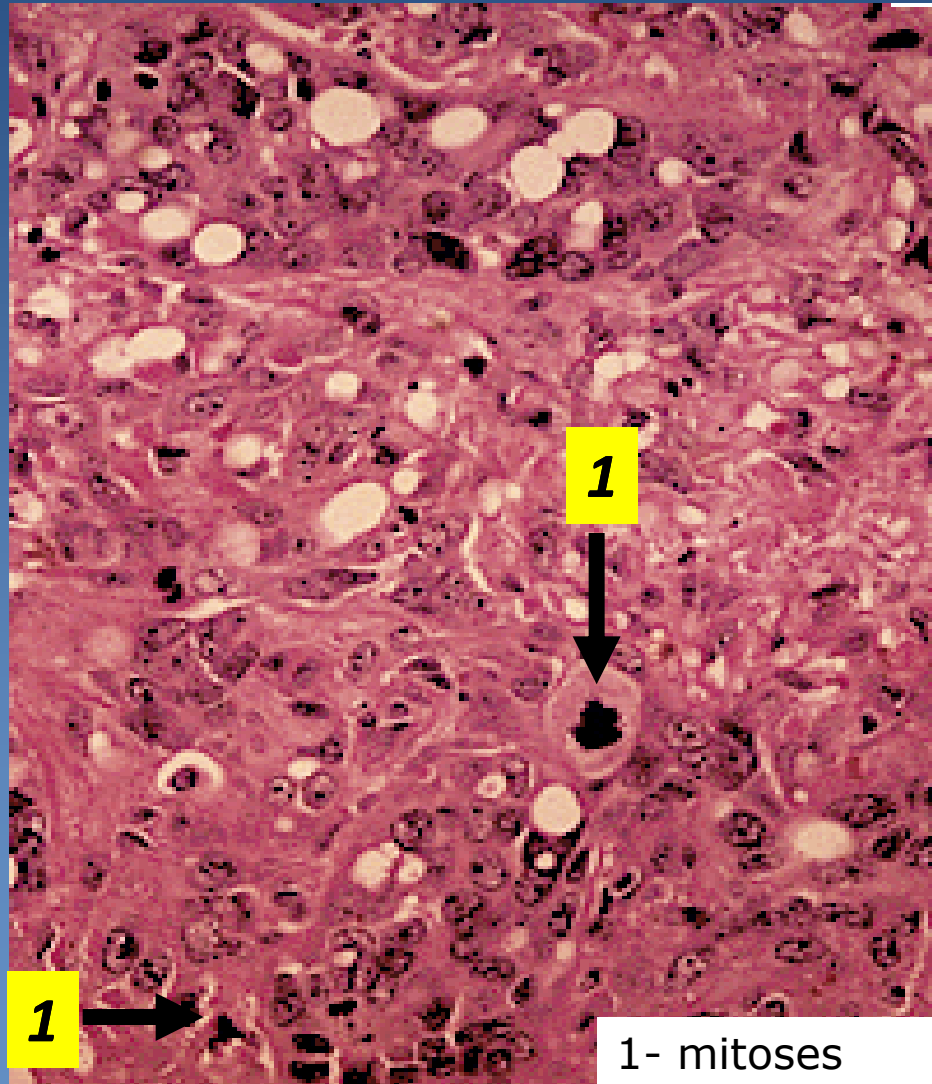


RV angiosarcoma

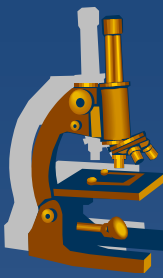
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# Angiosarcoma

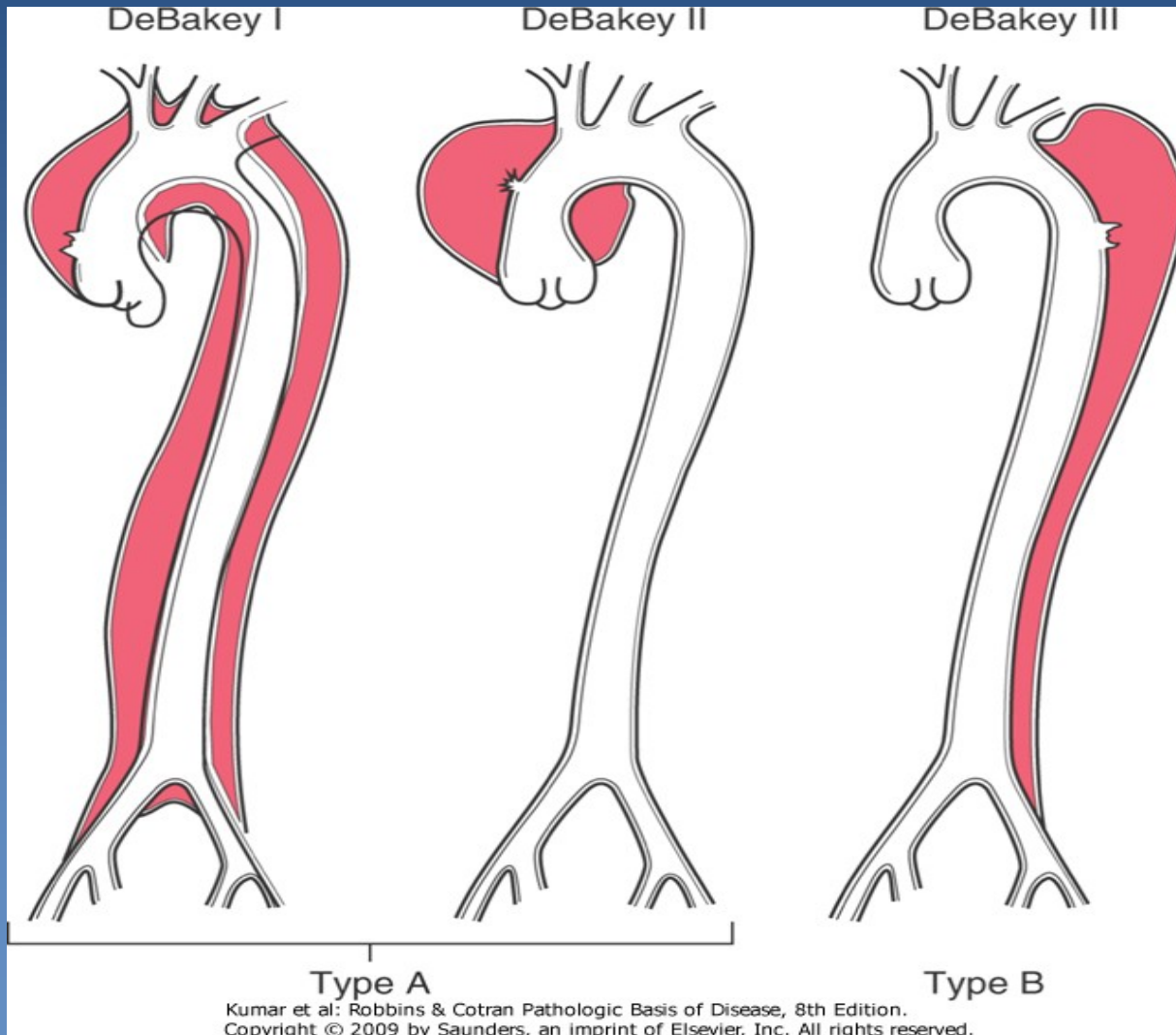
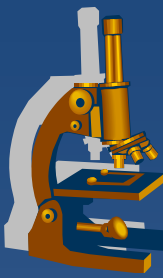


# Aortic dissection



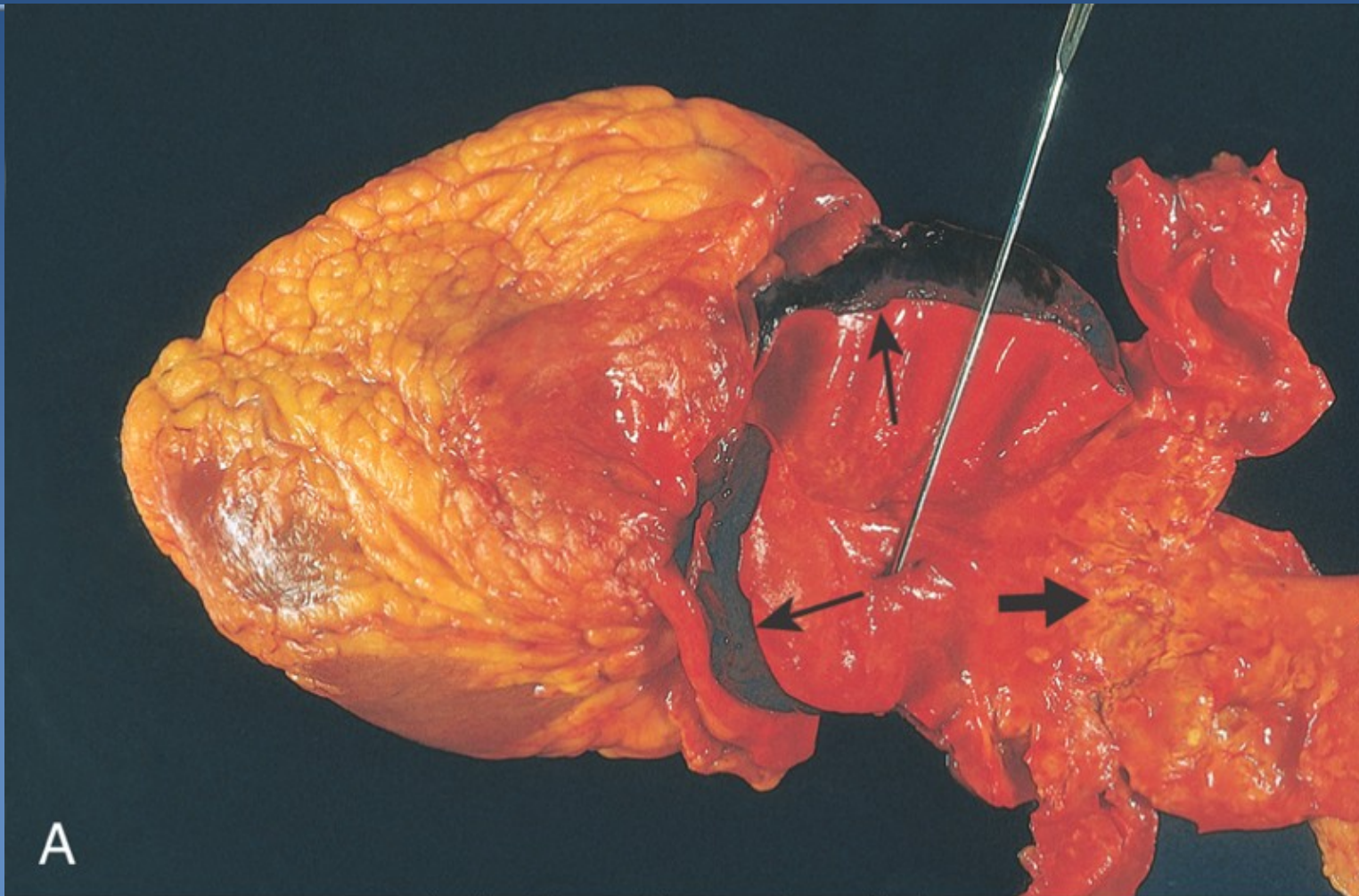
- ✗ tear in aortic intima - intramural bleeding through media, false lumen, possible „double-barreled“ aorta
- ✗ typical in ascending aort, 1–8 cm above aortic valve
- ✗ ante– and retrograde spread to the aortic root
- ✗ common thrombosis in false lumen
- ✗ risk of external rupture (→ **hemoperikardium**), progression at the aortic branches (→ **variable organ's ischemia**), **heart failure**
- ✗ predisposition – hypertension, Marfan sy, cystic medial necrosis, ...

# Aortic dissection





# *Aortic dissection*



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# VASCULITIS

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- × Vessel wall inflammation
- × **Classification** according **cause**: infectious x non-infectious  
(commonly immune-mediated, ANCA+/ANCA-)
- × **Type (size)** of vessel involved: Large-vessel  
Medium-vessel  
Small-vessel

# Vasculitis



× **ANCA<sup>+</sup> vasculitis** (dangerous, even fatal within a few years, if not recognised)

- ⇒ *Wegener granulomatosis*
- ⇒ *Churg-Strauss syndrome*
- ⇒ *microscopic polyangiitis*

× **ANCA<sup>-</sup> vaskulitis:**

- ⇒ *polyarteritis nodosa*
- ⇒ *Kawasaki disease*
- ⇒ *giant-cell arteritis (Horton, temporal)*
- ⇒ *Takayasu arteritis*
- ⇒ *thrombangiitis obliterans (Bürger disease)*
- ⇒ *leukocytoclastic (alergic) vasculitis – cca 30%*

# ***Possible clinical signs of systemic vasculitis***



**ORL:** - repeated respiratory tract inflammation

- exudate rich in plasma cells + eosinophils

**Kidney:** - glomerulonephritis

**Lung:** - variable presentation of lung diseases + hemoptysis

**Skin:** - ulceration, necrosis, petechiae-purpura

**GIT:** - ischemic ulcerations (sharply demarcated, without HP, minimal inflammation)

**Chronic debilitating disease – clinical signs of tumor!!**



# ***Patient presentation***

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- fever, nausea, myalgia, arthralgia
  - skin purpura
- signs of nephritis
- abdominal pain



general malaise (~ severe influenza, long duration, resistant to usual therapy)  
sinusoid course (relapse --- remission --- relapse--)

# ***Etiology***

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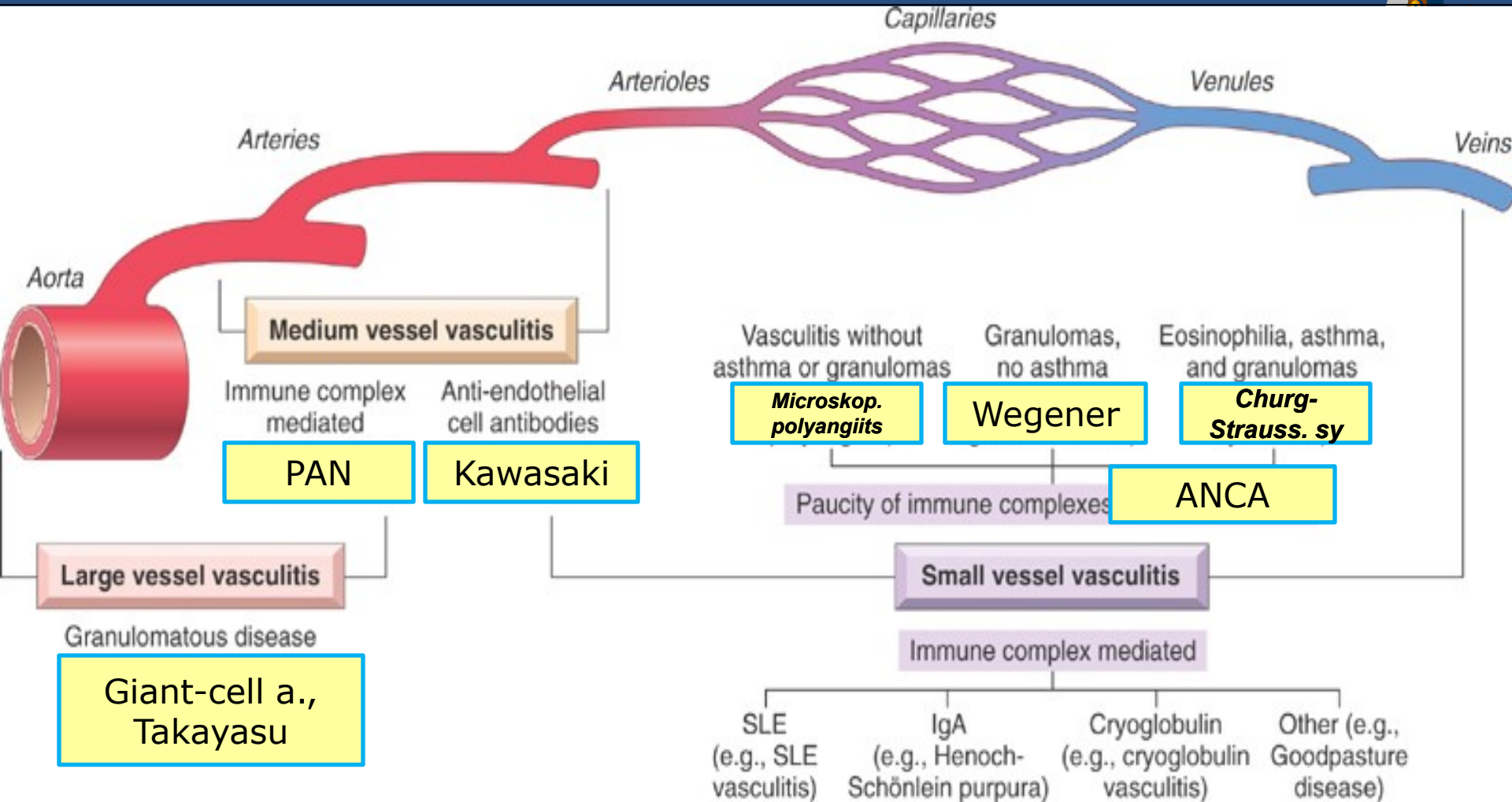
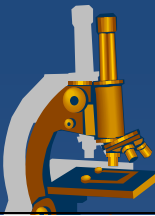


**× autoimmune process**

**× infection**

⇒ *ie. streptococcus, ...*

⇒ *direct cause of infective v., or trigger factor of pathological immune processes*



# ANCA+ vasculitis



## × incidence ?????

⇒  $\leq 20/1\text{mil. inhabitants}$

⇒ **age 65+ - 53/1mil. inhabitants**

## × prognosis:

⇒ *untreated ANCA<sup>+</sup> vasculitis  $\geq 80\%$  fatal in 2 yrs*

⇒ *treated ANCA<sup>+</sup> vasculitis :  $\geq 80\%$  survives 5 yrs*

⇒ *renal failure in elders  $>70$  yrs - in 40% due to ANCA<sup>+</sup> vasculitis*

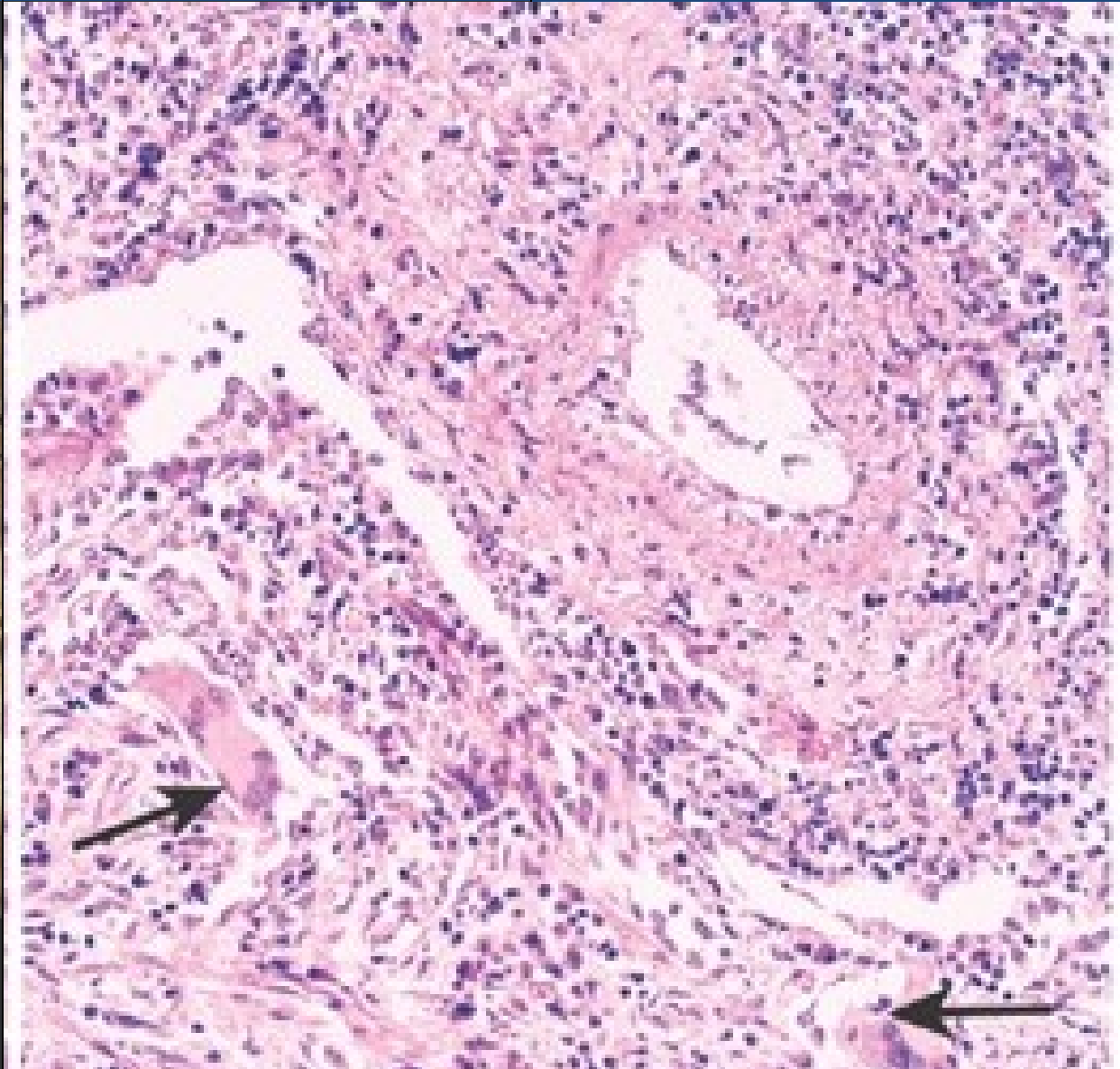


# *Wegener granulomatosis*

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- ✗ Persistent pneumonitis (95%) – nodular infiltrates
- ✗ Chronic sinusitis (90%) – ulcerations, event. destructive
- ✗ Renal disease (80%) – glomerulonephritis
- ✗ Other features: rashes, muscle pains, articular involvement, mono-/polyneuritis



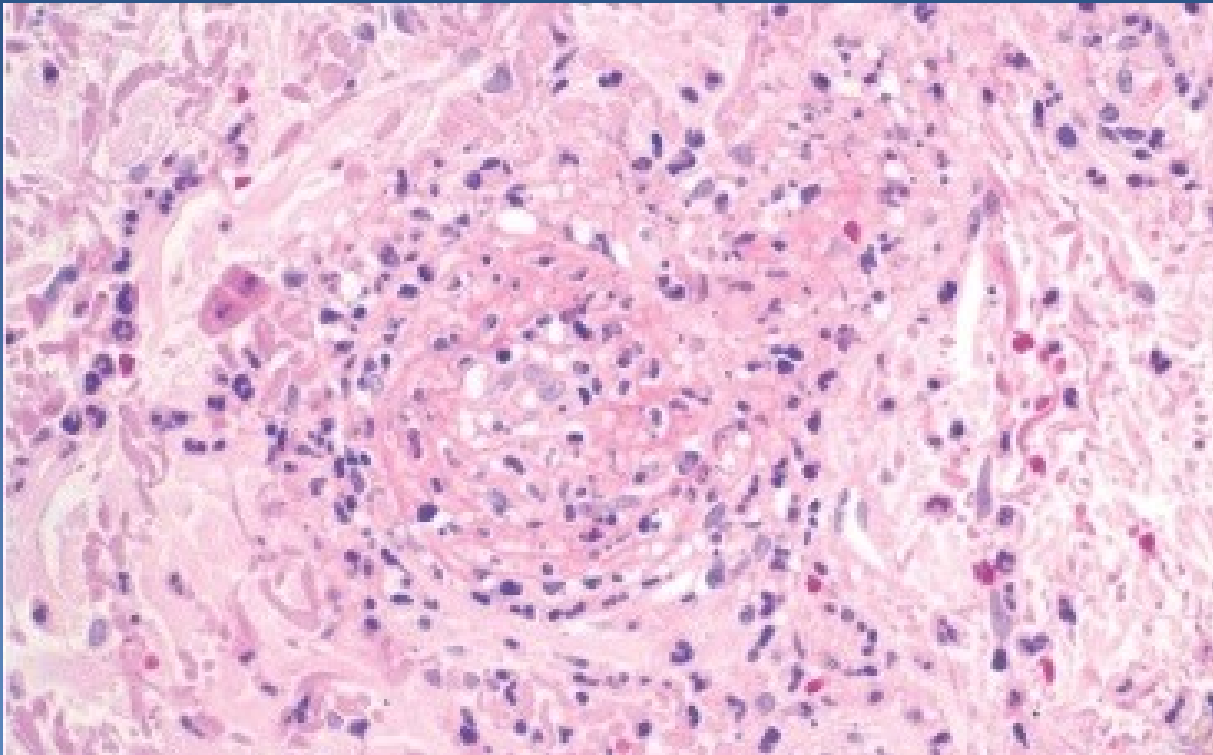
Small vessel vasculitis with giant-cell granulomatous reaction

# ANCA+ VASCULITIS: *microscopic polyangiitis*



- ✗ **ANCA** in approx. **70%** (remaining by immunecomplexes or antibodies)
- ✗ = **necrotizing vasculitis** arterioles, capillaries, venules (synonyms: leukocytoclastic v., hypersensitive v., allergic v.)
- ✗ : **SKIN**, kidney, lung, GIT, brain...
- ✗ highly variable etiopathogenesis (part of systemic connective tissue diseases; allergic response to exogenous antigens – bacteria, viruses, drugs)
- ✗ micro:
  - ⇒ *fibrinoid necrosis of vessel wall with neutrophils and chromatin fragments from neutrophil's nuclei - leukocytoclastic*
  - ⇒ *all lesions in the same stage of evolution* (X *polyarteritis nodosa*)

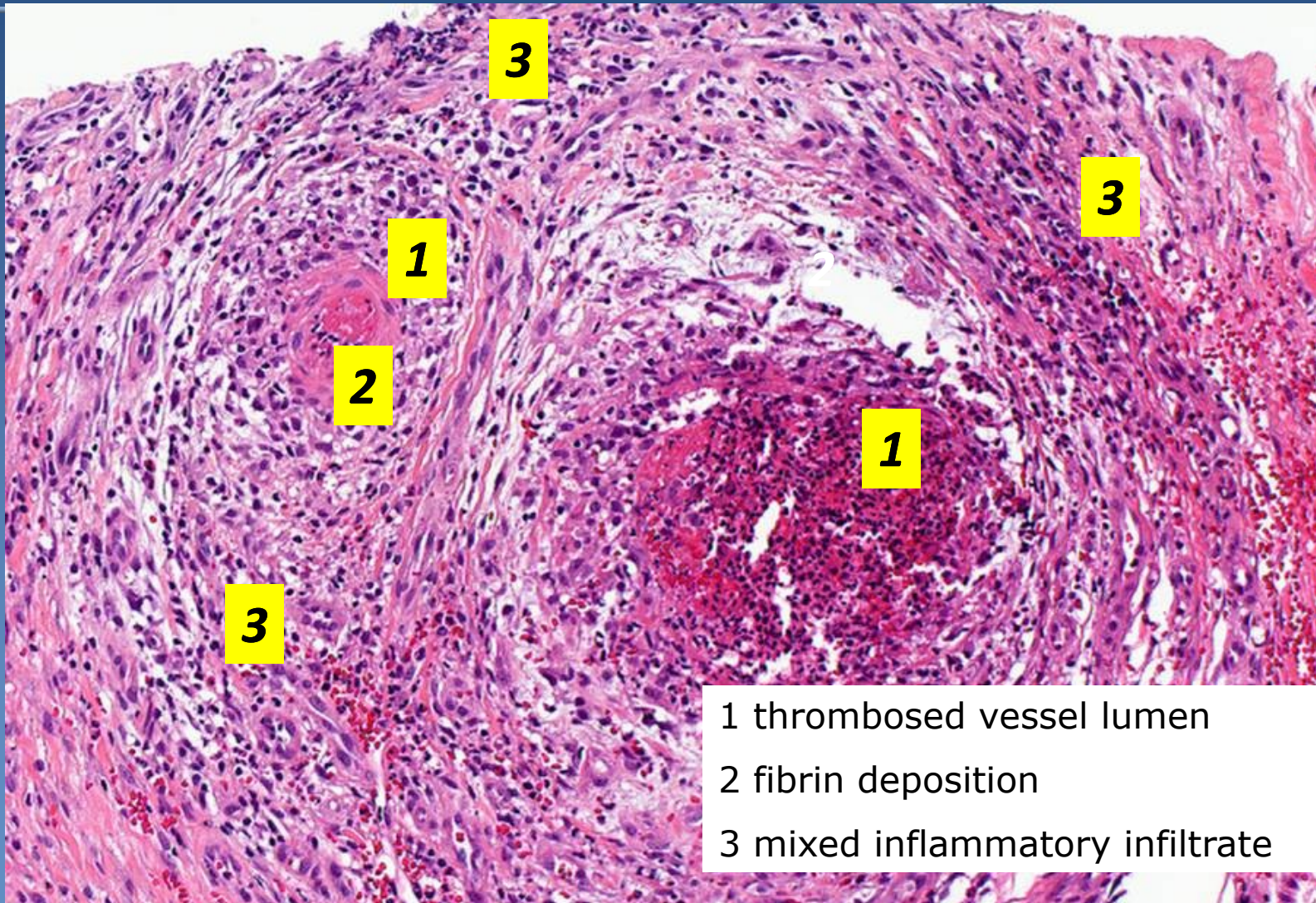
# *leukocytoclastic vasculitis*



nuclear fragments from neutrophils in a small vessel wall



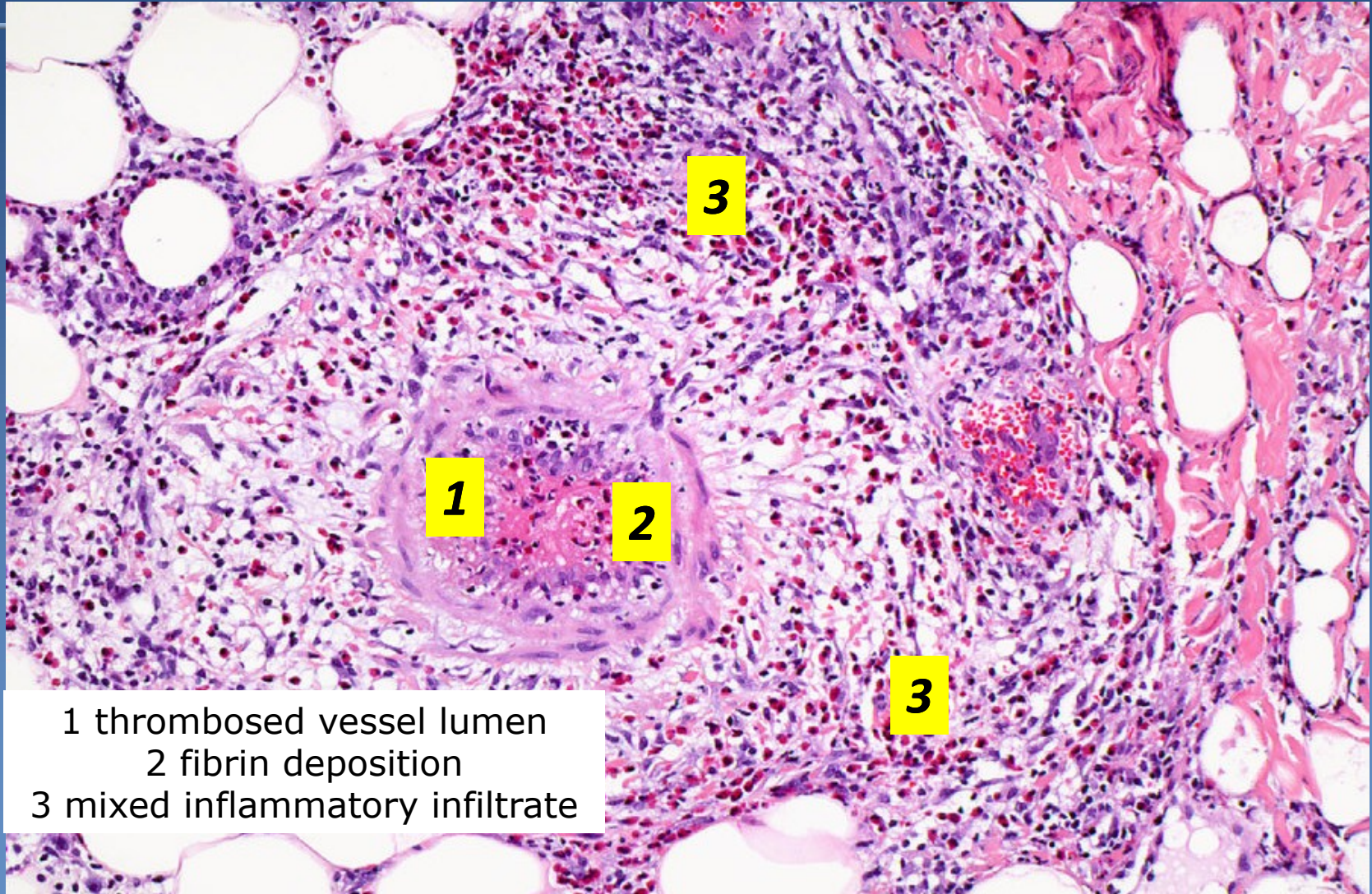
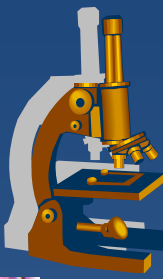
# *polyarteritis nodosa*



- 1 thrombosed vessel lumen
- 2 fibrin deposition
- 3 mixed inflammatory infiltrate



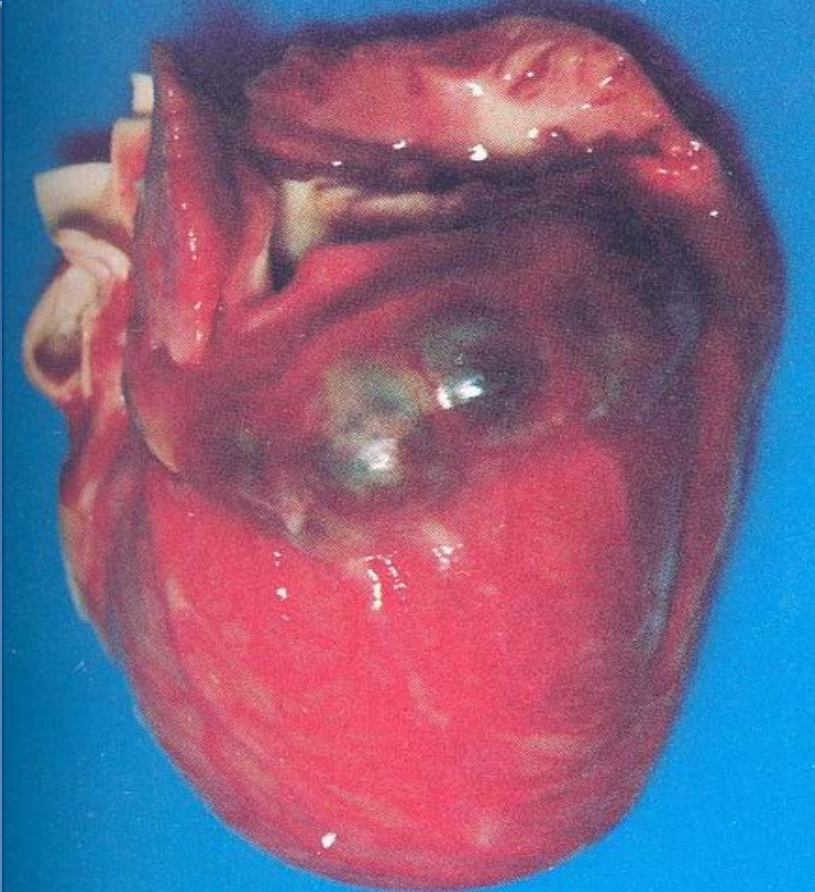
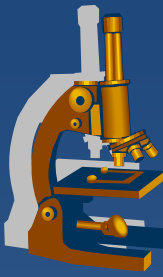
# *polyarteritis nodosa*



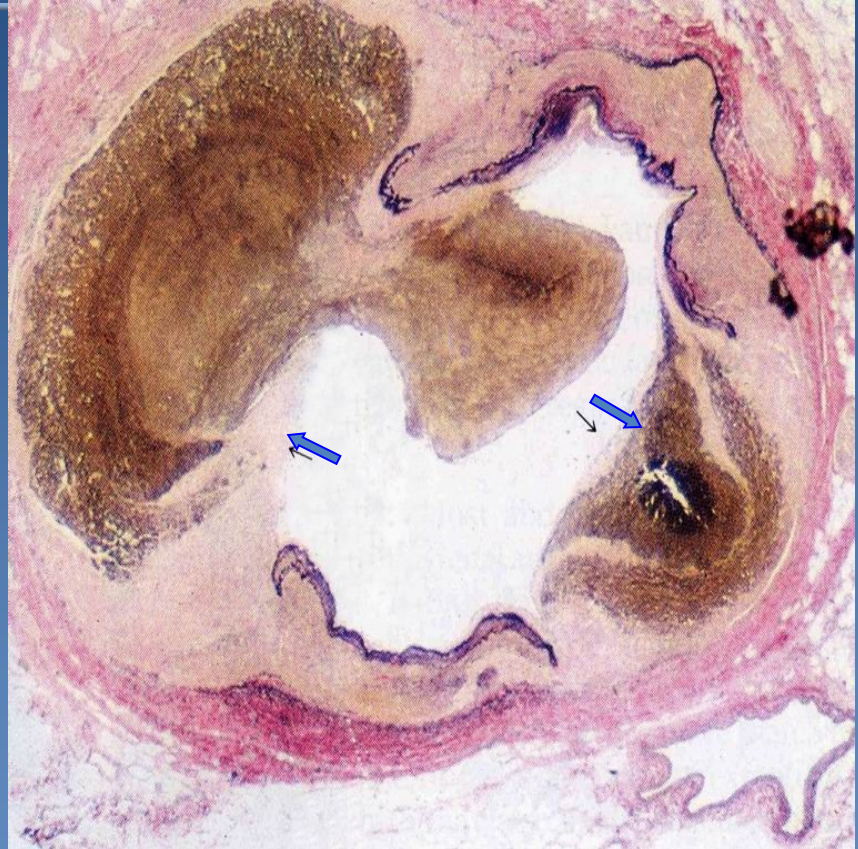
1 thrombosed vessel lumen  
2 fibrin deposition  
3 mixed inflammatory infiltrate



# *Kawasaki disease*



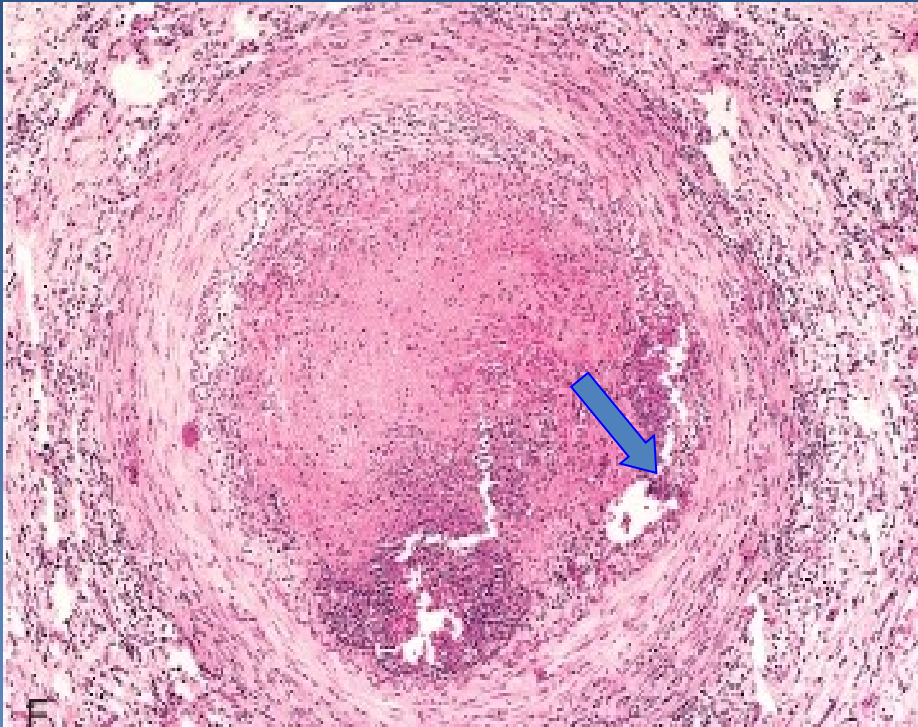
Coronary aneurysms in a child' heart



coronary artery with lamina elastica interna defects (arrows) and thrombotized aneurysms



# *Thrombangiitis obliterans* (*Bürger disease*)



Obliterative thrombosis with granuloma with central microabscess (arrow)



acral necroses



# *Infectious vasculitis*



- × Direct invasion of vascular wall by inf. pathogen
- × Primary angioinvasive microorganism
  - Fungi: Aspergillus, Mucor - thrombosis → ischemic necrosis
- × Localized vasculitis in focal infection
  - purulent – meningitis, pneumonia, abscess, fasciitis – pyogenic bacteria – secondary vasculitis
  - granulomatous, obliterative endarteritis – TB, tertiary syphilis, lepra
  - lymphocytic vasculitis – rickettsia (spotted fever, Q fever etc.), recurrent herpes, CMV
  - necrotizing vasculitis – anthrax

# *Infectious vasculitis*

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- ✘ **Septicemia** in systemic infection
  - possible thrombosis, mycotic aneurysm, infected infarction



