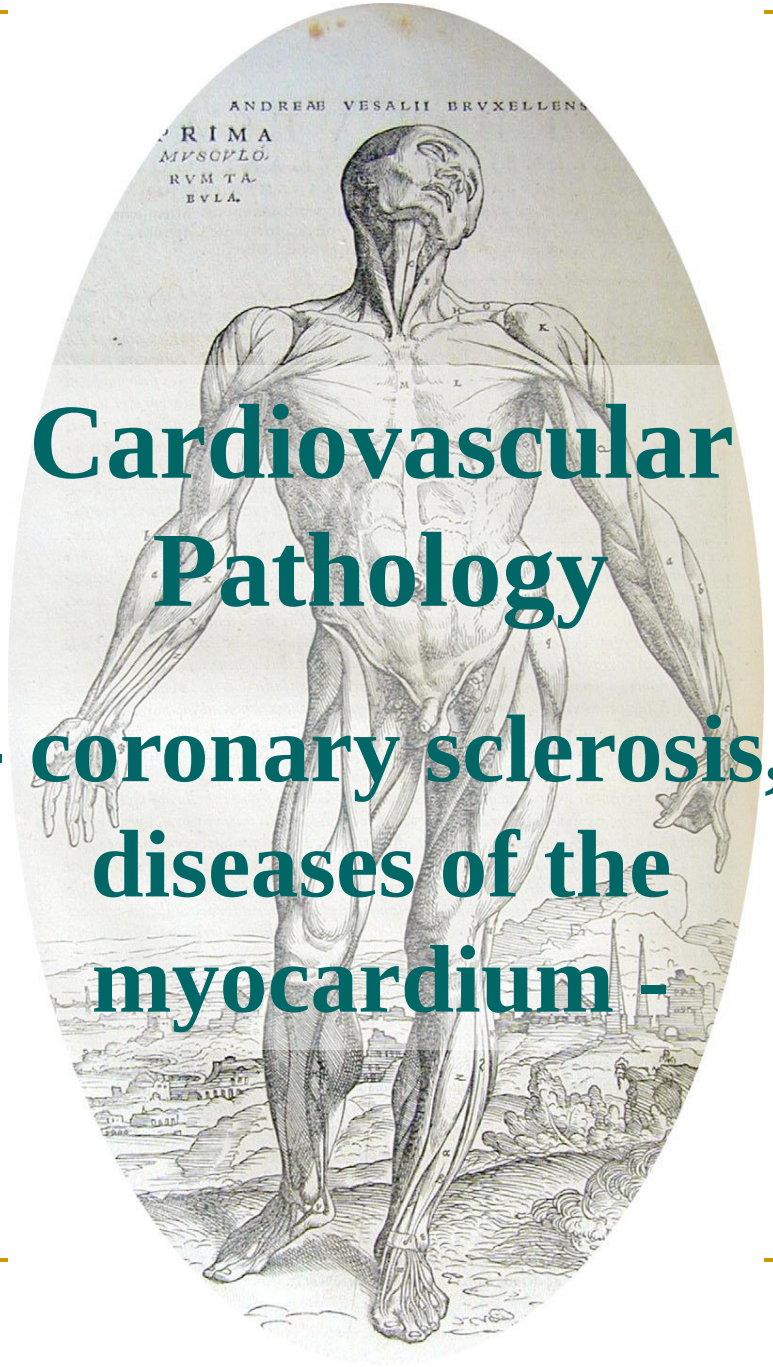


Cardiovascular Pathology

- coronary sclerosis, diseases of the myocardium -

Semmelweis University
2nd Department of Pathology

2017/2018 – Autumn Semester

Tibor Glasz MD PhD

Pathology of the coronary arteries

The system of coronary arteries

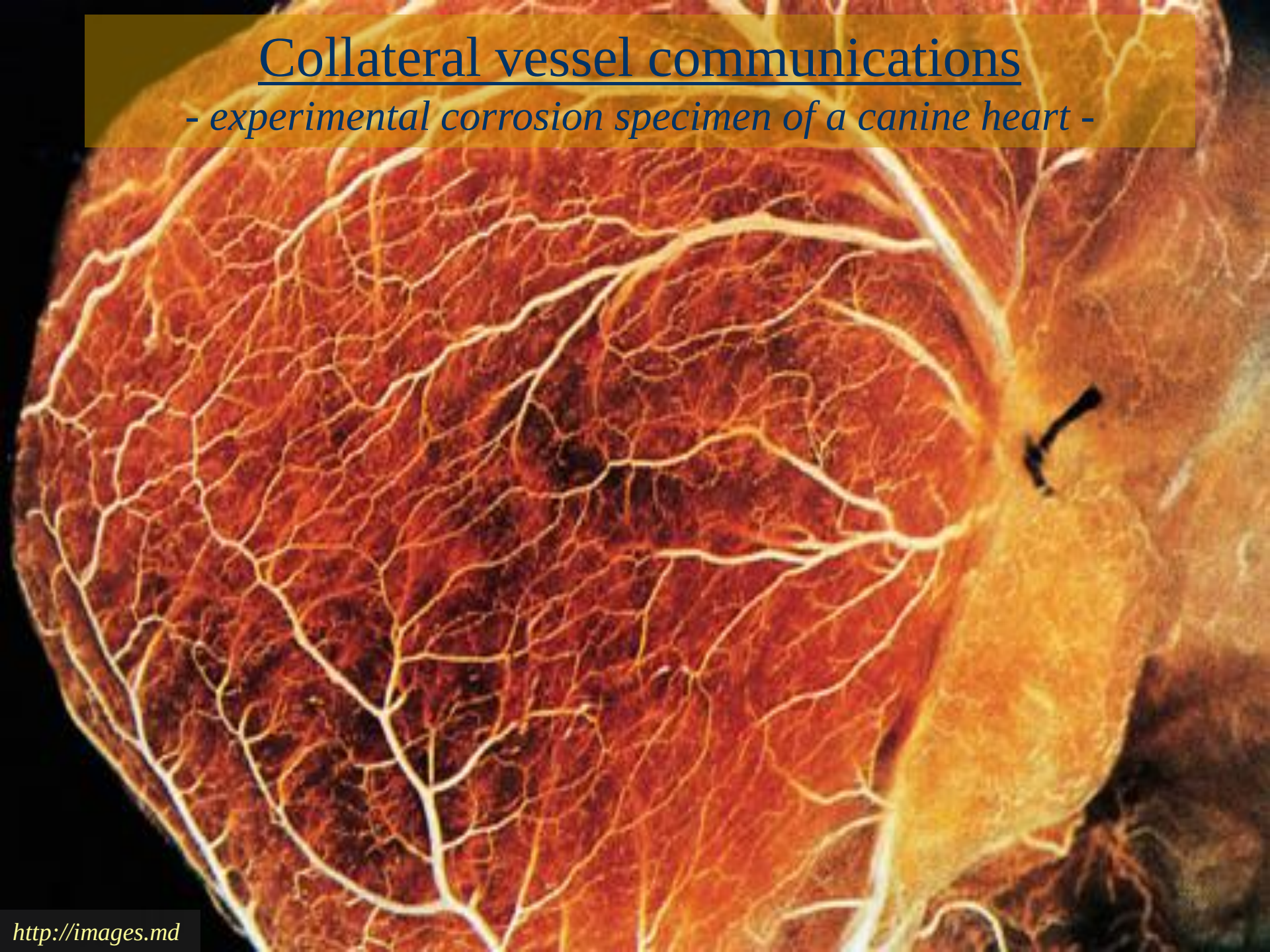
- Anatomy -

- subepicardial main branches
- epicardial side branches
- intramural small vessels
    - collateral arteries

Positional variations: intramurally running segments of the subepicardial large coronary arteries through formation of so-called muscle-bridges

Collateral vessel communications

- experimental corrosion specimen of a canine heart -



http://images.md

Coronary stenosis or occlusion

- Causes -

- up to **80-90% atherosclerosis**, atherosclerotic plaque
- less frequently: plaque hemorrhage
- thrombosis
- embolus
- very rarely: congenital developmental anomalies (coronary hypoplasia, anomalies of coronary anatomy – e.g. right coronary artery going out from the left side of the aortic wall)
- inflammations
- autoimmune diseases
- muscular spasms of the coronary wall (Prinzmetal's 'variant' angina)
- coronary kinking
- muscle bridges

Coronary arteriosclerosis

- according to extension within a coronary artery -

- *central* coronary artery disease
  - very good bypassing results

- *peripheral* coronary artery disease
  - small-vessel-disease, no bypassing possible

- *diffuse* coronary artery disease
  - the most frequent form, bypassing offers only limited success

Coronary arteriosclerosis

- according to coronary artery topography -

- Arteriosclerosis on a single coronary artery: *one-vessel-disease*
  - clinically anginal pain frequently localized to the thorax, with a history of not longer than 3 years

- Arteriosclerosis on two coronary arteries: *two-vessel-disease*

- Arteriosclerosis on three coronary arteries: *three-vessel-disease*
  - clinically anginal pain frequently radiating into the arms, neck and dorsal parts, with a history of longer than 3 years

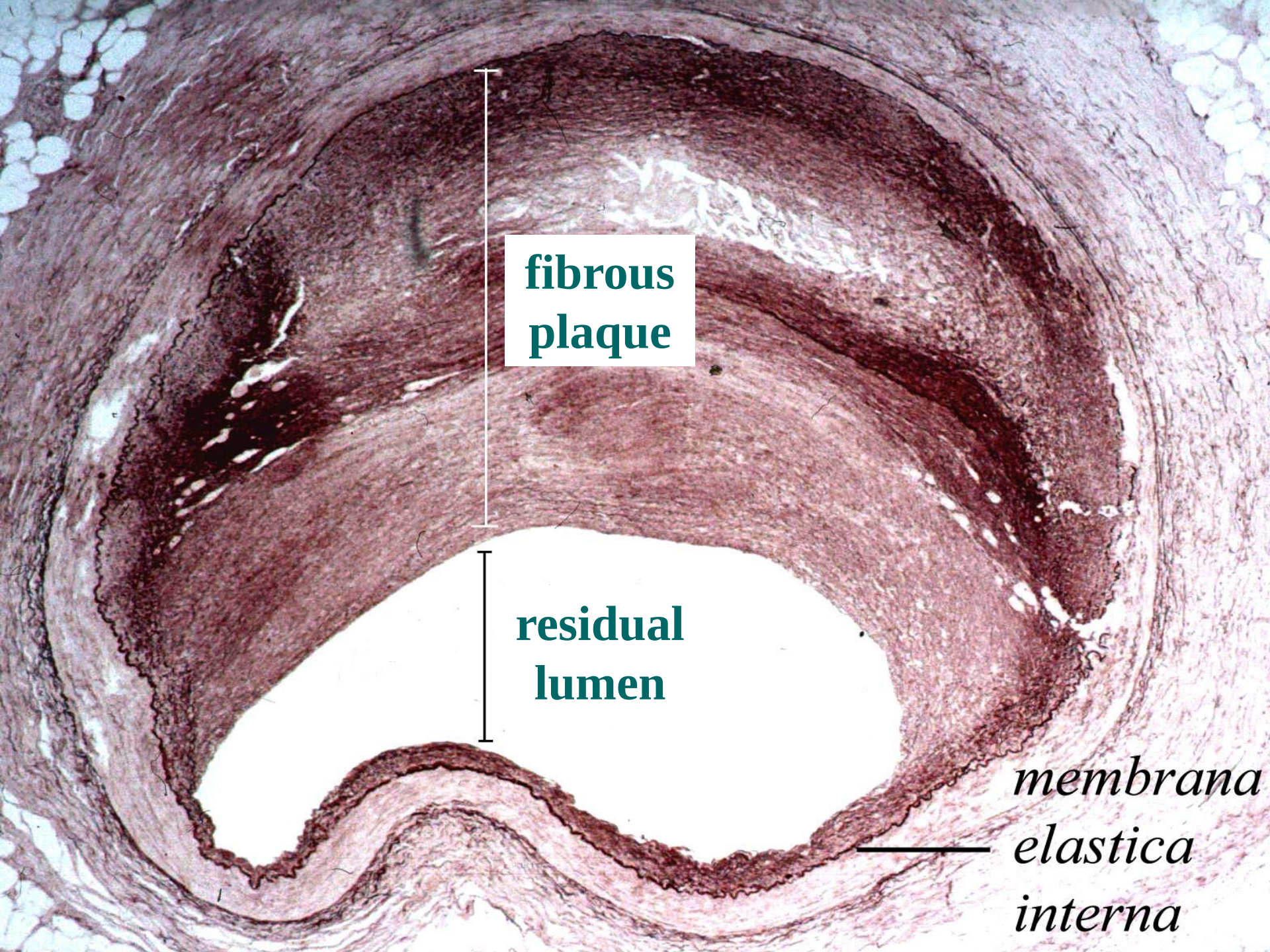
Coronary arteriosclerosis

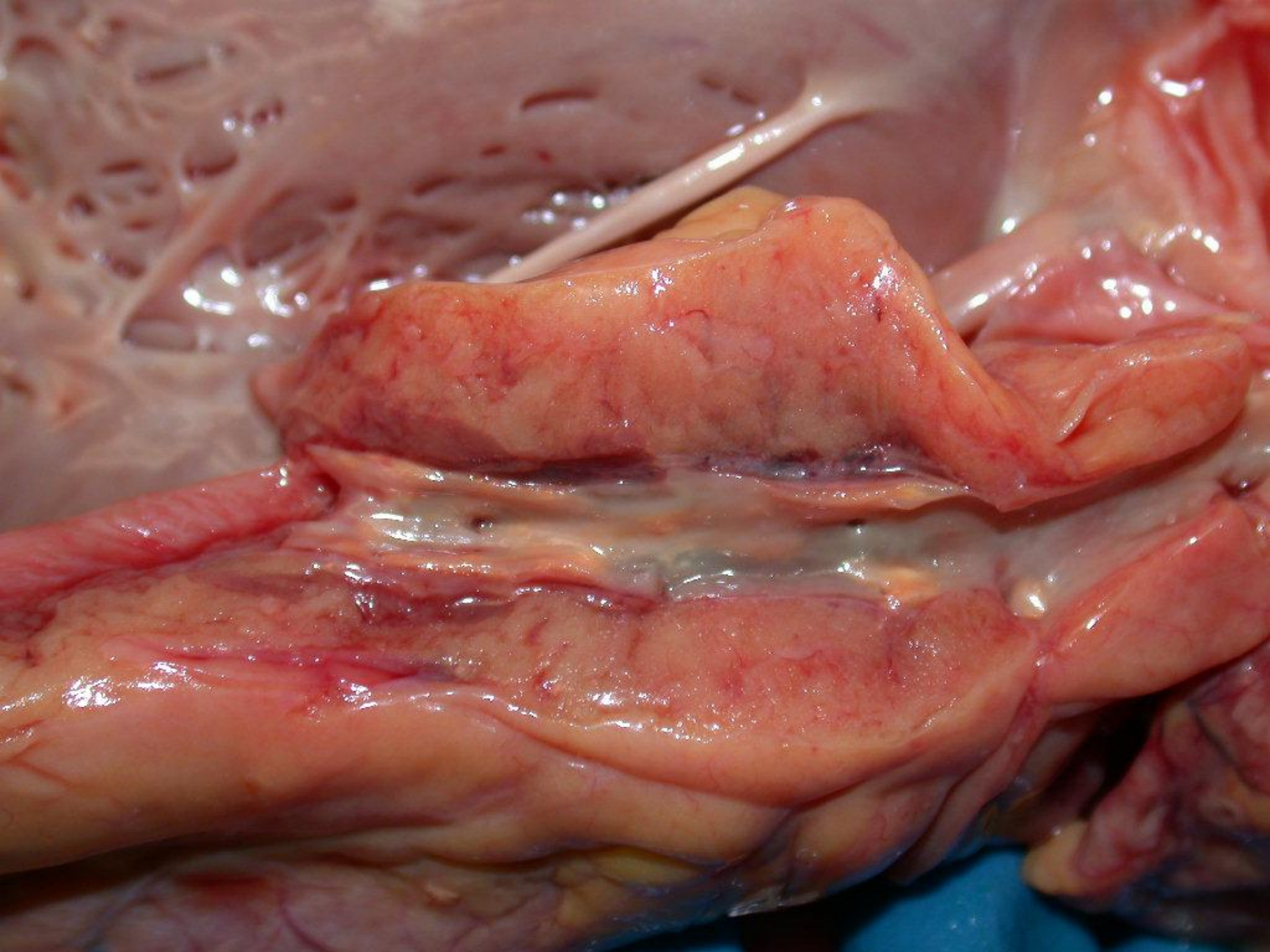
- according to severeness of the disease: grades -

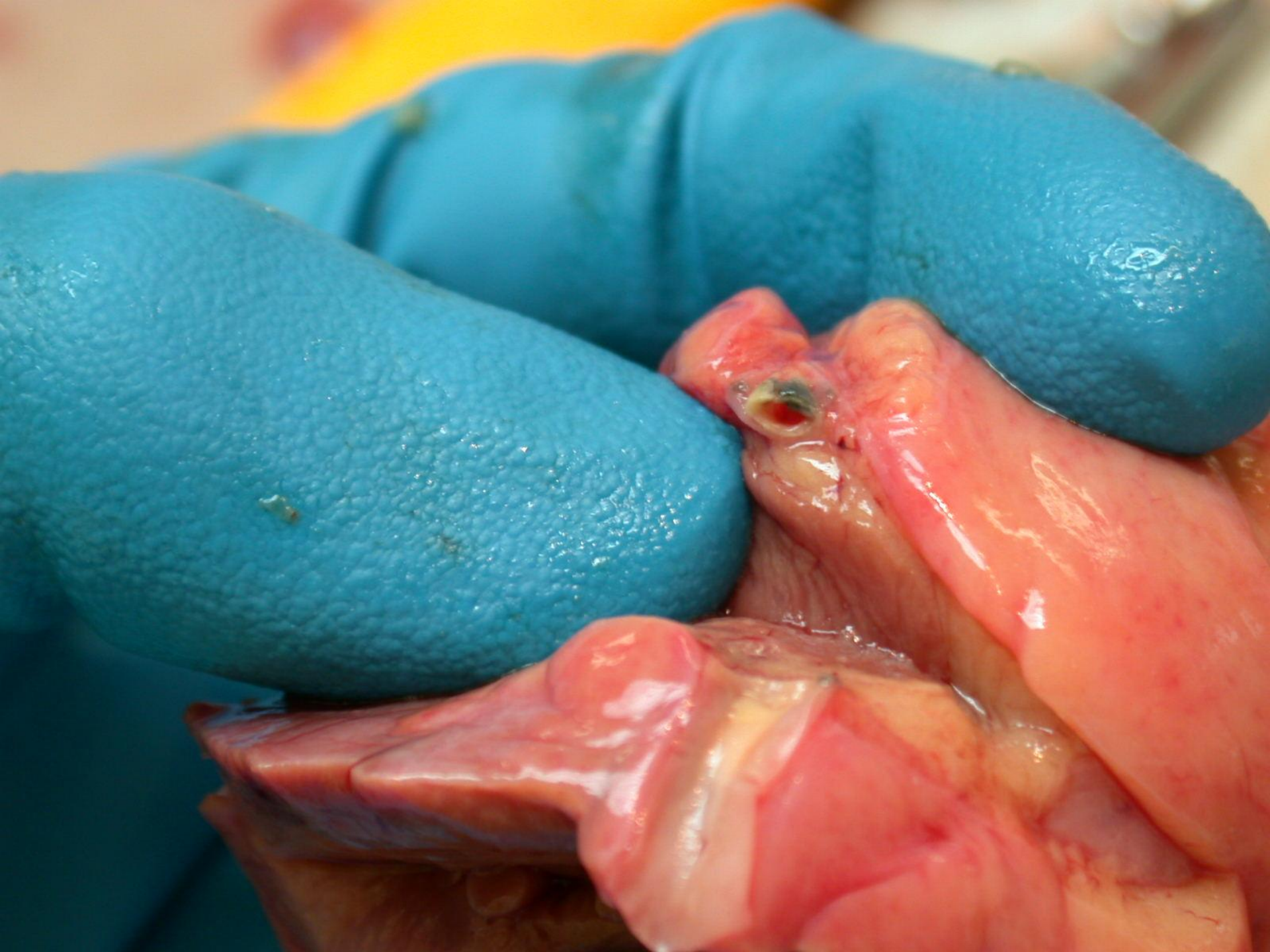
- low-grade coronary arteriosclerosis: stenosis < 50% of the native lumen

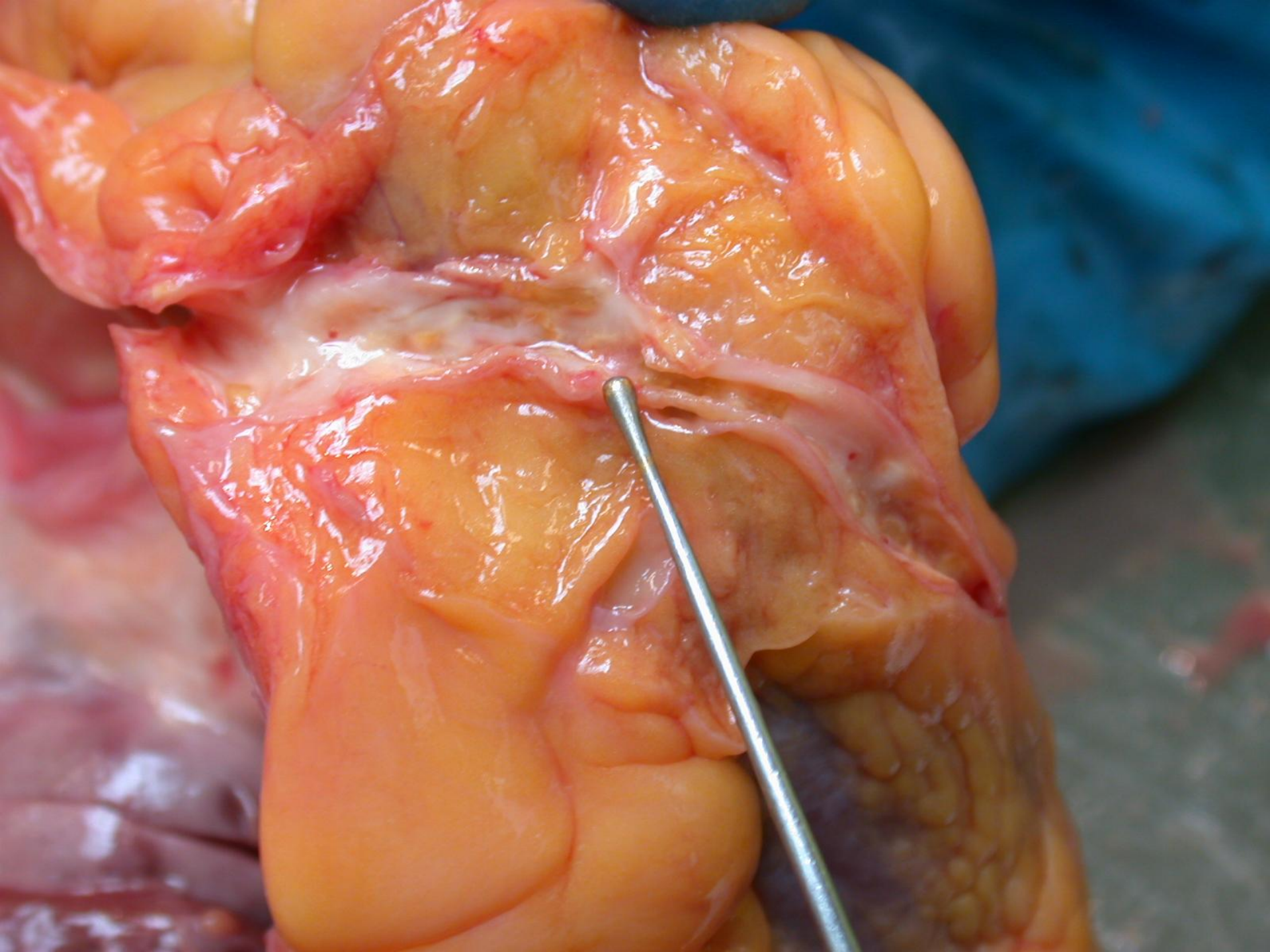
- intermediate coronary arteriosclerosis: stenosis > 50%, but <75% of the native lumen
    - ECG in rest yet normal

- high-grade coronary arteriosclerosis: stenosis >75% of the native lumen
    - ECG on exercise is abnormal: coronary heart failure


fibrous plaque
residual lumen
membrana elastica interna







Coronary plaques, the problem of instability

- Bernoulli's law and the 'steal'-phenomenon -

- stable plaques: high %-age of connective tissue: *fibrous plaque*
- unstable plaques: high %-age of lipid substances: *atheroma*

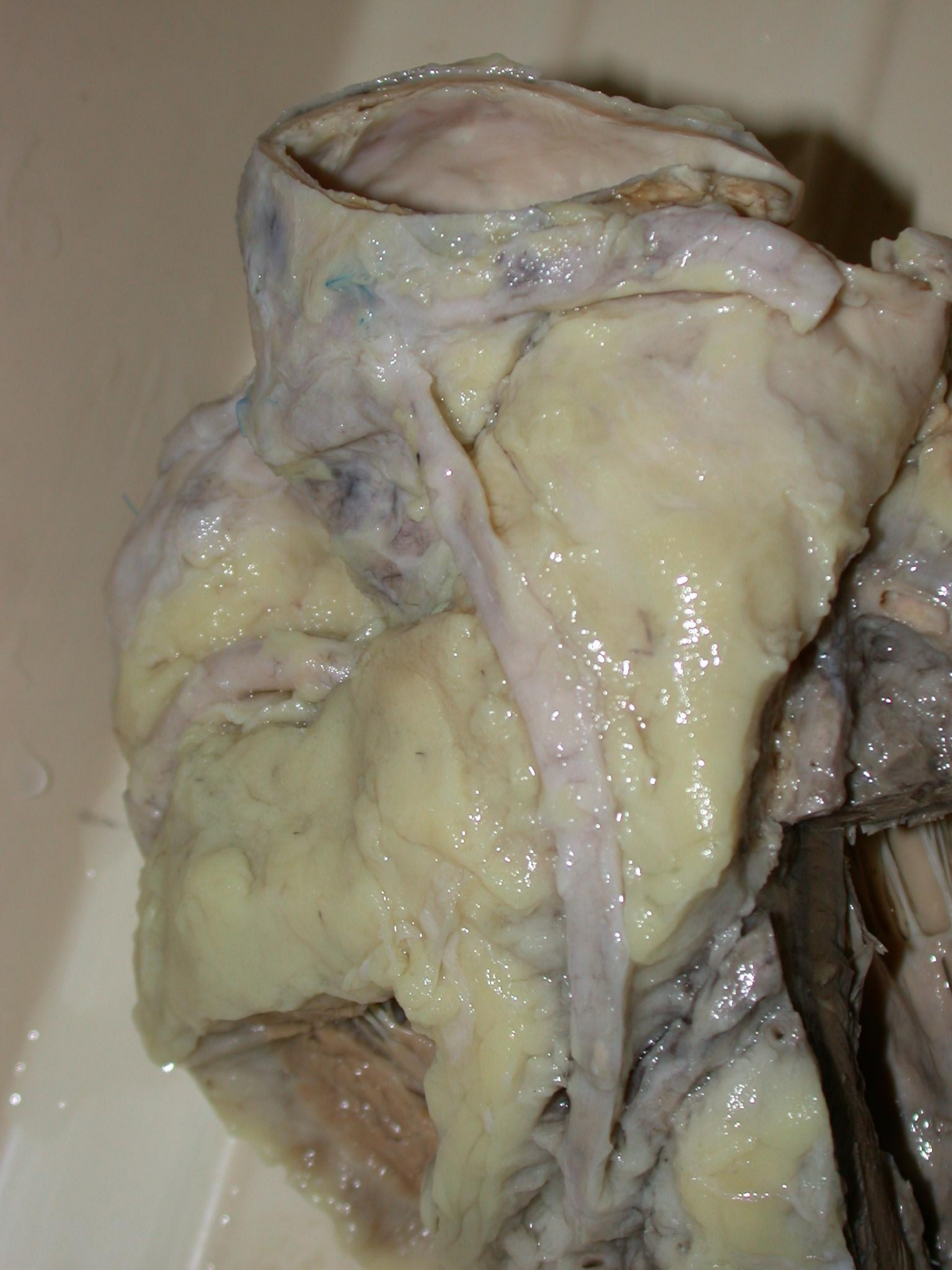
- at stenotic segments: increased blood flow speed causes decreased intraluminary pressure (*Bernoulli's phenomenon*) – suction effect on stenosed vessel parts
- poststenotically: slower blood flow, higher hydrostatic pressure
- and yet: flexibility differences between sclerotic-rigid and neighbouring elastic wall segments (so-called wind-kettle function of arteries)
- mechanic overload on plaque periphery: dissection, plaque rupture and hemorrhage

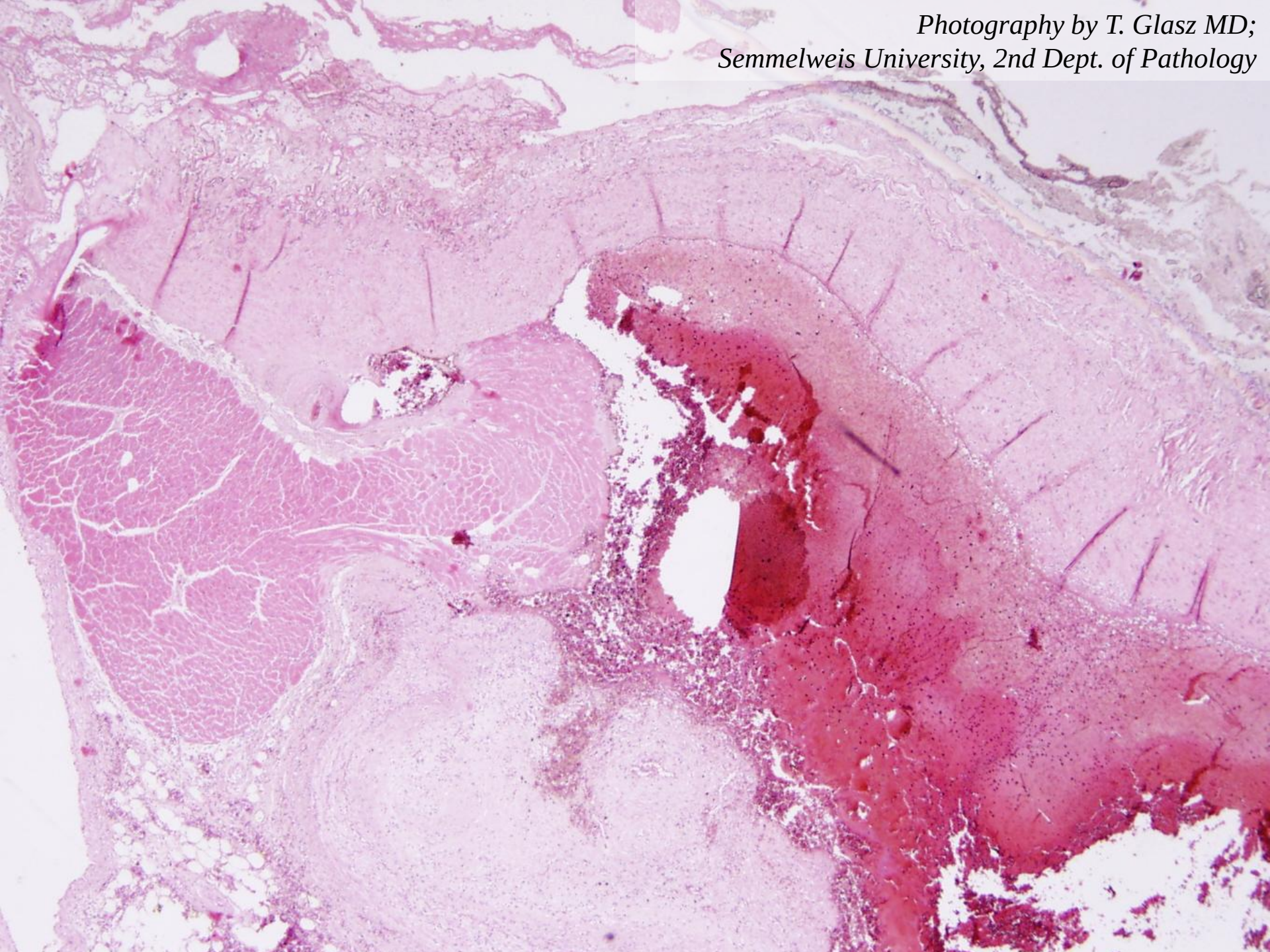
Restitution of the coronary flow

- conservative (medication based) therapy
- invasive:
  - angioplasty,
  - endarterectomy
  - stent implantation

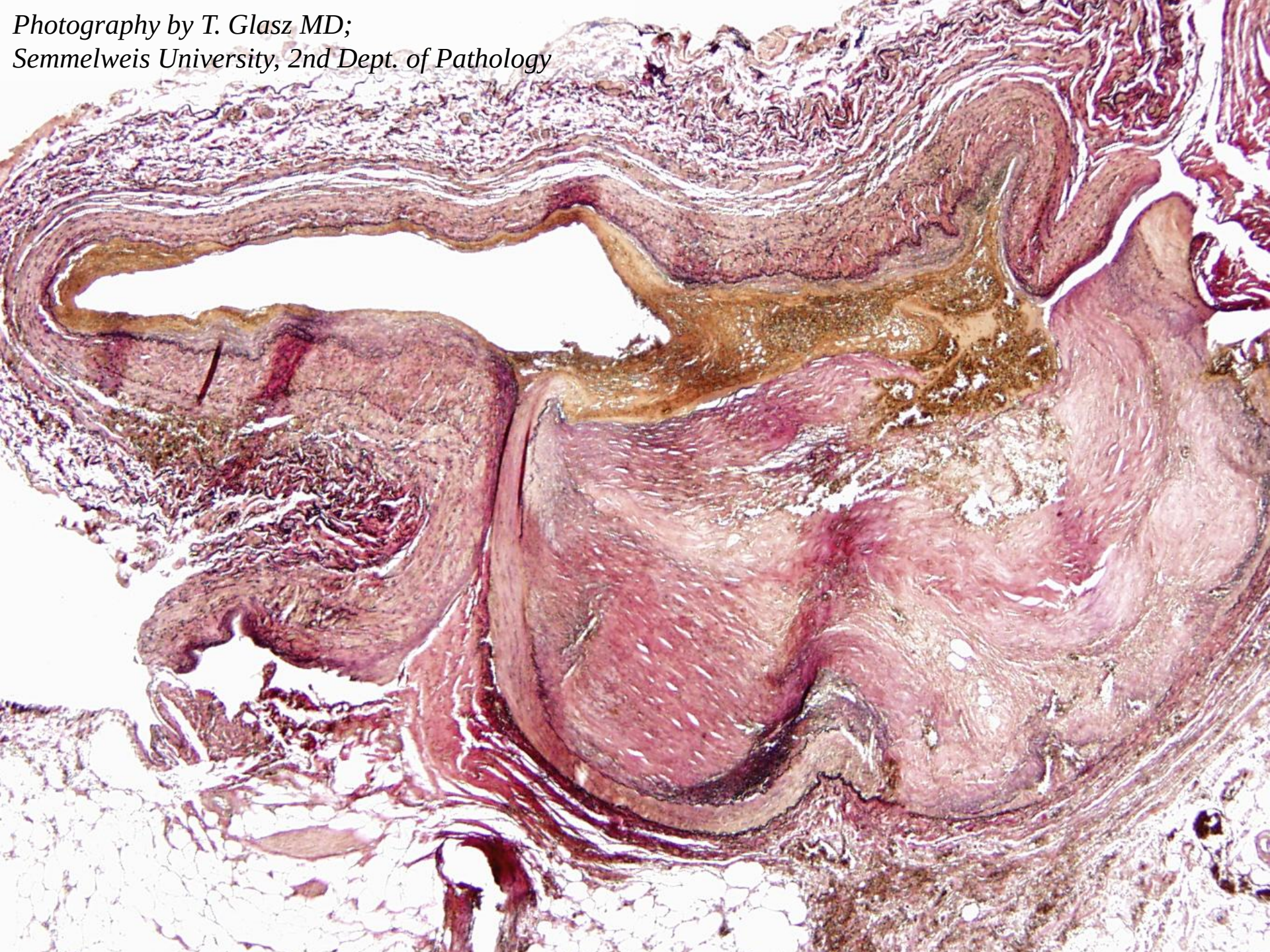
} PCI – percutaneous coronary interventions

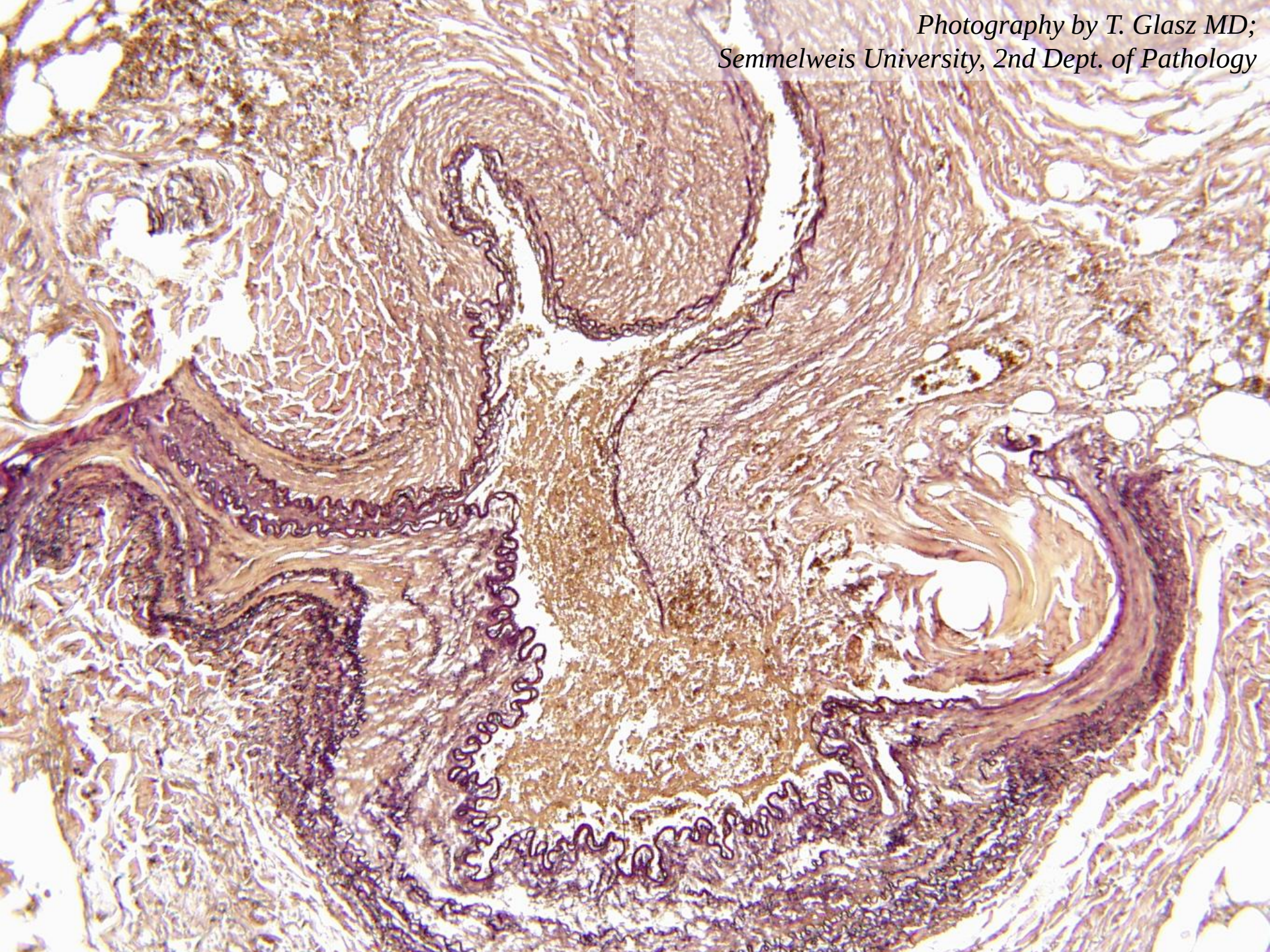
- bypass operation (open heart intervention: CABG – *coronary artery bypass grafting*)

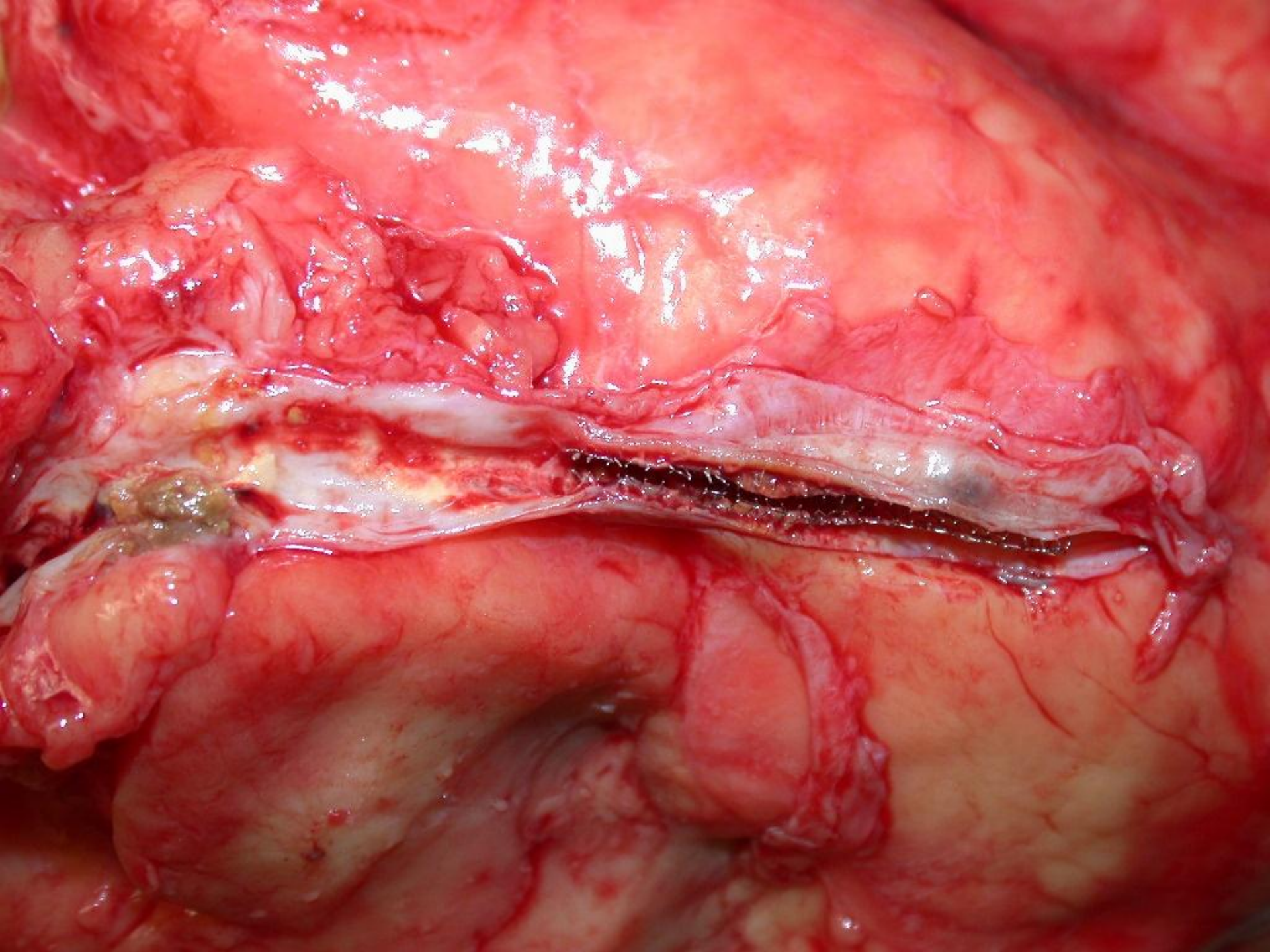




Photography by T. Glasz MD;
Semmelweis University, 2nd Dept. of Pathology


Photography by T. Glasz MD;
Semmelweis University, 2nd Dept. of Pathology


Photography by T. Glasz MD;
Semmelweis University, 2nd Dept. of Pathology



Ischemic heart disease

Ischemic heart disease

- Definition -

Ischemic heart disease is the general term for clinico-pathologic appearances that develop on insufficient oxygen supply to myocardium and consequent myocardial damage.

Formerly known as *coronary heart disease*.

Causes of ischemic heart disease

- Causes of insufficient myocardial oxygen supply -

A. Alteration of coronary arteries

1. Diseases of the subepicardial main branches

- **stenosing atherosclerotic plaque (over 90%!)**
- complicated plaque (hemorrhage or usuration+thrombosis)
- arterial dissection
- embolus
- so-called ‘steal’-syndrome (e.g. myocardial arteriovenous malformations; coronary-subclavian-steal-syndrom after coronary bypass grafting /CABG/ by means of the internal mammary artery /IMA/)

2. Diseases of the intramyocardial small vessels

- so-called small-vessel-disease (diabetes mellitus, amyloidosis, etc.)
- DIC, thrombocyte aggregation
- arterial spasm of small vessels
- perivascular fibrosis

Causes of ischemic heart disease

- Causes of insufficient myocardial oxygen supply -

B. Extracoronary causes of a relative myocardial oxygen deficiency (relative coronary insufficiencies)

- muscular hypertrophy (heart weight > 500g)
- aortal or aortic valve stenosis
- anemia
- shock
- diminished pO_2 in the air
- pneumonia
- enhanced myocardial oxygen demand of any kind (e.g. physical excerise)

Clinico-pathologic syndroms of ischemic heart disease

1. Angina pectoris

2. Myocardial infarction (‘heart attack’)

3. Sudden cardiac death

4. *Chronic* ischemic heart disease
   (so-called ischemic cardiomyopathy)

Angina pectoris

- first described by Heberden in 1768
- *definition*: variably strong, thoracally based attacks of pain of cardial origin
- primarily a clinical syndrome without corresponding macro- o. micromorphologic alterations
- *stable angina*: pain attacks on body exercise; generally there is a high-grade stenosing subepicardial coronary arteriosclerosis, where well developped intercoronary collaterals can yet prevent an infarction
- *unstable angina*: precursor of infarction; pain attacks also in rest
- *Prinzmetal's angina*: described by Prinzmetal in 1959; pain attacks on muscular spasms of variably sclerotic coronary vessels; complaints are experienced in rest and are limited in time

Sudden cardiac death

- *definition*: death within 1 hour after onset of symptoms in an apparently healthy or chronicly diseased individual
- incidency: 30 deaths / week / 1 million persons in the western world
- in the background there is very often a **high-grade coronary arteriosclerosis** (75%)
- *further causes*: extracoronary *functional* heart disease (cca. 20%) such as electromechanic instability (sick sinus disease, AV-node disease, WPW-syndrome, ventricular flutter, bradycardia) or *structural* abnormalities (vitia, cardiomyopathies, infectiv endocarditides, myocarditides, dysfunction of valvular prostheses, heart wall rupture). In 5% of the cases no detectable cause of death.
- histologically coagulation myocytolyses in up to 67% >> pathogenetic role of sympatico-adrenal hyperactivity, stress situations, physical exercise

Adams-Stokes syndrome

- *definition*: sudden cardiac arrest
- symptomatically quick onset of weakness, dizziness (*vertigo*), collapse
- physically: no systole, no pulse, no heart sounds, circulatory arrest, quick loss of blood pressure, tonal-clonal cramps >> *exitus letalis*
- chances of survival depend on length of the critical situation
    - a few seconds: '*forme fruste*' with slight vertigo
    - 10 seconds: facial paleness, collapse, muscular clonus, pupils dilated
    - 20-40 seconds: tonal cramps, cyanosis, loss of control on sphincter function (miction, defecation)
    - over 3 minutes: chances of survival very thin

Adams-Stokes syndrome

- *cause*: primarily **ischemic heart disease**, especially acute myocardial infarction >> ventricular fibrillation
- *further causes*: cardiac (rheumatic myocarditis, cardiomyopathy, cardiac tumours) and non-cardiac (metabolic and/or electrolite alterations, medicaments, thyreotoxicosis, carotic sinus-hyperesthesia)
- arrhythmias causing an Adams-Stokes syndrome (so-called electric catastrophies):
    - hypodynamic alterations: complete AV-block, sinus bradycardia with partial AV-block
    - hyperdynamic alterations: ventricular fibrillation (a dreaded complication of a myocardial infarction), paroxysmal ventricular tachycardia

Chronic ischemic heart disease
(so-called ischemic cardiomyopathy)

- direct cause of death in 40% of all ischemic forms of heart disease

- *definition*: chronic ischemic damage of myocardium

- *causes*: **severe coronary arteriosclerosis**, muscular cardiac hypertrophy (>500g), aortic hypoplasia, coronary hypoplasia >> long-term myocardial hypoxia

- *macroscopy*: atrophy, normotrophy, hypertrophy equally possible

- *microscopy*: variable picture with atrophic and compensationally hypertrophic muscle cells, microinfarctions (< 10mm), focal fibroses, interstitial fibrosis, myocytolytic foci – especially subendocardially

Chronic ischemic heart disease
(so-called ischemic cardiomyopathy)

- *Forms of cellular damage of cardiac muscle* : coagulation necrosis and single cell necroses (so-called myocytolyses)

  - *Coagulation necrosis* : seen in myocardial infarction; atonic death of muscle fibers (irreversible relaxation) >> fiber lengthening and meandering reactive to intraventricular pressure: so-called *wavy fibers*

  - *Liquefaction myocytolysis*: disappearance of the sarcoplasm with retained reticular skeleton of the myocardium >> no inflammatory reaction >> scarring through collapse and condensation of residual sarcolemmata and reticular fibers

  - *Coagulation myocytolysis*: tetanic cell death on metabolic basis; cellular necrosis in irreversible contraction; in pheochromocytoma, after heart transplantation, electric shock

Myocardial infarction

Myocardial infarction

Definition

- *acute*: myocardial necrosis localized to a circumscribed area of coronary blood supply, resulting from an acute ischemic insult exceeding the ischemic reserve capacities of the heart muscle tissue.
- *chronic*: cardiac muscular scarring over 1 cm in diameter

Classification according to extension

- regional extension
- transmural *versus* subendocardial

Epidemiology

- in the western world myocardial infarction is typically a disease of the 8th-9th decade of life

- dramatic difference in Hungary: myocardial infarction is typical under the age of 65! (hungarian data for the prevalence and mortality by myocardial infarction are 2.5x greater than those in the EU)

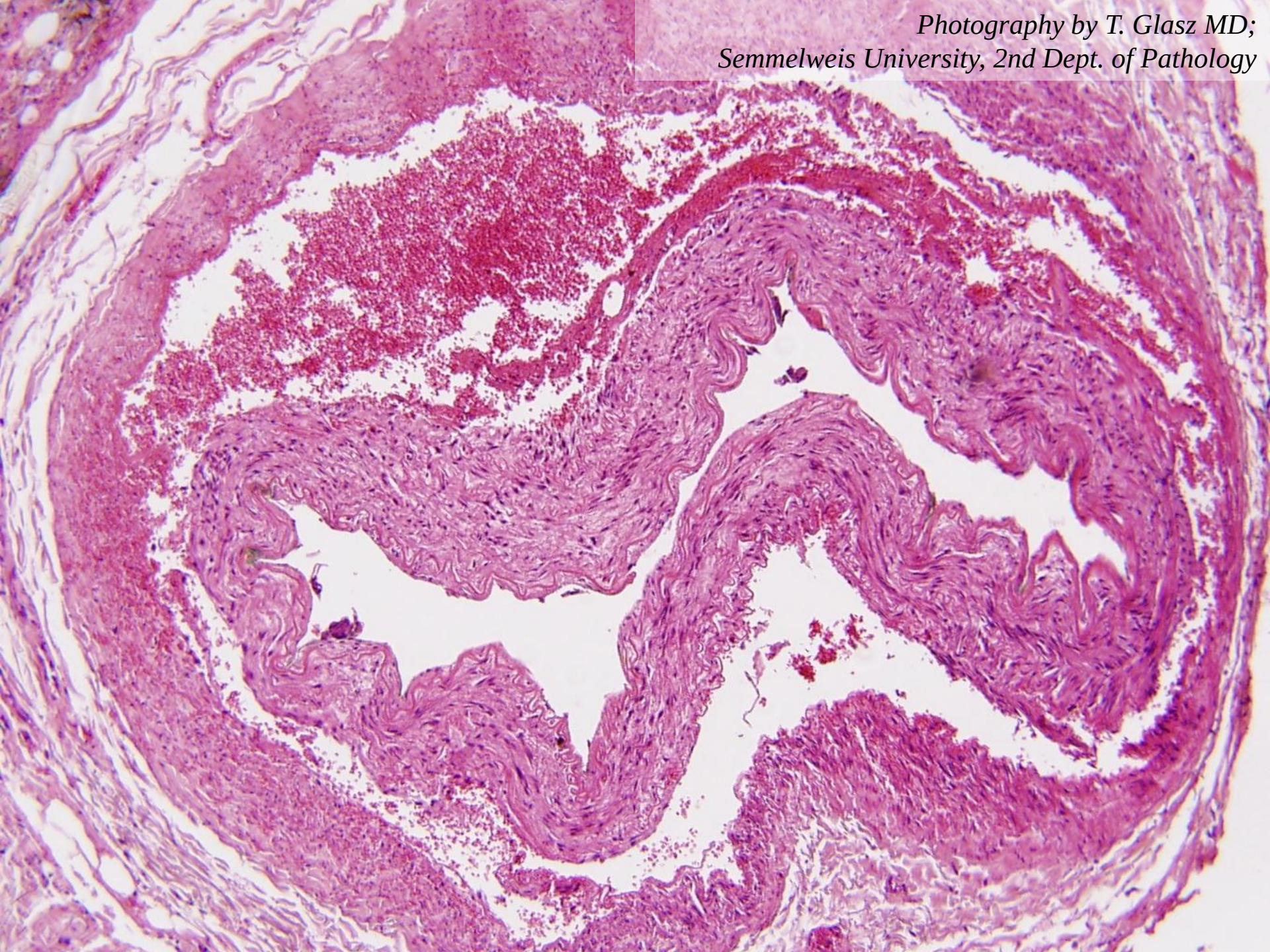
- women suffer a myocardial infarction 8 years later than men

Myocardial infarction

– Causes –

Causes of infarction are causes of the acute ischemic insult

- **high-grade coronary arteriosclerosis** (especially the so-called unstable plaques with complication: rupture, hemorrhage)
- coronary arterial dissection
- coronary embolism (very rarely)
- intermediate coronary arteriosclerosis with relative hypoxic periods (pneumonia, body exercise, low pO_2 of air)
- extreme stress


Photography by T. Glasz MD;
Semmelweis University, 2nd Dept. of Pathology

Transmural myocardial infarction

- Infarction through the entire thickness of the myocardial wall: from endocardium to epicardium/subepicardial fat tissue

- 5 possible localisations:
  - anterior
  - posterior
  - lateral
  - septal
  - circular

Anterior transmural myocardial infarction

- cause is an occlusive insult in the left anterior descending (LAD) branch

- 40-50% of all infarctions

- most frequent localisation: apical part of the anterior wall and ventral two-thirds of the septum

Posterior transmural myocardial infarction

- cause is an occlusive insult in the right coronary artery (RCA), or in the circumflex artery (RCX)

- 20-30% of all infarctions

- infarctions are especially large, if the dominant artery is the RCA

- topographical extension: posterior wall of the left ventricle, dorsal third of the septum, sometimes the paraseptal part of the right ventricular posterior wall

Lateral transmural myocardial infarction

- cause is an occlusive insult in the circumflex artery (RCX),or in the marginal artery

- 15-20% of all infarctions

Circular transmural myocardial infarction

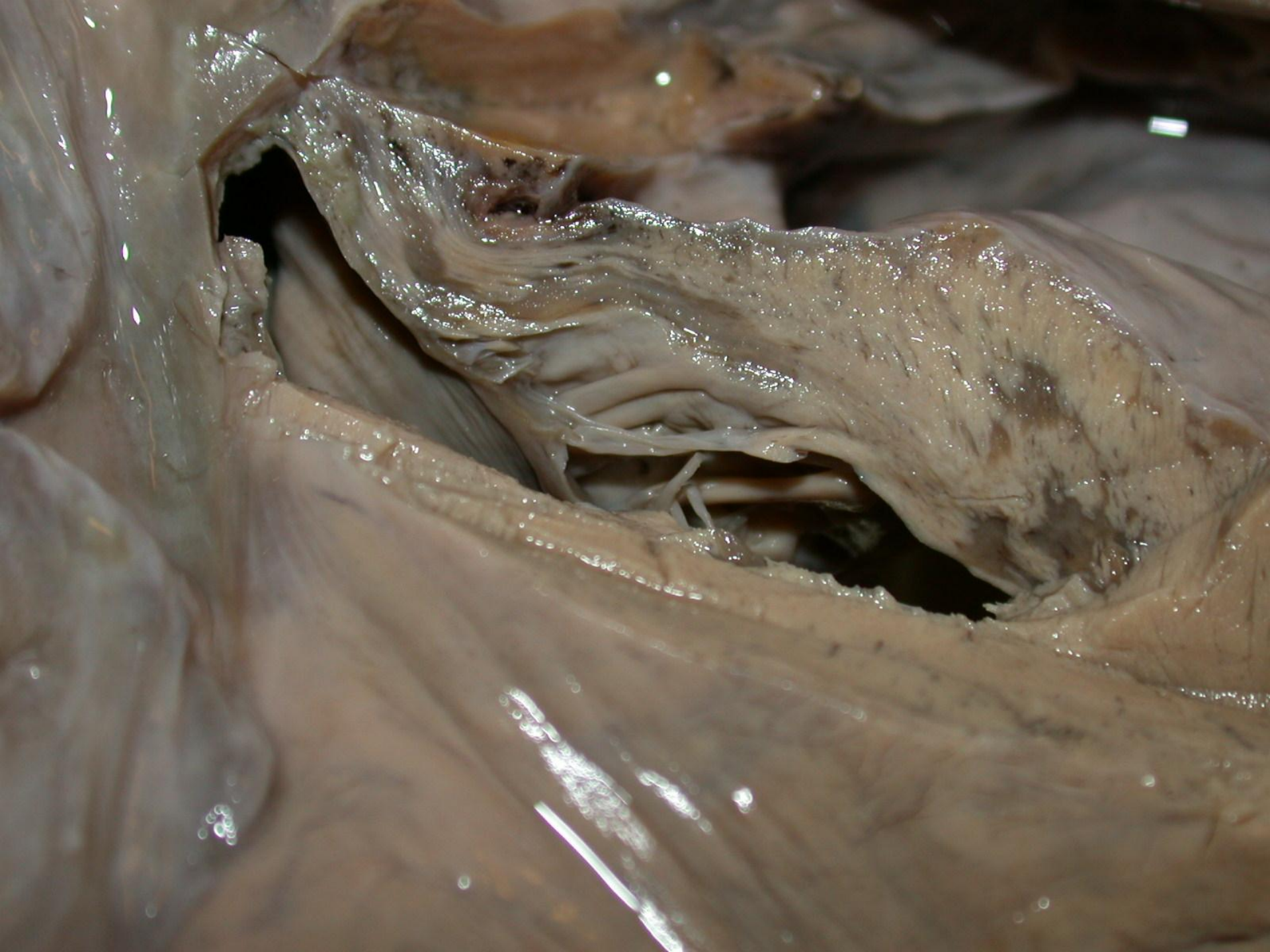
- cause is synchronic or subsequent occlusive insults in possibly 2-3 main branches within the time frame of a few hours
- very rare
- topographical extension: 60-75% of the left ventricular myocardium

Septal transmural myocardial infarction

- cause is an occlusive insult in the coronary artery branch responsible for the supply of the affected myocardial area

- very rare

- yet a minute focus of an infarction in this area can be lethal, if localized on the innervation conducting system (esp. upper third of the muscular septum) >> complete electro-mechanical block >> so-called malignant arrhythmias

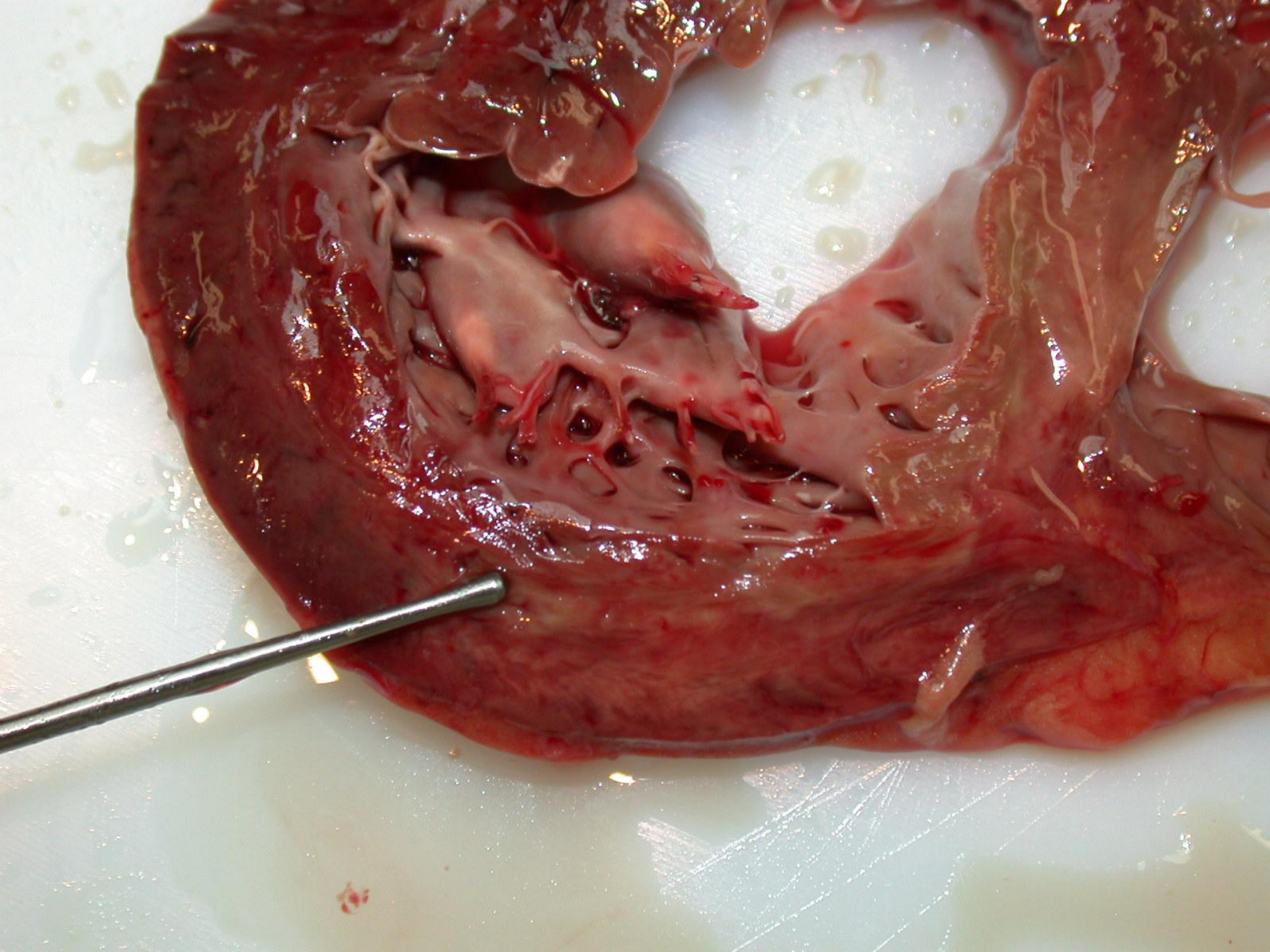


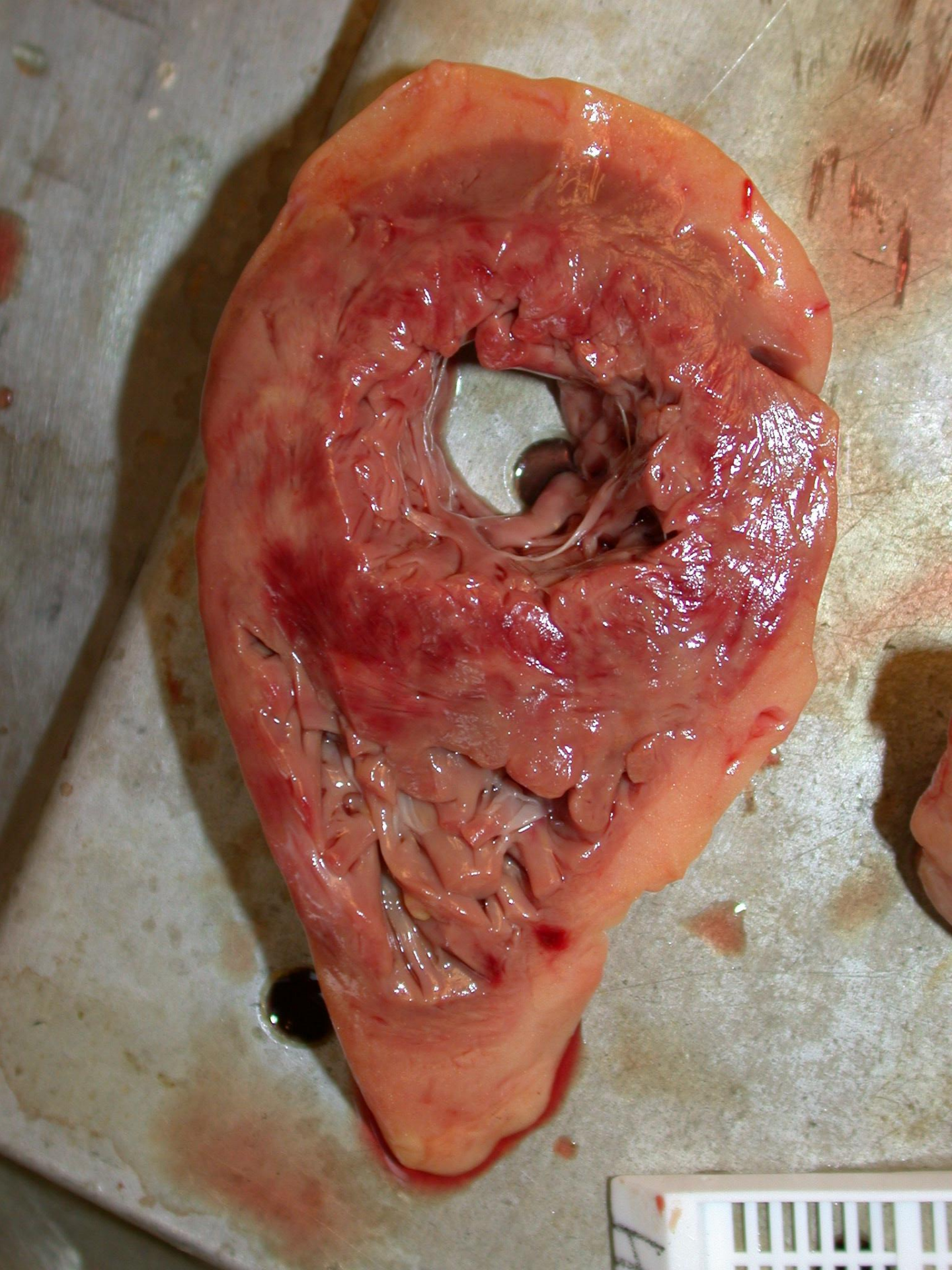
Developmental phases of myocardial infarction

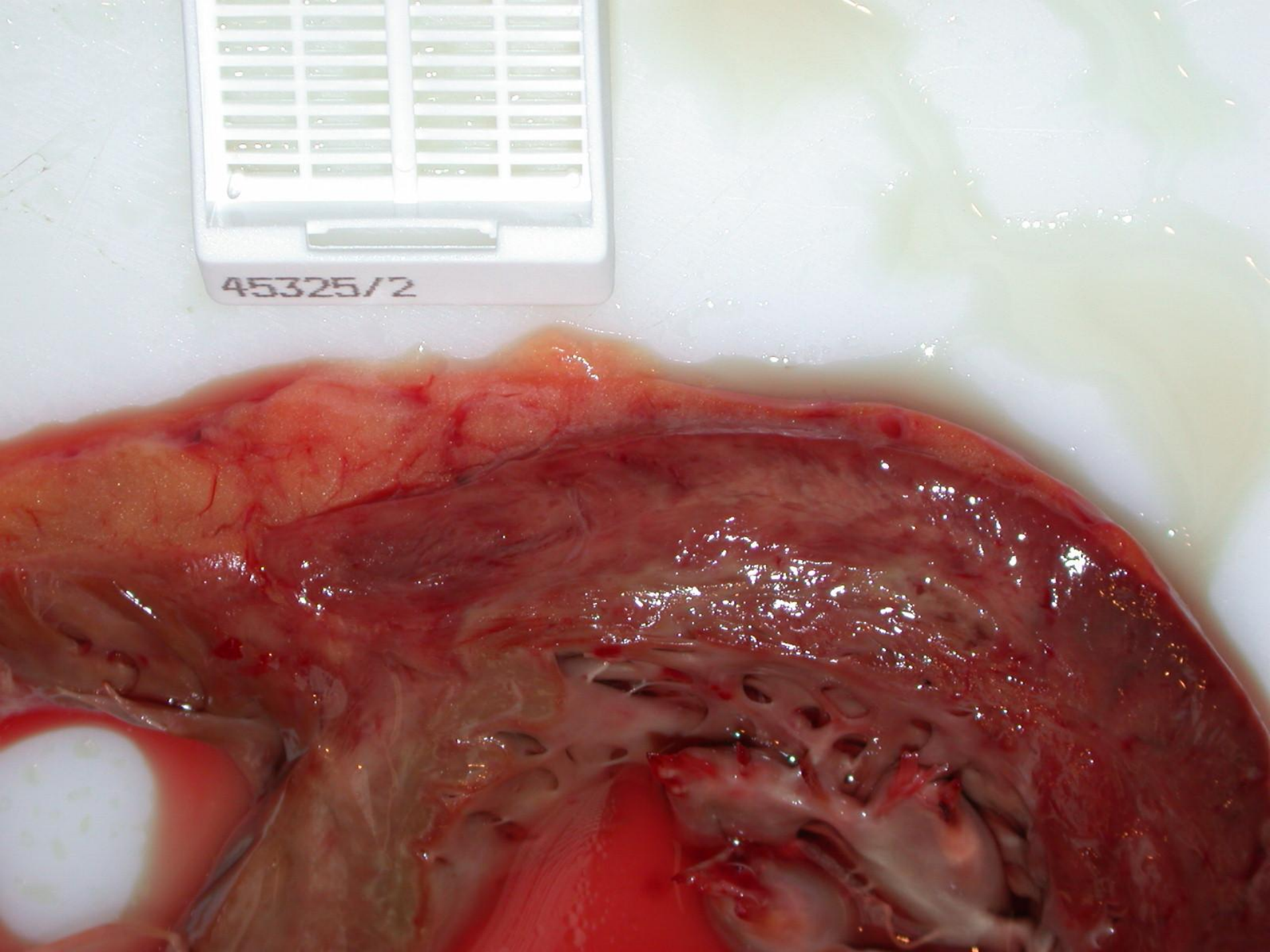
Postinfarctional periods:

- 5-6 hours: *microscopically* swelling of fibers with intact striation. Nuclei pale, swollen, ruptured, lobulated. Interstitium yet intact. *Macroscopically* no visible alterations. *Clinically* rescue manoeuvers for saving the necrobiotic (dying) myocardium yet possible (e.g. thrombolytic therapy)

- 15 hours: *microscopically* lengthening, thinning and meandering of necrotic muscle fibers. *Macroscopically* the first alterations appear : Paling and slight swelling of the affected myocardial area.





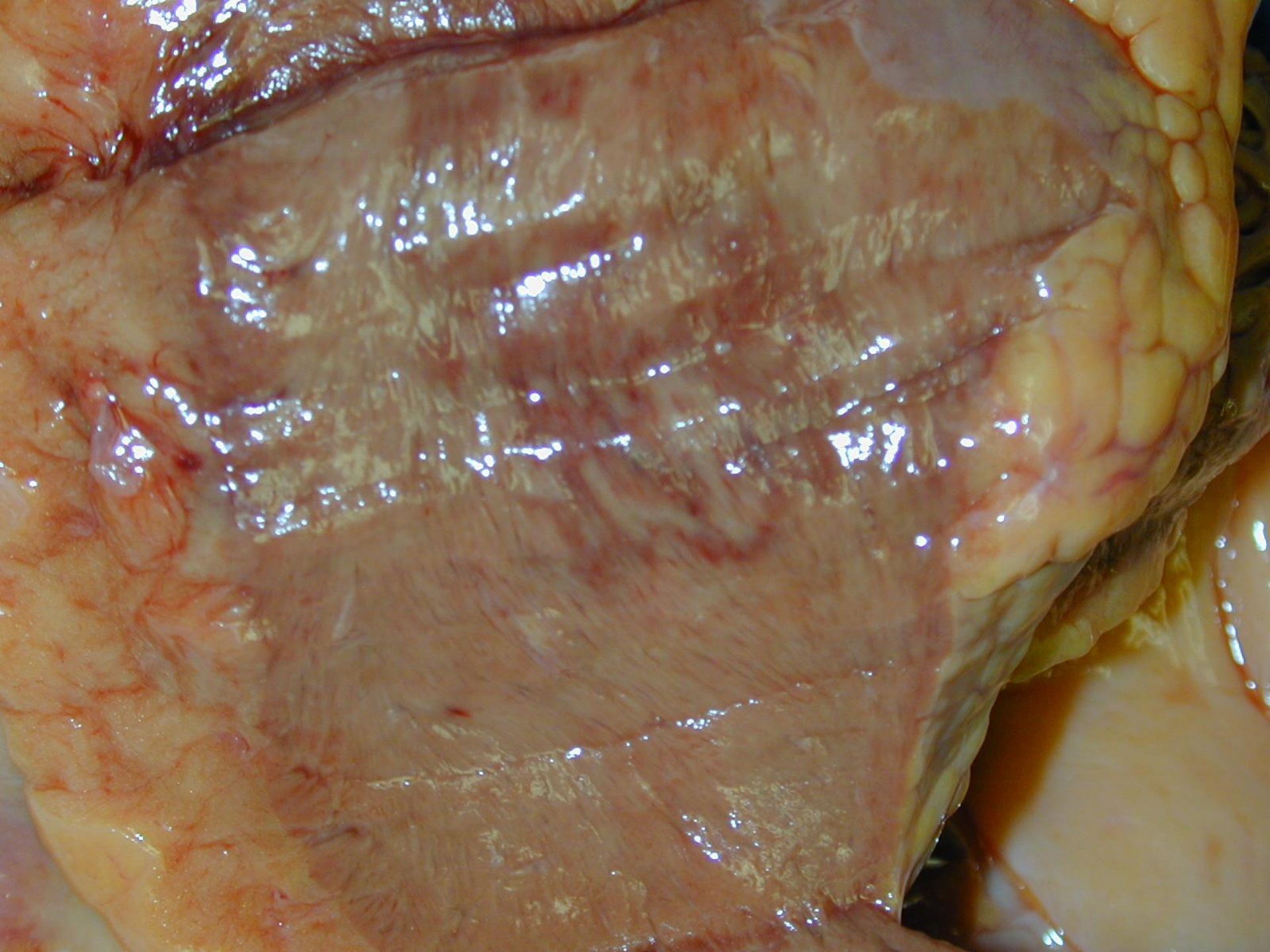

45325/2

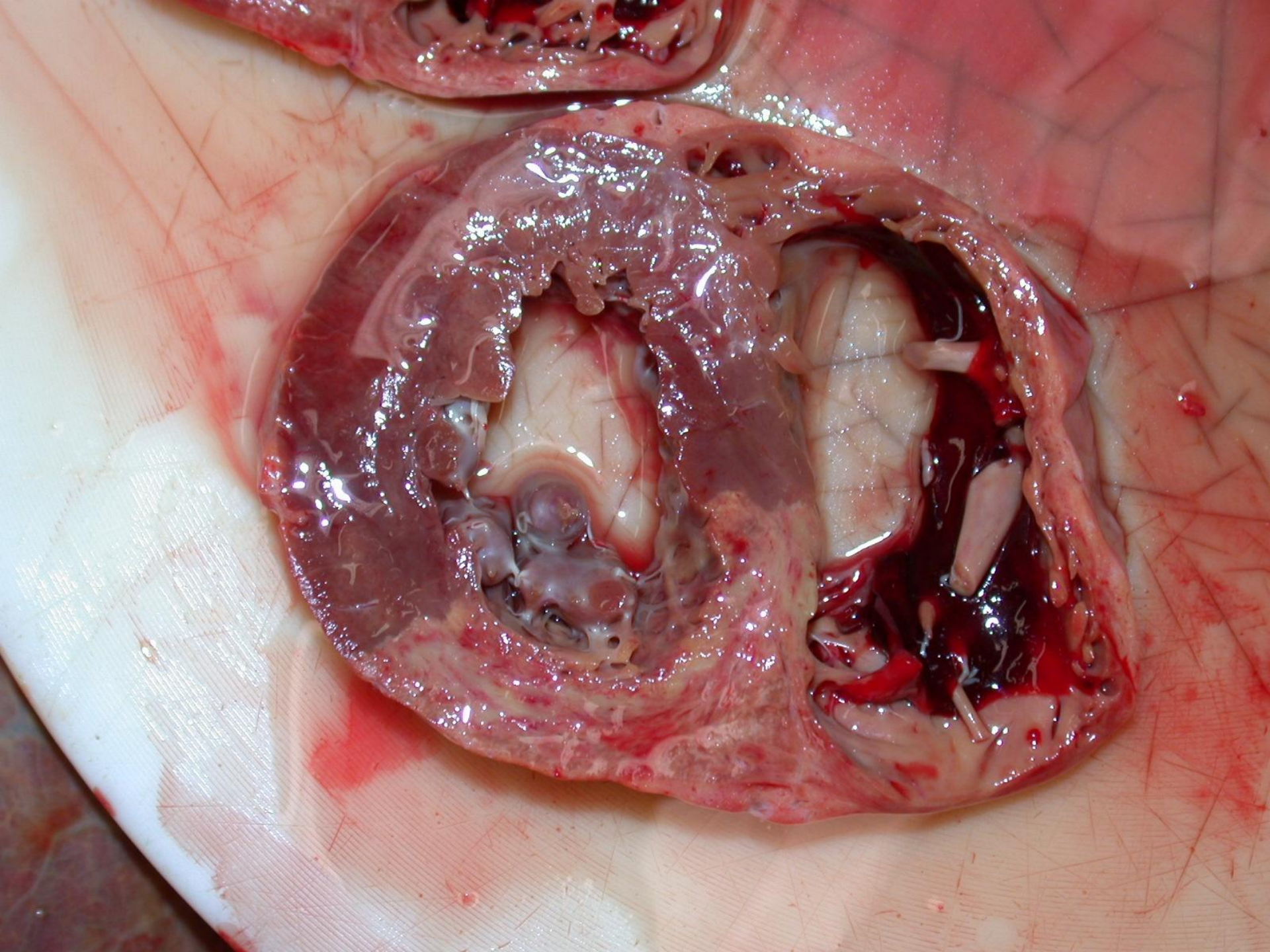
Developmental phases of myocardial infarction

Postinfarctional periods:

- 36 hours: *macroscopically* are the central infarction areas already slightly yellowish. Peripherally develops a hemorrhagic zone of demarcation.

- 3-4 days: *macroscopically* is the infarcted area clayish yellow with geographically irregular periphery and hemorrhagic demarcation. Synchronously (1-5. postinfarction day) the cytoplasmic striation of the myocytes disappear *under the microscope* with accompanying homogenesation and hypereosinophilia. Nuclear decoloration progresses. The interstitial connective tissue fibers undergo fragmentation. Infiltration of growing numbers of granulocytic inflammatory cell elements.



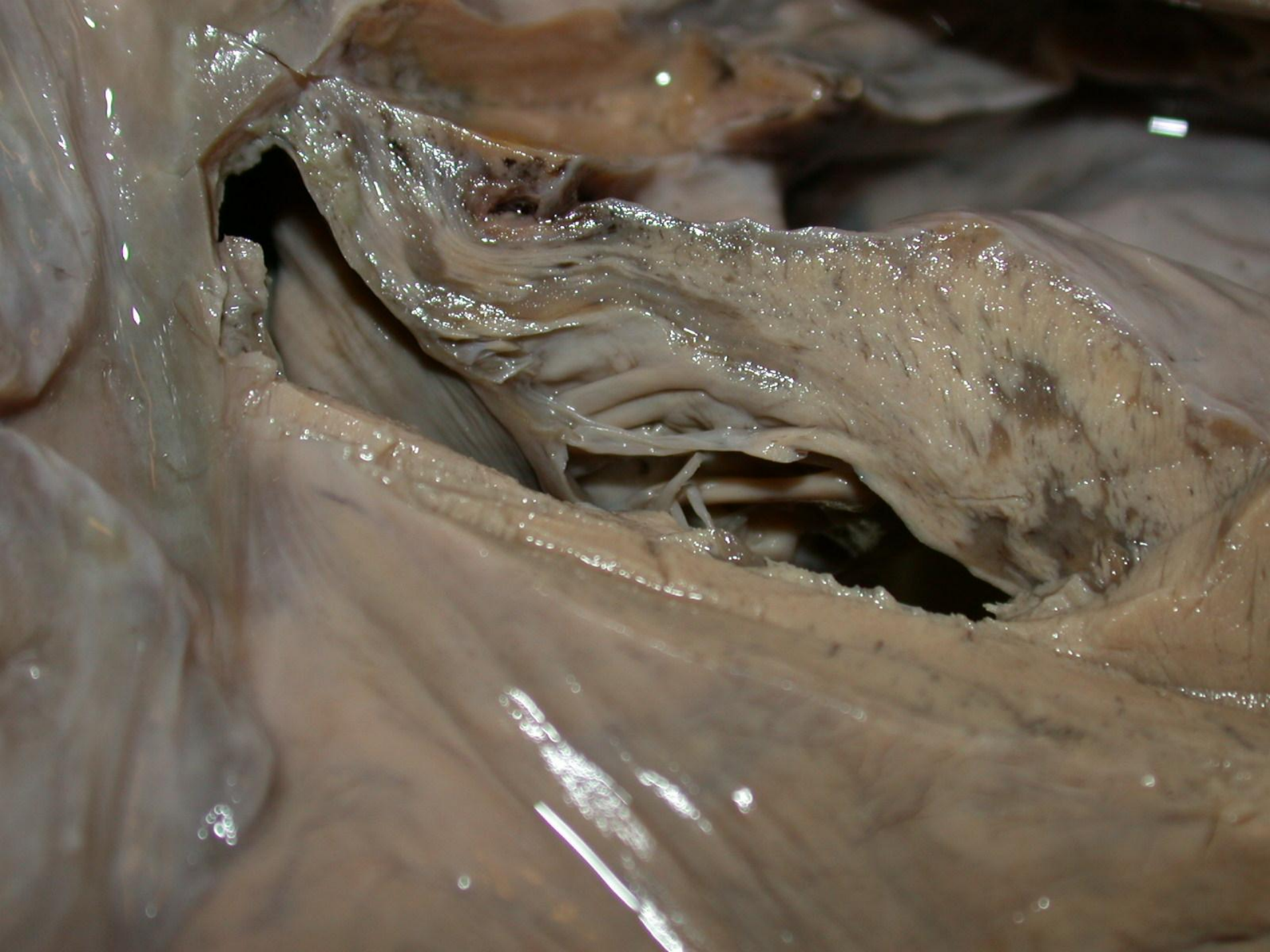


Developmental phases of myocardial infarction

Postinfarctional periods:

- 1 week: *microscopically* phagocytosis of the necrotic tissue begins with gathering of macrophages and fibroblasts. Highest danger of a myocardial rupture!

- 2 weeks: *microscopical* signs of reparation develop with laterally beginning granulation. Granulocytes disappear to give place for lymphocytes, plasmacells and eosinophils. At the same time (10. postinfarction day) the infarction zone turns *macroscopically* greyish with fading demarcation and signs of shrinking.

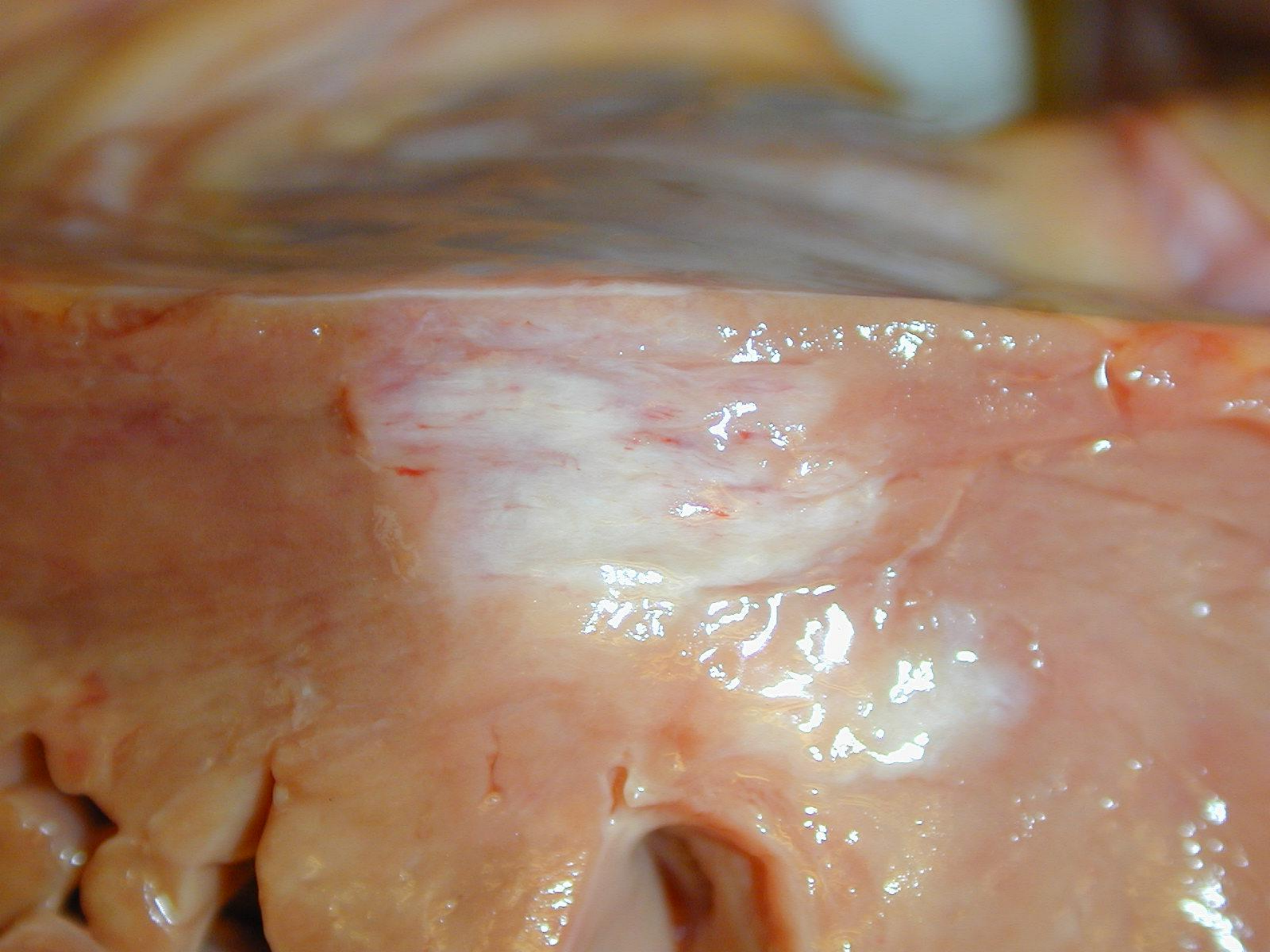


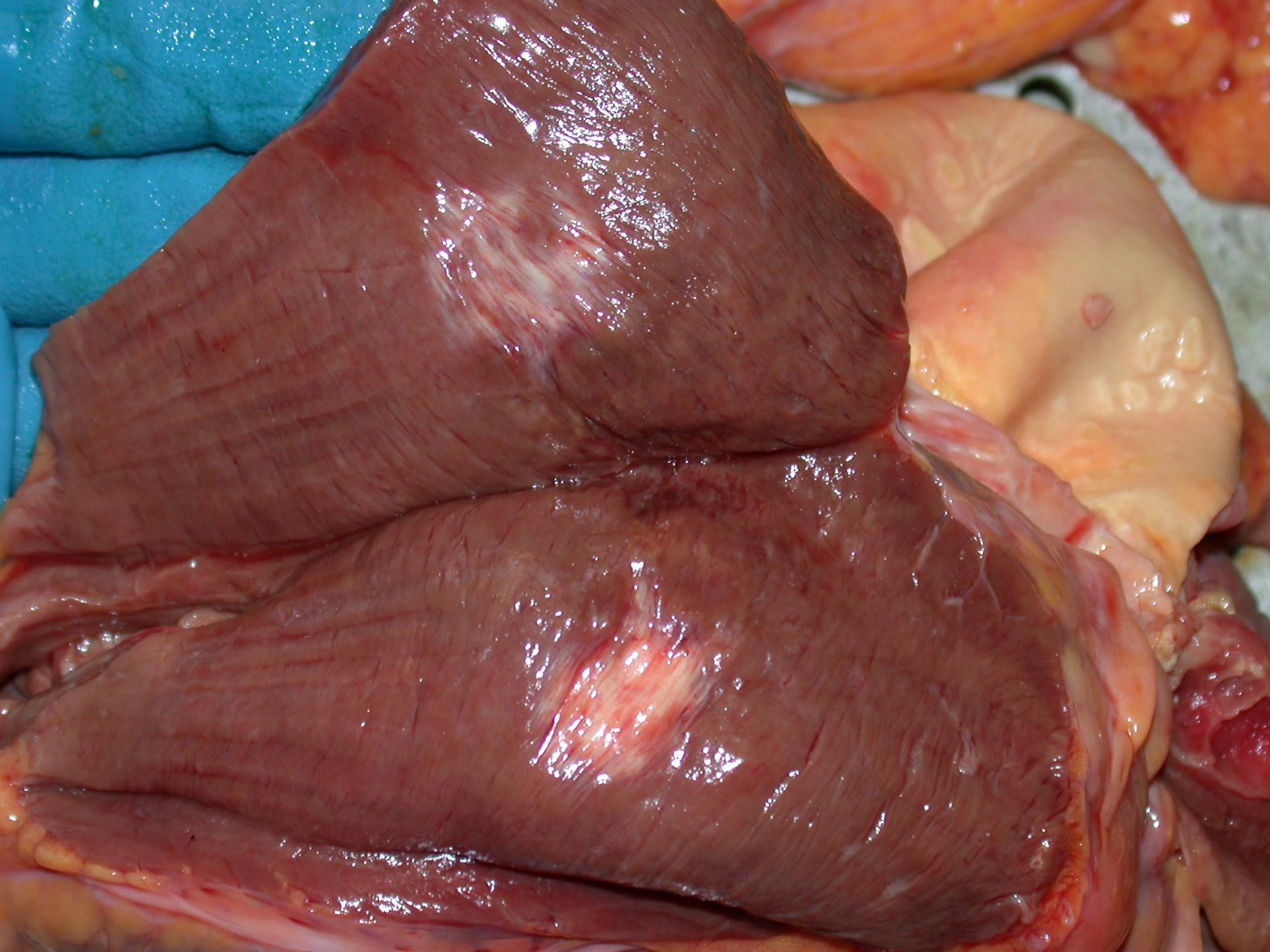
Developmental phases of myocardial infarction

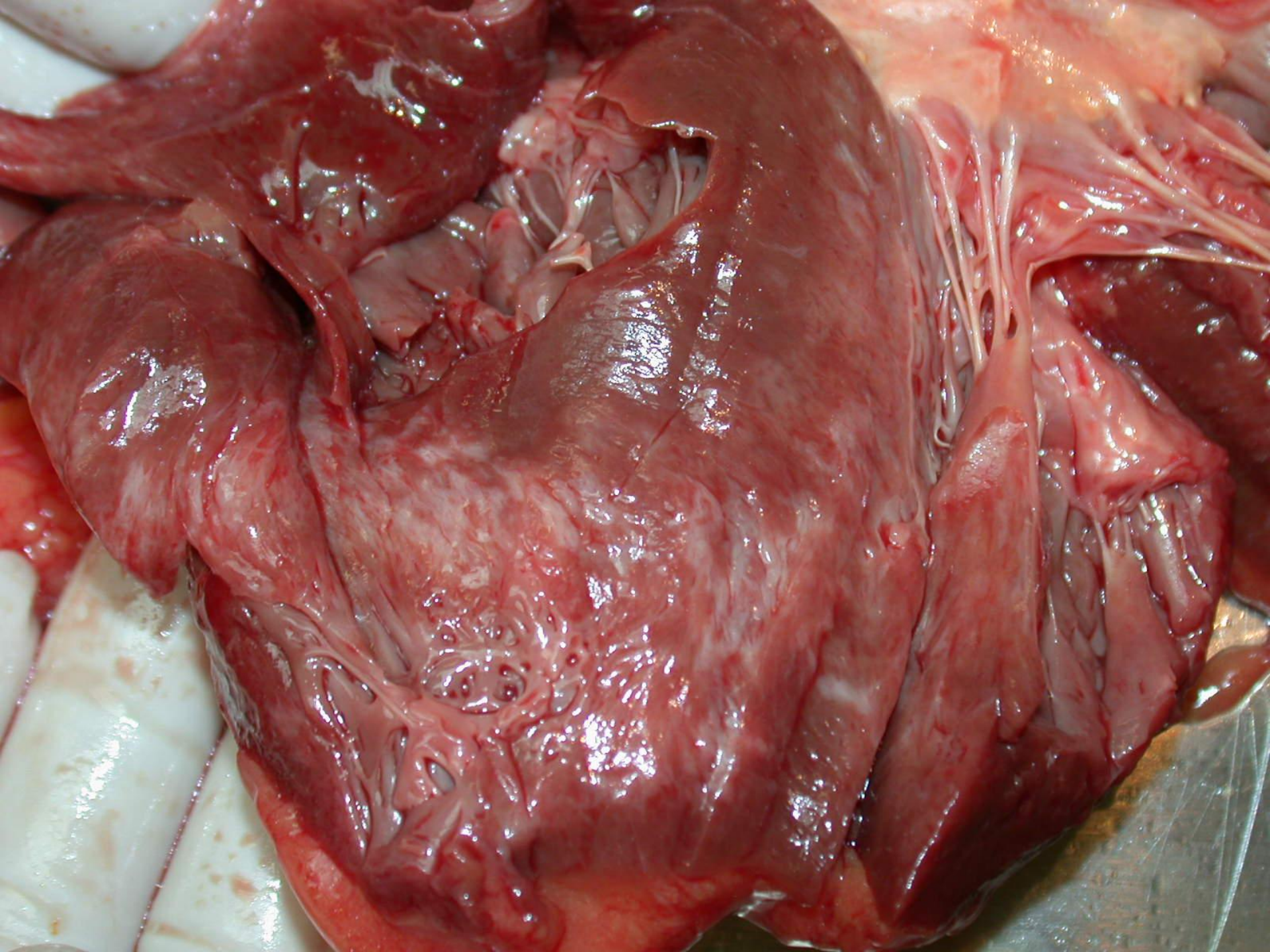
Postinfarctional periods:

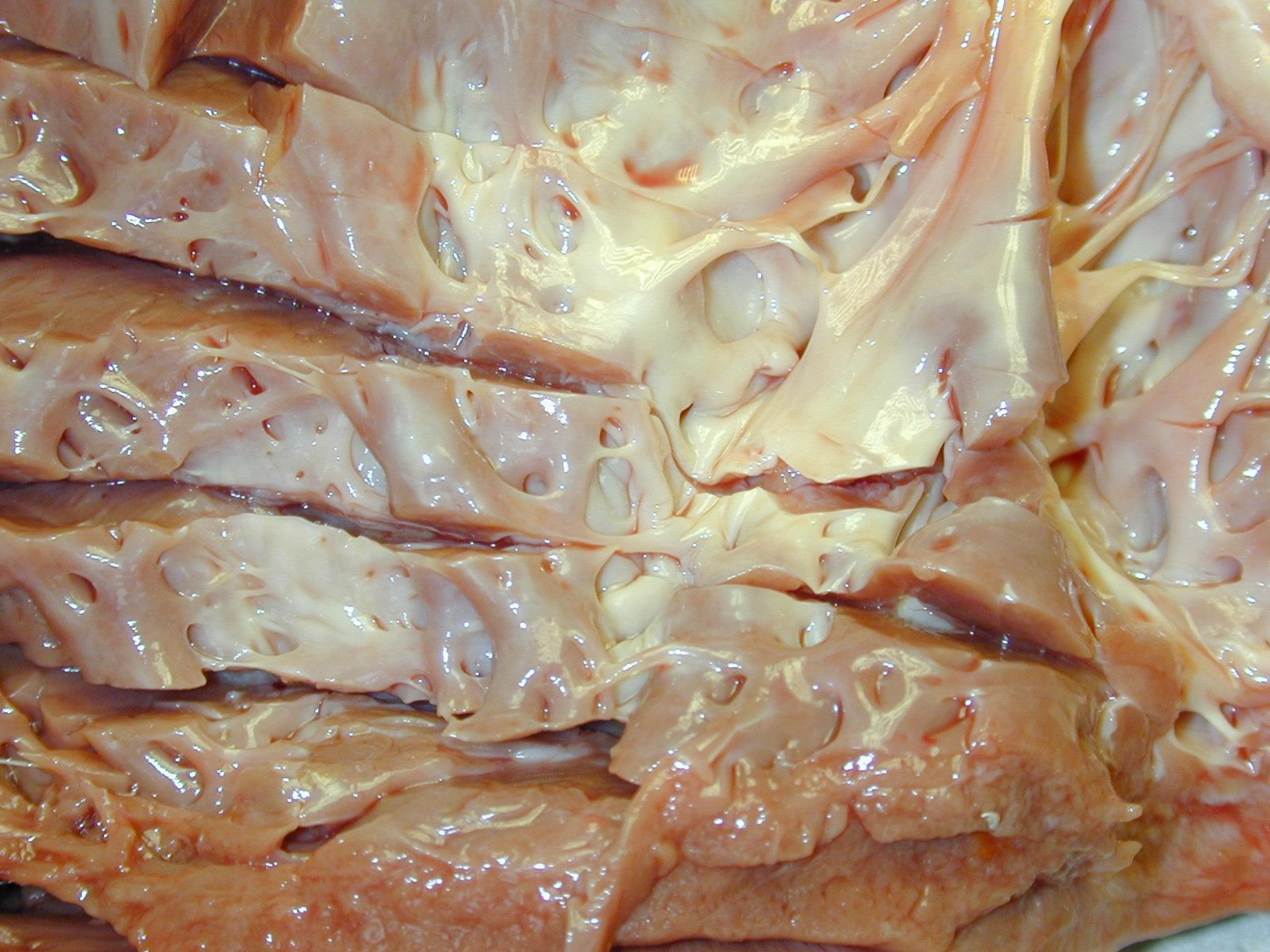
- 3 weeks: resulting from fibroblastic activity granulation tissue will be *microscopically* replaced by a loose connective tissue, with a collagen content growing with time.

- 6 weeks: final stage both *micro- and macroscopically* with development of scar tissue.









Paradox myocardial infarction

- *Definition:* acute myocardial infarction, that with respect to its age does not correspond to the occlusion of its relevant supplying artery (supplying artery with *chronic* occlusion, whereas *acute* infarction in the corresponding myocardial area)

- *Prerequisite anatomy*: well functioning collateral communications between supplied myocardial areas.

- *Mechanism of pathogenesis*: blood supply of a myocardial area of a coronary artery with *chronic* occlusion is done by collaterals from one of the neighbouring areas >> acute occlusion (e.g. thrombosis) of the supplying artery of the neighbouring area >> *acute* myocardial infarction of the area with *chronic* coronary occlusion

Progressiv myocardial infarction

- *Definition:* acute myocardial infarction, developping peripheral to a chronic infarction area

- *Mechanism of pathogenesis* : derangement of the perifocal (periinfarctional) microcirculation, or backward growing of the coronary thrombosis >> growing extension of the infarction with always newly involved infarction zones >> so-called *wavefront-phenomenon*

Subendocardial myocardial infarction

- *Definition:* a myocardial infarction limited to the inner (subendocardial) third of the ventricular wall

- the subendocardium represents a ‘strategic zone’ of the myocardium: highest interstitial pressure within the whole myocardium >> microcirculation is periodical: only possible during diastole, whereas capillary blood supply ceases during systole >> limited oxygenisation reserves of subendocardium

- in coronary heart disease the subendocardium is the most vulnerable area

Subendocardial myocardial infarction

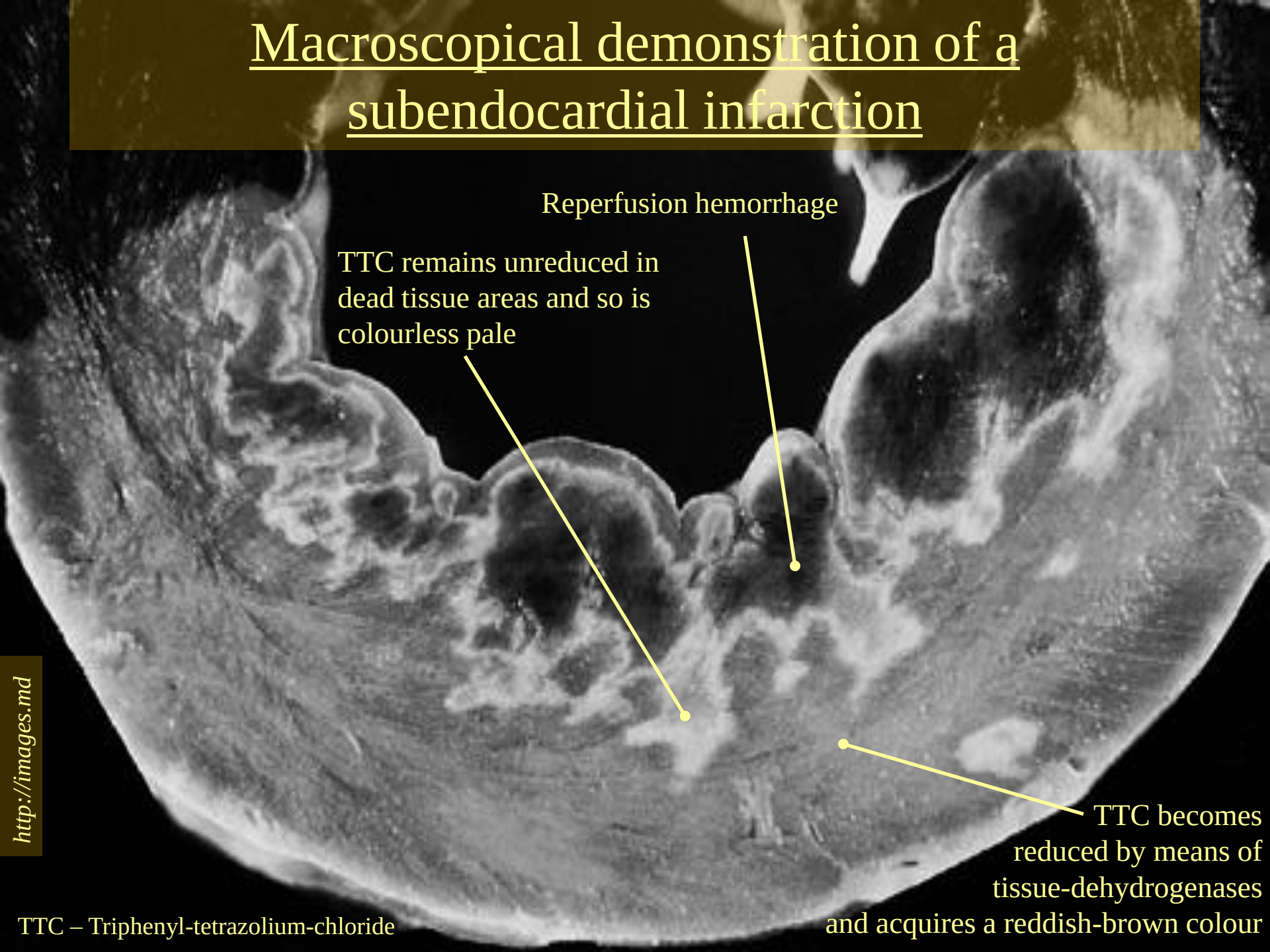
- *microscopically:* patchy picture with microinfarctions as large as 10 mm, liquefaction- and coagulation myocytolyses beside normal myocytes

- *macroscopically*: geographically irregular, partially fading peripheral zones

- reparation already in the 1. postinfarction week and from the richly vascularised granulation tissue quickly develops the subepicardial scarring

- by means of a *wavefront*-mechanism out of a subendocardial infarction can develop a transmural one.

Macroscopical demonstration of a subendocardial infarction



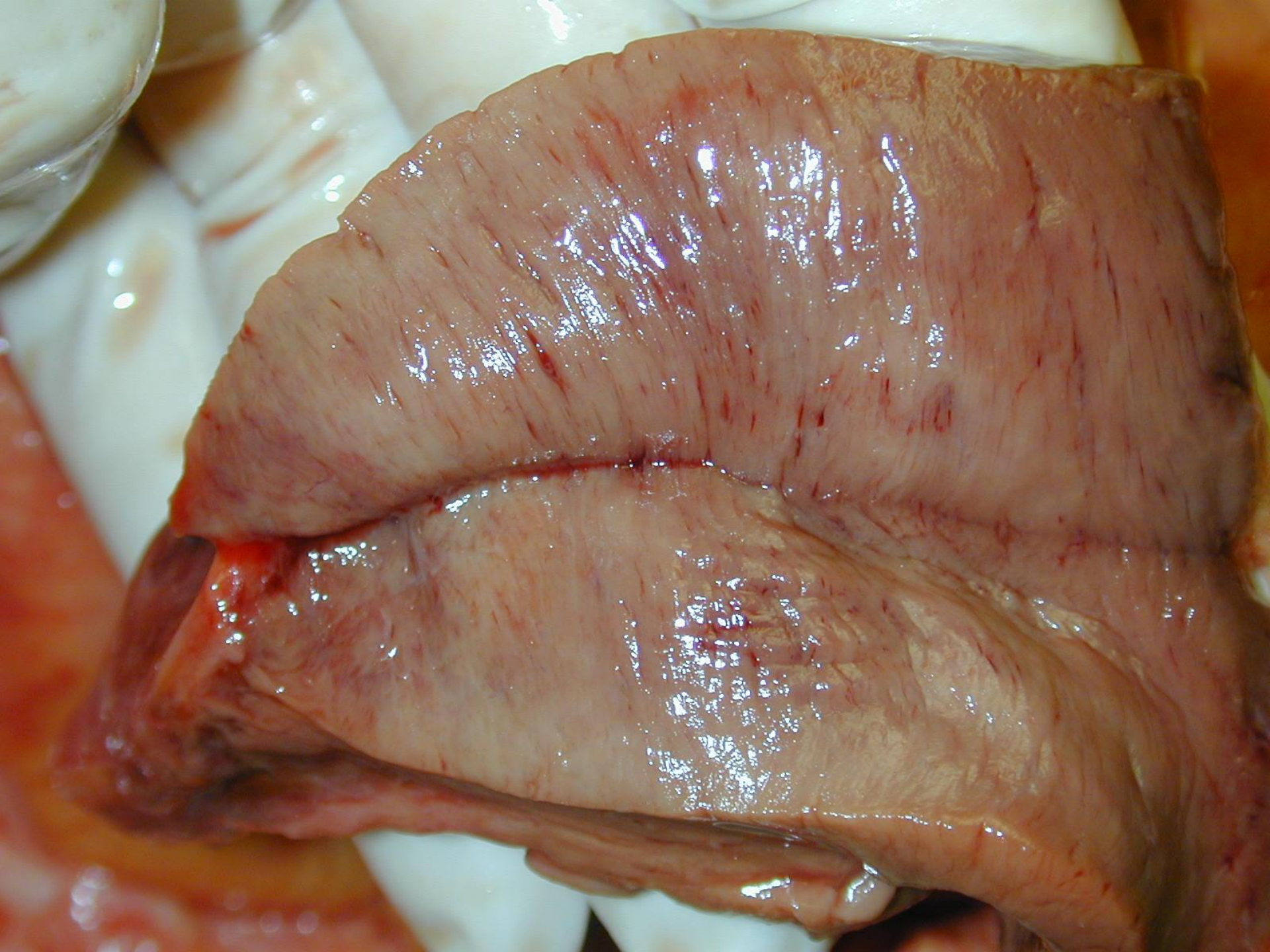
http://images.md

TTC – Triphenyl-tetrazolium-chloride

Complications of a myocardial infarction: left heart failure and cardiogenic shock

- failure of the left ventricular pump function from a slight congestion through severe circulatory insufficiency to a cardiogenic shock

- *background*: electro-mechanic dissociation (electric catastrophy – yet with a minute infarction in the upper septum!); ventricular fibrillation; with widely extended infarction there remains only an insufficient quantity of working musculature >> an infarction involving at least 40% of the left ventricular myocardium causes **cardiogenic shock**



Complications of a myocardial infarction: left heart failure and cardiogenic shock

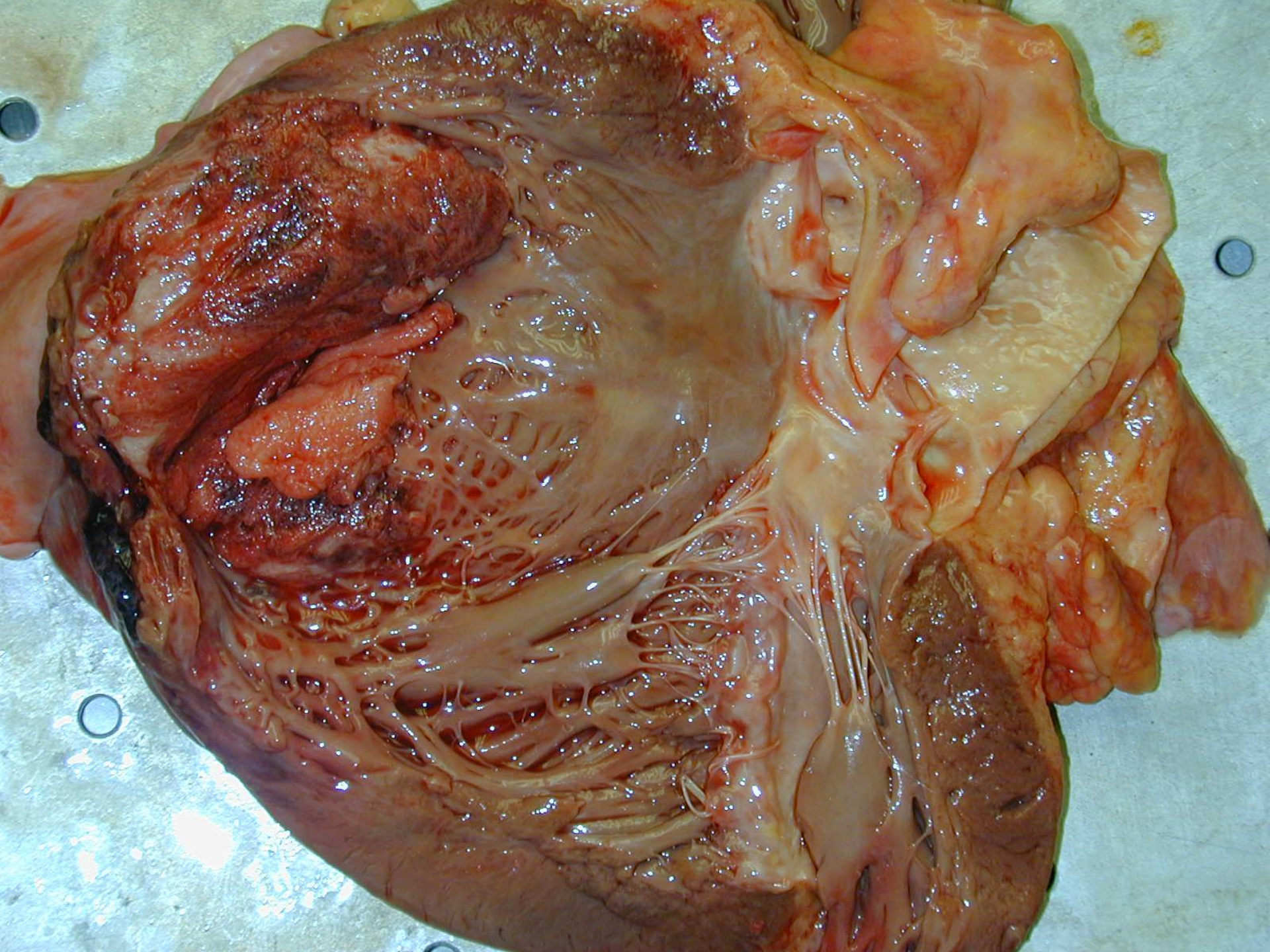
- *vitious circle of cardiogenic shock*: pump insufficiency with lower circulatory volume >> enhanced sympathetic tonus >> systemic vasoconstriction >> further hemodynamic overload of the heart
- *clinical appearance*: dyspnoe; pulmonary edema to the extreme of an *asthma cardiale*; drop of blood pressure; skin paleness with 'cold sweat'; acrocyanosis; oliguria; derangement of cerebral functions
- cardiogenic shock develops in some 10% of patients with infarction and is generally a complication of the 2. or 3. subsequent heart attack
- mortality of cardiogenic shock is dramatically high: 80% with, and 90-100% without therapy

Complications of a myocardial infarction: left ventricular aneurysm

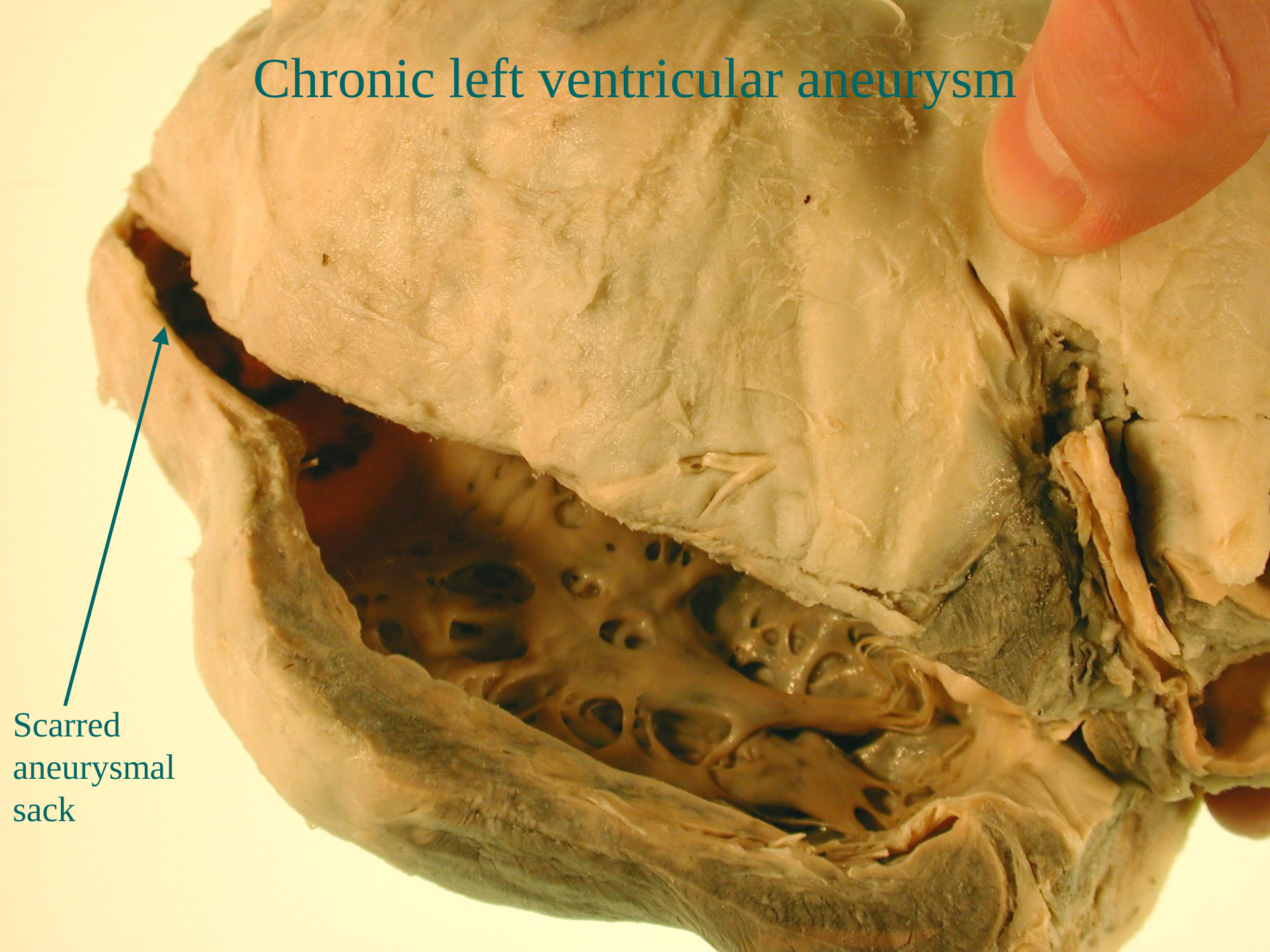
- *Definition*: variable degree of ventricular wall thinning and sacculation
- *Frequency*: develops in 15% of patients with infarction
- *Background*: infarcerated myocardium or postinfarctional scar tissue represents low mechanic resistence >> gradual outbulging (sacculation) of the affected area >> ventricular aneurysm
- *acute ventricular aneurysm*: in the acute phase of infarction (during the 1. postinfarctional week, in the phase of dead tissue degradation by means of macrophages) >> often gives rise to a ventricular wall rupture!
- *chronic ventricular aneurysm*: after scarring of the infarcerated myocardial area (after months to years) – practically doesn't rupture

Complications of a myocardial infarction: left ventricular aneurysm

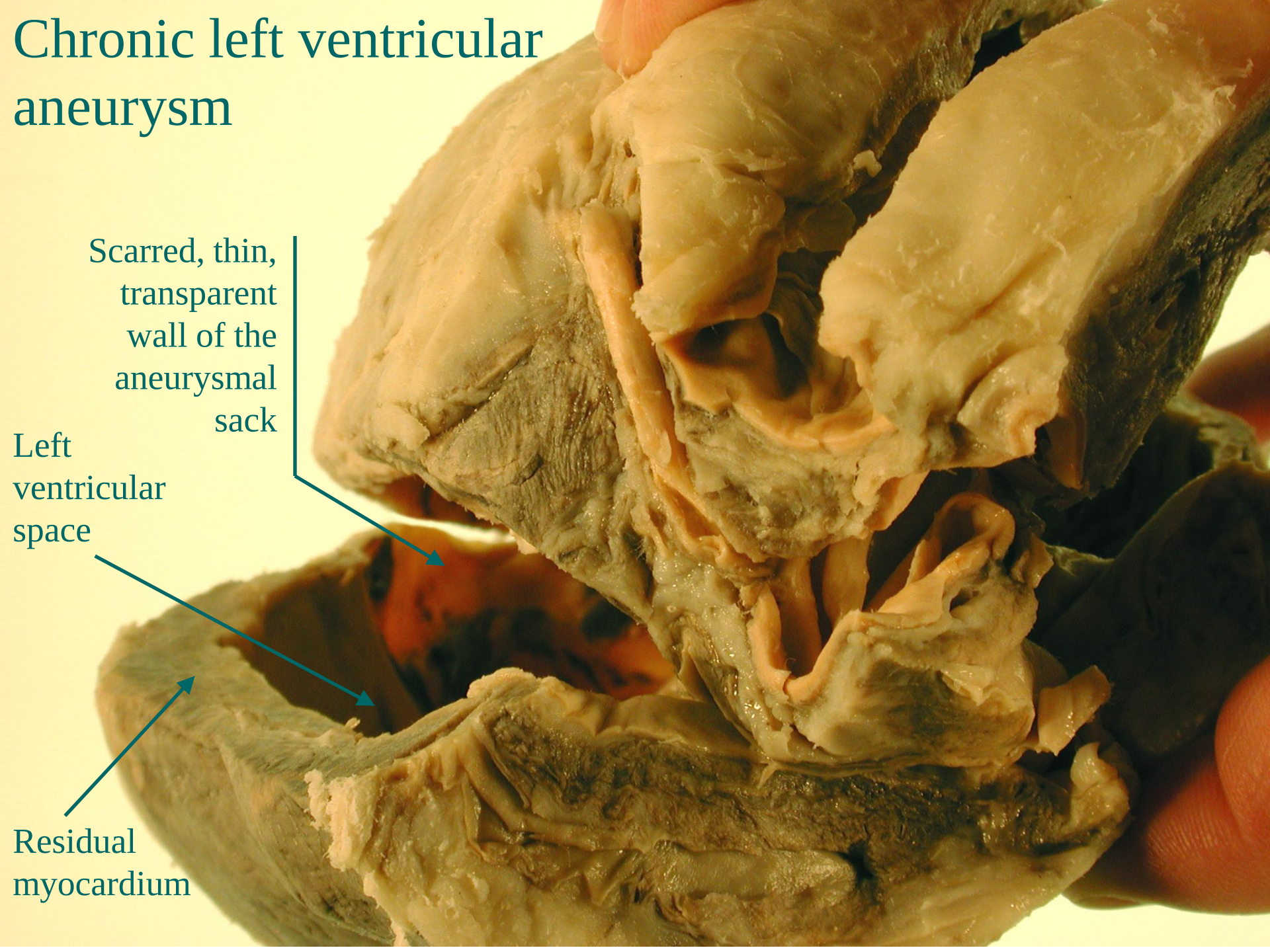
- derangements of myocardial motion capacities after infarction:
  - hypokinesis (impairment of muscular wall motility)
  - akinesis (complete arrest of myocardial movements in the affected area)
  - **paradox pulsation** – typical for ventricular wall aneurysms with large cavity comperable to the remaining lumen of the ventricle and a passive motion reversed to normal parietal pulsation >> blood volume oscillating between ventricular space and aneurysmal lumen >> enhanced work overload of the already damaged myocardium and further limitation of coronary blood flow >> left ventricular decompensation
- in the aneurysmal sack: thrombosis (50% of the cases) >> danger of embolisation (in 5% of cases)

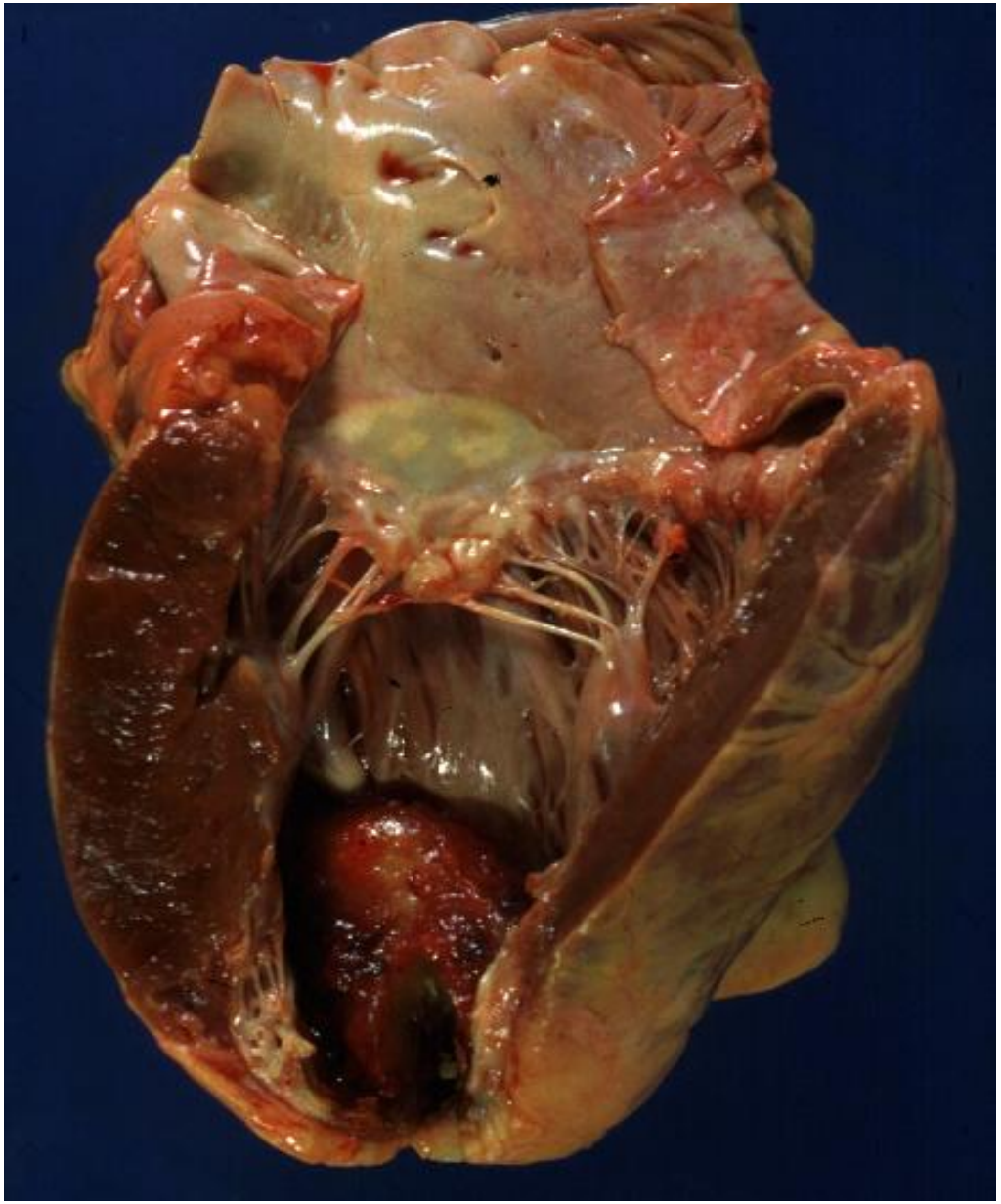


Chronic left ventricular aneurysm



Chronic left ventricular aneurysm



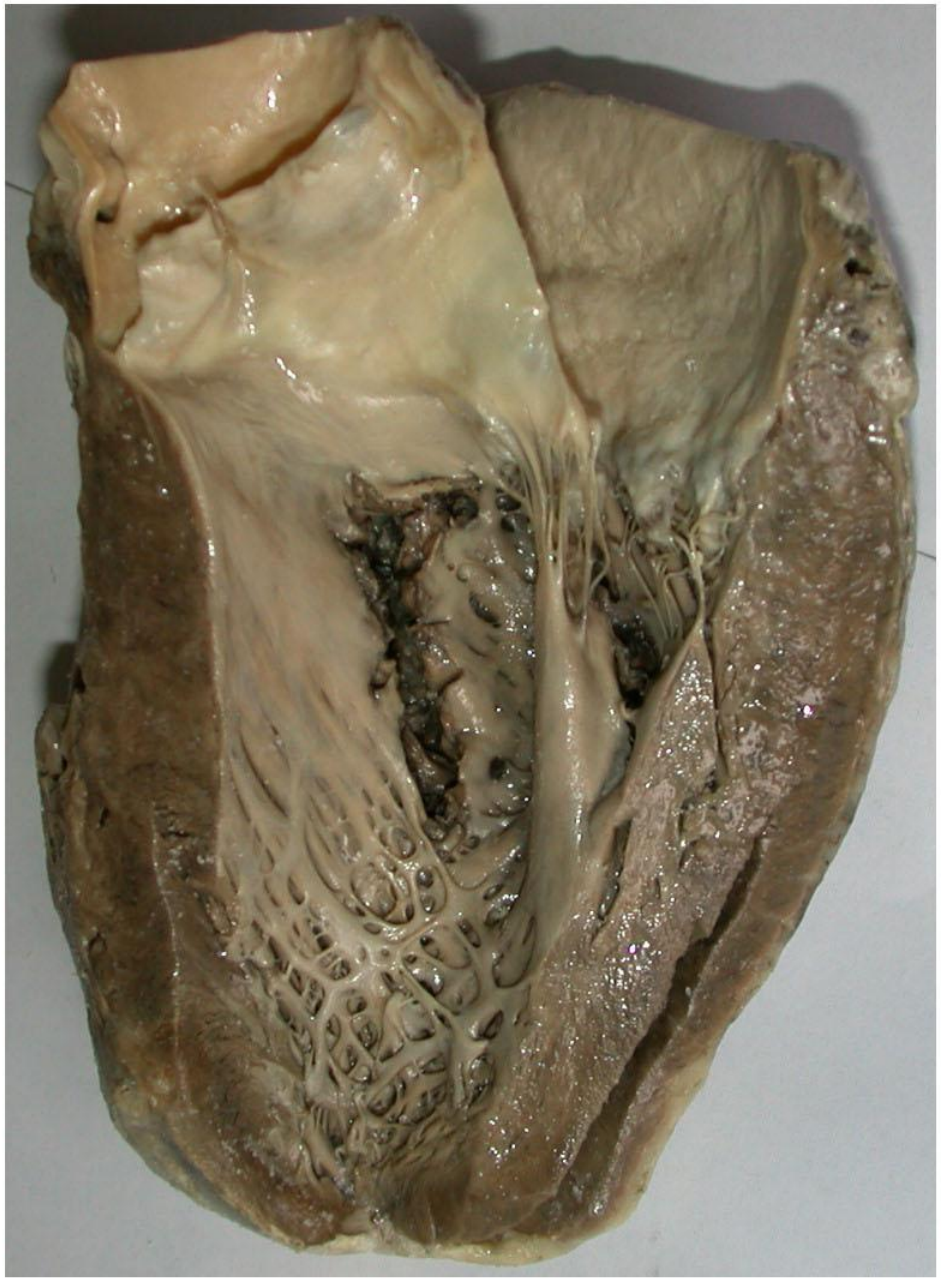


Complications of a myocardial infarction: septal rupture and defect

- *frequency*: 1-2% of all infarctions; in the 2-4. postinfarction day

- *drasticly progressing clinical picture*: anginal pain attack, hypotension, acute heart failure (possibly cardiogenic shock)

- *hemodynamically*: septal defect with a left-to-right shunt >> the left sided heart failure is quickly followed by a right heart failure. Furthermore, part of the oxygenated blood escapes to the right heart without supplying the coronary system. In complicated cases the pump function is further compromized by a damage of the conduction system >> severe arrhythmias or ventricular fibrillation.



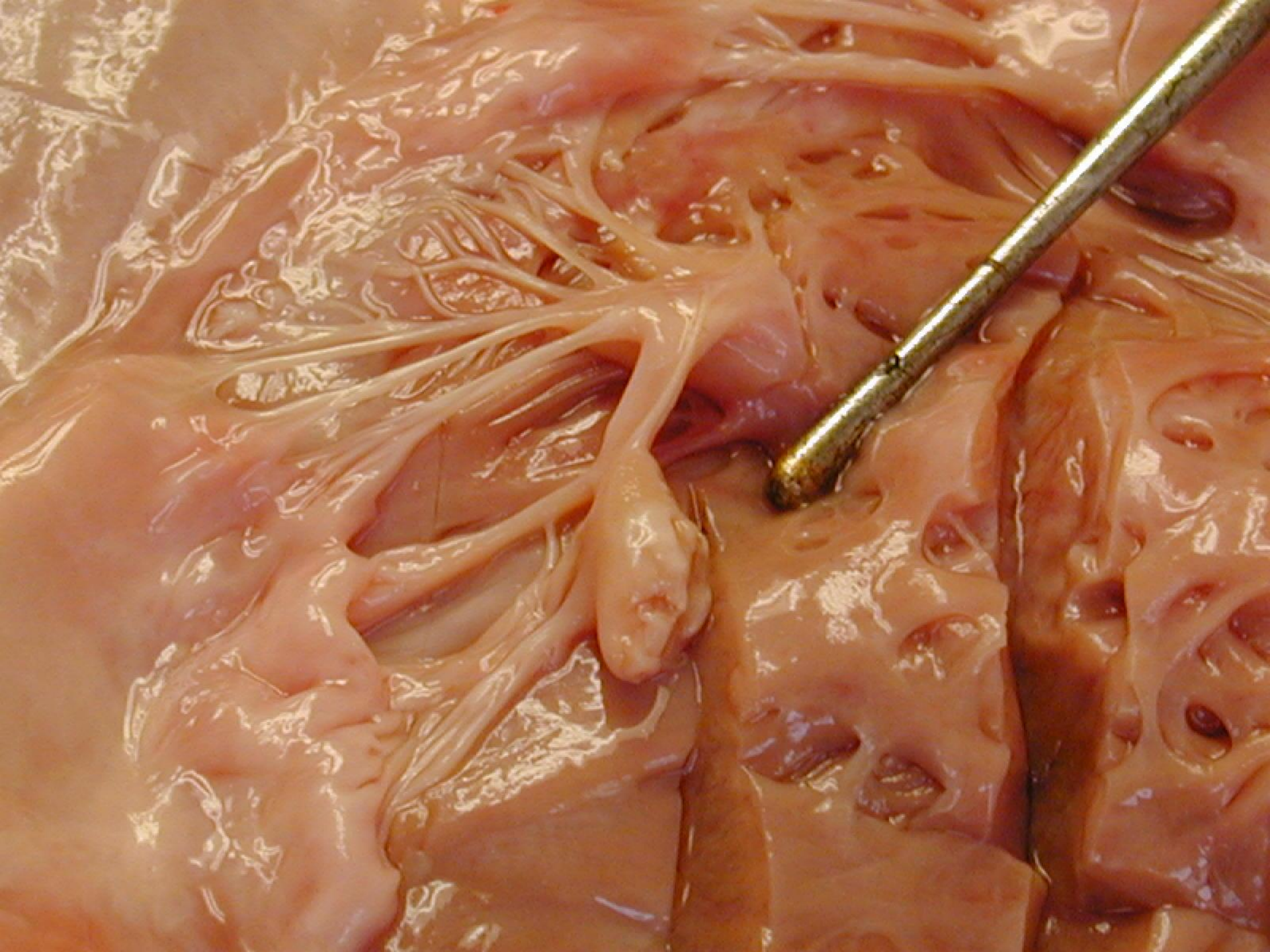
Complications of a myocardial infarction: papillary muscle dysfunction, rupture of cordae

- papillary muscles are from the metabolic, pathophysiologic and pathologic point of view part of the subendocardium

- functional derangement of the papillary muscles is to be detected already during attacks of *angina pectoris*

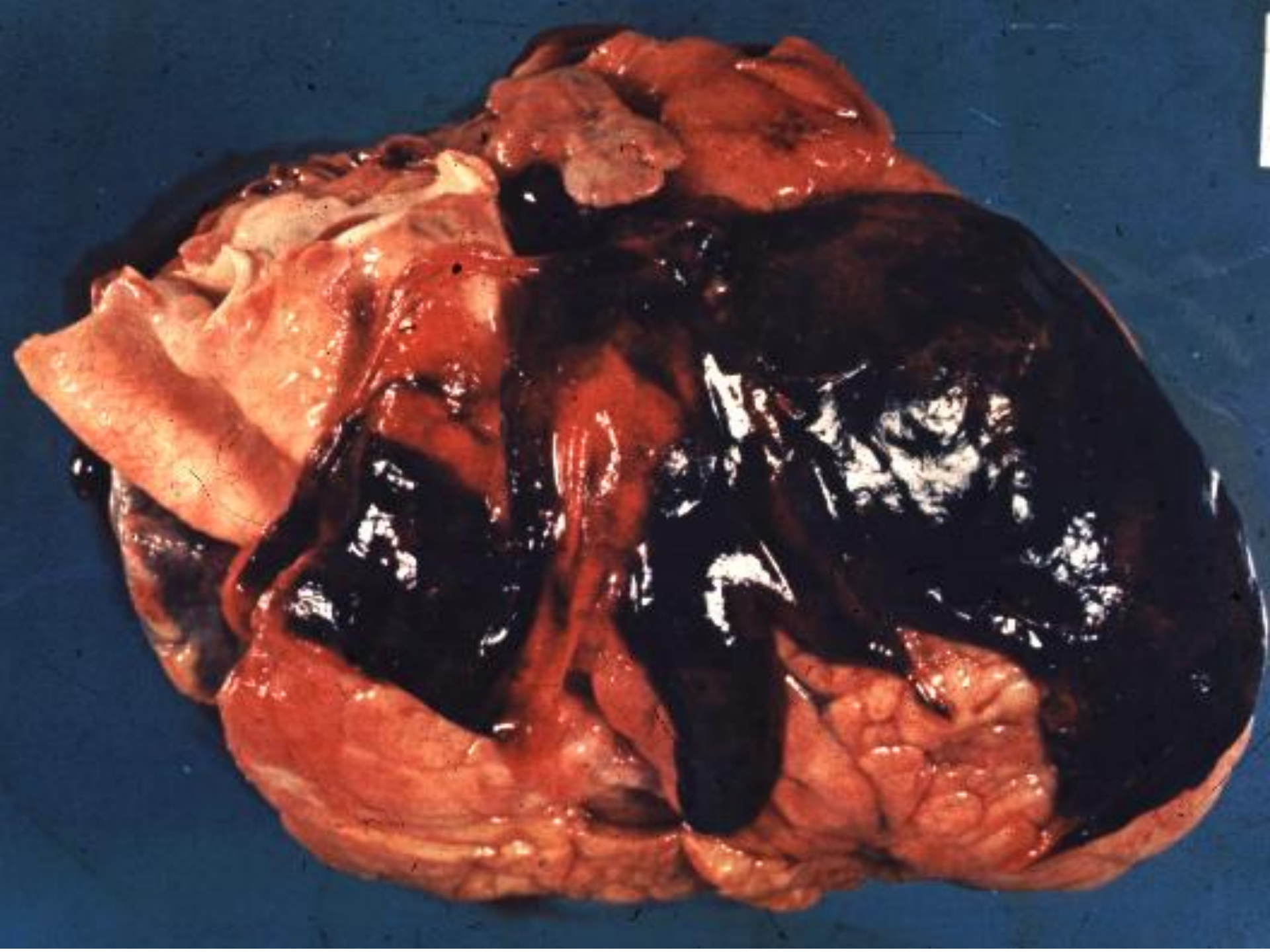
- in infarction: definitive damage of papillary muscle function, most frequently on the 2-7. postinfarction day

- rupture of papillary muscle or that of cordae is a life threatening situation >> sudden, severe valvular vitium and cardiac failure >> emergency implantation of a valve prosthesis is mandatory



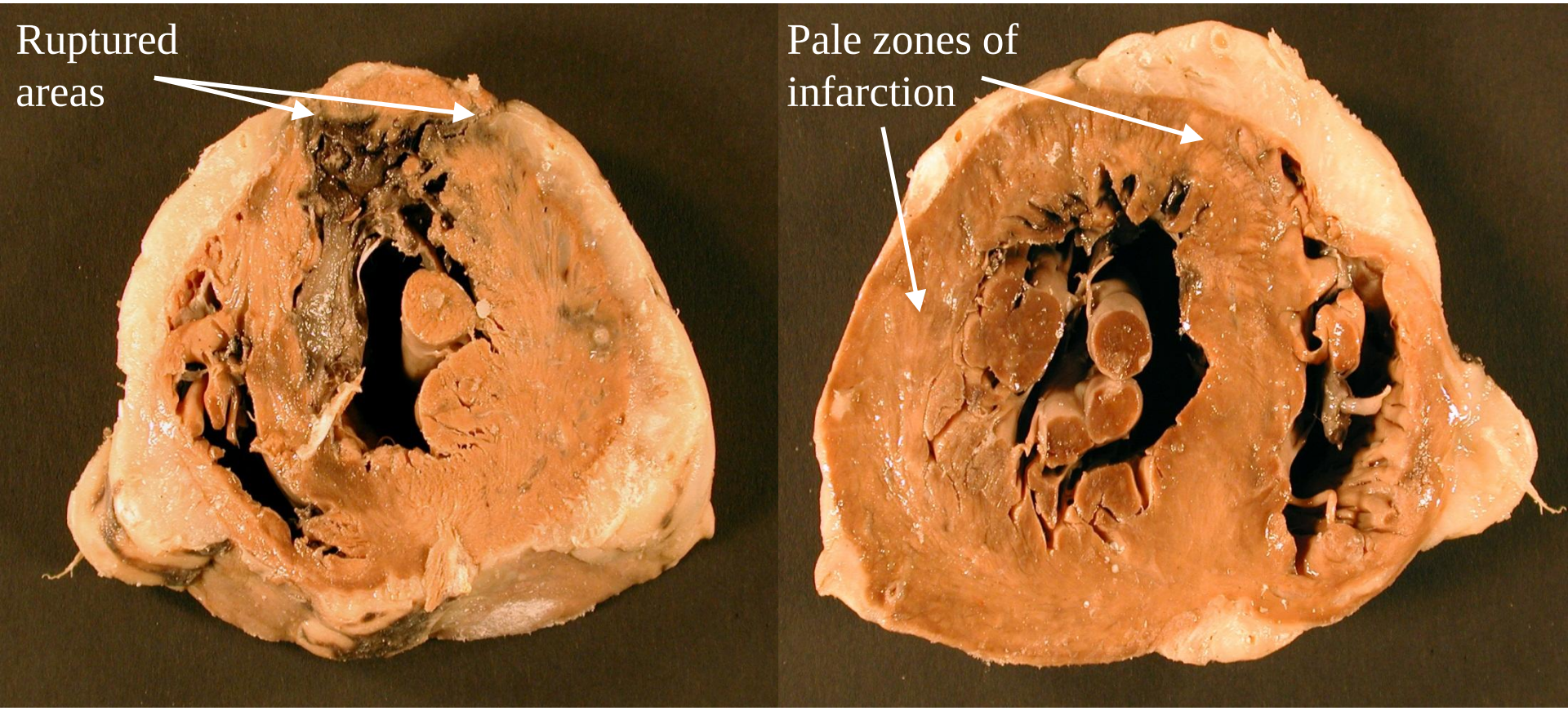
Complications of a myocardial infarction: muscular wall rupture, pericardial tamponade

- *frequency:* 10-20% of all lethal infarction cases; most frequently on the 3-5. postinfarction day
- *complications*: pericardial tamponade >> electro-mechanic dissociation >> sudden cardiac death
- small rupture results in slowly progressive development of a tamponade >> emergency surgery is yet possible
- sometimes introductory event is the formation of an acute myocardial aneurysm
- *predisposing factors for cardiac wall rupture*: **transmural infarction;** high age; female sex; steroide therapy; hypertension; few collaterals; myocardial fibrosis

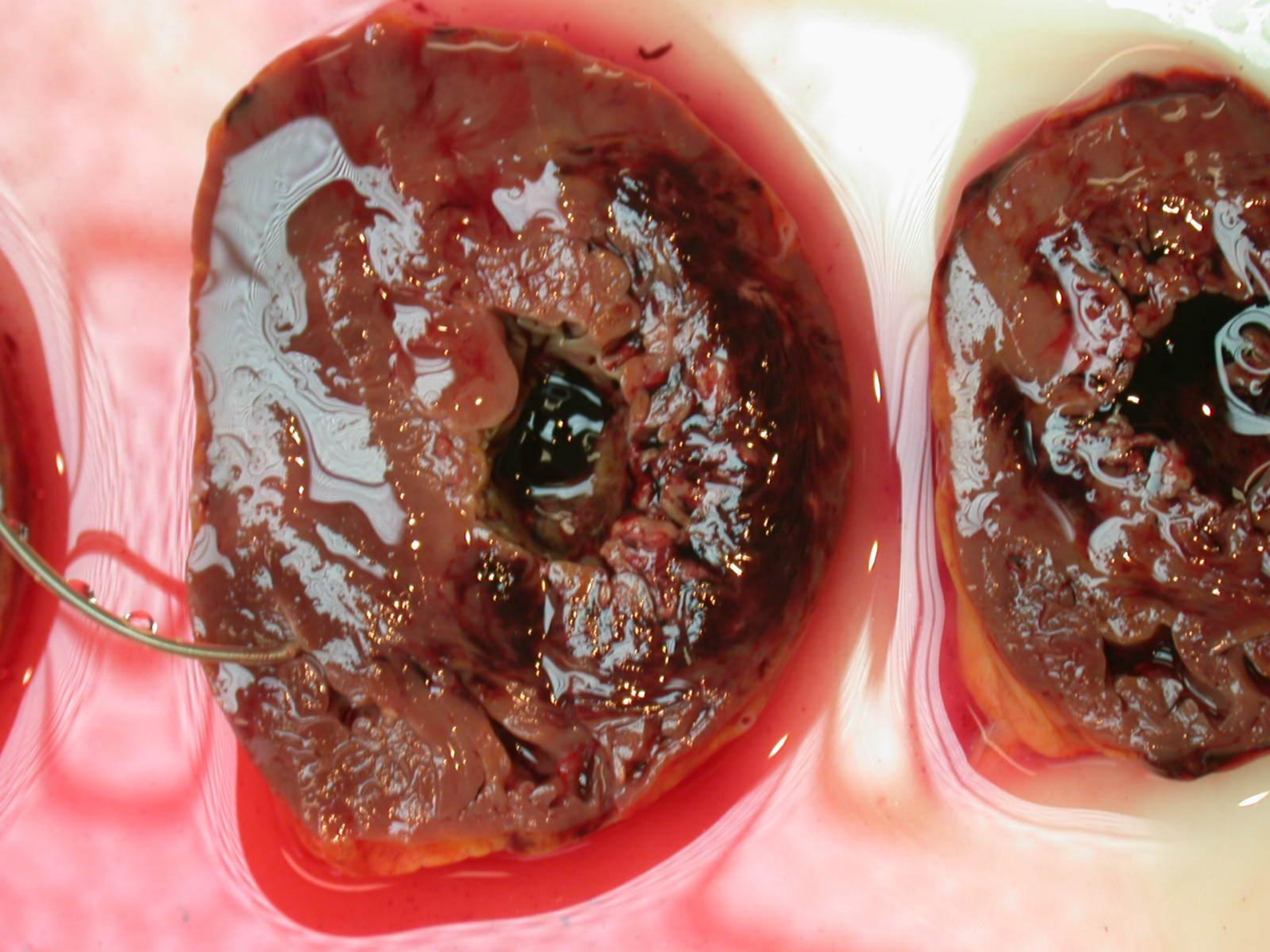


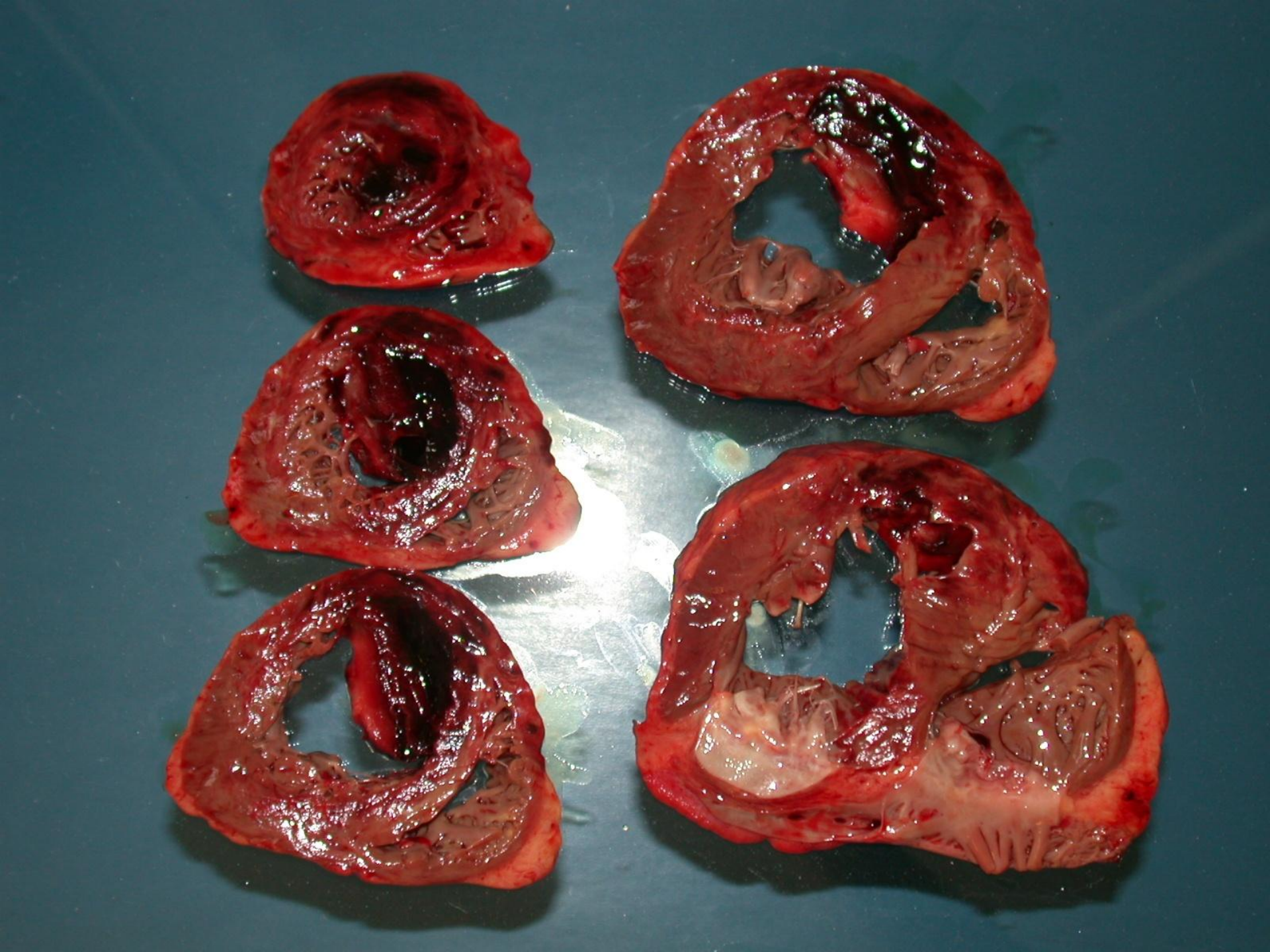

Myocardial rupture,
pericardial
tamponade

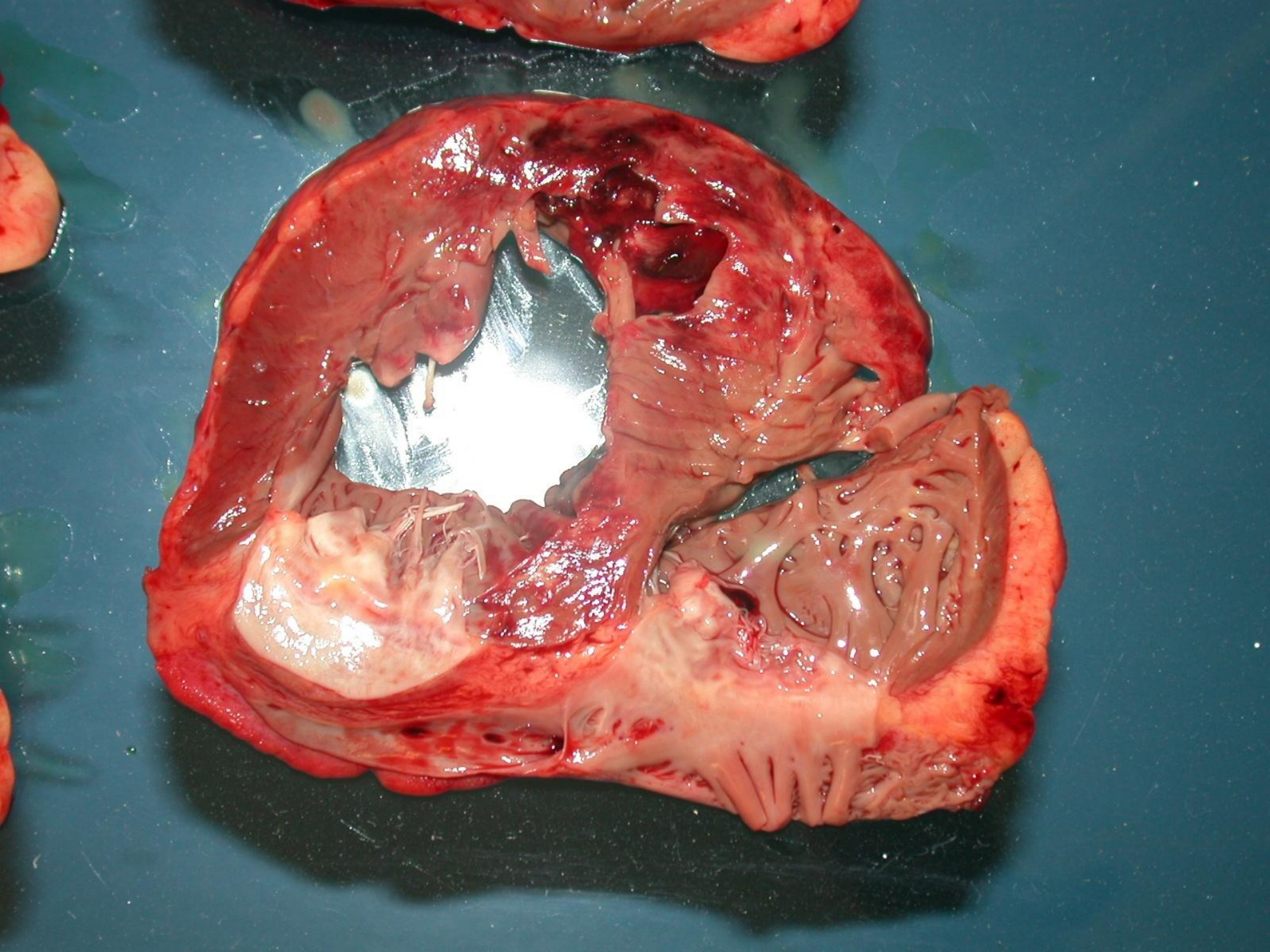
Myocardial rupture, pericardial tamponade



Acute myocardial infarction. Myocardial rupture.







Cardiomyopathies

Cardiomyopathies

Definitions:

- *primary (idiopathic) cardiomyopathies*: progressive chronic myocardial failure of unknown origin that after variously long periods lead to a therapy resistant circulatory insufficiency.

- *cardiopathies or secondary cardiomyopathies*: progressive, diffuse myocardial diseases, that may be identical to the idiopathic forms in their clinical and pathologi-cal presentation, yet can be derived from a detectable origin.

Therapy is possible only by heart transplantation.

Primary (idiopathic) cardiomyopathies

The following 3 groups are defined according to basic clinico-pathological differences:

(a) dilatative (congestive) cardiomyopathy

(b) hypertrophic (obstructive) cardiomyopathy

(c) restrictive (obliterative) cardiomyopathy

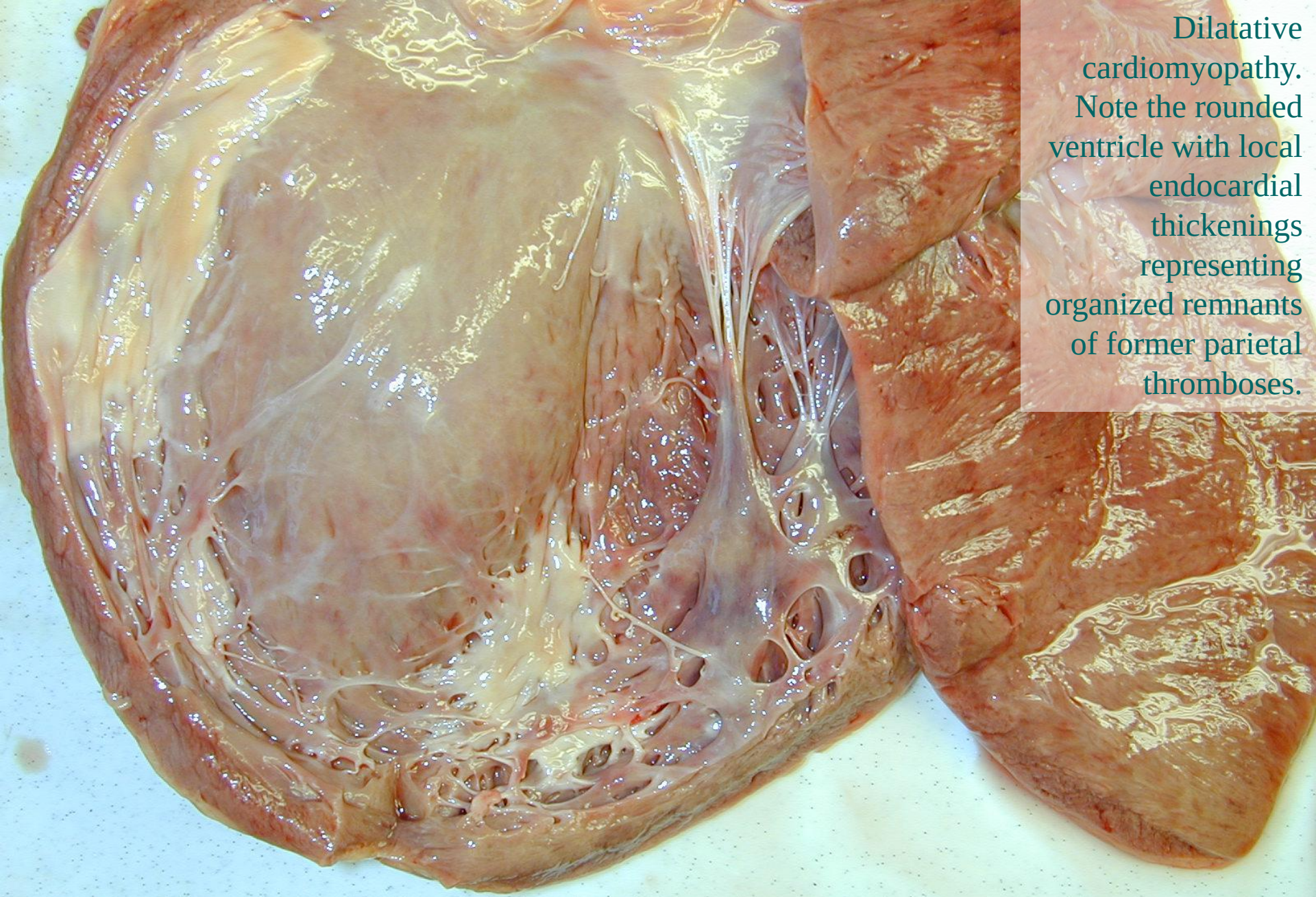
Dilatative/congestive cardiomyopathy (DCM)

- *Morphology* -

- *morphologic criteria*: severely enlarged heart (weight sometimes 3 times the normal – *cor bovinum*) with extremely dilated, ball-shaped ventricles, rounded apex, from basis to apex progressively thinning wall and parietal thrombi.

- further macroscopic alterations: atrial thrombosis; myocardium loose, patchy-fibrotic, pale; valves secondarily and relatively insufficient. Coronary arteries and valves morphologically intact!

- *microscopy*: no diagnostic alterations, only signes of a muscular hypertrophy (enlarged muscle fibers and nuclei) and secondary signes of a relative coronary insufficiency (myocytolysis, microinfarctions-microscars, interstitial fibrosis, single fiber necroses)



Dilatative cardiomyopathy. Note the rounded ventricle with local endocardial thickenings representing organized remnants of former parietal thromboses.

Dilatative/congestive cardiomyopathy (DCM)

- *Clinical aspects* -

- presentation in all age-groups, yet, most frequently in the young

- appearance sporadic, only seldom familiar (here genetic background possible), sometimes molecular biologic traces of enteroviral genom detectable (viral myocarditis in the anamnesis?)

- the clinical picture is that of a slowly developping, therapy resistant circulatory insufficiency

- begins slowly, lingering over the years with atypical complaints, the diagnosis is established generally in the stage of the circulatory insufficiency

- the end-diastolic volume increases progressively, the ejection fraction decreases

- leads in 5-10 years to death

Dilatative/congestive cardiomyopathy (DCM)

- *Molecular characteristics* -

- cardiac muscle contractility is secured by the strength of the sarcomeric contraction as well as by its transmission from sarcomer to sarcolemma and further to the extracellular matrix

- the connection between sarcomer and sarcolemma is given by the dystrophin-sarcoglycane proteincomplex

- certain mutations of the dystrophin gene (on the X-chromosome) lead to selective absence of the dystrophin in the myocardium (>>DCM) but not in the skeletal musculature (e.g. no Duchenne-Becker's muscle dystrophy)

- mutation of the δ-sarcoglycane gene >> DCM

- mutation of the distal part of the myocardium-specific actin (contacting part between actin and dystrophin with the help of a protein named desmin) and mutations of desmin >> DCM

- further mutations of e.g. binding structures between neighbouring muscle cells, or that of the energy production can lead to DCM

Hypertrophic/obstructive cardiomyopathy (HCM)

- *Morphology* -

- *macroscopically*: severely enlarged heart (weight sometimes 1000g – *cor bovinum*) with a disproportionate left heart hypertrophy especially at the septum >> decreased ability to dilatation ('*compliance*') and stenosis of the way leading out from the ventricle with cardiac insufficiency >> hence synonym terms: '*asymmetrical septal hypertrophy*' (ASH); '*idiopathic hypertrophic subaortic stenosis*' (IHSS)

- *microscopically*: a diagnostic picture: (a) extreme hypertrophy of the muscle fibers; (b) enlarged, bizarr nuclei with pale perinuclear rim (*halo*); (c) very typically irregular-chaotic, syntitially woven fiber connections: beside normal end-to-end connections there are end-to-side and side-to-side fiber connections. This chaotic micromorphology explaines the clinicallly often experienced cardiac arrhythmias.

Hypertrophic/obstructive cardiomyopathy (HCM)

- Clinical aspects -

- ethiology and pathogenesis unknown, the genetic background is however proven (HCM is an inherited disease)

- clinical symptomes appear only around the 30th year of life

- first angina and dyspnoe on body excersize

- conduction abnormalities are often seen (arrhythmias)

- sudden cardiac death is possible

- with the disease at end stage, there is a therapy resistant cardiac insufficiency

Hypertrophic/obstructive cardiomyopathy (HCM)

- Molecular characteristics -

- generally it is a familiar disease with autosomal dominant inheritence and varying penetrance

- rarely sporadic appearance through *de novo* mutations is possible

- HCM is a disease of the sarcomer: as well the thick (myosin) as the thin (actin, tropomyosin, etc.) filament genes may be affected

Restrictive/obliterative cardiomyopathy (RCM)

- General comments -

- a rare disease

- important is the restricted ability of the heart ventricle to dilate (reduced diastolic filling)

- the ventricle is capable neither of contracting nor of expanding to the desirable degree

- the combined systolic and diastolic derangement leads to cardiac insufficiency

- the disease is generally detected very late, in the stage of cardiac insufficiency

- according to classic understanding basis of the disease lies in the parietal endocardium, namely (a) an *endocarditis parietalis fibroplastica secundum Loeffler*; or (b) an *endomyocardial fibrosis*

Restrictive/obliterative cardiomyopathy (RCM)

- *Endocarditis parietalis fibroplastica secundum Loeffler* -

- in the background there is a severe peripheral and interstitial eosinophilia (sometimes even an eosinophilic leukemia)

- it is a lethal disease

- the atypical, degranulated, circulating eosinophils cause endo-myocardial necrosis by their toxic substances >> thickening and scarring of the endocardium and the subendocardium >> formation of parietal thrombi >> organisation of thrombi >> the very rigid endocardium leads to myocardial motility derangements

Restrictive/obliterative cardiomyopathy (RCM)

- *Endomyocardial fibrosis* -

- endocardial changes as with Loeffler's endocarditis, yet without an eosinophilia

- it is most frequently seen in the first 2 years of life, in adults rare

- the proliferating connective tissue that thickens the parietal endocardium infiltrates also into the subendocardial myocardium

- prognosis depends on dimensions of the disease: focal endocardial thickenings can remain symptomless, whereas a diffuse disease leads quickly to cardial decompensation and death

Museum of Pathology;
2nd Dept. of Pathology; Semmelweis University

Secondary cardiomyopathies: cardiopathies

- diffuse myocardial diseases of known origin >> important, that with the therapy of the causative circumstances also the cardiac status gets relief or will even be cured

- (a) *Alcoholic cardiomyopathy* – the most frequent cause, that leads to a **dilatative type cardiac disease**. No coronary sclerosis. First symptoms are arrhythmias without congestive signes. Beside a normal coronarogram angina pectoris is possible. At the beginning the developping heart insufficiency can be reversed by alcohol abstinence and specific supportive cardiotherapy. With continued alcohol abuse an irreversible circulatory decompensation will follow. Cause of death is often embolisation from parietal thrombi.

- (b) *Peripartal (pregnancy-linked) cardiomyopathy* – in the 3rd trimester of pregnancy or within 6 weeks after birth. Disease characteristics as with a **dilatative type cardiopathy**. Specific therapy makes a complete recovery possible.

Secondary cardiomyopathies: cardiopathies

- (c) *Hemochromatosis* – genetic derangement of iron uptake and -stockage. Iron reserves appear pathologically also in parenchymal cells causing functional alterations in many organs: liver, pancreas, heart, skin, etc. The clinical appearance of the heart disease that of a **DCM**. Later the myocardium develops progressiv rigidity through accumulating iron contents, so the clinical picture turns into one resembling a **RCM**. Macroscopically the myocardium is stiffened, dark coloured. Microscopically the muscle fibers are massively overloaded with iron containing hemosiderin pigment (positive Prussian-blue reaction).

- (d) *Amyloidosis* – the amyloid protein is deposited in the myocardial interstitium and in small vessels >> thickening of myocardium all over the heart (especially in the left ventricle). A cardiac insufficiency with lung edema and systolic functional decrease develops typically in an unexpected, abrupt manner. Myocardium stiffened and rigid with a waxy-glassy hue on the cut surface >> the clinical presentation is that of a **RCM**. Microscopically amyloid is seen as a homogenous eosinophilic material (congo-red staining positive).

Secondary cardiomyopathies: cardiopathies

- (e) *Sarcoidosis* – in 8% of patients with sarcoidosis also cardiac disease develops. Sarcoidotic granulomas appear in the pericardium and myocardium (most frequently in the upper third of the interventricular septum and in the papillary muscles). The clinical picture is dominated by arrhythmias. The overall picture as with **RCM**. Arrhythmias may lead to sudden cardiac death.

Cardiac decompensation

Cardiac decompensation

- *General comments* -

- it is the end stage of severe heart diseases; prognosis bad

- the clinical progression is defined by the basic disease, age, overall status and other factors (e.g. social status of the patient)

- *acute* cardiac decompensation: as with myocardial infarction, valve rupture in destructive endocarditis

- *chronic* cardiac decompensation: as with non-treated hypertension, chronic valvular endocarditis, cardiomyopathies

- pump failure (*forward failure*) – disturbance of contractility

- filling failure (*backward failure*) – disturbance of dilatation

- at the beginning cardiac decompensations are generally one sided: either left- or right heart failure, which can later combine

Cardiac decompensation

- *Left heart failure* -

- causes are:
    - ischemic heart disease
    - hypertension
    - vitia (other than a mitral stenosis)
    - diseases of the myocardium (cardiomyopathies)

- *backward failure*: congestion of the lungs with chronic pulmonary edema, 'heart failure cells', brown stiffening of the lungs (*induratio brunea pulmonum*)

- clinically: dyspnoe; orthopnoe; nocturnal respiratory complaints; frequent and blood-stained coughs; (when combined with right heart failure:) hydrothorax with compression and atelectasis of the lungs (*atelectasia e compressione*); cerebral hypoxia with sleepiness (*stupor*) and rarely hypoxic encephalopathy up to coma; decreased renal filtration, salt and water retention, peripheral edemas

Cardiac decompensation

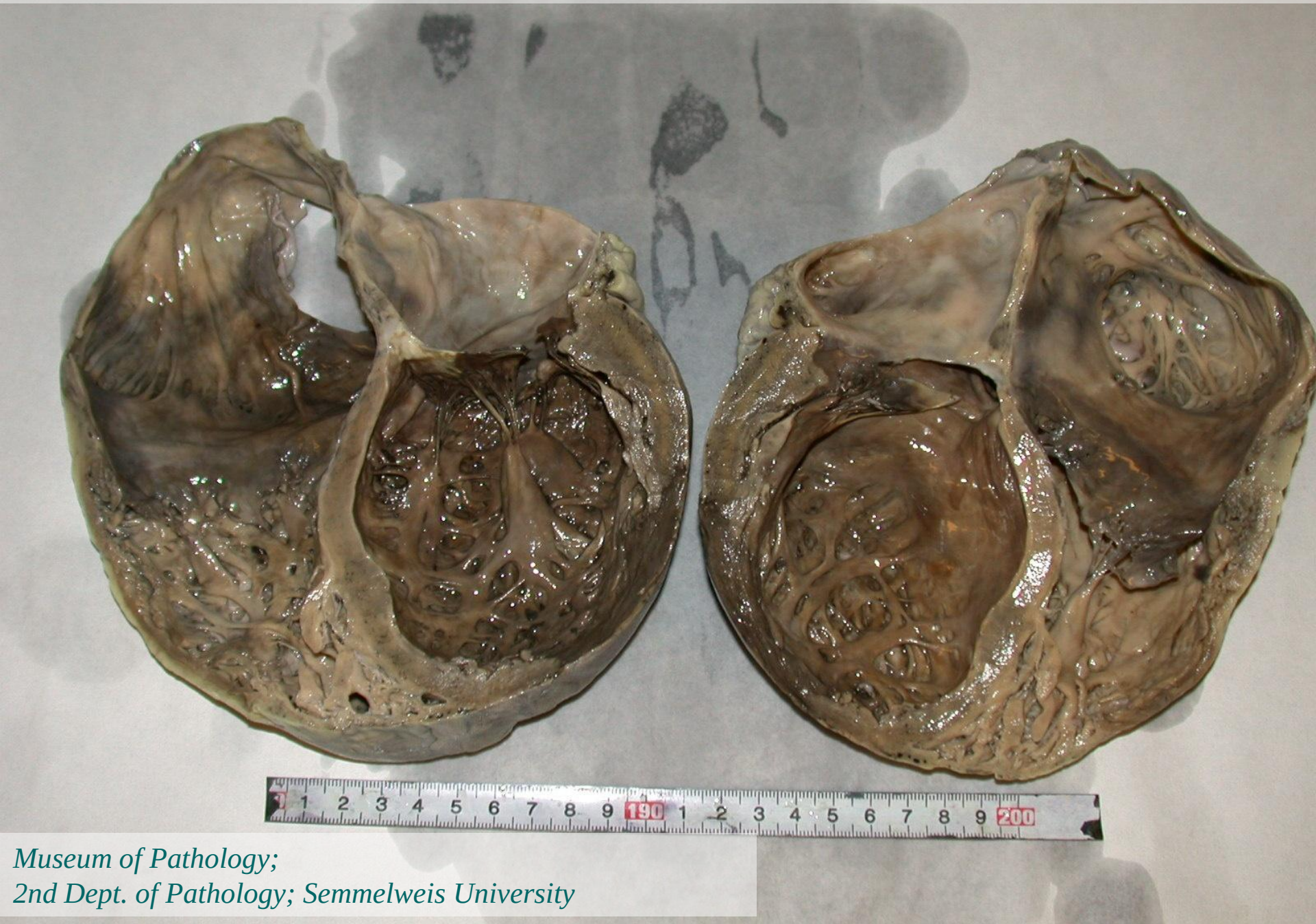
- *Right heart failure* -

- most frequently in combination with a left heart failure – congestive cardiac decompensation

- isolated right heart failure develops in only 15% of the cases, especially with
    - mitral stenosis
    - some congenital vitia
    - cor pulmonale
    - pulmonary fibrosis

- clinically: congestion of the superficial jugular veins; lower limb edema (*anasarca*); sometimes hydrothorax; hypoxic encephalopathy as with left heart failure; liver congestion with development of a severe nutmeg liver and a so-called cardiac cirrhosis; hepato-splenomegaly; congestive gastroenteritis; ascites

Cardiac decompensation. Cavities of both sides are tremendously dilated.



Museum of Pathology;
2nd Dept. of Pathology; Semmelweis University

Tumors of the heart

Primary cardiac tumors

- Benign
  - Myxoma 25%
  - Lipoma 8%
  - Papillary fibroelastoma 8%
  - Rhabdomyoma 7%
  - Mesothelioma of the AV-Nodule 2%
- Malignant
  - Angiosarcoma 7%
  - Rhabdomyosarcoma 5%
  - Mesothelioma 4%
  - Fibrosarcoma 3%

Secondary cardiac tumors

- in 5% of all malignancy-related death cases cardiac metastases can be found

- primary tumor locations in order of frequency are

    - pulmonary carcinoma

    - mammary carcinoma

    - renal cell carcinoma

    - malignant melanoma

    - lymphoma / leukemia

Myxoma

- most frequent tumor of the heart

- originates from the parietal endocardium

- macroscopy: a soft, greyish-reddish, sessile or steeled, varyingly large tumor

- microscopy: very loose, myxoid stroma with disseminated small vessels, on the surface a covering layer endothelium

- danger of complication in approx. 50% of the cases is systemic embolisation from fragmented tumor particles

- the lesion can unequivocally be detected radiologically

- therapy: operative resection; healing rate high; recurrences infrequent

- familiar appearance as a so-called ‘Carney-syndrome’ possible: multiple cardiac myxomas, sometimes extracardiac (e.g. cutaneous) myxomas, patchy dermal pigmentation, endocrine hyperfunction >> in case of a myxoma, echocardiography of closer relatives is indicated

- differential diagnosis against an organized parietal thrombus is both macro- and micro-scopically often probematic

Papillary fibroelastoma

- it is probably a residuum of an organized thrombus

- a bunch-like formation at the semilunar and cuspidal valves with hairy, repeatedly bifurcating, thin branches and endothelial lining on the surface, usually measuring cca. 1cm

- most frequent localisation: aortic valves >> danger of complication: stenosis or occlusion of the coronary ostia with angina pectoris or even sudden cardiac death

Rhabdomyoma

- most frequent in new-borns and small children

- possible presentation with tuberous sclerosis

- no real tumor, but a hamartoma*

- in the left ventricular myocardium multiple nodules, sometimes with elevation of the endocardial inner surface

**Hamartoma – a tumor-like lesion with tissue components, that are also present under normal conditions of the presenting localisation, the morphologic composition and percentage relations of which being however abnormal.*

Mesothelioma of the AV-nodule

- a typically cystic tumor in the location of the AV-nodule measuring from microscopically small up to even 3 cm

- the tumor is connatal, that develops during the embryonal period, primarily in females

- danger of complication: recurrent fits of Adams-Stokes' syndrome already in childhood; complete AV-blockage; sudden cardiac death of unknown origin in a young person >> often makes the implantation of a pacemaker necessary