- Atherosclerosis is a chronic disease primarily of the elastic arteries and a large and medium-sized muscular arteries. The basic lesion - the atheroma, or fibrofatty plaque - consists of a raised focal plaque within the intima, having a core of lipid (mainly cholesterol and cholesterol esters) and a covering fibrous cap. In small arteries plaques are occlusive, compromising blood flow to distal organs and causing ischemic injury, but in large arteries they are destructive, weakening the affected vessel wall, causing aneurysms or rupture of favoring thrombosis.

- Atherosclerosis is one of arteriosclerosis. Arteriosclerosis literally means "hardering of the arteries"; more accurately it refers to a group of disorders that have in common thickening and loss of elasticity of arterial walls. Atherosclerosis accounts for more death and serious morbidity than any other disorder. Although any artery may be affected, the aorta and the coronary and cerebral systems are the prime targets, and so myocardial infarction, cerebral infarction, and aortic aneurysms are the major consequences of this disease. Atherosclerosis also takes a toll through other consequences of acutely or chronically diminished arterial perfusion, such as gangrene of the legs, mesenteric occlusion, sudden cardiac death, chronic ischemic heart disease and ischemic encephalopathy.

risk factors

- 1) hyperlipidemia, dislipidemia
- 2) hypertension,
- 3) cigarette smoking,
- 4) diabetes,
- 5) age,
- 6) male,
- 7) hereditary predisposition,
- 8) emotional stress.

- LPLD, LPLD/LPHD
- Hypercholesterolemia

Theories

- Infiltration by cholesterol & lipids (Hypercholesterolemia, hyperlipidemia) – Anichkov
- Neuro-metabolic (emotional stress – changing in the regulation of lipid metabolism) – Myasnikov
- Immunologic theory
- Receptor theory – deficiency of specific lipoprotein receptors
- Thrombogenic theory
- Viral theory

Clinical & morphological types

- Atherosclerosis of aorta
- Atherosclerosis of coronary arteries
- Atherosclerosis of cerebral arteries
- Atherosclerosis of mesenteric arteries
- Atherosclerosis of arteries of low extremities
- Atherosclerosis of renal arteries

Stages of atherogenesis

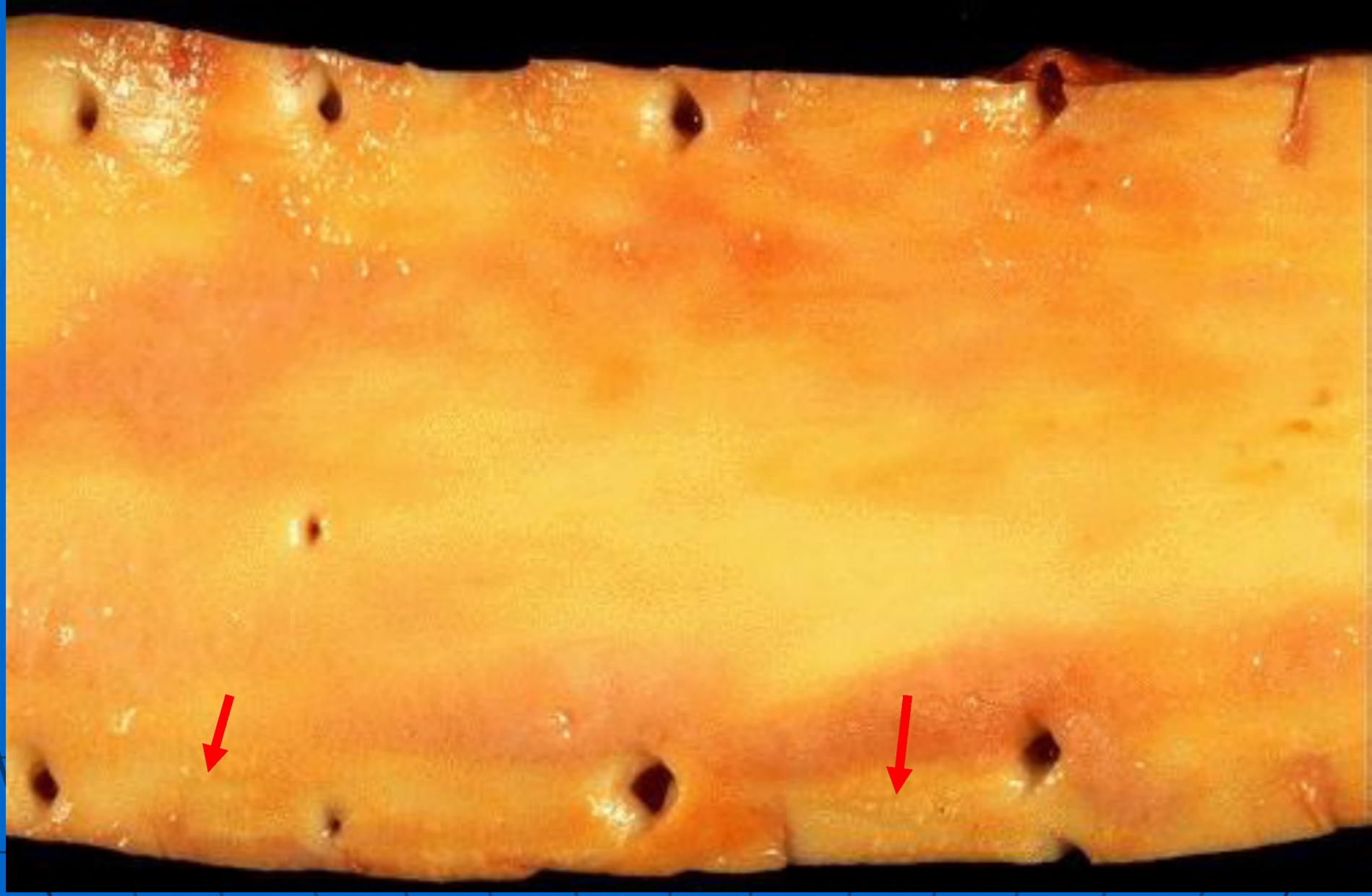
- Fatty spots & bands
- Atheromatous (fibrous) plaque
- Complicated lesions
- Atherocalcinosis

Microscopic stages of atherosclerosis

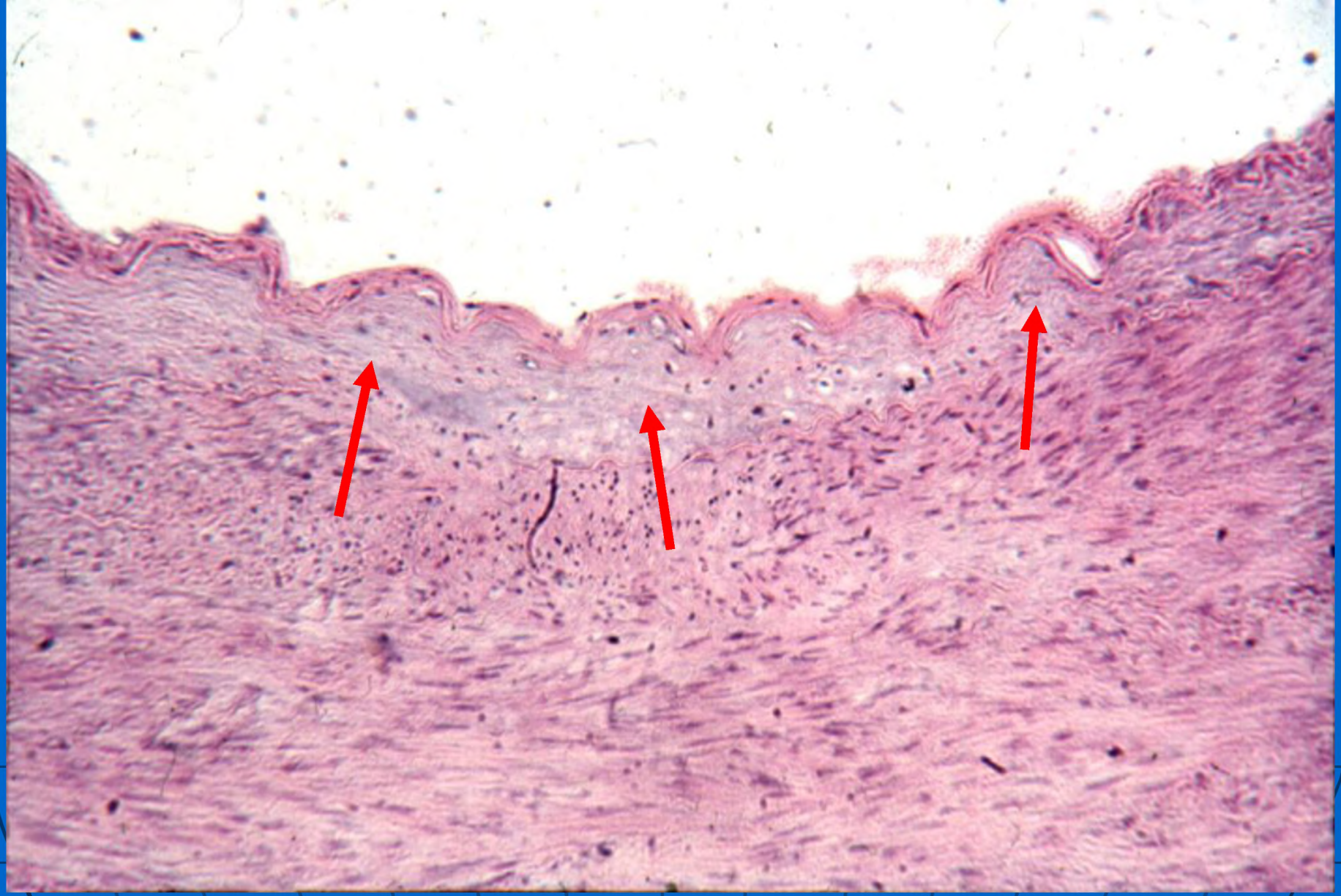
- Prelipid stage
- Stage of lipoidosis
- Stage of liposclerosis
- Atheromatosis
- Ulceration
- Atherocalcinosis

Pathogenesis and morphogenesis of atherosclerosis

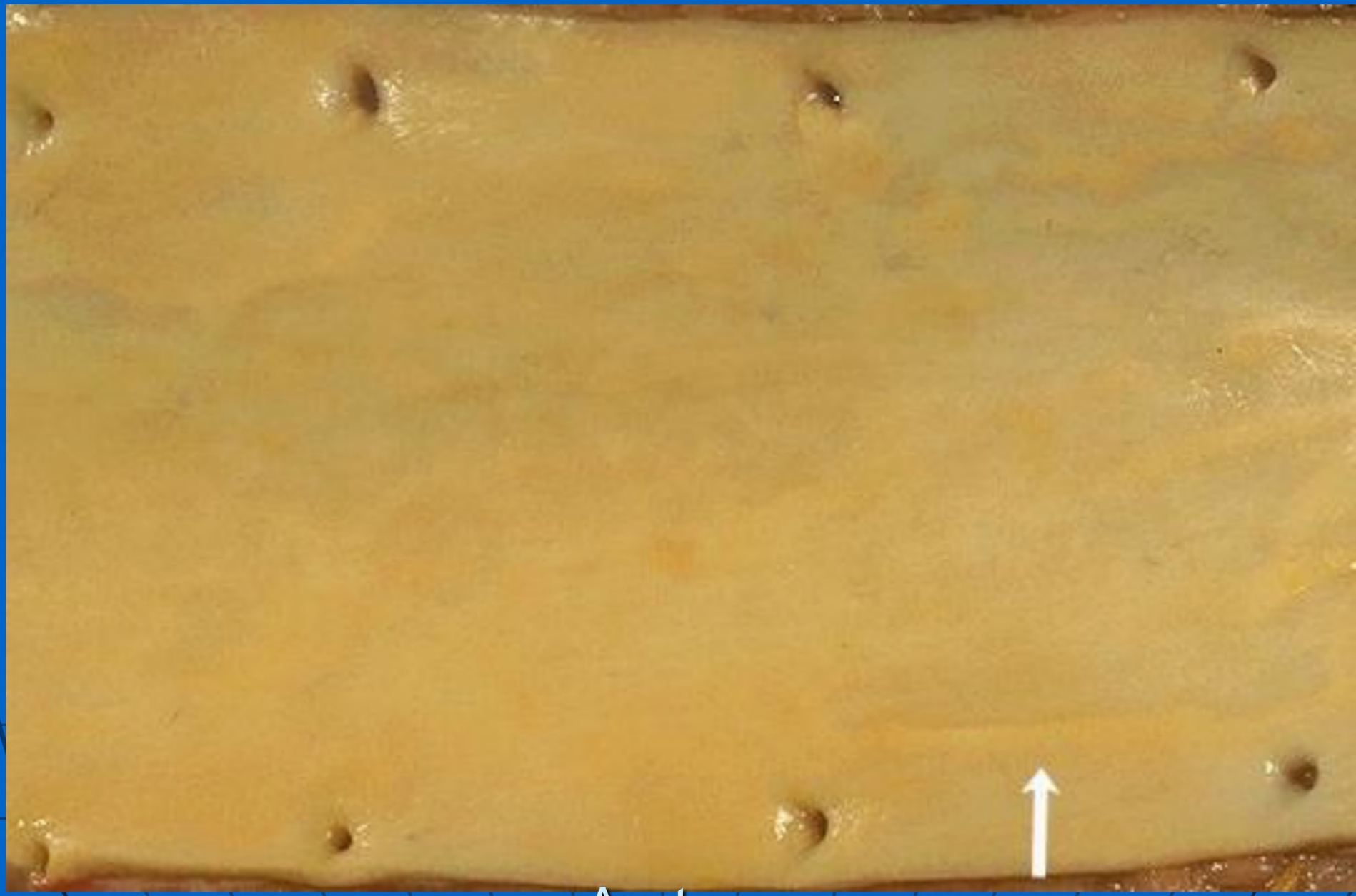
- Prelipid stage. The accumulation of glycosaminoglycans in the arterial intima and mucoid edema, an increase in the permeability of the endothelium and intima membranes.
- Lipoidosis. Focal accumulation of cholesterol, lipoproteins and proteins in the intima. Transformation of macrophages and smooth muscle cells of arteries into foamy (xantom) cells due to the accumulation of lipid products in them.
- Liposclerosis. The proliferation and subsequent maturation in the arterial wall of fibroblasts and other cells under the influence of bioactive substances secreted by activated xanthoma cells.
- The stage of complicated lesions includes atheromatosis, ulceration, and calcification of the fibrous plaque. Disintegration of xanthoma cells and lipid masses, smooth myocytes of the middle shell (atheromatosis). Torn plaque stimulates thrombosis (ulceration or ulcerative atheromatosis), hemorrhages, embolism and aneurism formation. Focal calcification of atheromatous masses (atherocalcinosis).



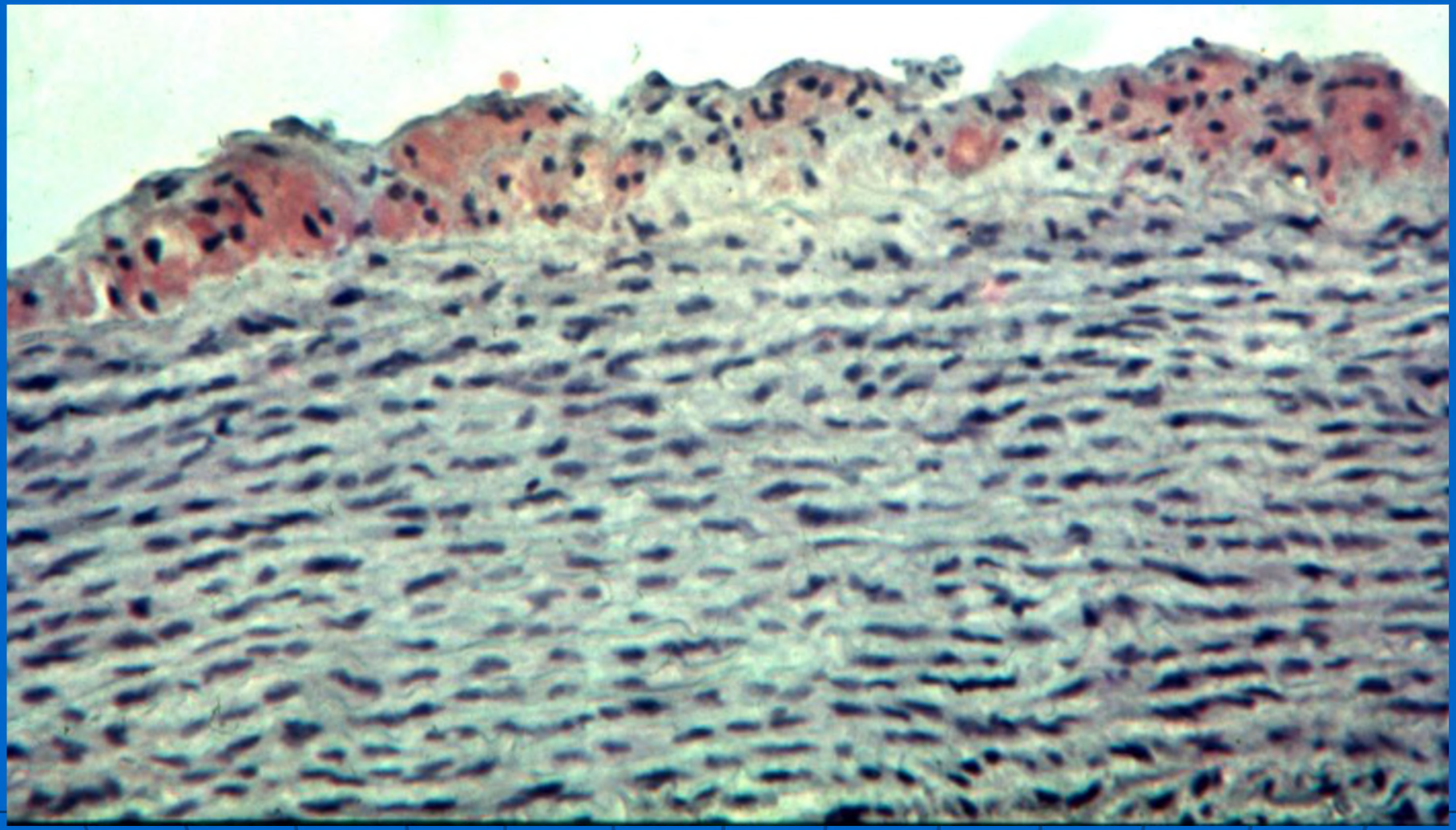
Aorta:
Fatty spots & bands



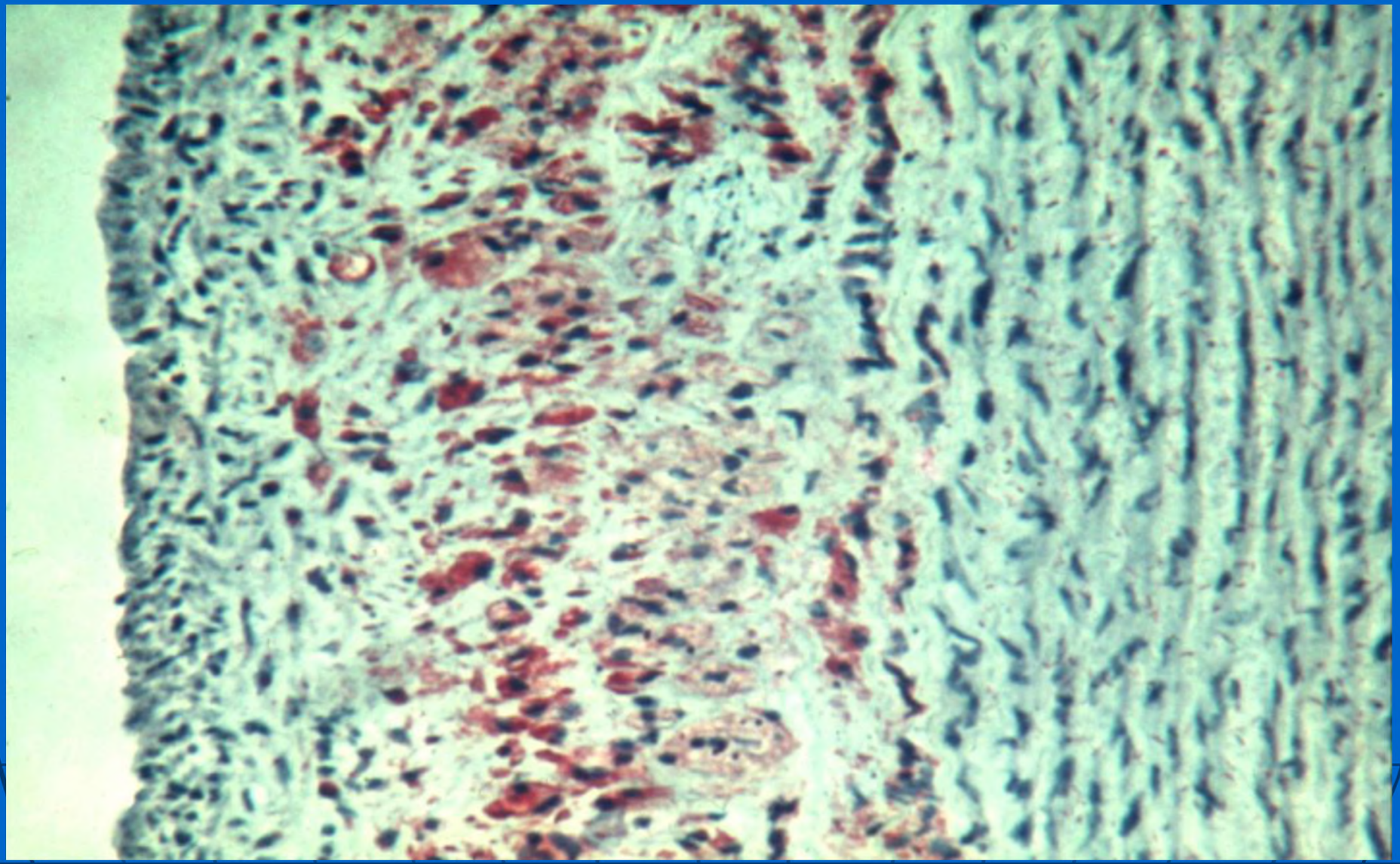
Aorta: prelipid stage :



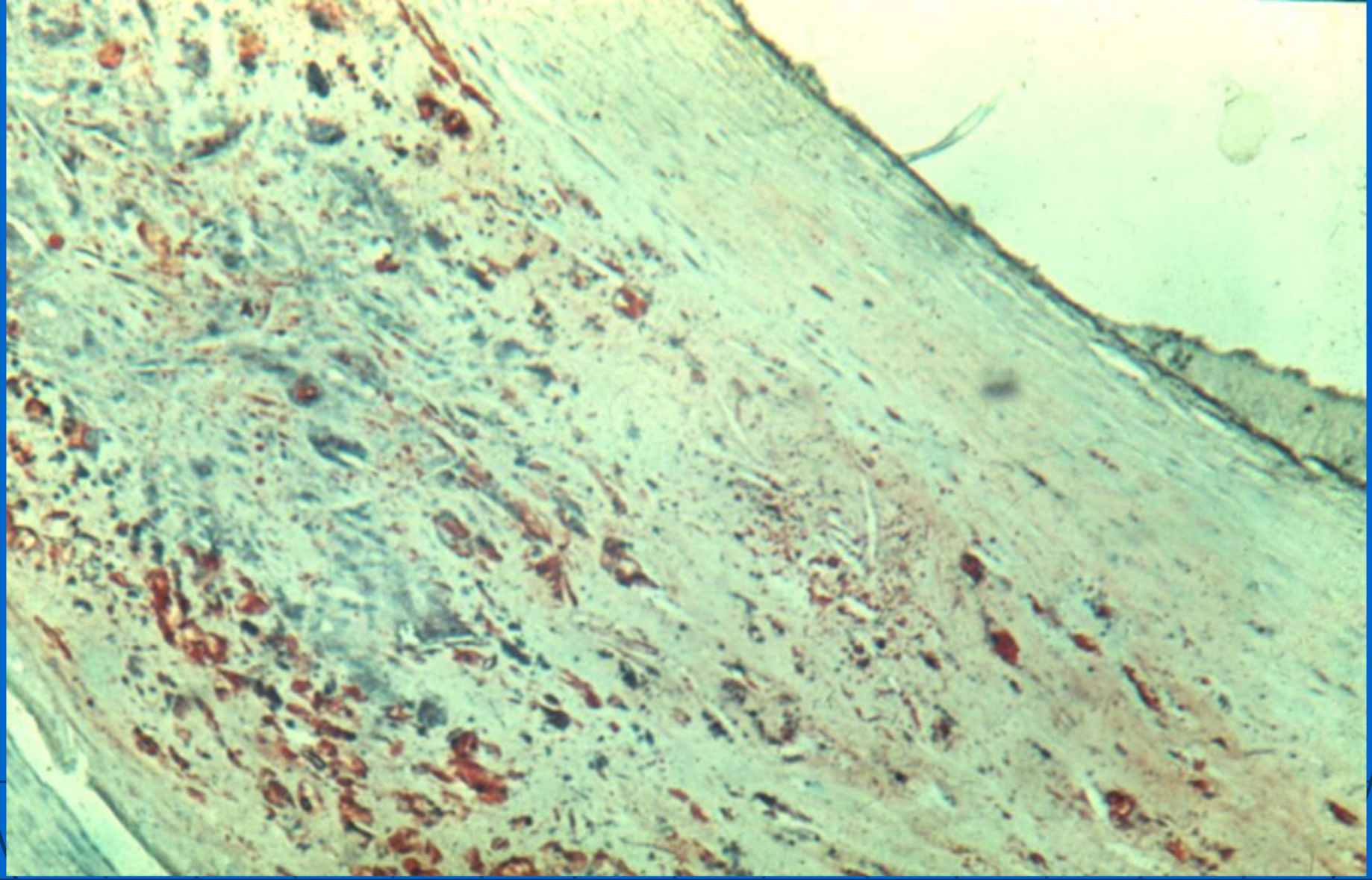
Aorta:
Fatty spots & bands



Aorta:
deposition of lipids in the intimae



Aorta:
lipoidosis in the intimae

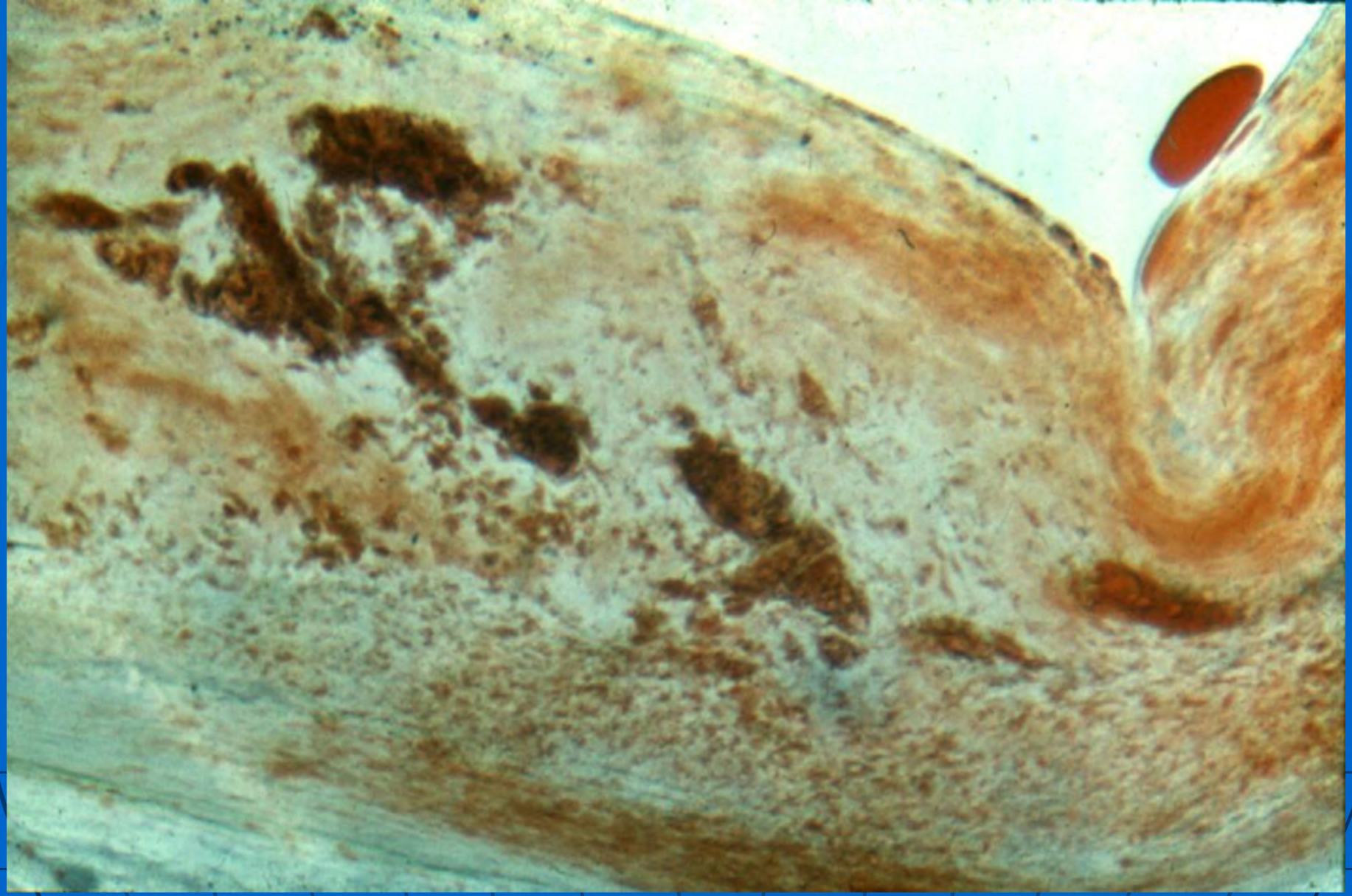


Aorta:
liposclerosis in the intimae

Atheromatous plaque

Atheromatous plaque have three principal components:

- 1) cells, including smooth muscle cells, macrophages, and other leukocytes;
- 2) connective tissue extracellular matrix, including collagen, elastic fibers, and proteoglycans;
- 3) intracellular and extracellular lipid deposits



Aorta, atheromatosis in the intimae:
deposition of lipids, fibrosis

Plaque rupture and erosion

- Atherosclerosis is not a continuous, linear process but rather a disease with alternate phases of stability and instability.
- Sudden and unpredictable changes in symptoms appear to be related to plaque disruption. Plaques prone to rupture have a large lipid core, low smooth muscle cell density, high macrophage density, thin fibrous cap–disorganized collagen and high tissue factor concentration. The lipid core forms a cellular mass within the collagen matrix of the plaque.

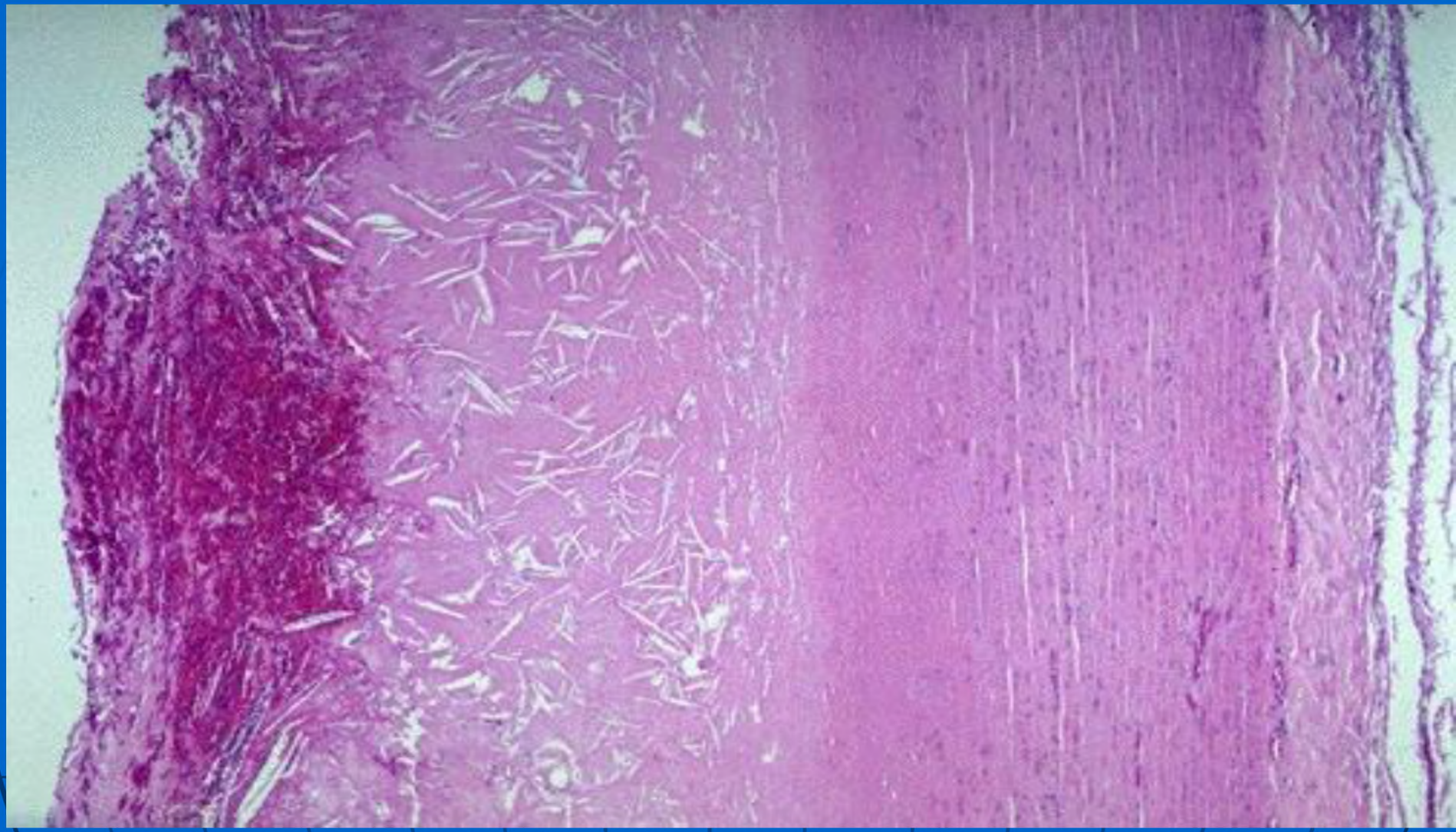
Plaque rupture and erosion

- After foam cell death, the lipid core may be created by active dissolution of collagen by metalloproteinases and not just by passive accumulation. The lipid core of plaques prone to rupture has a high concentration of cholesteryl esters with a high proportion of polyunsaturated fatty acids. A lower proportion of polyunsaturates is observed at the edge of disrupted plaques as compared with their centre. The relative proportion of the different fatty acids could influence local platelet and thrombus formation.

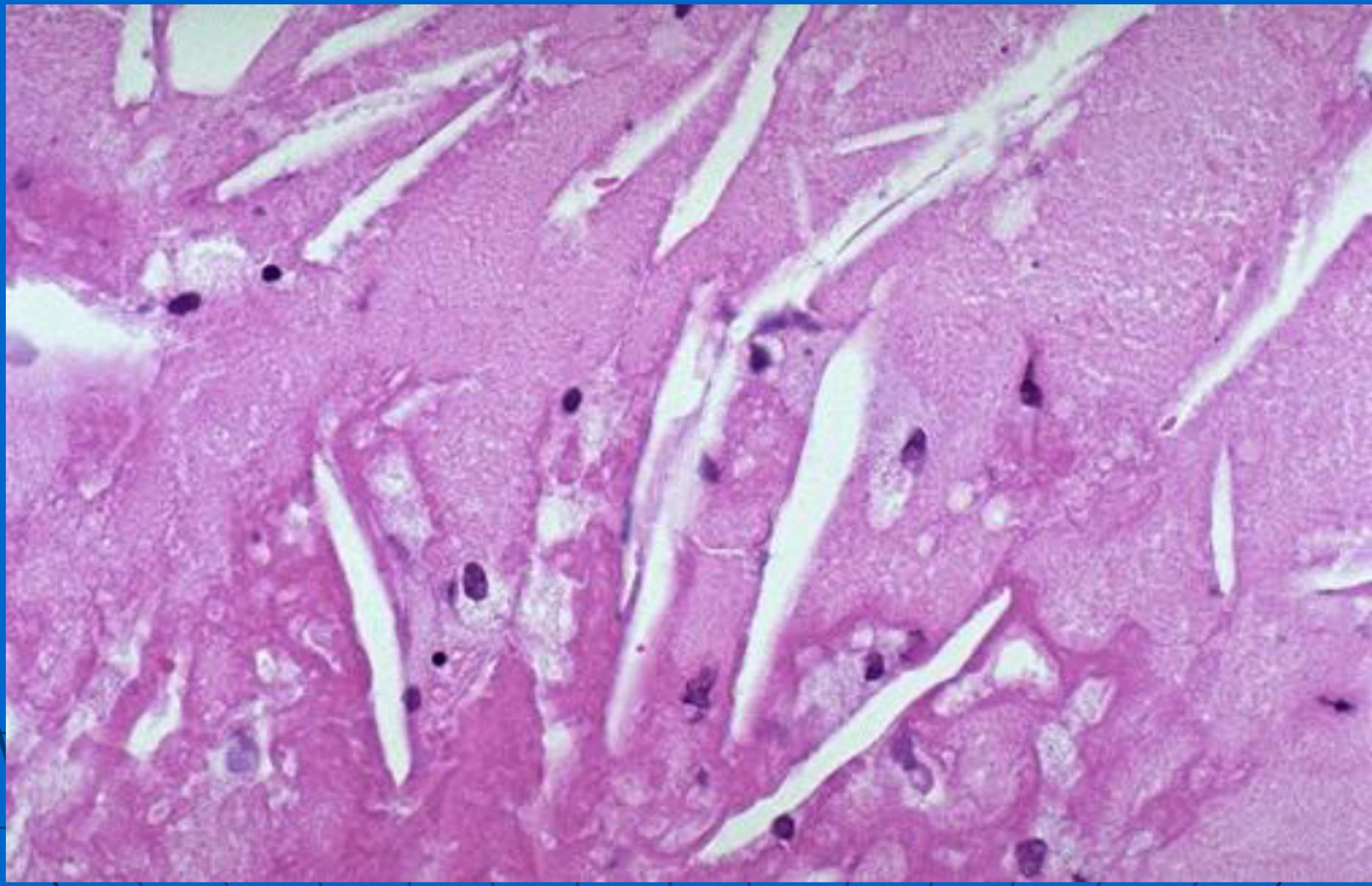
Plaque disruption may result from various combinations of the following:

- *Active rupture* is likely related to secretion of proteolytic enzymes by the macrophages which may weaken the fibrous cap.
- *Passive plaque disruption* is related to physical forces occurring at the weakest point of the fibrous cap, which widely corresponds with the thinnest part of the fibrous cap, at the junction of the plaque and the adjacent 'normal' wall. The vulnerability of the plaque may depend on the circumferential wall stress, as well as the location, size and composition of the lipid core, and the impact of flow on the luminal surface of the plaque.

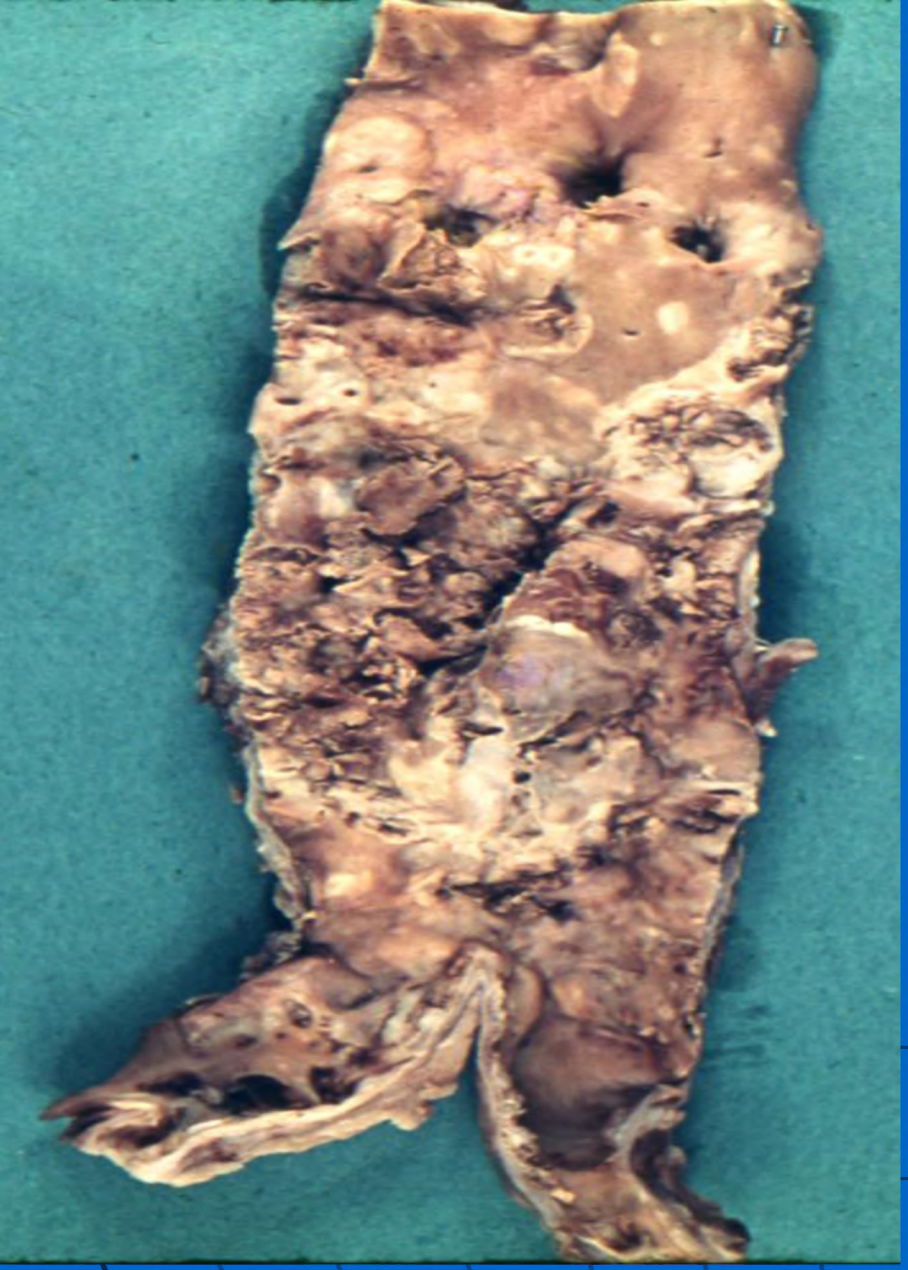
- Besides plaque rupture, *plaque erosion* has been described as one of the underlying mechanisms in acute coronary syndromes. Plaque erosion seems to be more common in women, diabetics and hypertensive patients; some evidence exits that it more commonly occurs on high-grade stenosis and on stenosis located in the right coronary artery. A recent study showed a 40% prevalence of plaque erosion in sudden coronary death, and a 25% prevalence in acute myocardial infarction, with a higher prevalence in women than in men. For plaque rupture these figures were 37% in women vs 18% in men.
- When erosion occurs, thrombus adheres to the surface of the plaque whereas, when the plaque ruptures, thrombus involves the deeper layers of the plaque, down to the lipid core; when this latter situation is not accommodated by positive remodelling, it might contribute to the growth and rapid progression of the plaque.

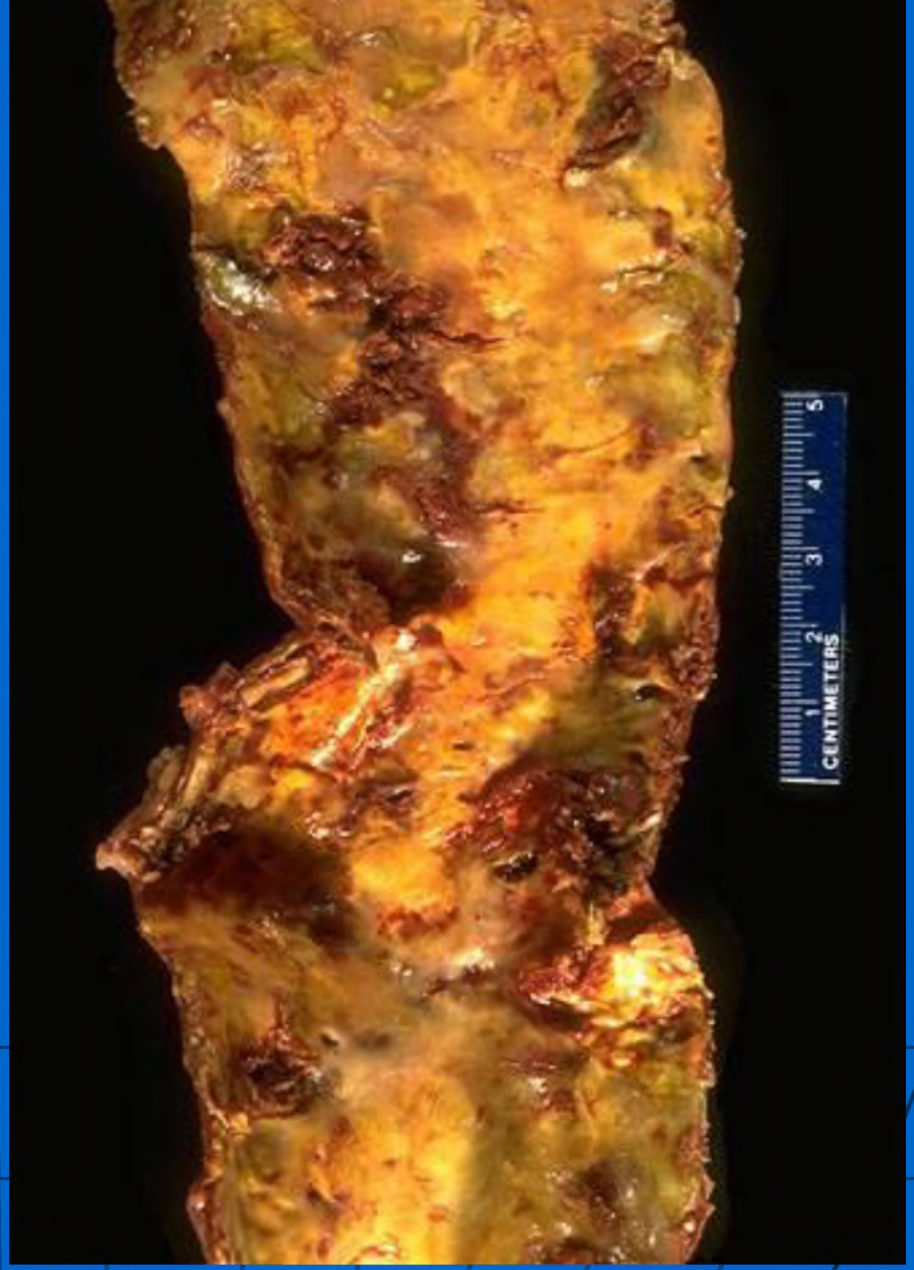


Aorta: atheromatosis in the intimae, deposition of cholesterol



Aorta: atheromatosis in the intimae, deposition of cholesterol





Aorta. Atheromatous (fibrous) plaque. Complicated lesions. Atherocalcinosis.

Inflammation

- The fibrous cap usually has a high concentration of type I collagen and can support high tensile stress without breaking. However, it is a dynamic structure with a continuous equilibrium between collagen synthesis modulated by growth factors and degradation by metalloproteases derived from activated macrophages. In addition, apoptosis of smooth muscle cells can weaken the cap tissue and favour plaque rupture.
- Macrophage infiltration has been demonstrated consistently in pathological studies: the proportion of macrophages is six to nine times greater in ruptured plaques than in stable plaques. The presence of macrophages reflects an inflammatory process which is also characterized by the presence of activated T-lymphocytes at the site of plaque rupture. These T-lymphocytes can release various cytokines that activate macrophages and promote smooth muscle cell proliferation. It has been suggested that these cells produce metalloproteases that digest the extracellular matrix.

Thrombosis

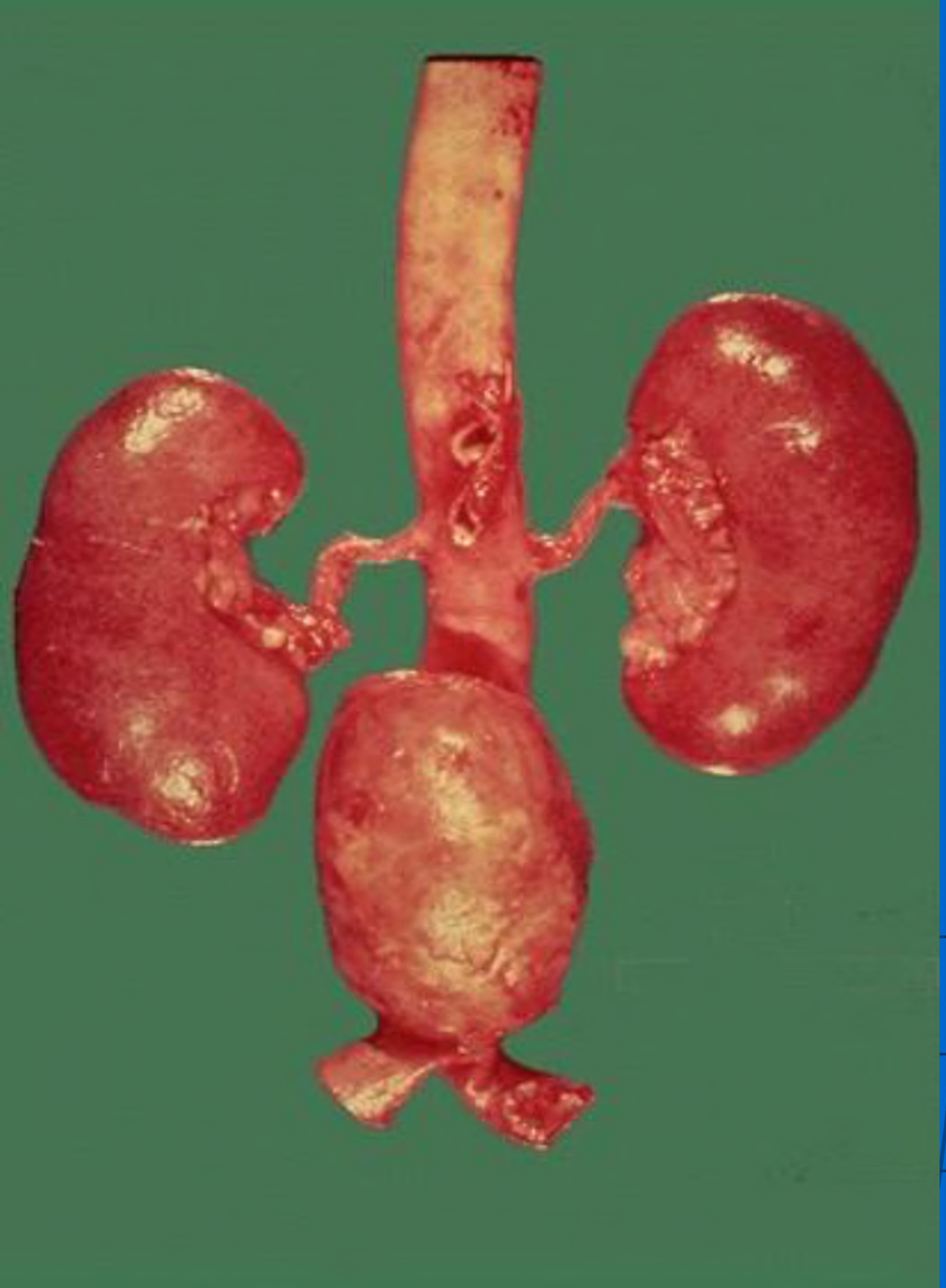
- Thrombosis is induced at the site of plaque rupture or erosion. It may lead to rapid changes in stenosis severity, and may result in subtotal or total vessel occlusion. The lipid-rich core, which is exposed after plaque rupture, is highly thrombogenic and has a greater concentration of tissue factor than other components of the plaque.

Vasoconstriction

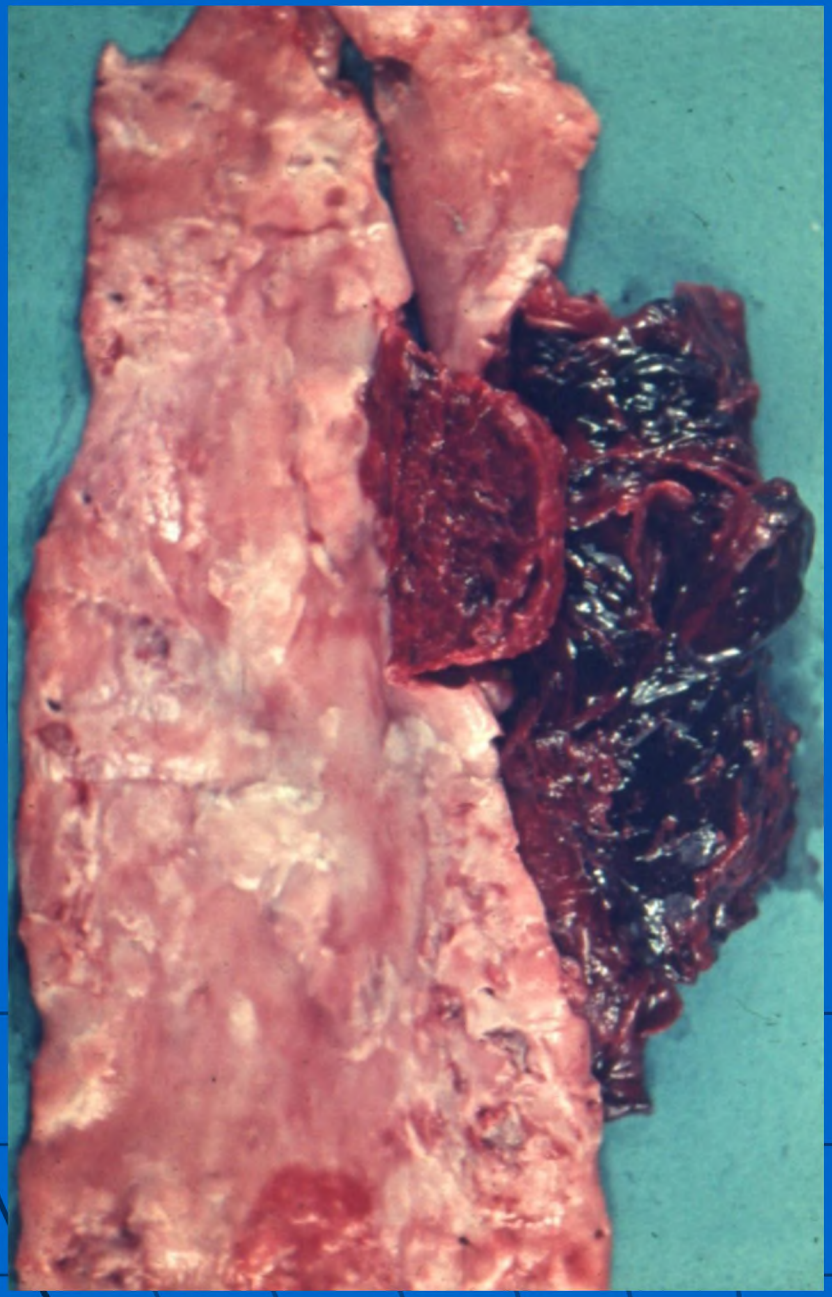
- The platelet-rich thrombus can release vasoconstrictor substances such as serotonin and thromboxane A2 that induces vasoconstriction at the site of plaque rupture or the microcirculation. This vasoconstrictor effect is the dominant factor in Prinzmetal variant angina characterized by transient, abrupt constriction of a coronary segment not preceded by an increase in myocardial oxygen demand. These episodes of acute transmural ischaemia are provoked by localized coronary vasospasm, which severely constricts or occludes one or more large epicardial coronary vessels.

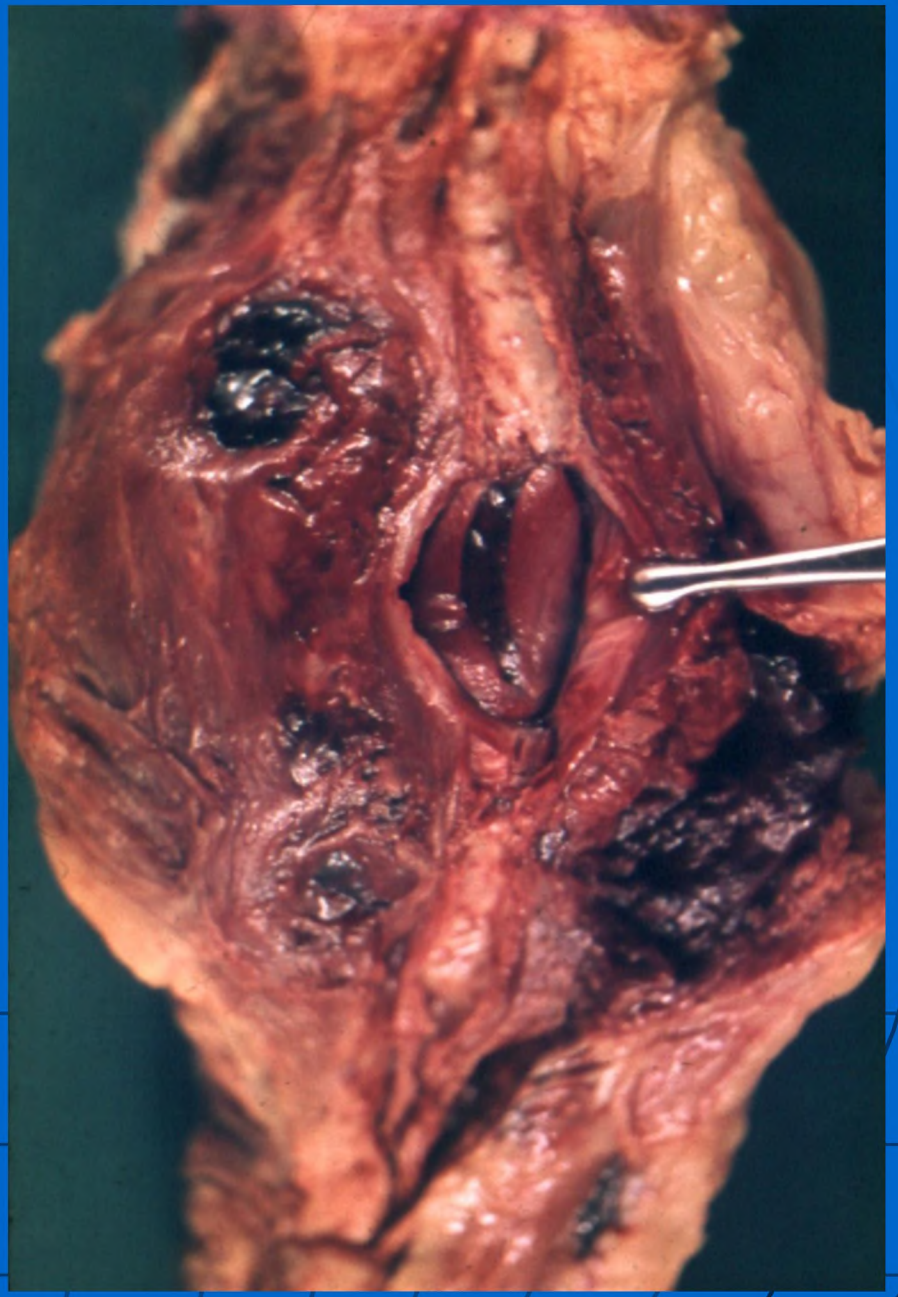
The "complicated lesions" of atherosclerosis, defined by the following changes, have the most clinical significance:

- almost always, atheromas in advanced disease undergo patchy or massive calcification;
- focal rupture or gross ulceration, or both, of the luminal surface of atheromatous plaque may result in exposure of highly thrombogenic substance that induce thrombus formation or discharge of the debris into the bloodstream, producing microemboli (cholesterol emboli or atheroemboli);
- superimposed thrombosis, the most feared complication, usually occurs on fissured or ulcerated lesions; thrombi may partially or completely occlude the lumen;
- hemorrhage into plaque may occur, especially in the coronary arteries from rupture or their overlying cap or the thin-walled capillaries that vascularize the plaque;
- in some cases the underlying media of aorta or other vessel wall undergoes considerable pressure or ischemic atrophy with loss of elastic tissue, causing sufficient weakness to permit aneurismal dilation.

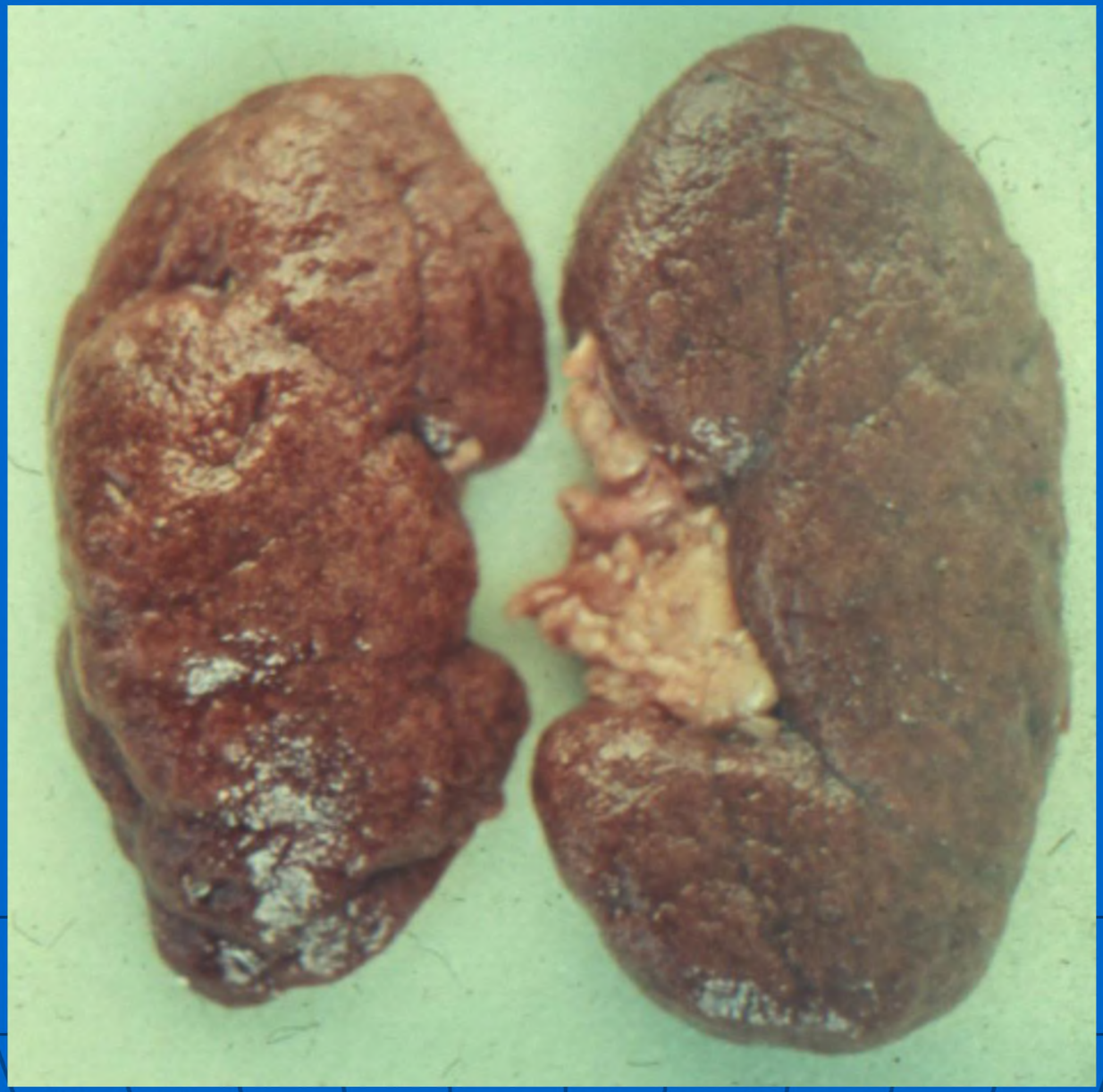


Aorta. Complicated lesions, aneurysmal dilation

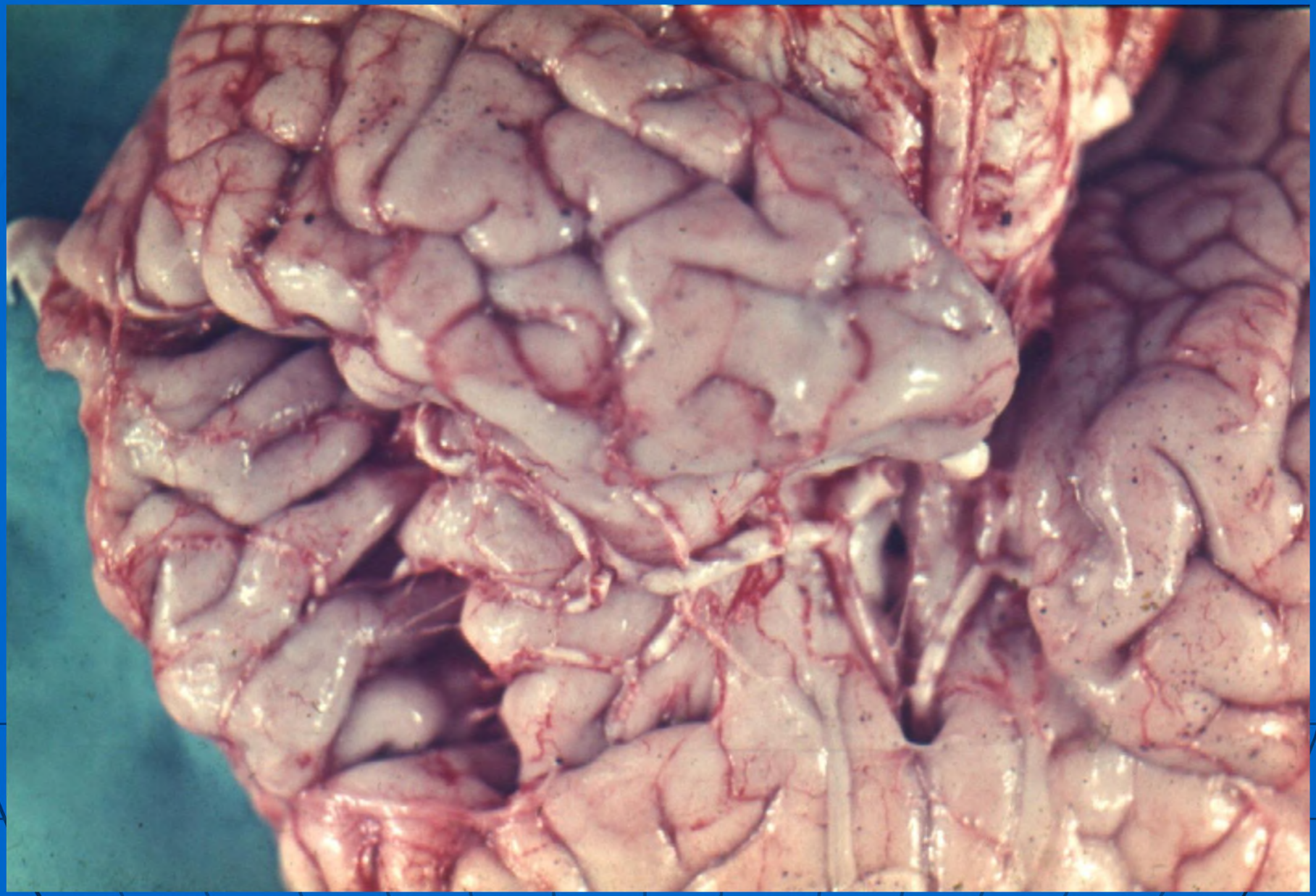




Aorta. Complicated lesions, aneurysmal dilation

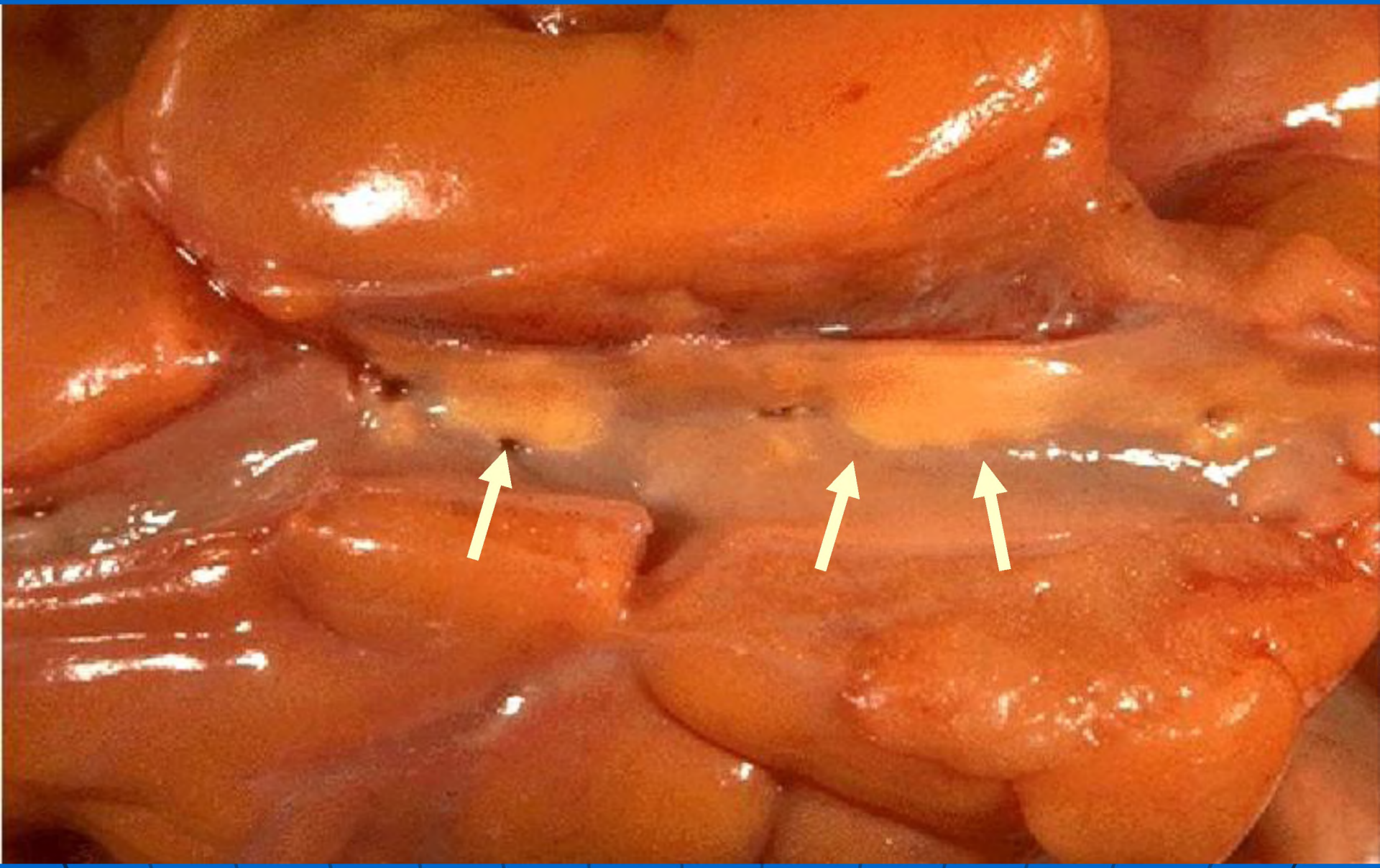


Kidneys with atherosclerotic nephrosclerosis - coarse retracted scars, wrinkled surface of the kidneys

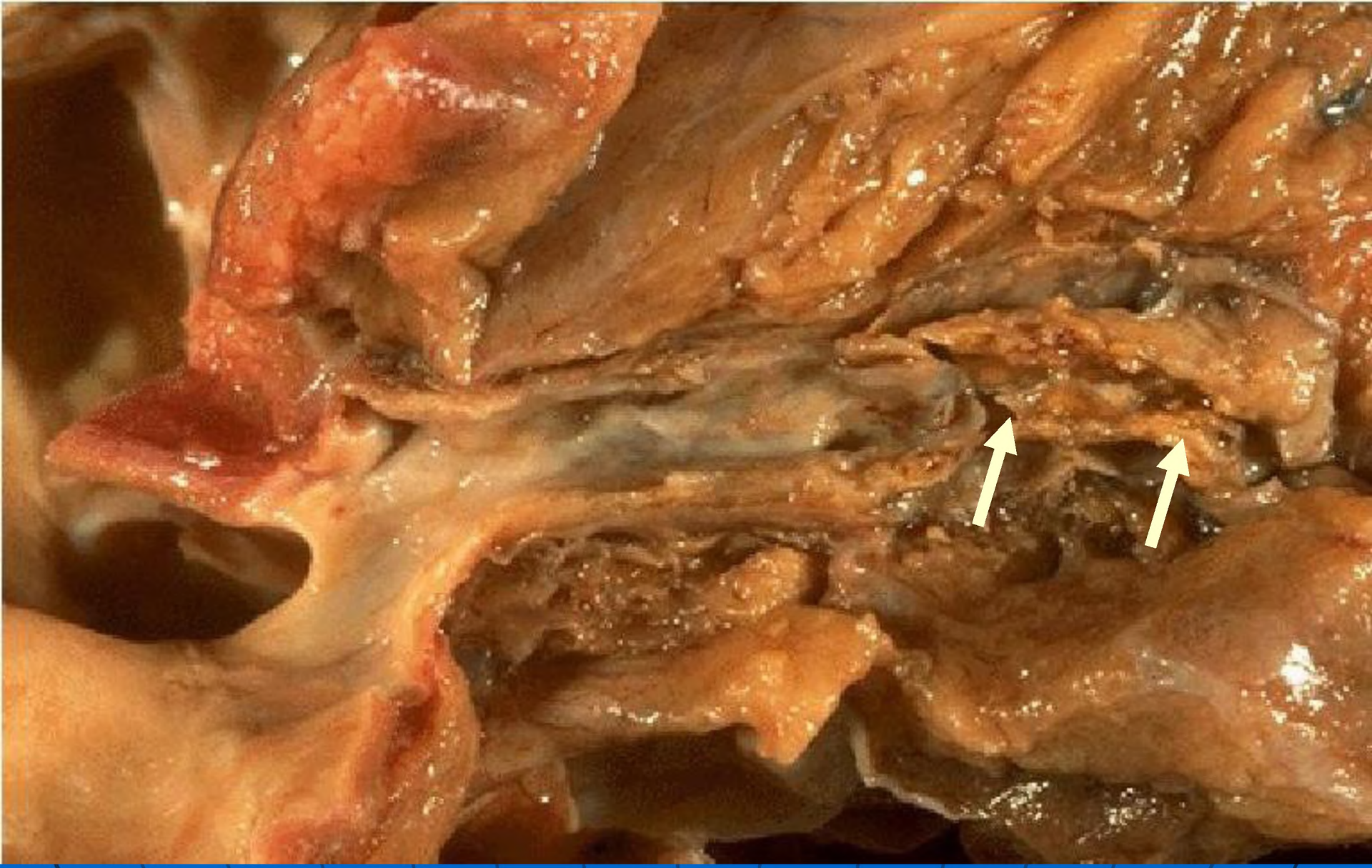


Brain with atherosclerotic plaques in the cerebral arteries.

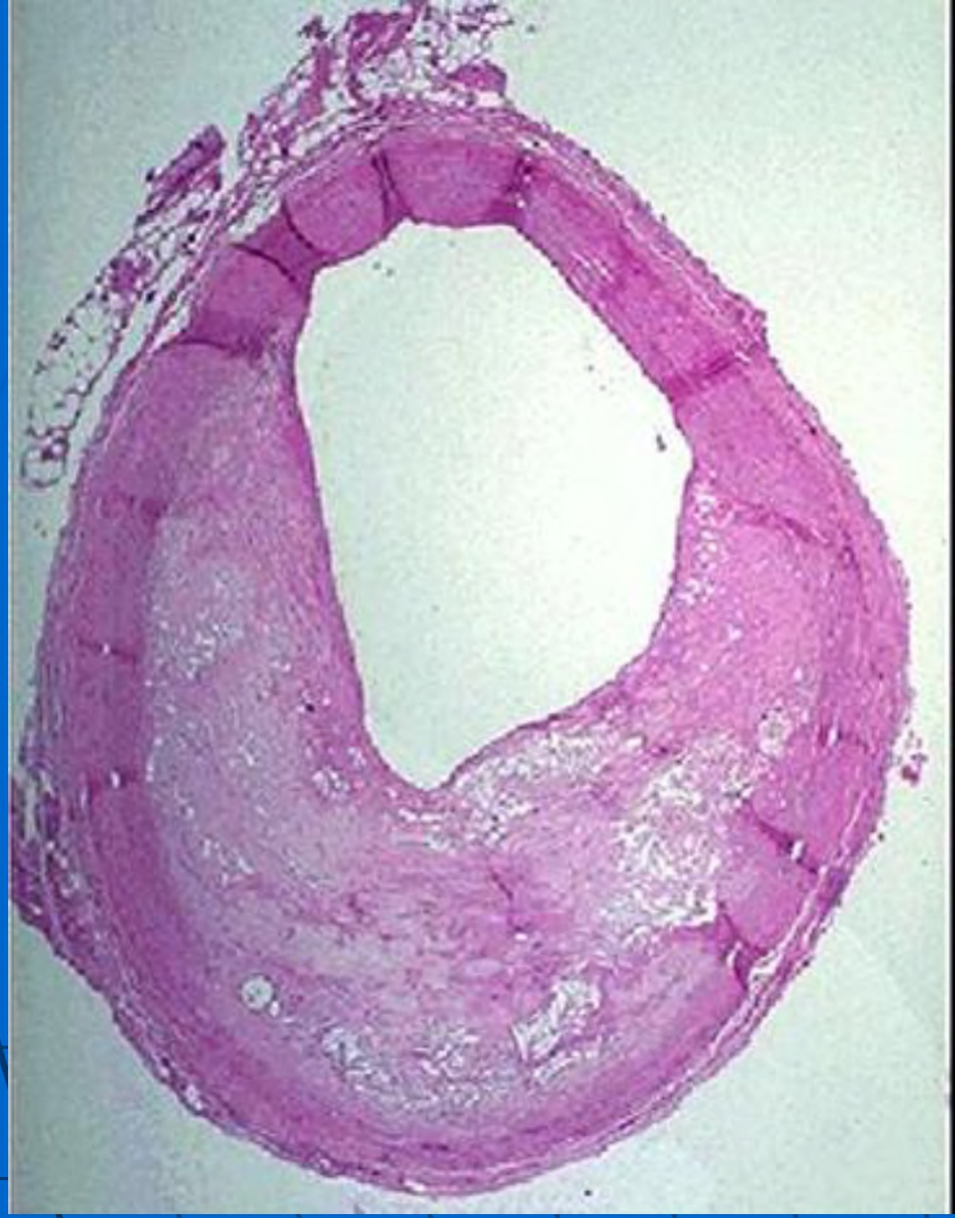
Coronary artery in cross section with varying degrees of atherosclerotic stenosis in different areas.

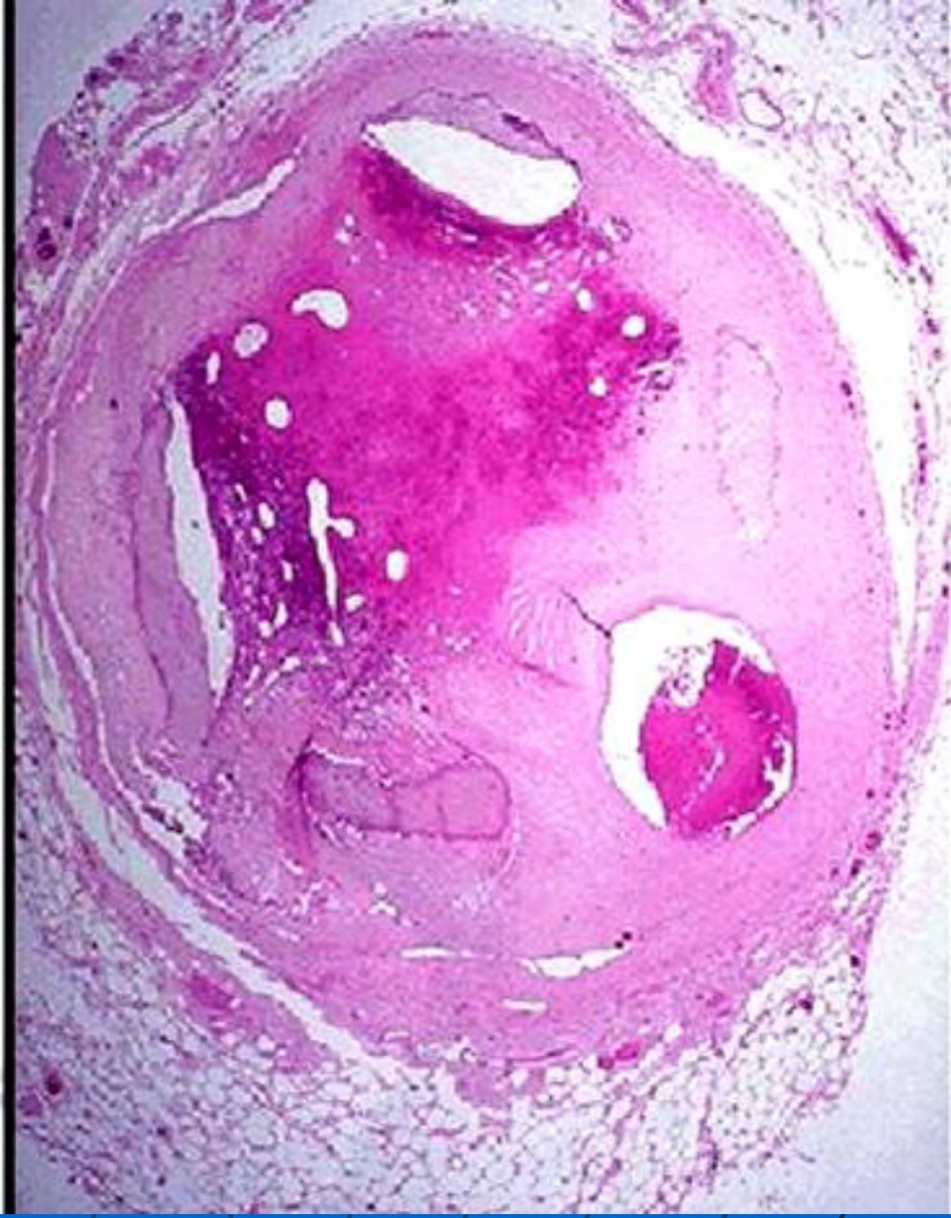


Atherosclerotic plaques
in the coronary artery.

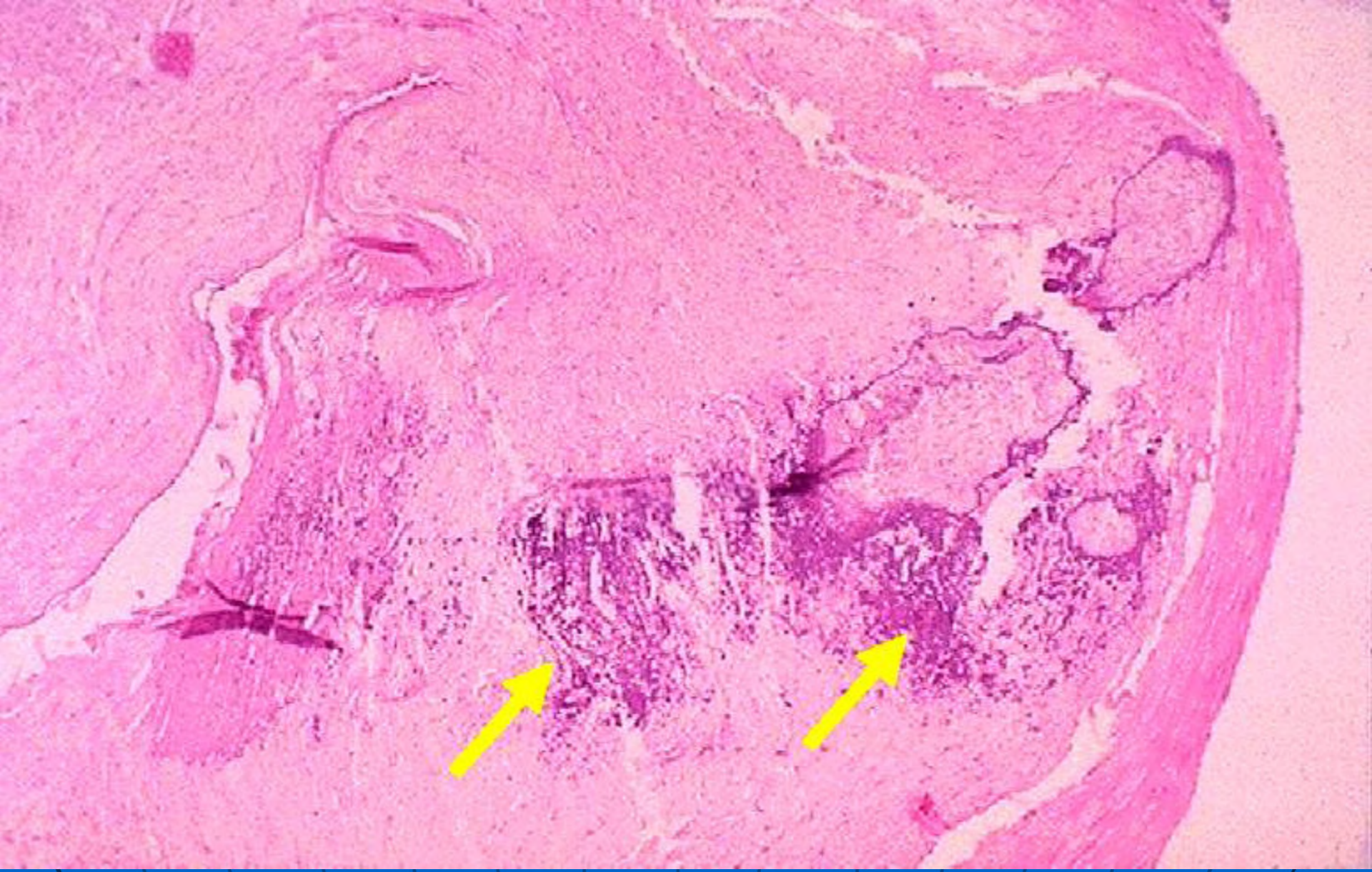


Atherosclerosis of the coronary artery
at the stage of ulcerative atheromatosis.

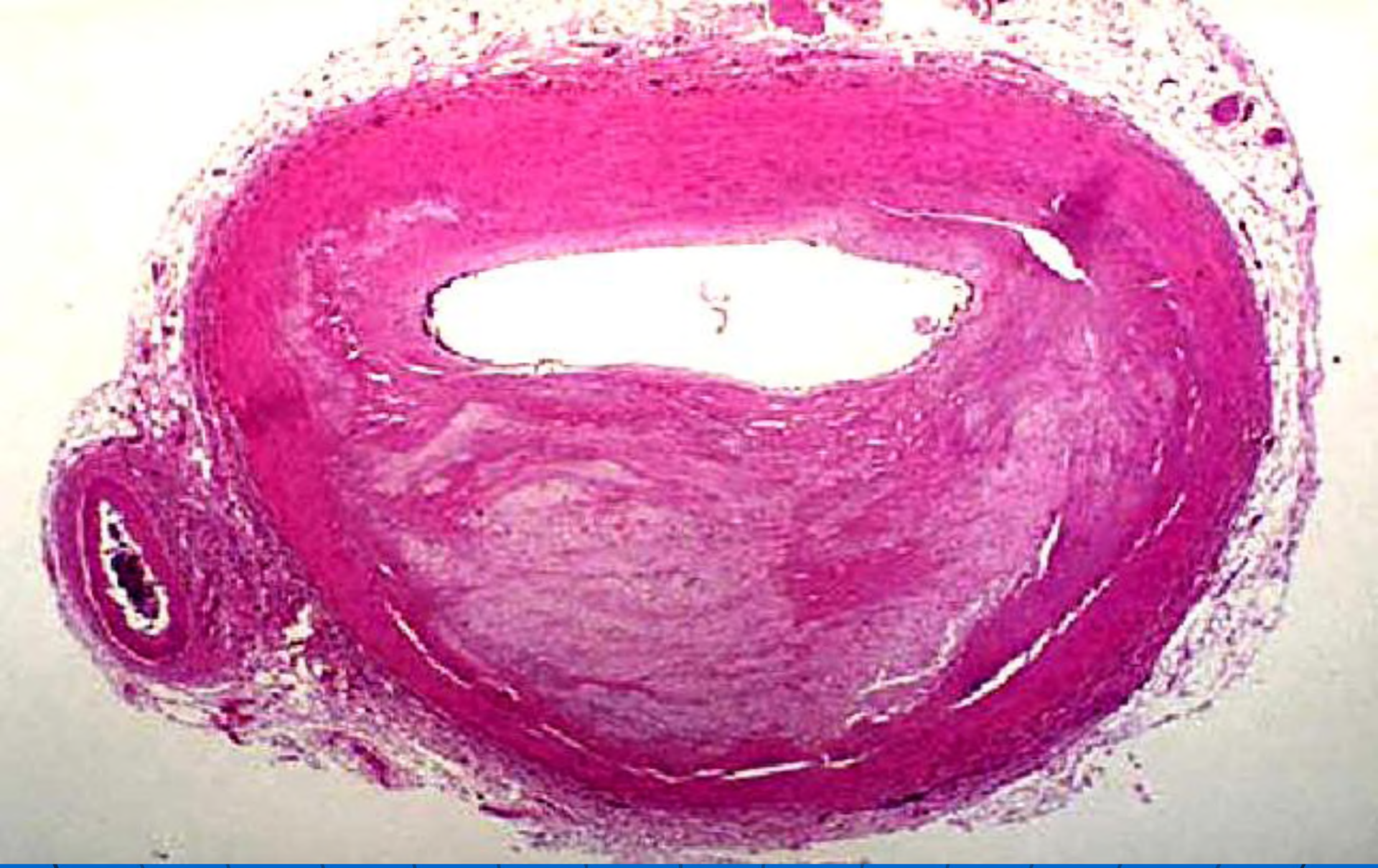




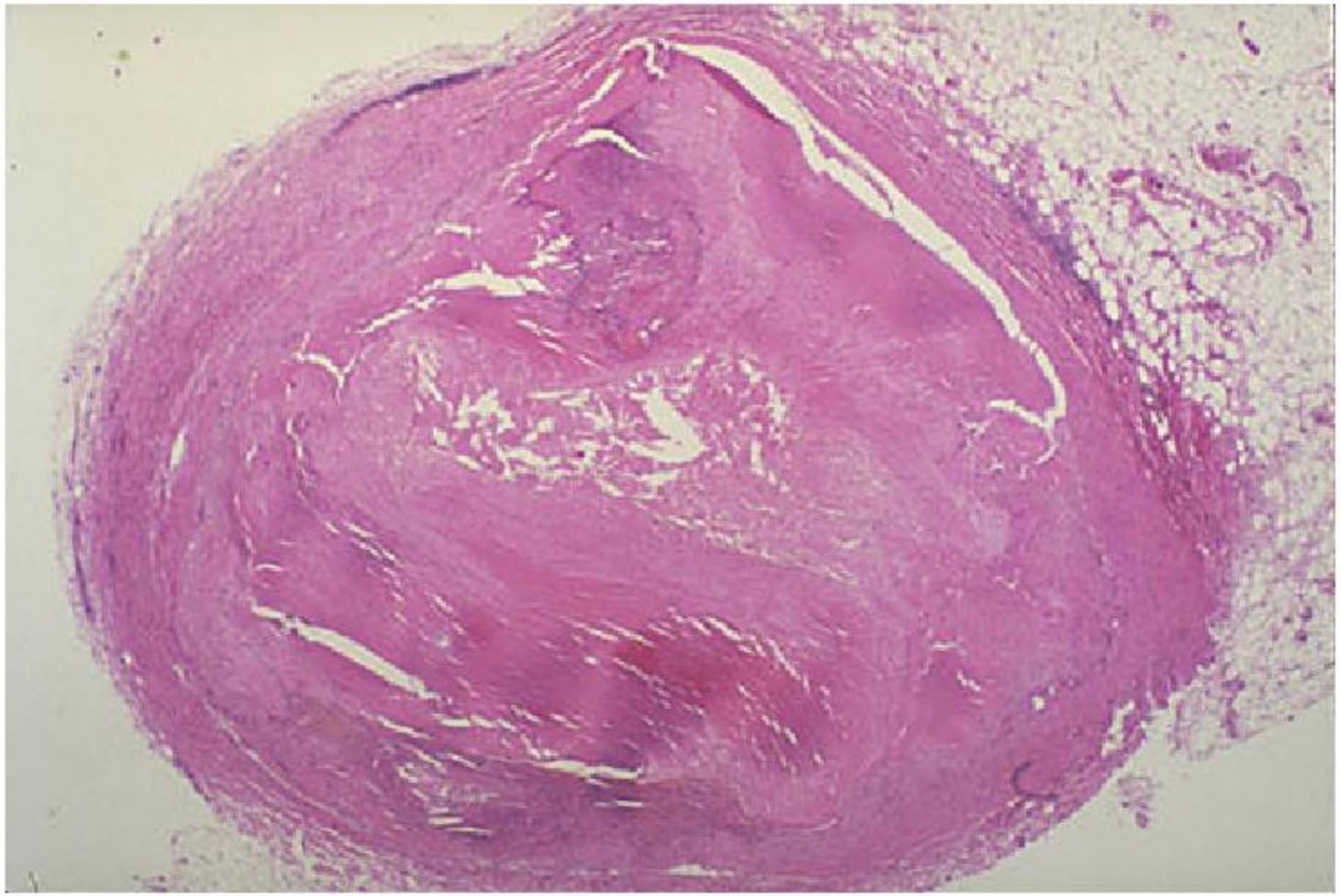
Stenosis of coronary artery
and coronary artery with recanalized thrombus.



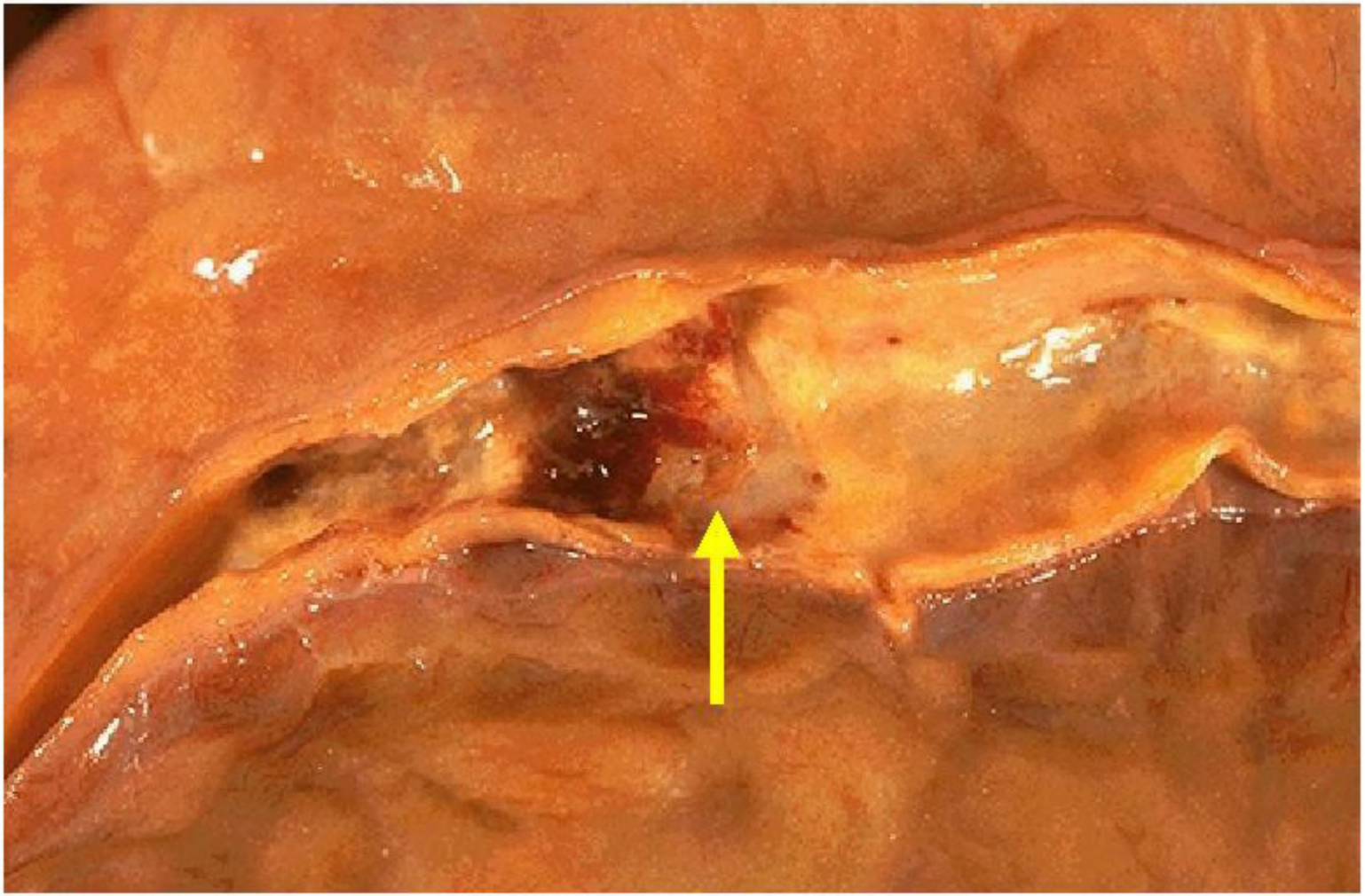
Stenosing atherosclerosis of the coronary artery. Stage of atherocalcinosis (arrows).



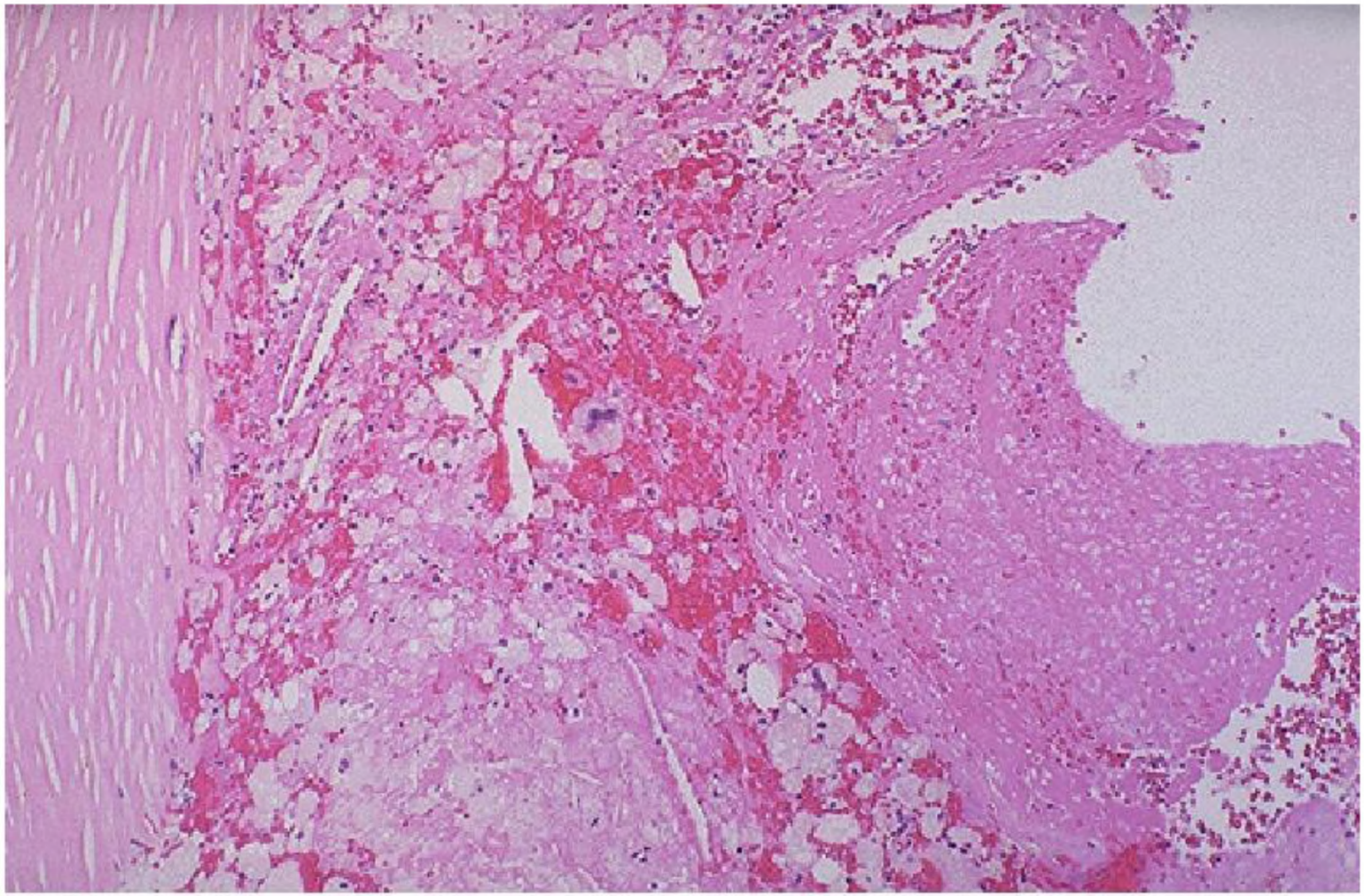
Stenosis of the coronary artery by 75% or more always manifested by angina.



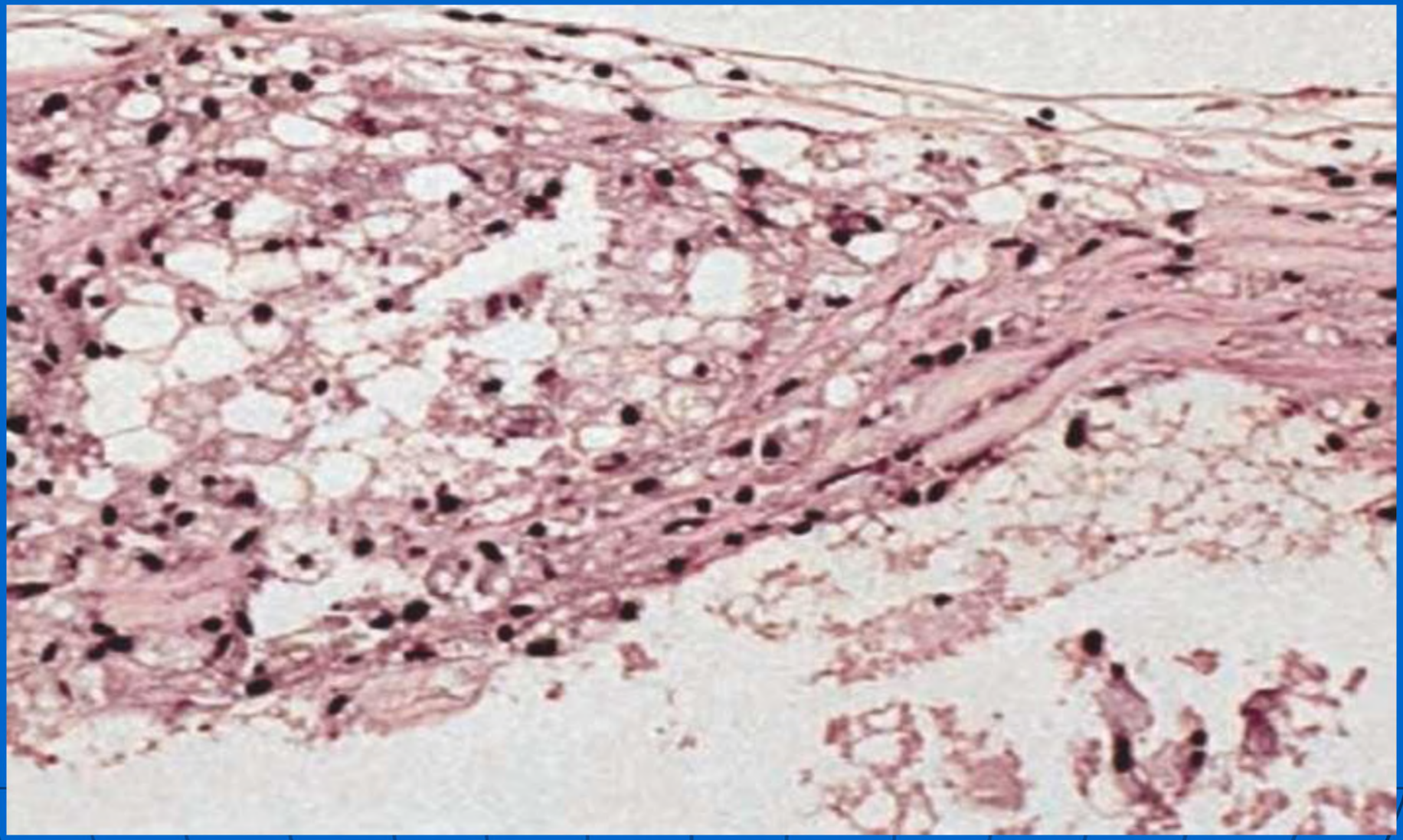
Если окклюзия венечной артерии нарастает постепенно, успевают развиться коллатерали.



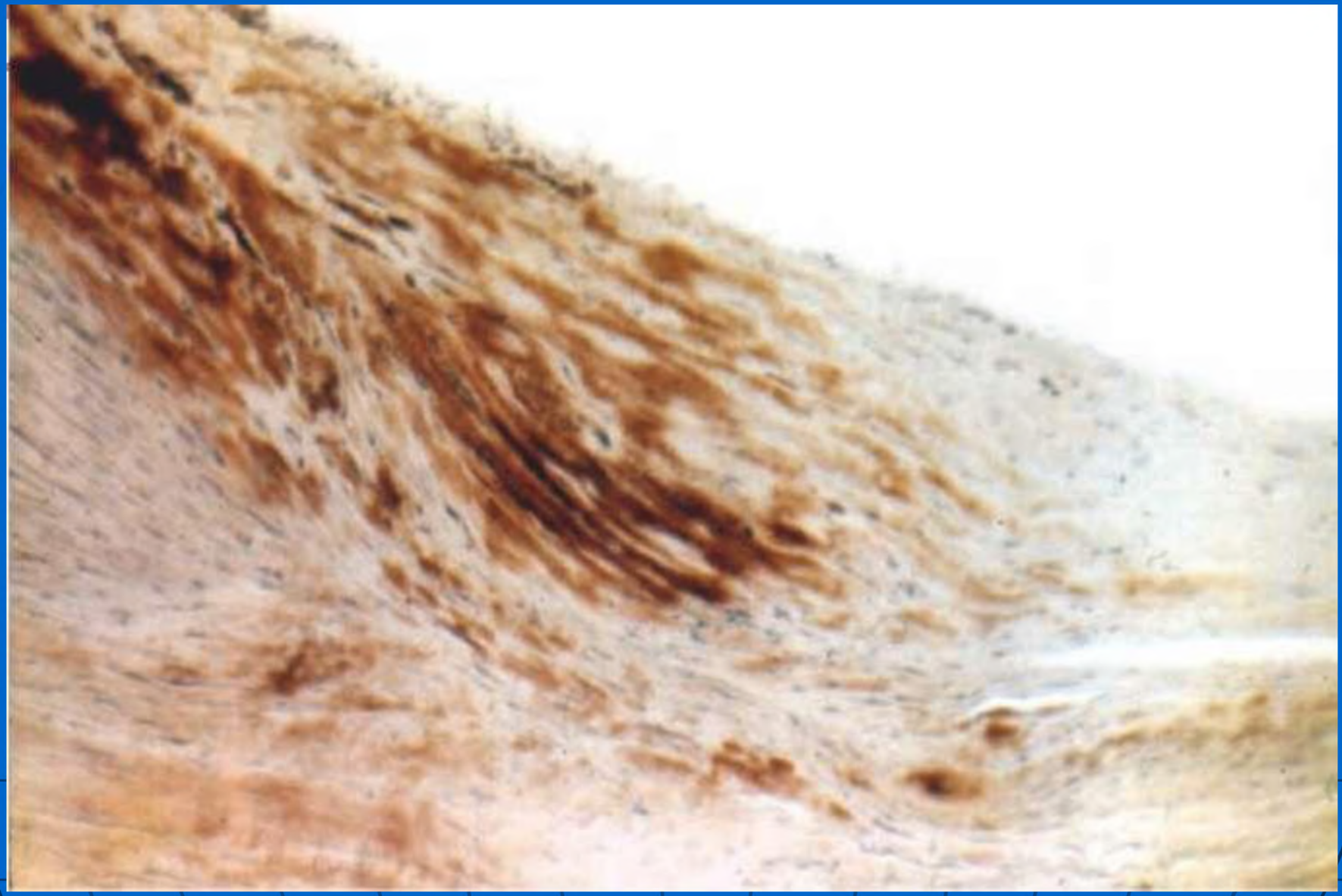
Кровоизлияние в атероматозную бляшку с разрывом ее покрышки, которая перекрывает просвет венечной артерии в виде клапана - одна из наиболее частых причин остановки кровотока по артерии.



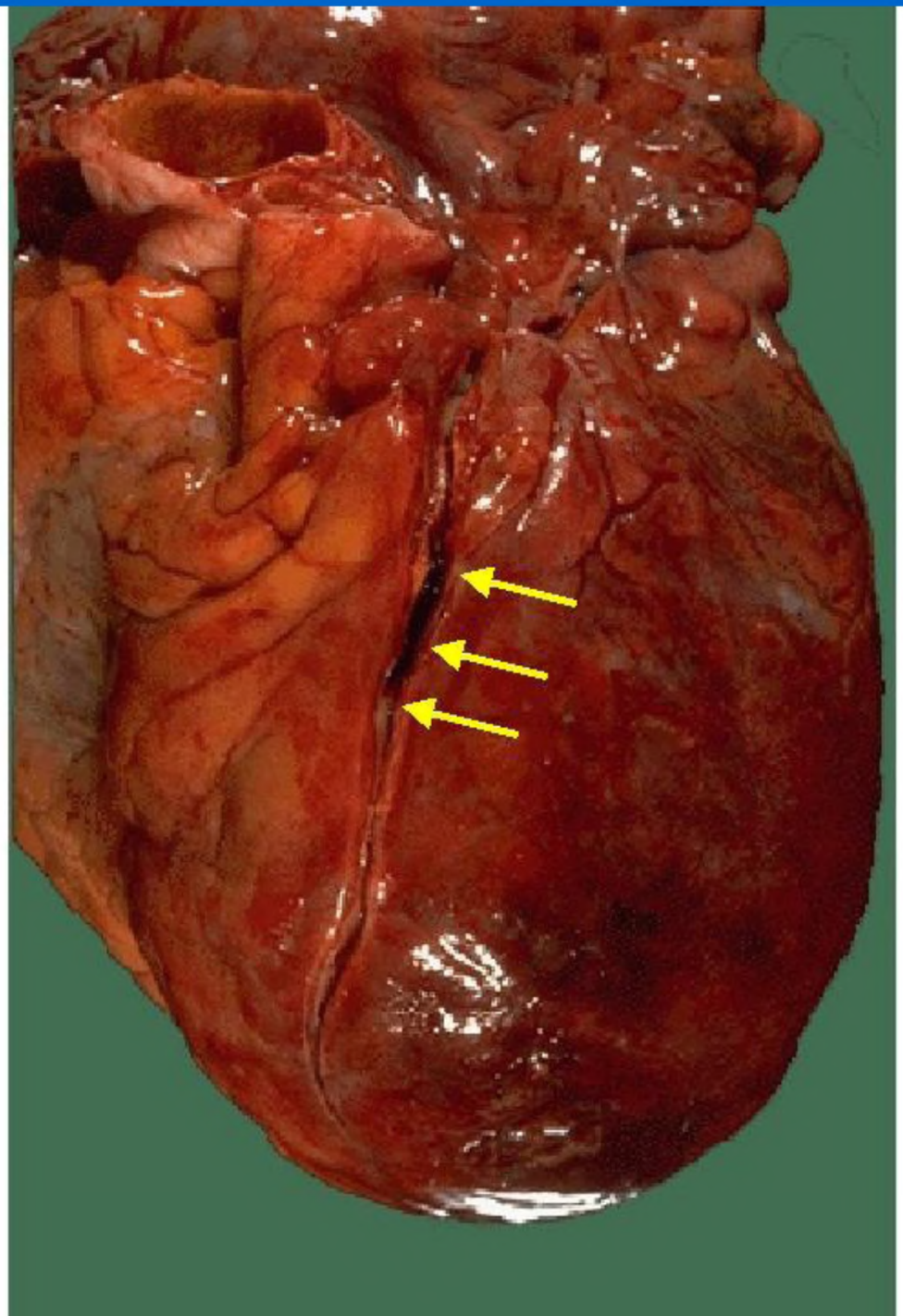
Кровоизлияние в толщу атероматозной бляшки и пристеночный тромб. В бляшке видны щели на месте растворившихся при проводке кристаллов холестерина, ксантомные клетки.



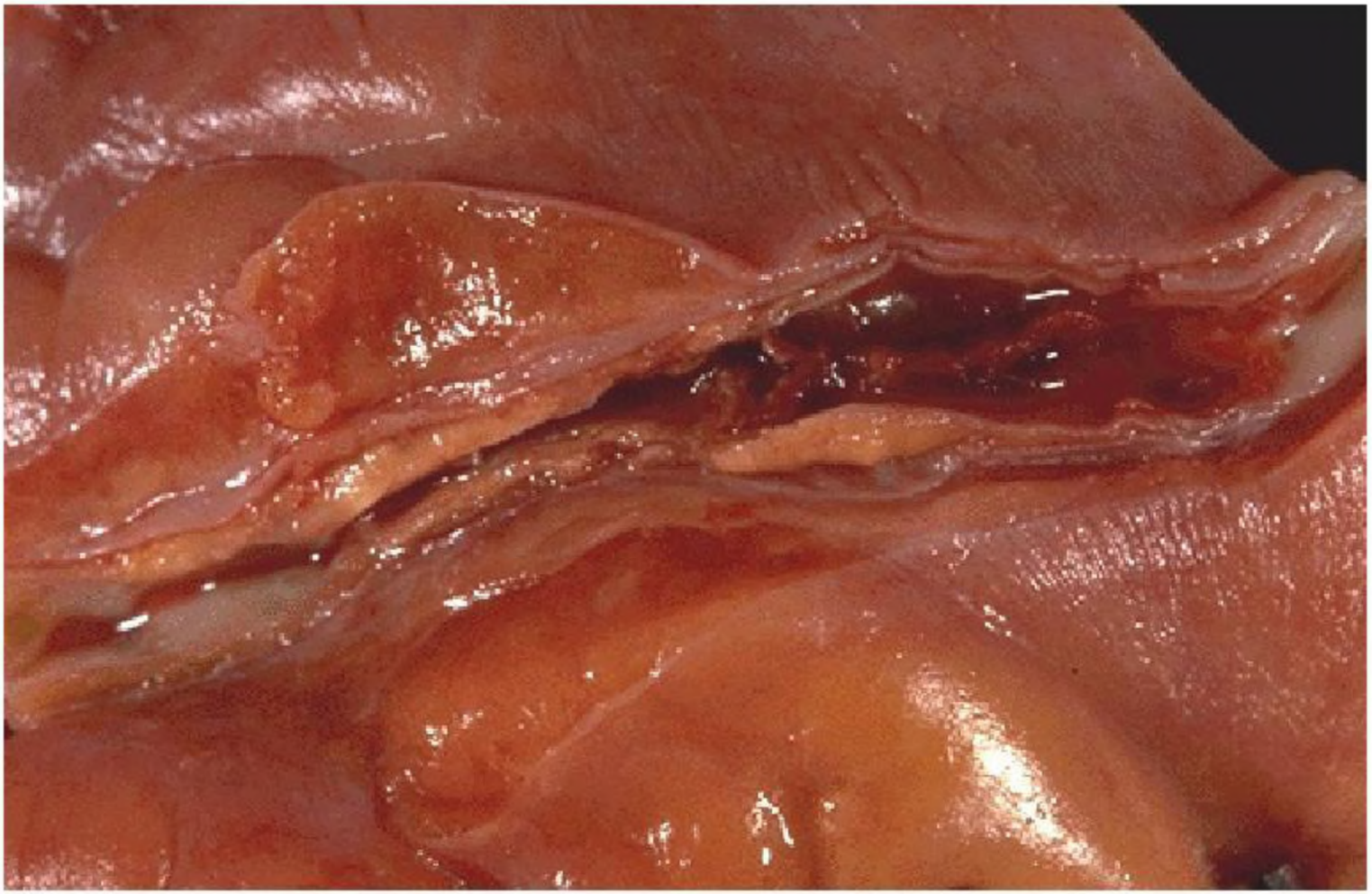
Unstable atherosclerotic plaque: loosening of the connective tissue of the capsule, accumulation of foam cells, diffuse infiltration by lymphocytes and macrophages, atheromatous masses in the large lipid core. Stained with hematoxylin and eosin.



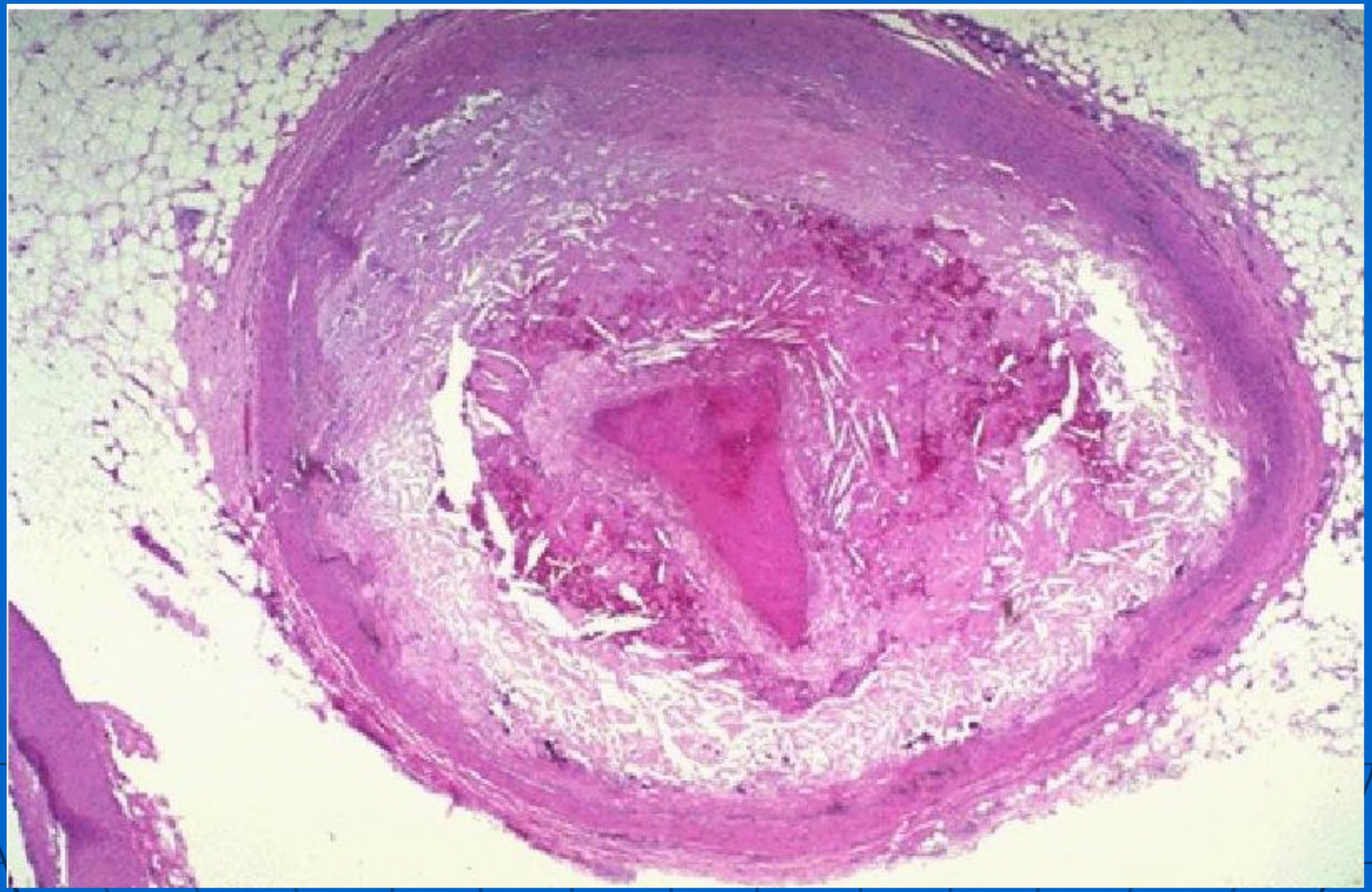
Unstable atherosclerotic plaque: lipid infiltration of plaque capsule. Stained with Sudan III.



Тромбоз передней нисходящей венечной артерии сердца.
Тромбоз — еще одна причина острого нарушения коронарного кровотока.



Тромбоз венечной артерии может приводить либо к внезапной смерти, либо к инфаркту миокарда.



Coronary artery thrombosis during atheromatous plaque. One can see the clefts in the place of cholesterol crystals dissolved during tissue placement.

Atherosclerotic lesions cause clinical disease by the following:

- slow, insidious narrowing of the vascular lumen, resulting in ischemia of tissues perused by the involved vessels;
- sudden occlusion of the lumen by superimposed thrombosis or hemorrhage into the atheroma, producing ischemia and if severe and prolonged infarction of the tissues in the perfusion zone;
- providing a site for thrombosis and then embolism;
- weakening the wall of a vessel, causing aneurysm or rupture.