Cardiovascular pathology: blood vessels
(degenerative changes, vasculitis)

Markéta Hermanová

- **Normal arterial structure:**

- **Intima** (endothelium+connective tissue)
- **Media** (elastic tissue; in medium sized arteries – smooth muscles)
- **Adventitia** (fibrous connective tissue)

- **Age related vascular changes:**

- Progressive fibrous thickening of the intima
- Fibrosis ans scarring of the muscular or elastic media
- Accumulation of mucopolysaccharide-rich ground substance
- Fragmentation of the elastic laminae

- **Arteriosclerosis:** „hardening of the arteries“, arterial wall thickening and loss of elasticity

- **Arteriolosclerosis** (hyaline and hyperplastic; related to hypertension)

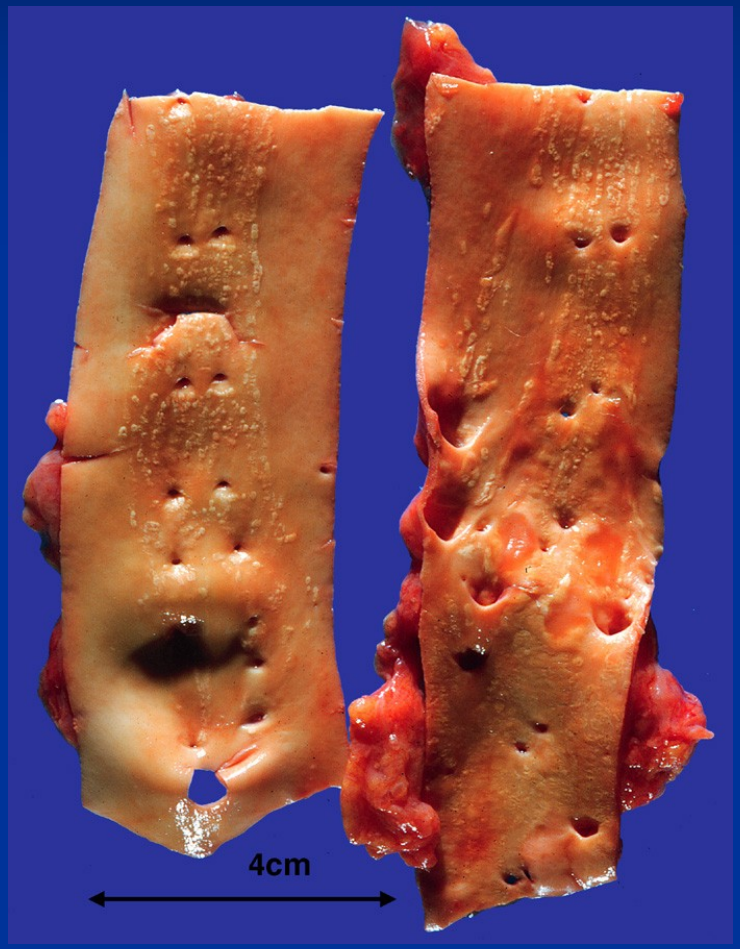
- **Monckenberg medial sclerosis-mediocalcinosis** (calcified deposits in muscular arteries in extremitites, older people)

- **Atherosclerosis**

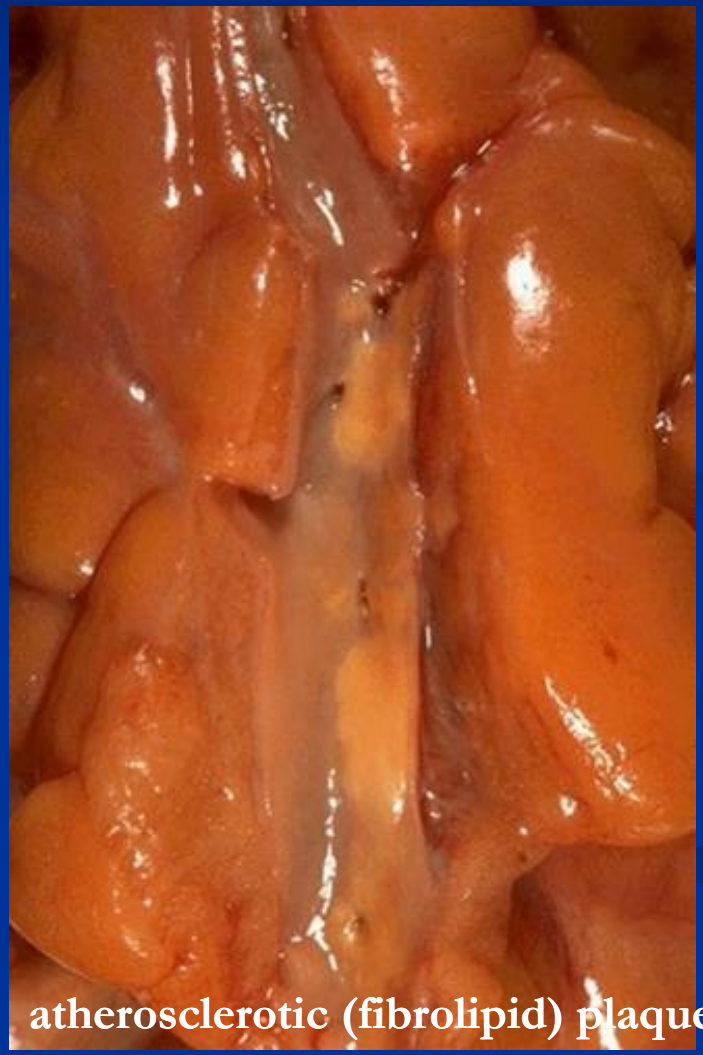
Atherosclerosis

- Large and medium-sized arteris
- Elevated lesions: **fatty streaks, atherosclerotic (fibrous+atheromatous) plaques and complicated lesions** (ulceration, thrombosis, calcification and bleeding)
- Major cause of organ ischaemia (e. g. Myocardial infarction)
- Risk factors: age, male gender, genetics, hypertension, smoking and diabetes, some infections (CMV, chlamydia pn., influenza,…), metabolic syndrome.
- ↑LDL, cholesterol, fibrinogen and fVII; ↓HDL

Atherosclerosis

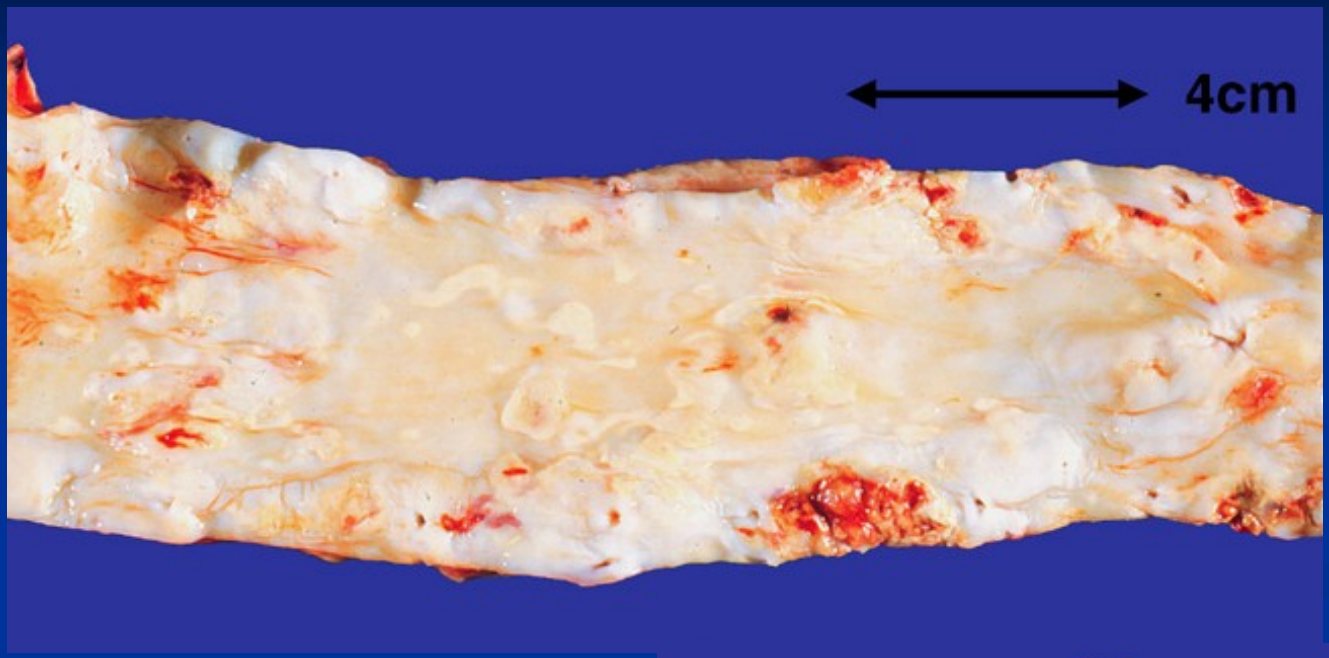


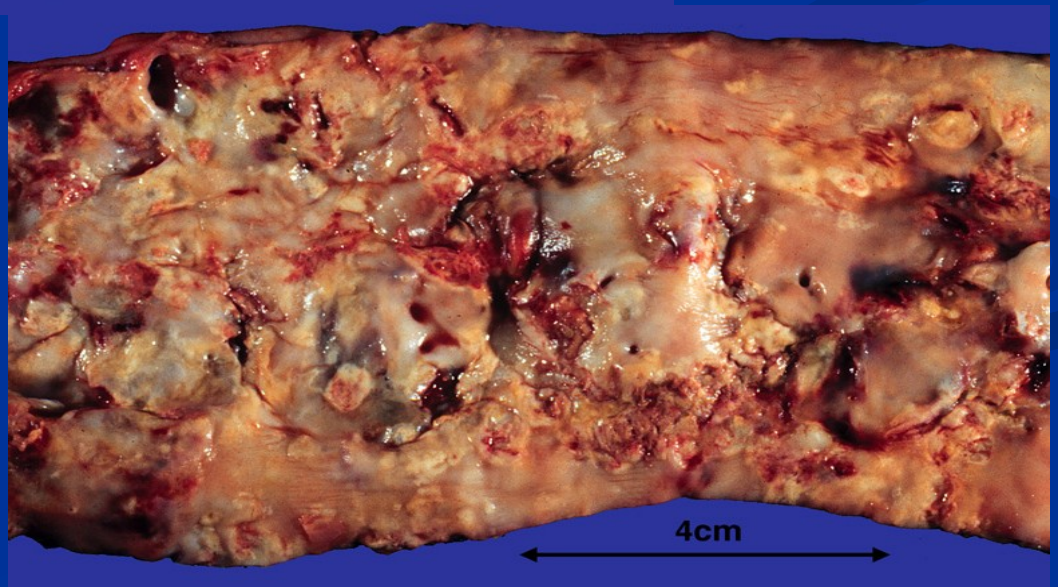
fatty streaks

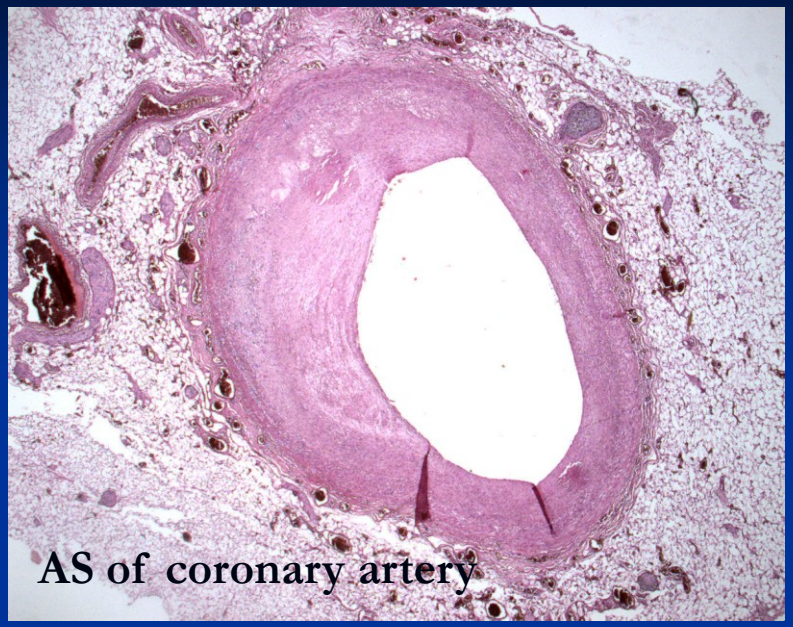


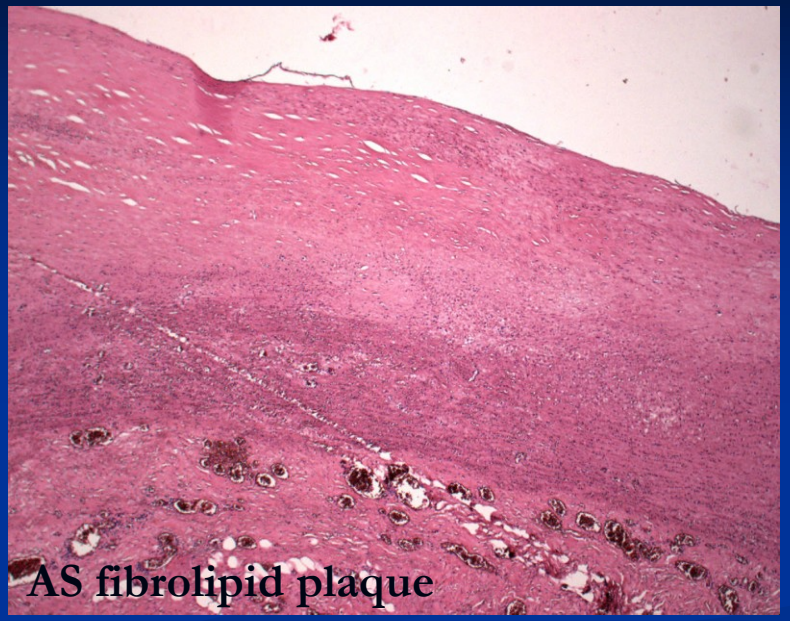
atherosclerotic (fibrolipid) plaques

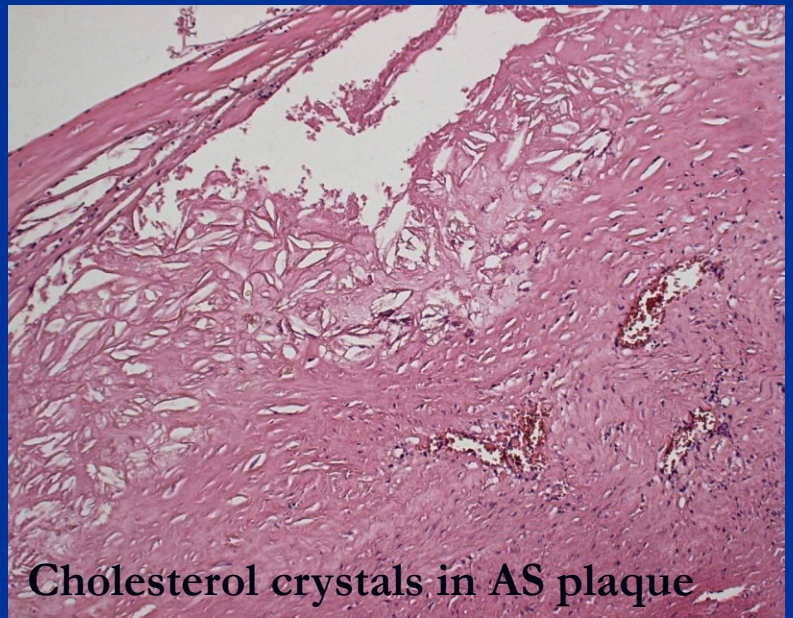
AS – complicated lesions

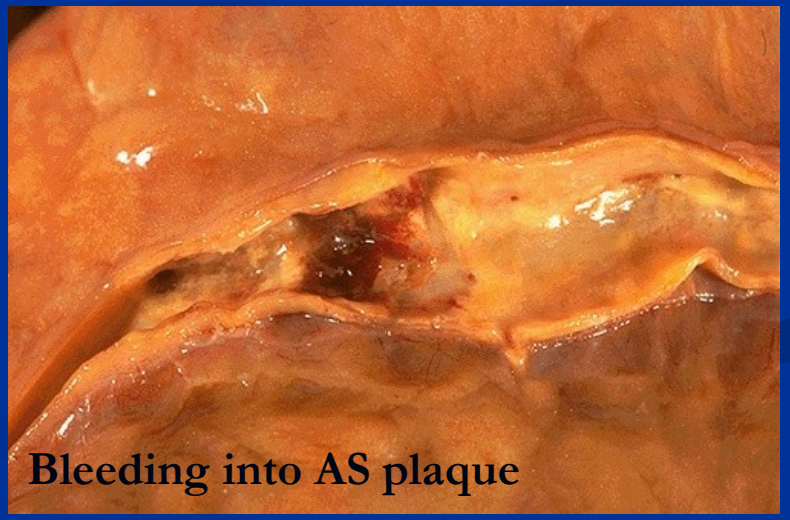





AS of coronary artery


AS fibrolipid plaque

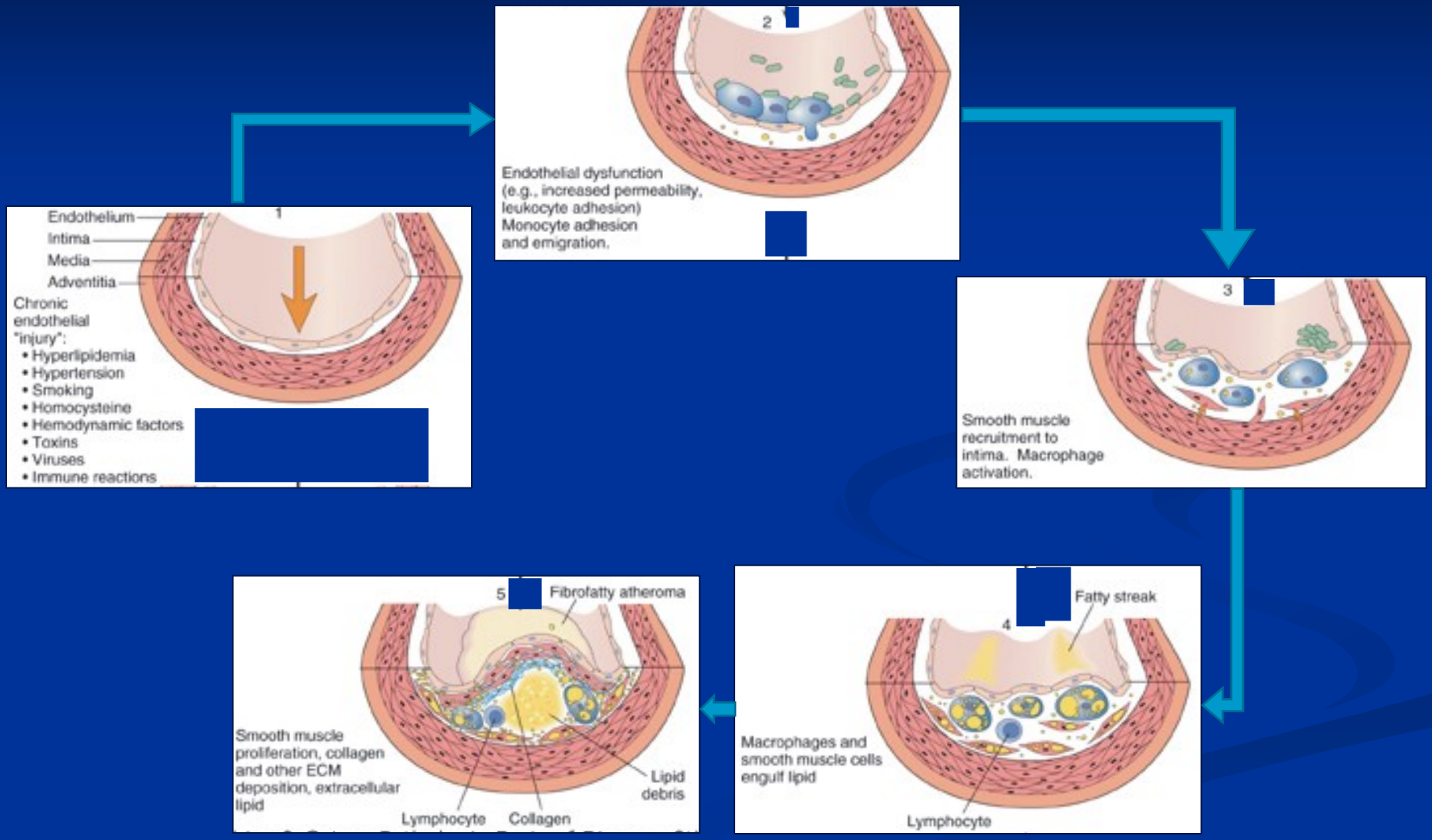

Cholesterol crystals in AS plaque


Bleeding into AS plaque

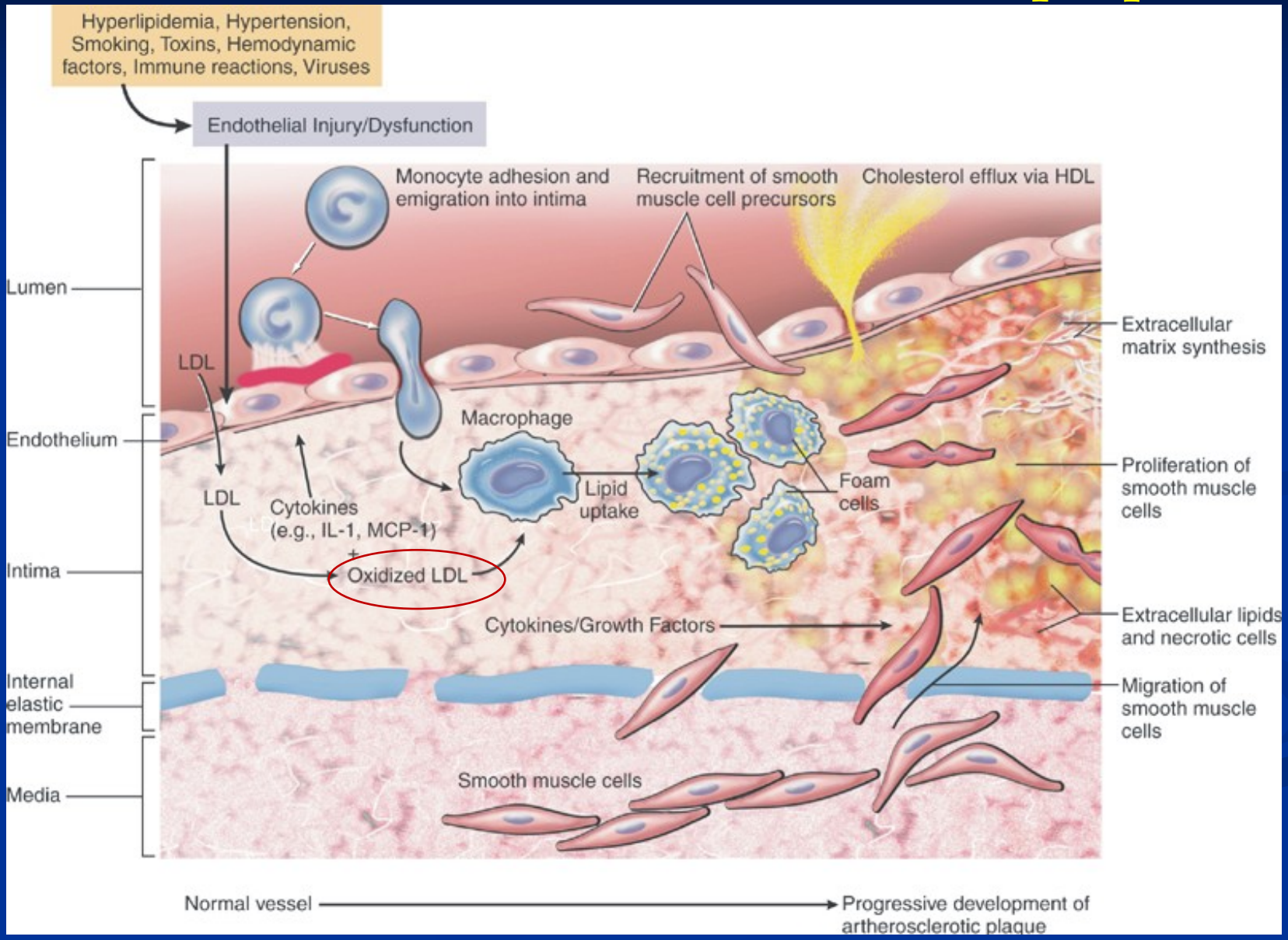
Pathogenesis of arteriosclerosis

- **Endothelial injury**
  - mechanical denudation, hemodynamic forces, immune complex deposition, irradiation, chemicals,…
  - Endothelial dysfunction: increased permeability, enhanced leukocyte adhesion, altered gene expression (expression of cell adhesion molecules, increased thrombogenisity)
- **Accumulation of lipoproteins**
- **Cellular reaction in the focus of injury**
  - monocyte adhesion to endothelium, migration into intima and transformation into macrophages and foamy cells
  - Platelet adhesion
  - Migration of smooth muscle cells from media into intima or smooth muscles recruitment from circulating precursors
  - Smooth muscle proliferation and production of proteins of ECM (collagen, elastin, proteoglycans)
  - Lipid accumulation (both extra- and intracellularly (in macrophages and smooth muscles)

Atherosclerosis - pathogenesis



Atherosclerosis – cell interactions in an atheromatous plaque



Morphology of atherosclerosis

- **Fatty streaks**

- **Atherosclerotic plaque (fibrous and atheromatous)**
  - cells (smooth muscle cells, inflammatory cells and macrophages,…)
  - ECM (collagen, elastic fibers, proteoglycans)
  - lipids (intra- and extracellular)

- **Complications**
  - Rupture, ulceration or erosion, thrombosis
  - Hemorrhage into a plaque
  - Atheroembolism
  - Aneurysm formation

Consequences of atherosclerosis

- Progressive lumen narrowing; occlusion of smaller arteries
- Acute atherothrombotic occlusion
- Embolisation of atheroscleroic debris causing distal vessel occlusion
- Rupture of abdominal atherosclerotic aneurysm
- Vasoconstriction

Clinical consequences

- Cerebral infarction
- Myocardial infarction
- Peripheral vascular disease with intermitent claudication
- Gangrene
- Aortic atherosclerotic aneurysm
- Carotid atheroma embolisation

Hypertension: increased systemic and local tissue blood pressure

- **Essential (primary)**
- **Secondary hypertension**

- **Borderline hypertension:** 140/90-160/95mmHg
- **Mild hypertension:** diastolic pressure 95-104mmHg
- **Moderate hypertension:** diastolic pressure 105-114mmHg
- **Severe hypertension:** above 115 mmHg

- **Benign** (gradual organ damage)
- **Malignant** (severe renal, retinal and cerebral damage)

- **Primary (essential) hypertension** (etiology unknown, multifactorial)
  - Genetic susceptibility
  - Excessive sympathetic nervous system activity
  - High salt intake
  - Abnormalities in renin-angiotensin-aldosteron system
- **Secondary hypertension**
  - Renal diseases
  - Endocrine causes (adrenocortical hyperfunctions, pregnancy induced, thyreopathies, acromegaly,…)
  - Coarctation of aorta, PAN, increased intravascular volume, increased cardiac output, rigidity of aorta
  - Drugs (e. g. Contraceptives, corticosteroids,…)
  - Hormones producing tumors: renin producing tumors, pheochromocytoma,……
  - Psychogenic causes, acute stress, increased intracranial volume,…

Pathological classification

- **Benign hypertension**
- Left ventricular hypertrophy – congestive heart failure – ventricular dilatation
- Acceleration of atherosclerosis
- Intimal proliferation and hyalinisation of the muscularis media in medium sized renal arteries and arterioles – benign nephrosclerosis

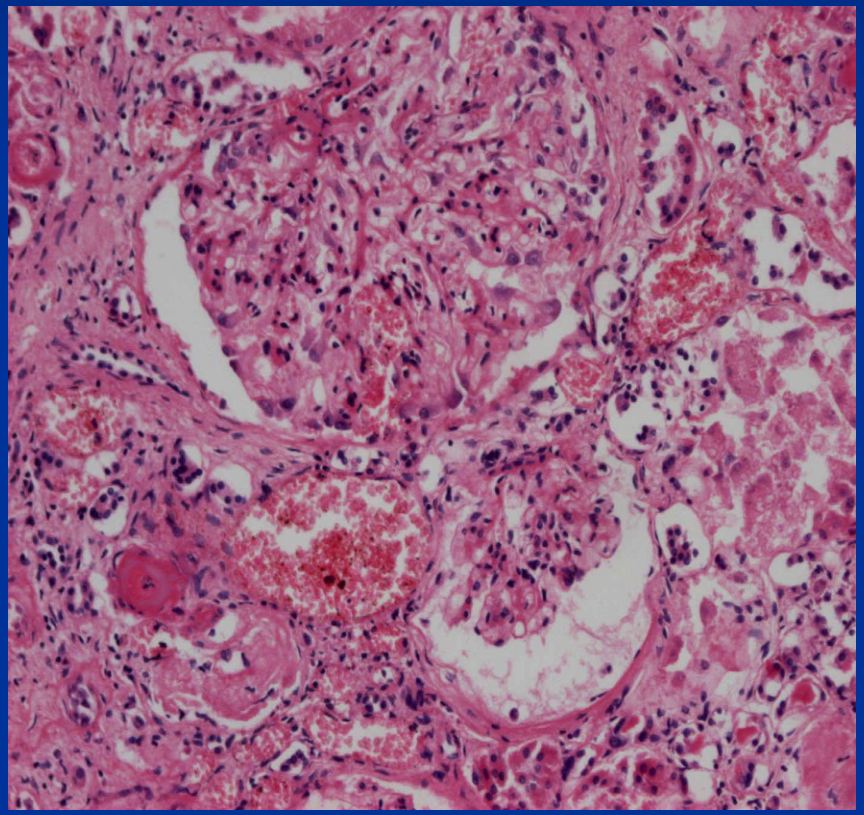
- **Malignant hypertension**
- Diastolic blood pressure usually above 130mmHg
- Progressive renal disease – renal failure (necrotising arteriolitis-fibrionoid necrosis of arterioles); accelerated hypertension
- Cardiac failure
- Papilloedemea and retinal haemorrhages
- Severe headache and cerebral haemorrhage

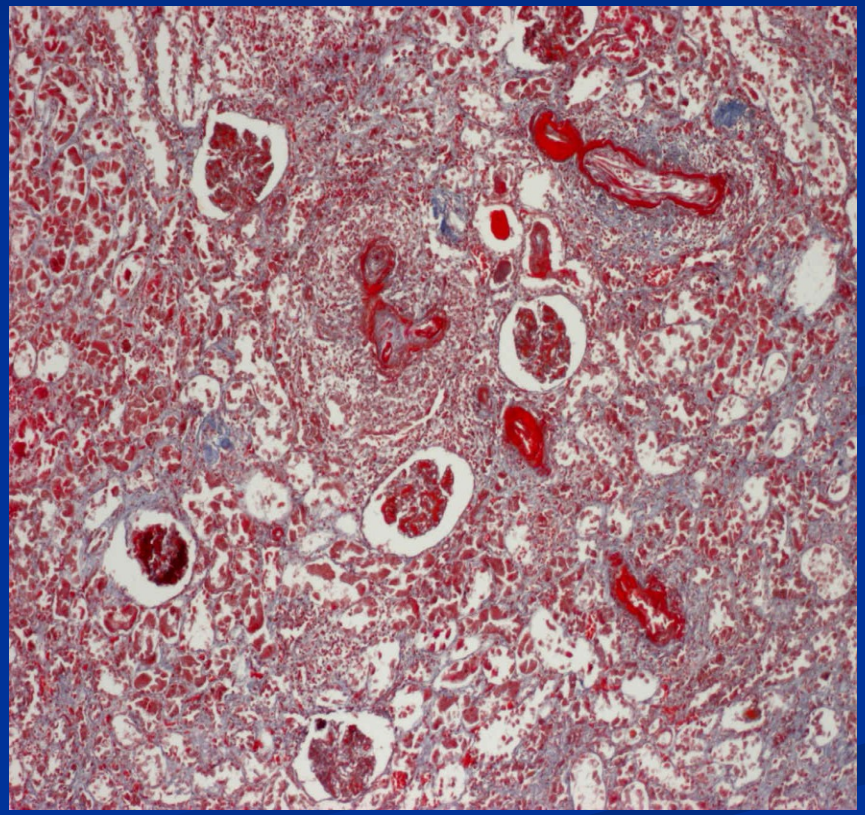
+ pulmonary hypertension

Diabetic vascular disease

- Premature atherosclerosis
- **Microangiopathies: damage of kidneys, nerves and retina** (abnormal glycosylation of proteins within the vessel wall; thickening but with increased permeability; micro-albuminuria; micro-aneurysms; capillary thrombosis (retina); damage of vessels supplying nerves)
  - Diabetic retinopathy
  - Diabetic glomerulosclerosis
  - Peripheral neuropathy
- Comlications: gangrene, renal failure, blindness

Malignant nephrosclerosis – fibrinoid necrosis of arterioles – necrotising arteriolitis

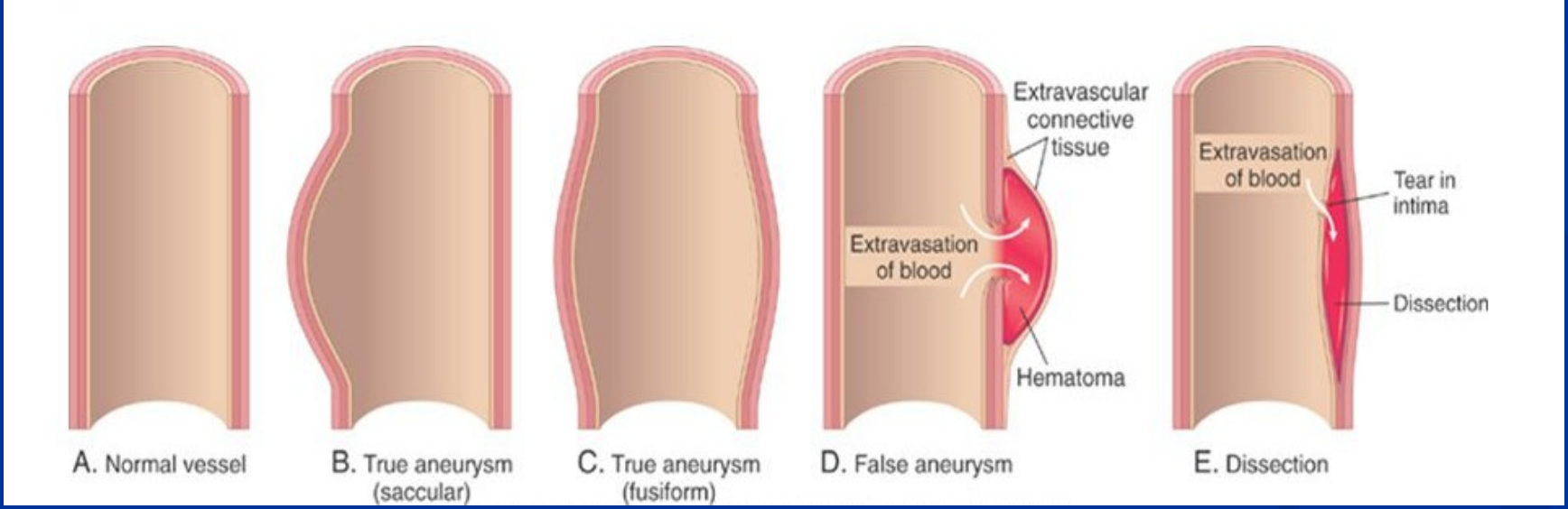


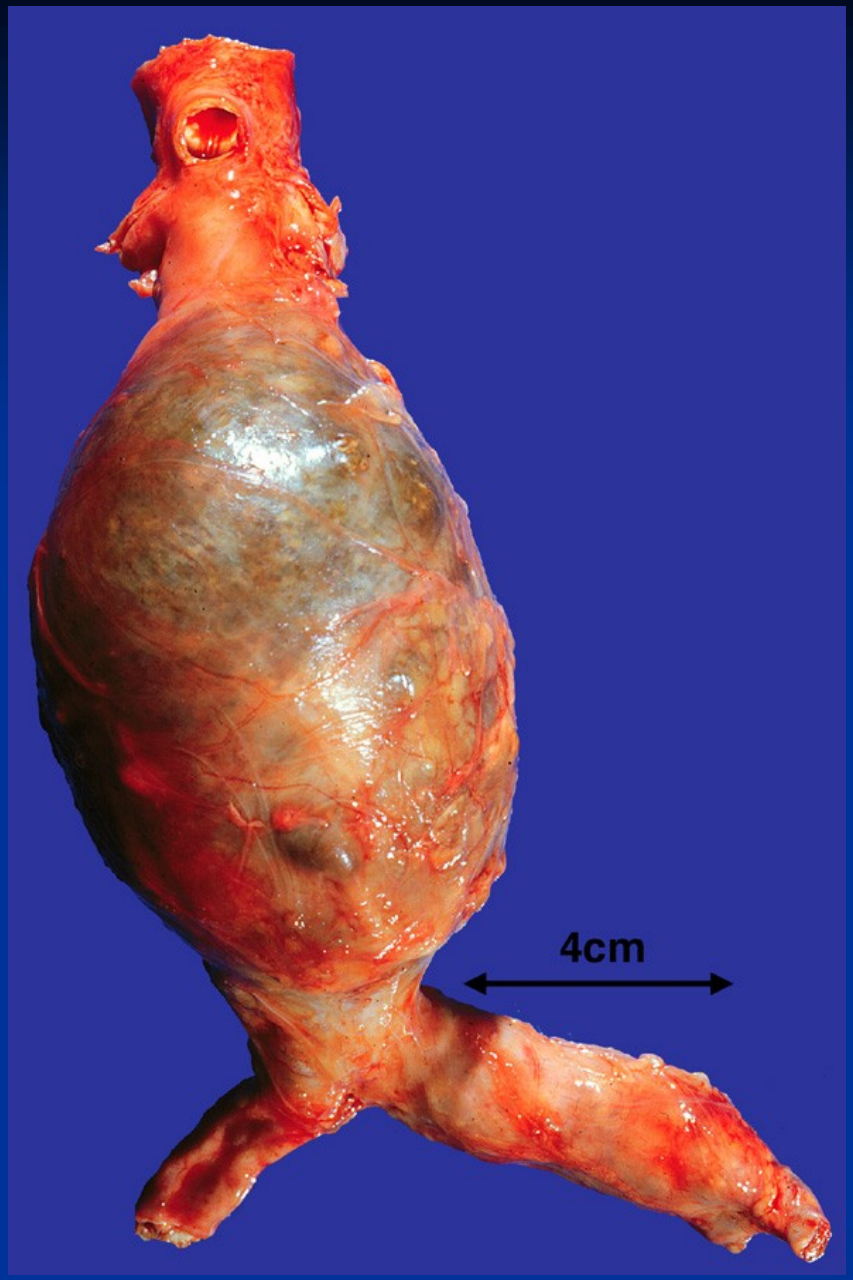


Aneurysms: localised, permanent, abnormal dilatation of a blood vessel

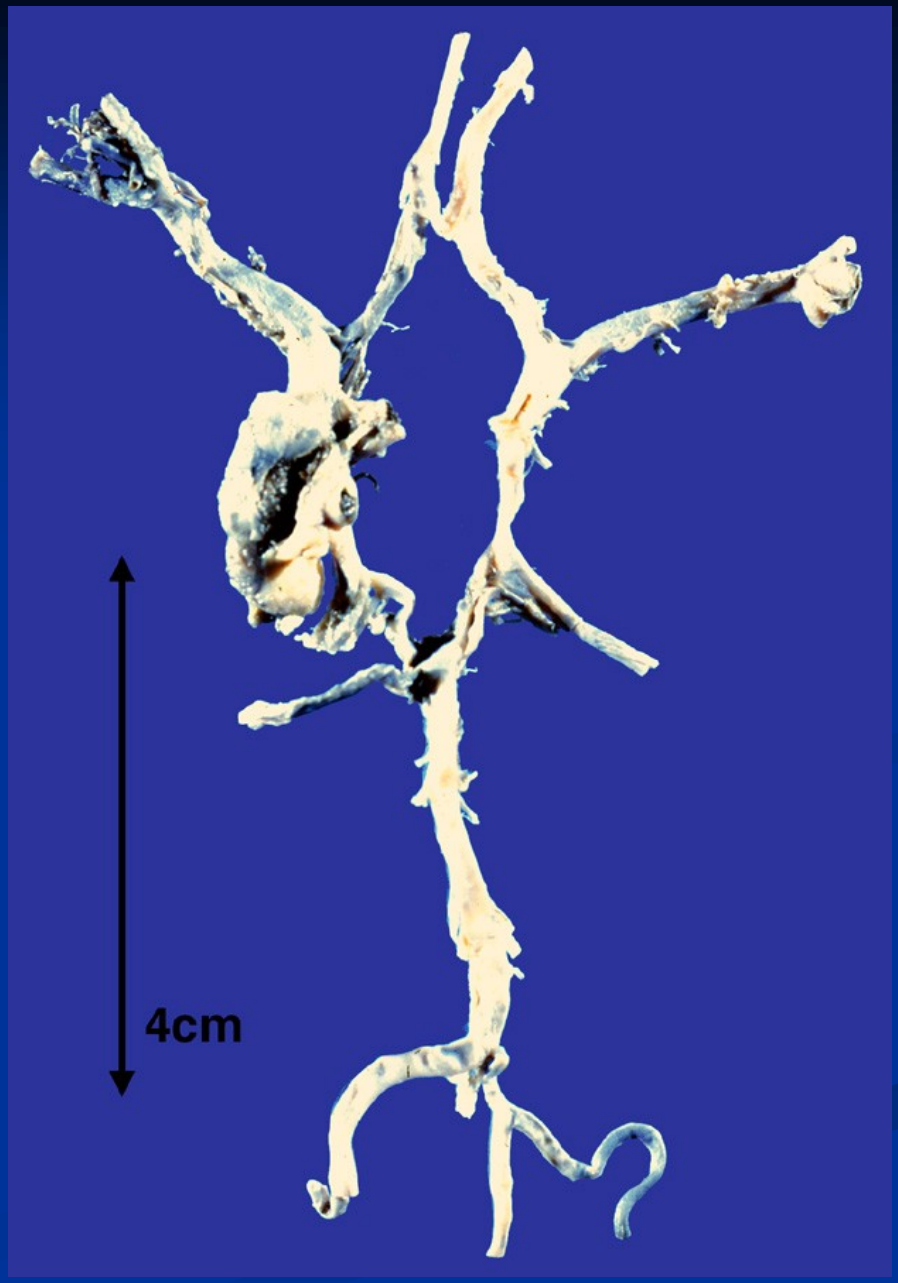
	Localisation of aneurysms	Clinical effects
Atherosclerotic	Lower abdominal aorta and iliac arteries	Abdominal mass, lower limb ischaemia, rupture
Aortic dissection	Aorta and major branches (intramural bleeding) ↑BP, Marfan sy, cystic medionecrosis	Loss of peripheral pulses, haemopericardium, rupture external or re-entry
Berry	Circle of Willis	SAH
Micro-aneurysms	Intracerebral capillaries	Intracerebral haemorrhage, as. hypertension
Syphilitic	Ascending and arch of the aorta	Aortic incompetence
Mycotic	Root of aorta (from endocarditis) Any vessels	Thrombosis or rupture, cerebral infarction or haemorrhage

Aneurysms


Extravascular connective tissue
Extravasation of blood
Hematoma
Extravasation of blood
Tear in intima
Dissection
A. Normal vessel
B. True aneurysm (saccular)
C. True aneurysm (fusiform)
D. False aneurysm
E. Dissection

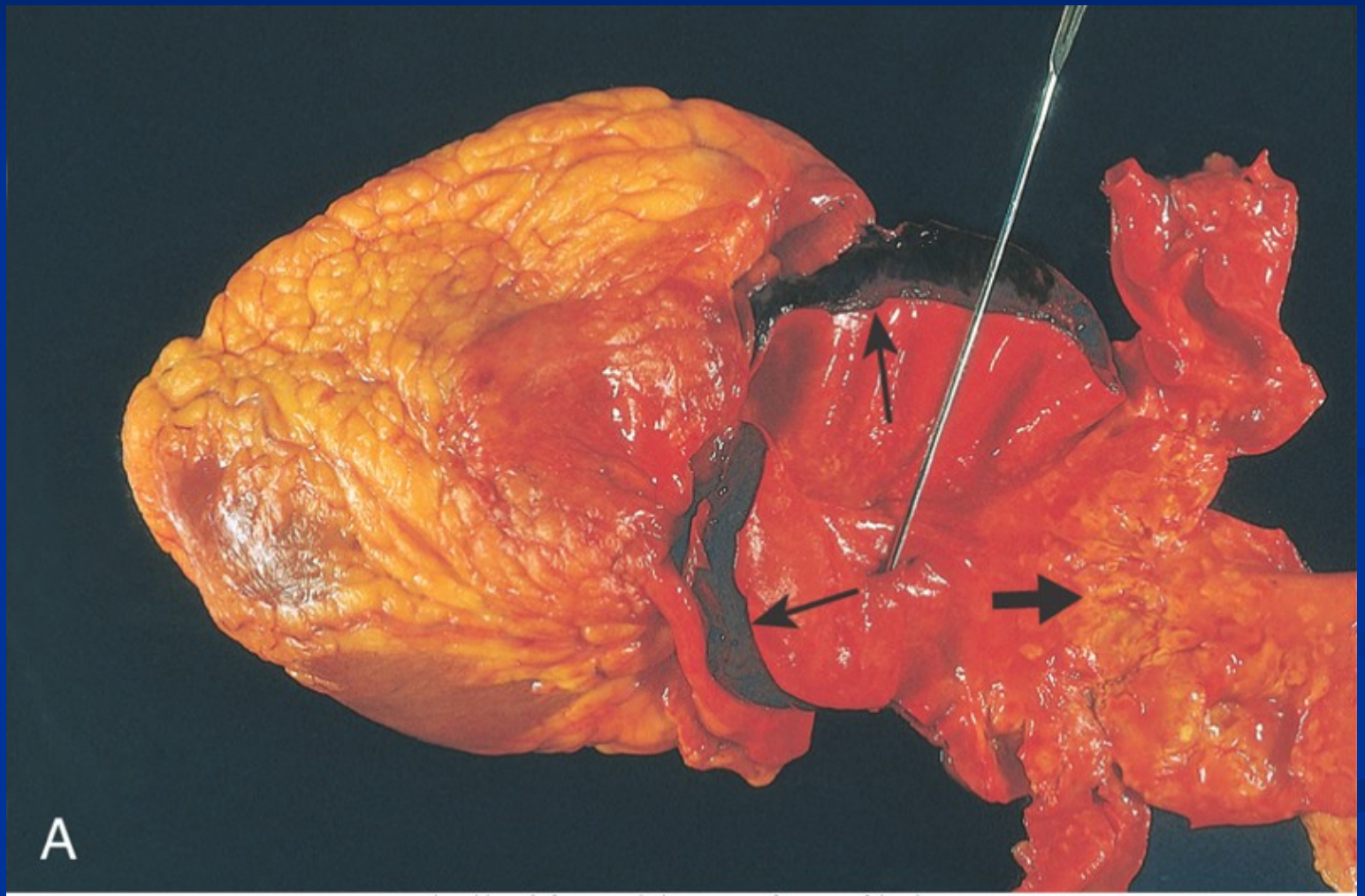


AS aneurysm – abdominal aorta



Berry aneurysm of circle of Willis

Aortic dissection



Pathogenesis of vasculitis

- **Infectious**
  - Bacterial
  - Rickettsial
  - Spirochetal (syphilis)
  - Fungal (aspergilosis, mucormycosis)→mycotic aneurysm, thrombosis, infarction
  - Viral (herpes zoster, varicella)

- **Immunologic**

- **Unknown/(immunologic)**
  - Giant cell (temporal) arteritis
  - Takayasu arteritis
  - Polyarteritis nodosa

Immune mediated vasculitis

- **Immune-complex-mediated**
  - Infection-induced (hepatitis B and C virus)
  - Henoch-Schonlein purpura (IgA+C3, small vessels)
  - SLE and rheumatoid arthritis
  - Drug-induced
  - Cryoglobulinemia
  - Serum sickness (reaction to protein in antiserum derived from non-human sources)
- **Antineutrophil cytoplasmic antibody (ANCA)-mediated**
  - Wegener granulomatosis
  - Microscopic polyangitis (microscopic polyarteritis)
  - Churg-Strauss syndrome
- **Direct antibody mediated**
  - Good-Pasture syndrome (anti-GMB antibodies)
  - Kawasaki disease (anti-endothelial antibodies)
- **Cell mediated**
  - Organ allograft rejection
- **Inflammatory bowel disease (ulcerative colitis, morbus Crohn)**
- **Paraneoplastic**

Large vessel vasculitis

- **Giant cell (temporal) arteritis**
  (granulomatous, extracranial branches of the carotid artery; +polymyalgia rheumatica)

- **Takayasu arteritis**
  (granulomatous; aorta and major branches; pulsless disease)

Medium-sized vessel vasculitis

- **Polyarteritis nodosa**
  (necrotizing, transmural; all stages coexist; in any organs with exception of the lung)

- **Kawasaki disease=mucocutaneous lymph node syndrome**
  (PAN-like vasculitis; coronary arteries affected; children)

- **Small vessel vasculitis**

- **Polyangiitis with granulomatosis/Wegener granulomatosis**
  (M>F; necrotizing granulomas of respiratory tract +necrotizing or granulomatous vasculitis+focal necrotizing often crescenting glomerulonephritis)

- **Churg-Strauss syndrome**
  (allergic granulomatosis and angitis: necrotizing vasculitis+granulomas with eosinophilic necrosis + allergic rhinitis, asthma bronchiale, eosinofilia)

- **Microscopic polyangitis (polyarteritis), hypersensitivity, leukocytoclastic vasculitis**
  (necrotizing vasculitis, palpable purpura of the skin and mucous membranes +often necrotizing glomerulonephritis, pulmonary capillaritis; lesions of the same age)

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

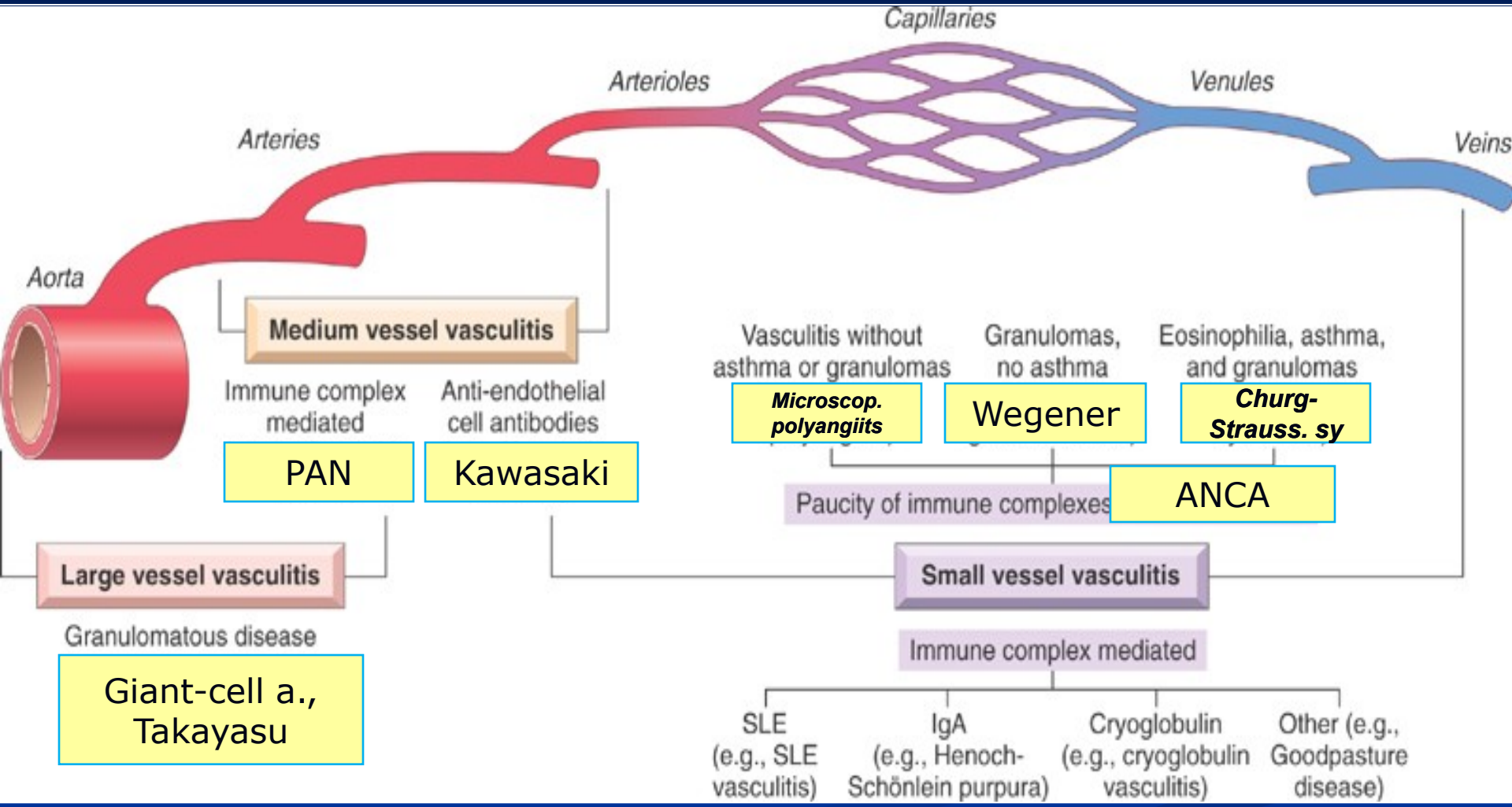
Skin: - ulceration, necrosis, petechiae-purpura

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

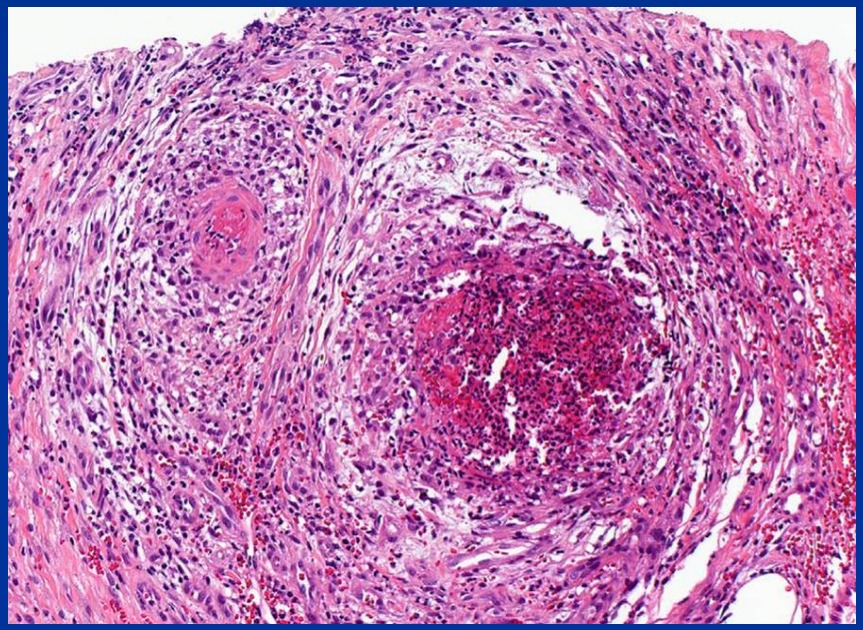
Patient presentation

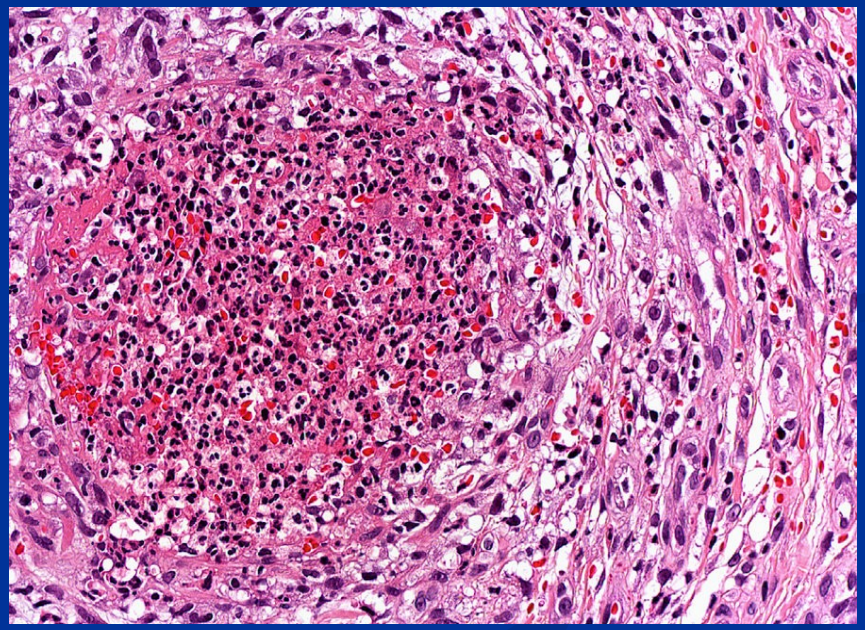
- **fever, nausea, myalgia, arthralgia**
- **skin purpura**
- **signs of nephritis**
- **abdominal pain**

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

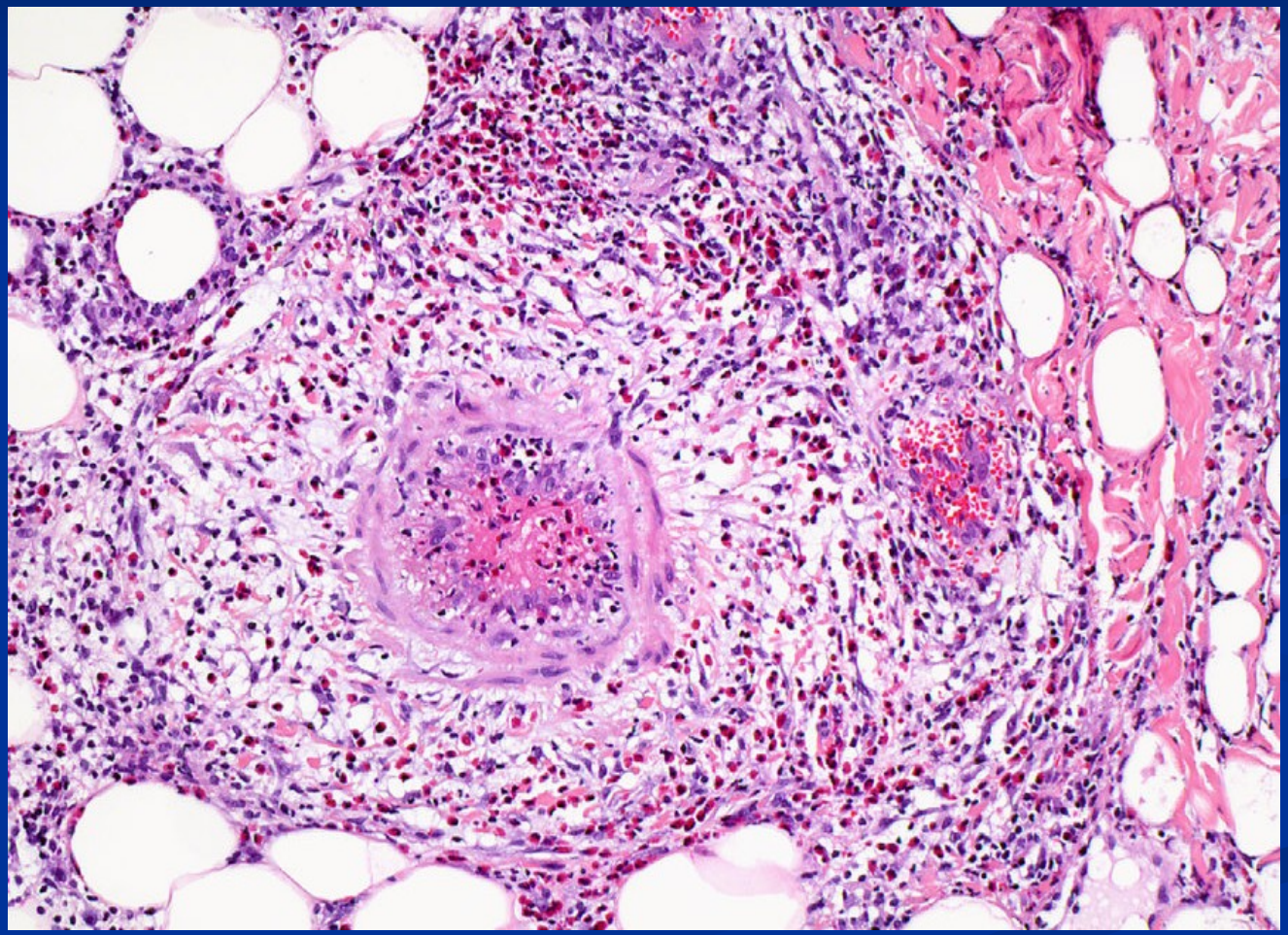

Capillaries
Arterioles
Venules
Arteries
Veins
Aorta
Medium vessel vasculitis
Immune complex mediated
Anti-endothelial cell antibodies
PAN
Kawasaki
Vasculitis without asthma or granulomas
Granulomas, no asthma
Eosinophilia, asthma, and granulomas
Microscop. polyangiits
Wegener
Churg-Strauss. sy
Paucity of immune complexes
ANCA
Large vessel vasculitis
Granulomatous disease
Giant-cell a., Takayasu
Small vessel vasculitis
Immune complex mediated
SLE (e.g., SLE vasculitis)
IgA (e.g., Henoch-Schönlein purpura)
Cryoglobulin (e.g., cryoglobulin vasculitis)
Other (e.g., Goodpasture disease)

Polyarteritis nodosa





Polyarteritis nodosa



Thrombangiitis obliterans (Buerger disease)

- Segmental, thrombosing, acute and chronic inflammation of medium-sized and small arteries
- Tibial and radial arteries (extension to veins and nerves of extremities)- all structures encased in fibrous tissue
- Cigarette smoking (hypersenzitivity to intradermally injected tabacco extracts)
- HLA-A9 and HLA-B5

Raynaud Phenomenon

- Paroxysmal pallor or cyanosis of the digits o the hands and feet; less frequently acral parts (nose, ears)
- Cold induced vasoconstriction of the digital arteries, precapillary arterioles, cutaneous A-V shunts
- Structural changes of the arterial wall absent; late in the course intimal thickening
- Late in the course: atrophy of the skin, subcutaneous tissues and muscles, ulcerations, ischemic gangrene

- Primary, usually uncomplicated
- Secondary (in SLE, scleroderma, atherosclerosis, Buerger disease), more severe

Venous thrombosis

- Immobility (post-operative phase, cardiac failure, bed rest, fractures, long flights…)
- Cancer (thromophlebitis migrans: superficial venous thrombi)
- Pregnancy and childbirth
- Oestrogen therapy (contraceptives, hormonal treatment of prostatic cancer,…)
- Haematological disorders (polycythaemia, factor V Leiden (mutated) and antithrombin III deficiency,…)

Thrombophlebitis and phlebothrombosis

- Deep venous thrombosis in deep leg veins: 90 % cases of thrombophlebitis and phlebothrombosis
- + periprostatic venous plexus, pelvic venous plexus, large veins in skull and the dural sinuses
- **Pulmonary embolism!!!!**

- In setting of infection and inflammation

- **Varicose veins of superficial veins of the upper and lower leg**
  - Dilated, tortuous veins
  - Increases intraluminal pressure and loss of vessel wall support
  - Superficial veins of the upper and lower leg
  - Familial tendency, pregnancy
  - Dilatation, stasis, congestion, oedema, pain, thrombosis, stasis dermatitis, varicose ulcers

- **Other varicosities**
  - **Esophageal varices** (in liver cirrhosis – in portal vein hypertension; the opening of porto-systemic shunts)
  - **Hemorrhoids** (primary varicose dilatation of the venous plexus at the anorectal junction)

- **Superior and inferion vena caval syndromes**
  - Neoplasms that compress the superior or inferior vena cava

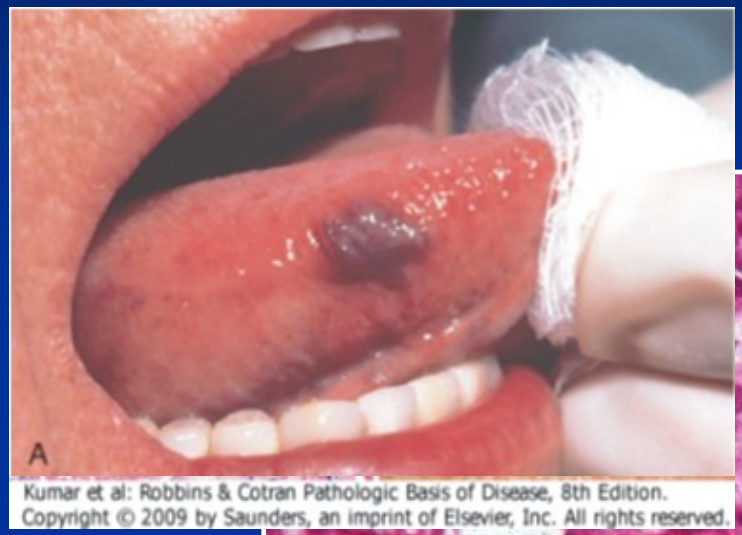
Vascular tumors and tumor-like conditions

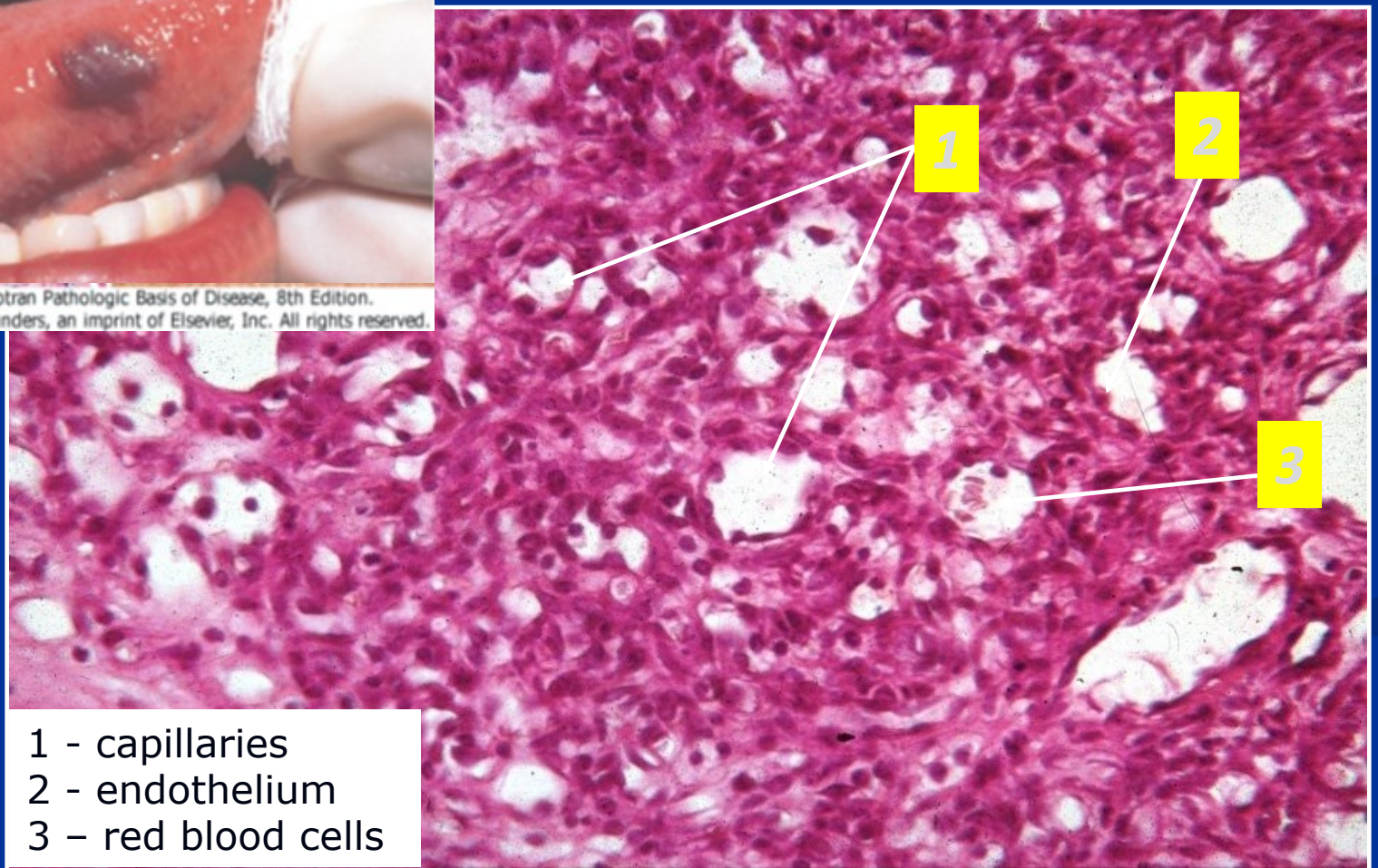
- Benign tumors
- Vascular tumors of intermediate malignancy
- Malignant vascular tumors

Benign tumors and tumor-like lesions

- **Hemangioma**
  - Capillary
  - Cavernous
  - Pyogenic granuloma (lobular capillary hemangioma)
- **Lymphangioma**
  - Capillary
  - Cavernous
- **Vascular ectasias**
  - Nevus flammeus
  - Spider teleangiectasia
  - Hereditary hemorrhagic teleangiectasia (Osler-Weber-Rendu disease)
- **Reactive vascular proliferations**
  - bacillary angiomatosis (opportunic infection of immunocompromised patients; G- Bartonella henselae, B quintana,…)
  - intravasculary papillary endothelial hyperplasia,…

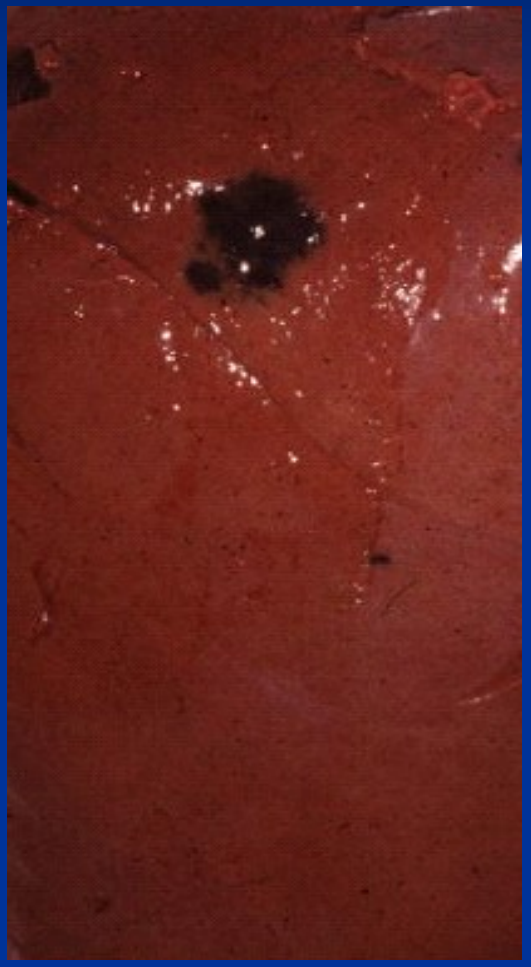
Capillary hemangioma

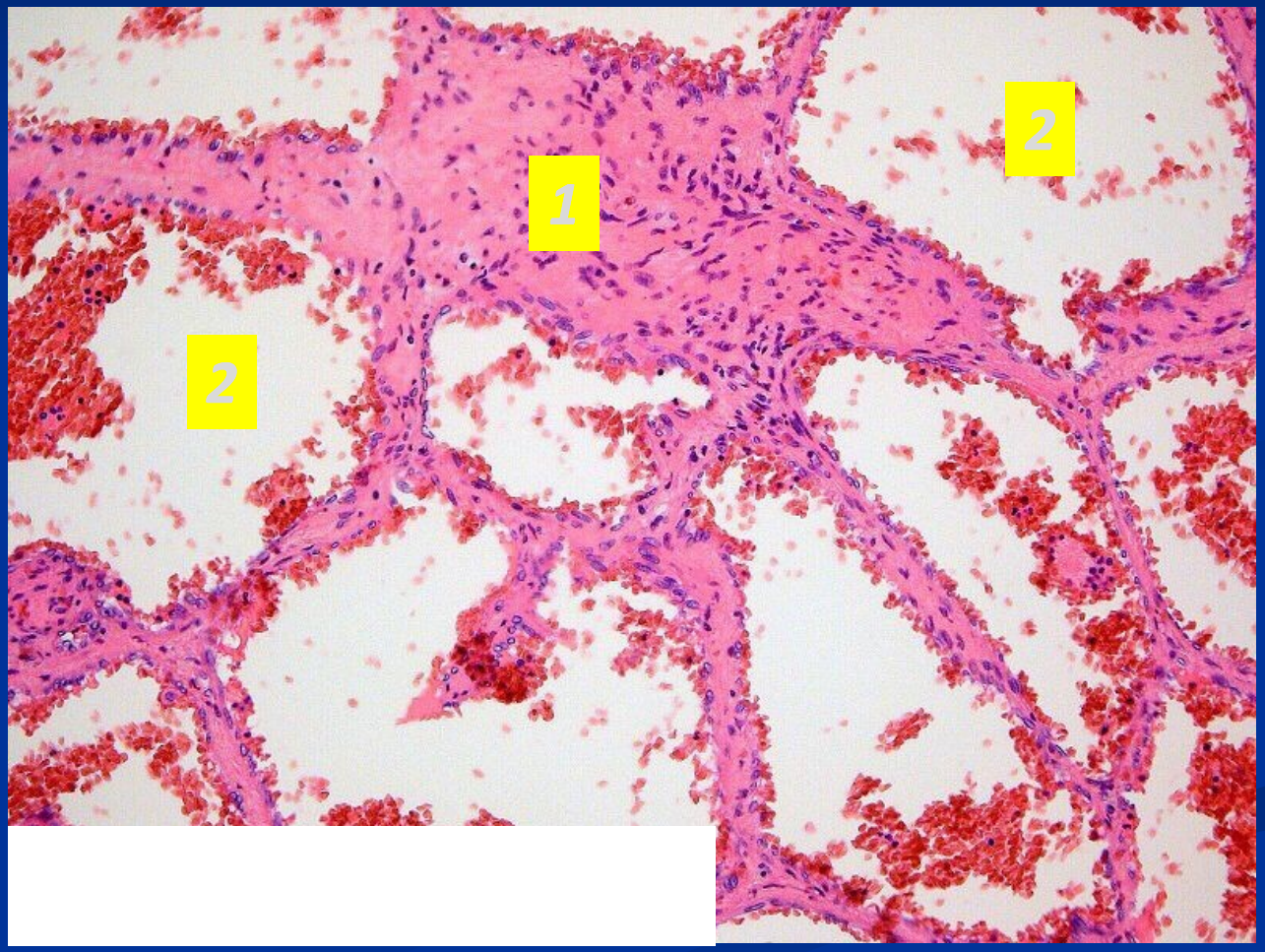




1 - capillaries
2 - endothelium
3 – red blood cells

Cavernous hemangioma





Vascular tumor of intermediate malignancy

- Kaposi sarcoma
- Hemangioendothelioma

Malignant neoplasms

- Angiosarcoma

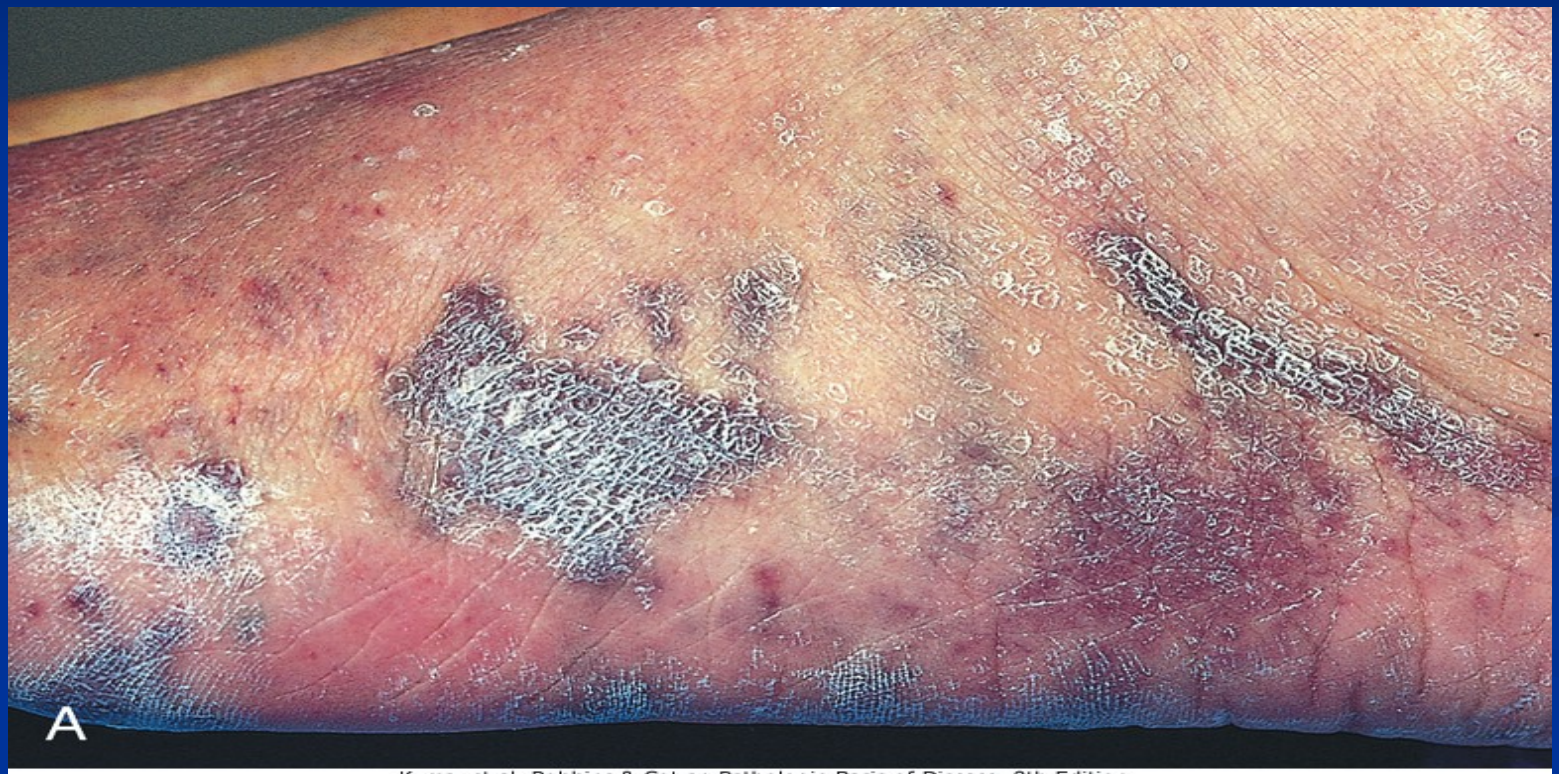
Kaposi sarcoma

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



Endomyocardial biopsy

- Performed **during catetrization procedure**
  (right internal jugular vein, femoral vein – right ventricular EMB;
  femoral artery – left ventricular EMB)
- Under fluoroscopic guidance
- **Risk of EMB:**

- Perforation with pericardial tamponade
- Arrhythmias
- Heart block
- Pneumothorax
- Puncture of central artheries
- Venous hematoma
- Pulmonary embolization
- Nerve paresis
- Vasovagal reaction
- Damage to the tricuspid valve
- Bleeding from the biopsy site
- Deep venous thrombosis

- **to evaluate heart transplant recipients for rejection**

(cellular rejection, vascular rejection)

In suspected:

- Cardiac amyloidosis, (glycogen, lysosomal storage disease,…)
- Myocarditis
- Cardiomyopathy (alcoholic, idiopathic, hypertrophic, ischemic, peripartum, restrictive,…)
- Cardiac tumors

- >1 region of the right heart septum
- Number of samples (5-10), 1-2 mm^3
- Fixation in 10% neutral buffered formalin, light microscopy
- Fixation in 4% glutaraldehyde, transmission electron microscopy
- Frozen samples for molecular studies

Classification of types of restrictive cardiomyopathy according to cause

- **Myocardial**

- Noninfiltrative

Idiopathic cardiomyopathy
Familial cardiomyopathy
Hypertrophic cardiomyopathy
Scleroderma
Pseudoxanthoma elasticum
Diabetic cardiomyopathy

- Infiltrative

Amyloidosis
Sarcoidosis
Gaucher´s disease (lysosomal storage disease)
Hurler´s disease (lysosomal storage disease)
Fatty infiltration

- Storage diseases

Hemochromatosis
Fabry´s disease (sfingolipidosis; ↓α-galactosidase)
Glycogen storage disease

- **Endomyocardial**

Endomyocardial fibrosis
Hypereosinophilic syndrome
Carcinoid heart disease
Metastatic cancers
Radiation
Toxic effect of anthracyclin
Drugs causing fibrous endocarditis (serotonin, methysergide, ergotamine, mercurail agents, busulfan)

Thank you for your attention …