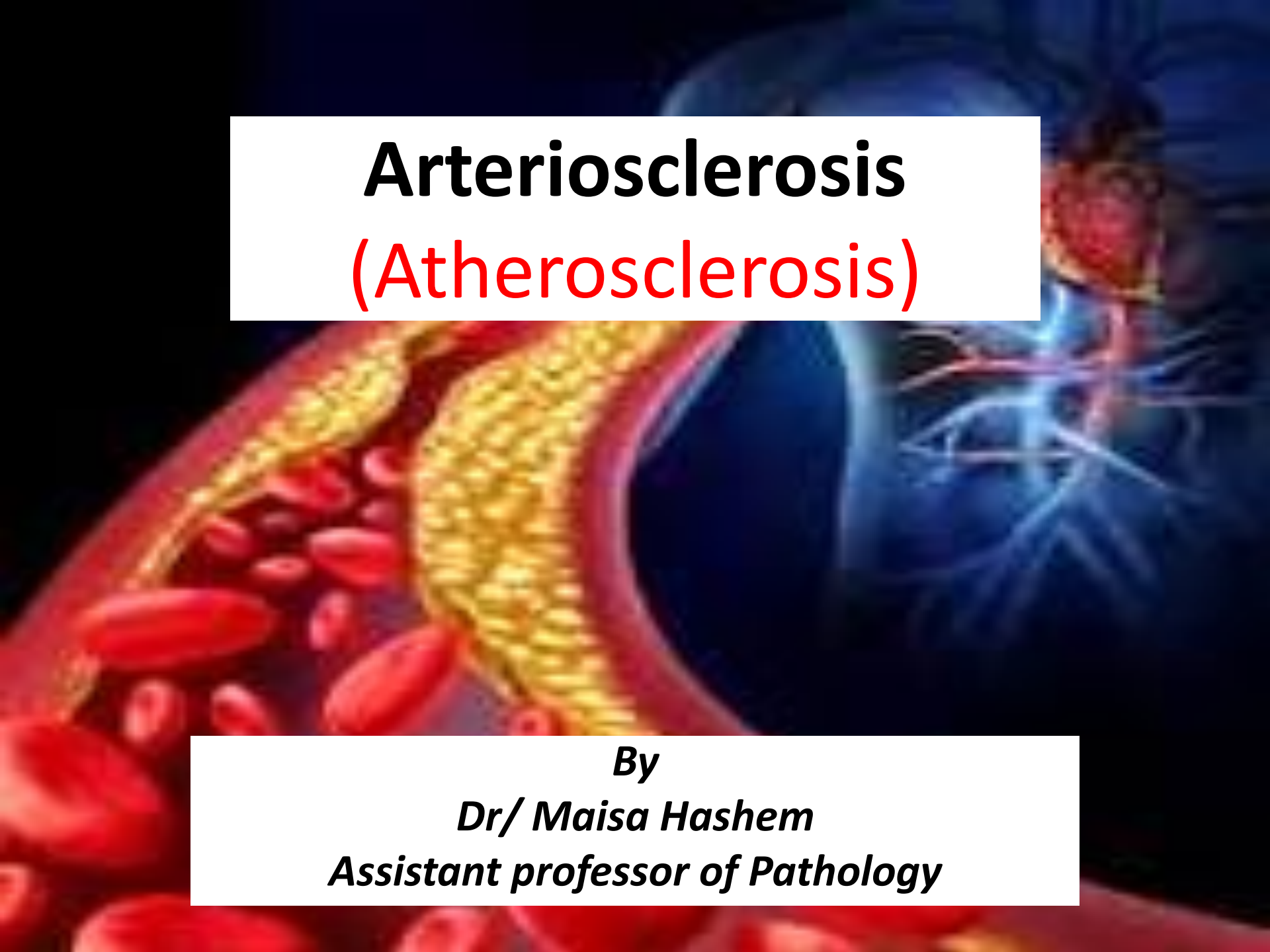

Arteriosclerosis
(Atherosclerosis)

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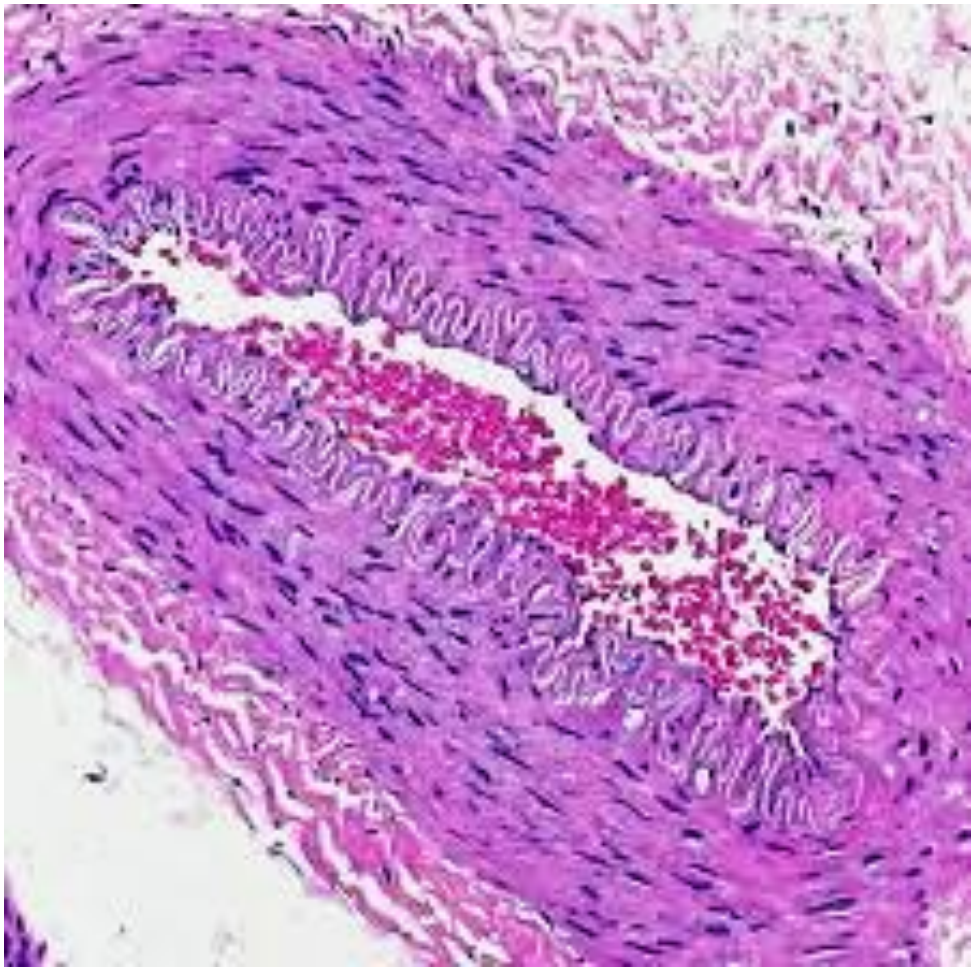
Learning objectives

After the lecture, students should be able to:

- Define the term atherosclerosis.
- list the risk factors for its development.
- Mention its pathogenesis.
- Describe the morphological changes that occur in vessel wall in the various stages of development of atheroma.
- Outline the common complications of atheroma.

The wall of the blood vessel is formed of:

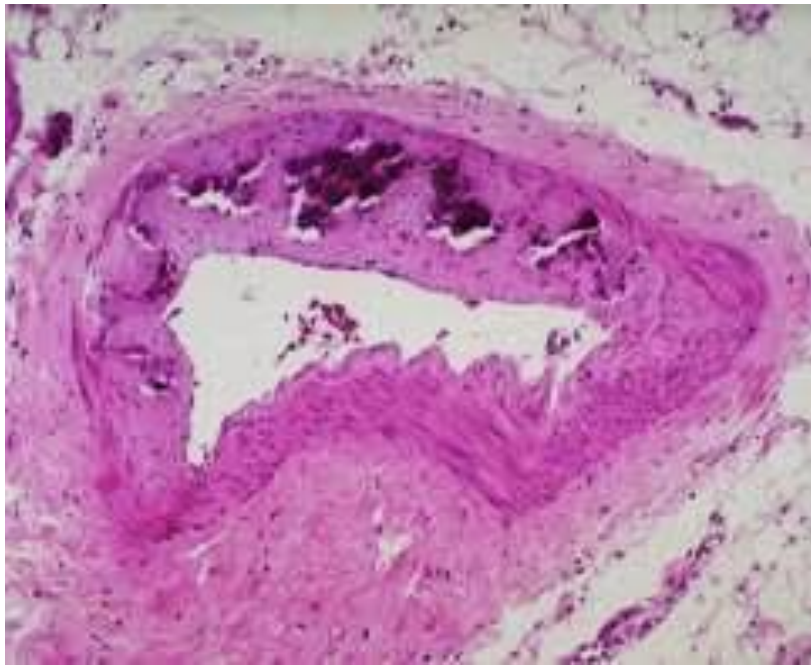
- **Tunica intima:** Features simple squamous endothelium, thin subendothelial connective tissue, and a prominent, often wavy internal elastic lamina (separating intima and media).
- **Tunica Media:** The thickest layer, consisting of several layers of circularly arranged smooth muscle cells interspersed with thin elastic and collagen fibers. The outermost edge may show a less conspicuous external elastic lamina.
- **Tunica adventia (Externa):** Contains collagen and elastic fibers, connective tissue, and sometimes *vasa vasorum* (small vessels supplying the artery wall).



Arteriosclerosis

Arteriosclerosis means hardening of the arteries. There are three types of arteriosclerosis;

1) **Arteriolosclerosis:** affects small arteries and arterioles and cause ischaemic injuries.
2) **MÖnckeberg medial sclerosis:** it affects muscular arteries in old people (>50 years). It is characterized by medial calcification. However these lesions do not encroach on the vessel lumen and are usually not clinically significant.
3) **Atherosclerosis:** it affects large elastic arteries (as aorta, carotid and iliac arteries) and muscular arteries (coronary and popliteal arteries).



Atherosclerosis

Definition: it is a common degenerative disease of arteries characterized by lipid deposition in subintimal connective tissue followed by fibrosis.

Predisposing (risk) factors:

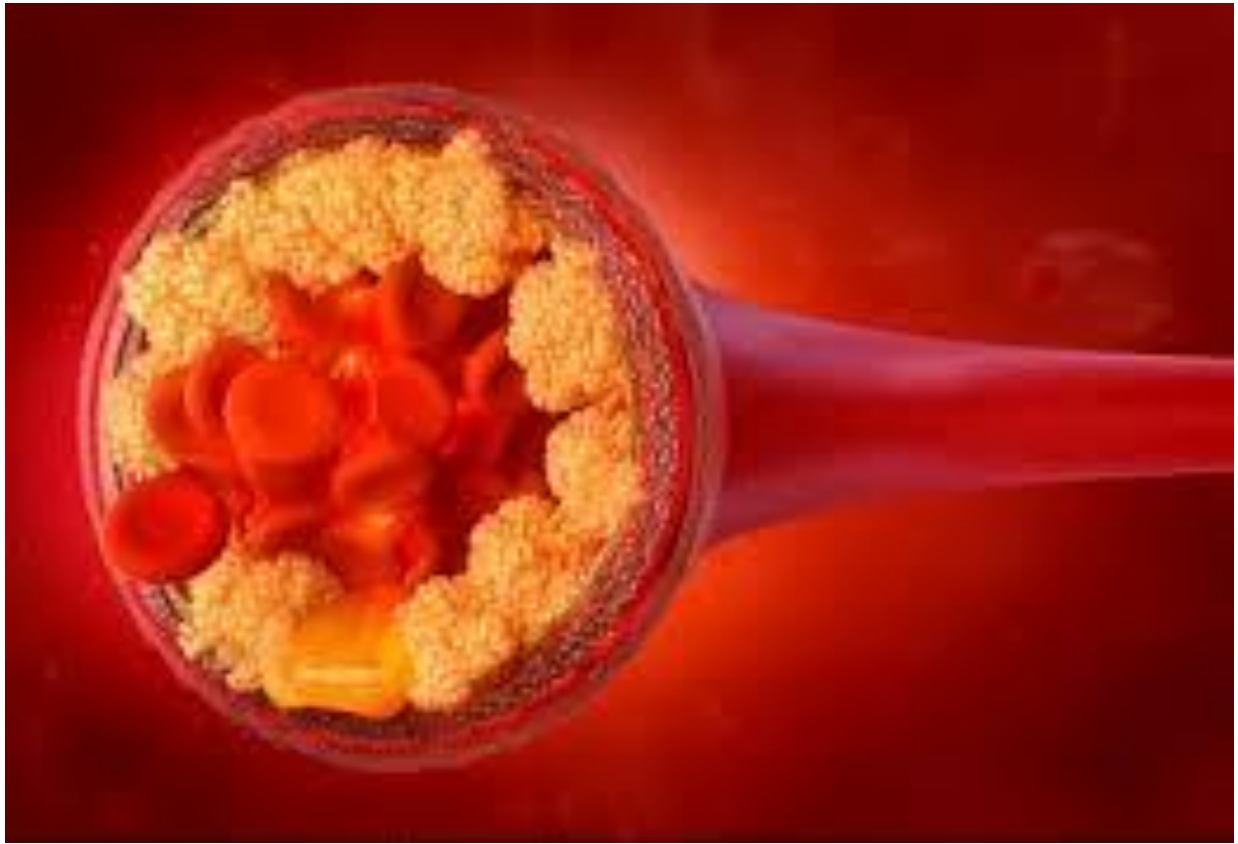
1) Non-modifiable risk factors:

- Hereditary: a familial tendency is usually present.
- Age: children are not affected by atherosclerosis. The incidence and severity increase as the age advance.
- Sex: atherosclerosis is higher in males. Estrogen decrease the incidence in females age of menopause.

2) Modifiable risk factors:

- Diet: excess intake of animal fat favors the development of atherosclerosis.
- Plasma lipids: high serum level of LDL is an important factor in the development of atheroma.
- Stress: it predisposes to atherosclerosis ; Hypertension increases the incidence and complications of the disease.
- Others: diabetes mellitus, cigarette smoking, alcohol consumption and lack of physical exercise.

- Atherosclerosis affects large arteries as aorta and its main branches, in addition to small arteries as the coronary, cerebral and renal.
- In the aorta; the lesions are more severe in the abdominal part, especially around the orifices of the intercostal and lumbar arteries.
- Note, medium sized arteries are rarely affected.



Theories of Atherosclerosis

1) Insudation theory: excess intake of animal fat cause hypercholesterolemia and increase plasma beta lipoproteins. Plasma passes constantly from the vascular lumen through the vessel walls. Repeated endothelial cell injury increase endothelial permeability to plasma lipoproteins. During its passage; some of the large beta lipoproteins are trapped in the subintimal connective tissue. the protein part get filtered, while the insoluble lipid retained and induce further fibrosis.

2) Thrombogenic theory: small fibrin thrombi form always over the intimal surface and heal by organization. When the thrombi are large, its center degenerates and shows lipid containing depris derived from the components of the thrombi.

- Now it is widely accepted that both mural thrombi and insudation of plasma lipids through the endothelium are involved in atheroma formation.

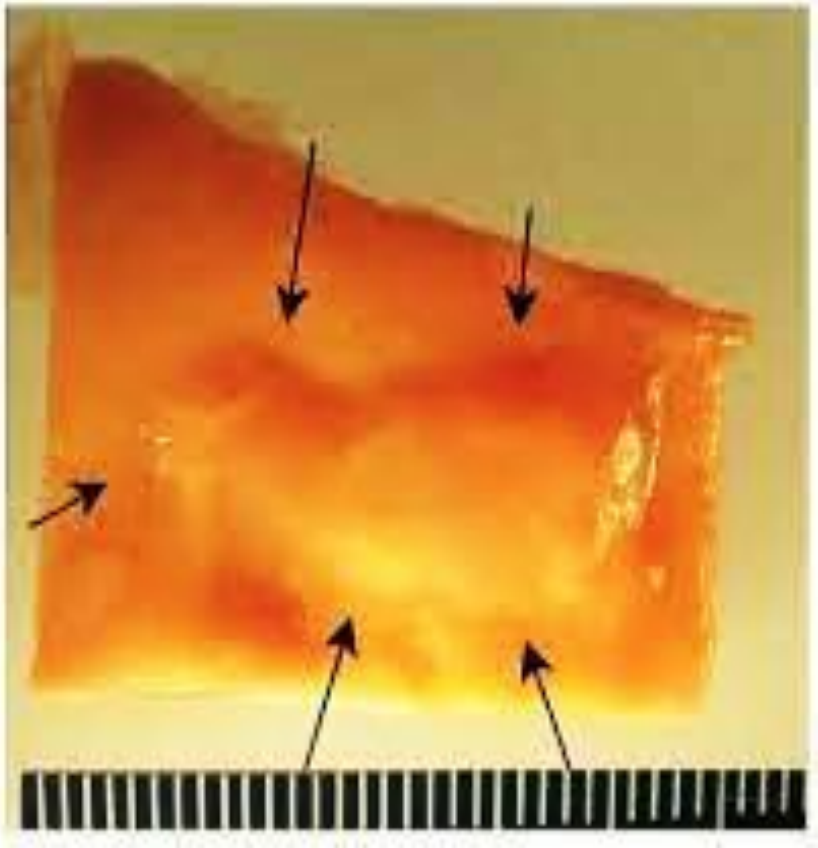
Pathogenesis of atherosclerosis

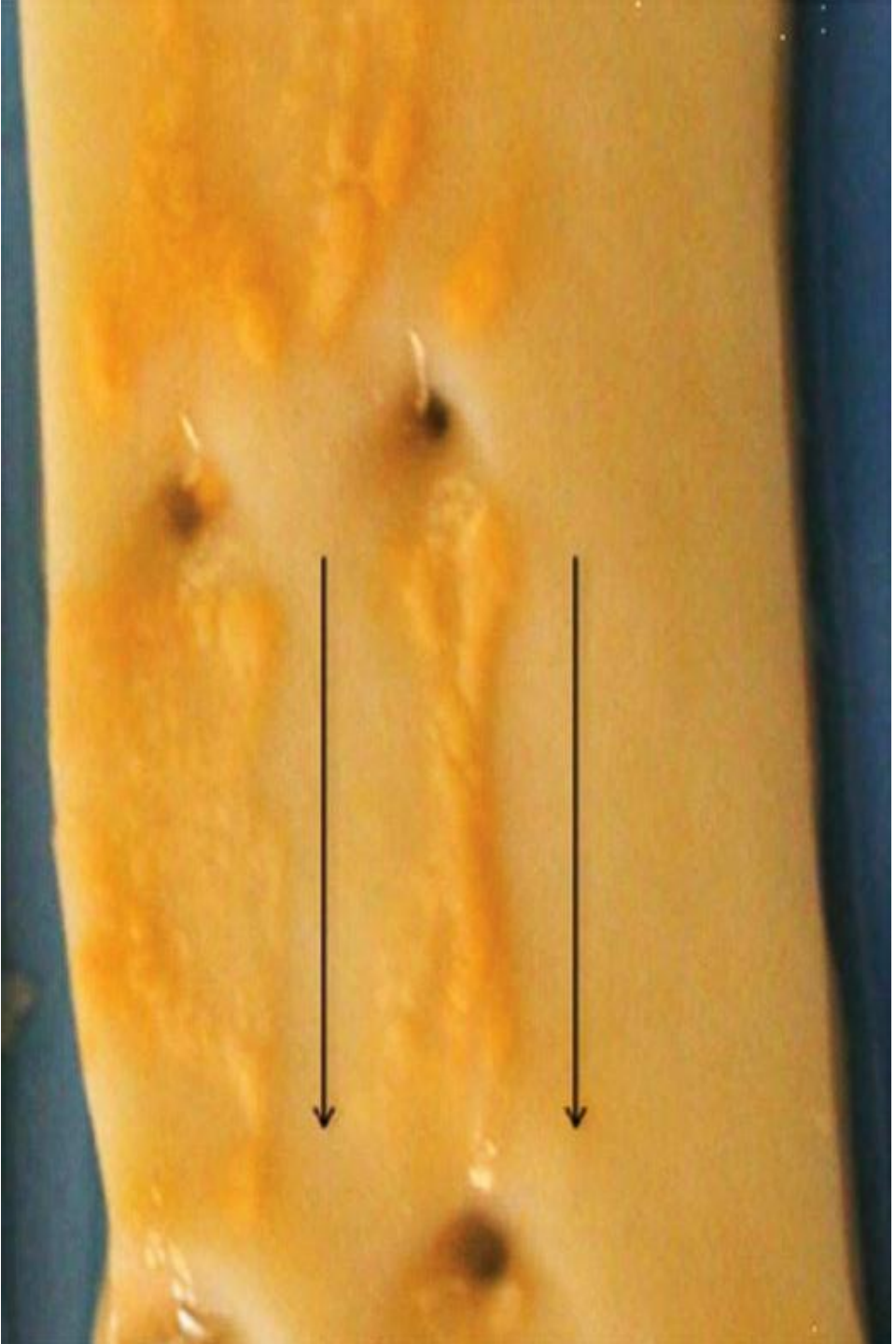
- It is a chronic inflammatory disease of the arterial wall.
- Combined risk factors as hyperlipidaemia, hypertension, smoking, hemodynamic disorders; all these factors produce endothelial cell injury.
- Endothelial cell injury allow recruitment of platelets and monocytes at intimal surface.
- platelets produce PDFG that allows recruitment and proliferation of smooth muscles of tunica media.
- Some monocytes enter the subintimal connective tissue and transform to macrophages.

- Due to hypertension and hyperlipidaemia; few fat droplets deposit on tunica intima and enter subintimal connective tissue.
- Some of these fat droplets are engulfed by smooth muscles and macrophages (foam cells), other fat droplets are free in the subintimal connective tissue.
- These lipid-laden macrophages and proliferated smooth muscles accumulate in aggregates produce fatty streaks.

Fatty Streaks

- Fatty streaks are the earliest lesions in atherosclerosis. They are composed of lipid-filled foamy macrophages. Initially; these fatty streaks appear as multiple minute flat yellow spots. Then, they coalesce into elongated streaks.
- These lesions are not significantly raised and don't cause any disturbance of blood flow.
- Fatty streaks are virtually seen in aortas of all children >10 years.
- Not all fatty streaks progress to advanced stages.



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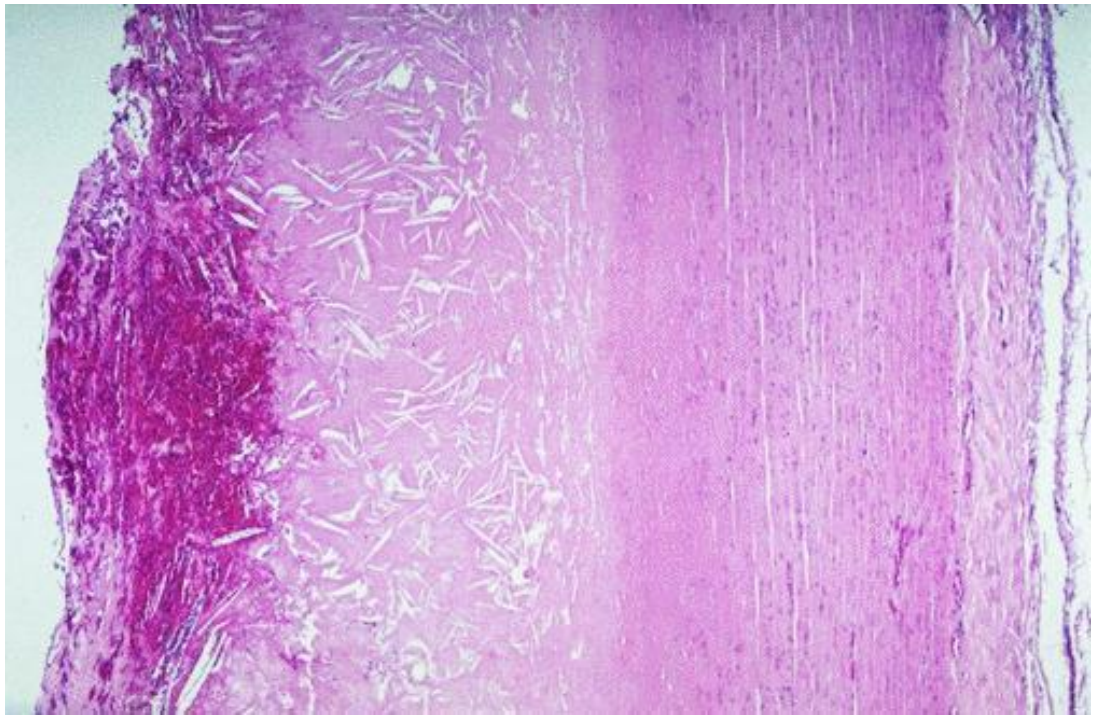
Atherosclerotic plaque/ atheroma

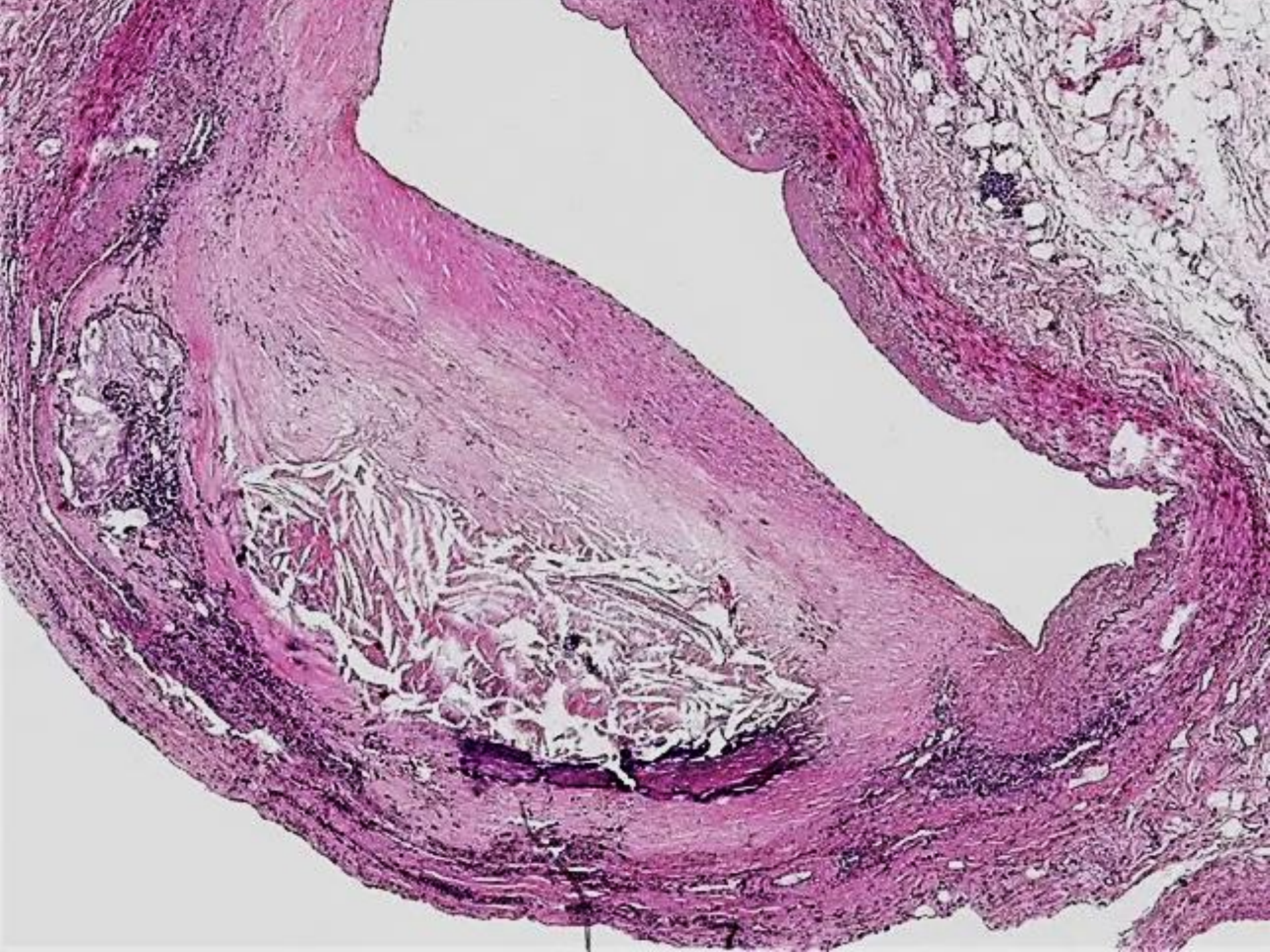
- The subintimal aggregates of foamy macrophages increase gradually in size. They are accompanied by proliferation of smooth muscles and collagen fibers.
- The smooth muscles proliferate and migrate to cover the fatty streaks forming fibrous caps.
- Beneath and to sides of the cap, there is proliferation of T-lymphocytes, macrophages and smooth muscles.

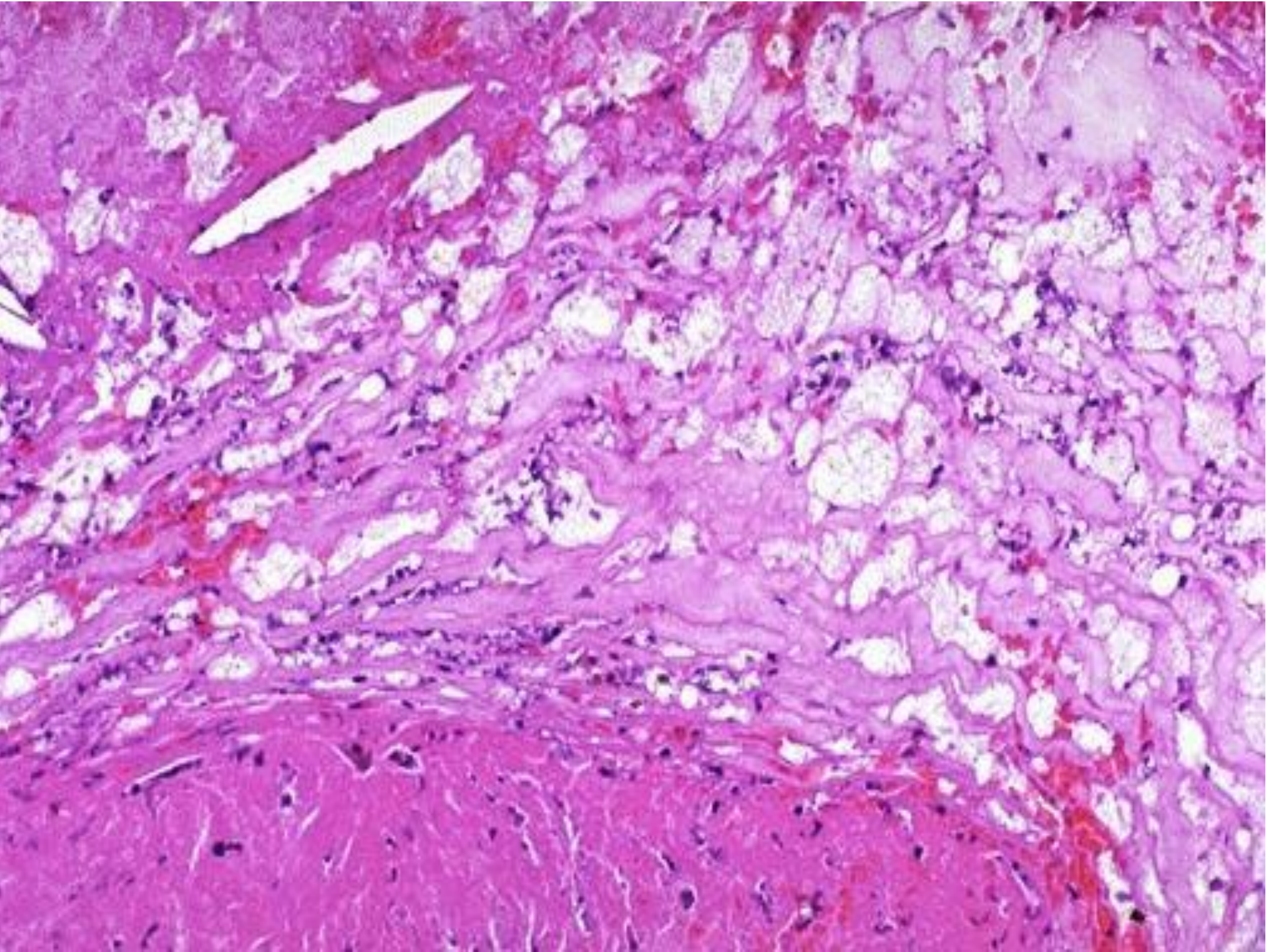
- The center of the atherosclerotic plaque undergo necrosis and dystrophic calcification.
- The plaque press on tunica media cause its thinning out.
- The center of the lesion may undergo neovascularization.
- The atherosclerotic/ atheromatous plaques impringe on the vascular lumen.
- Grossly; the atheromatous plaque appear as patchy, yellowish-white, elevated patches.
- The overlying endothelium may ulcerate and superimposed by thrombi.

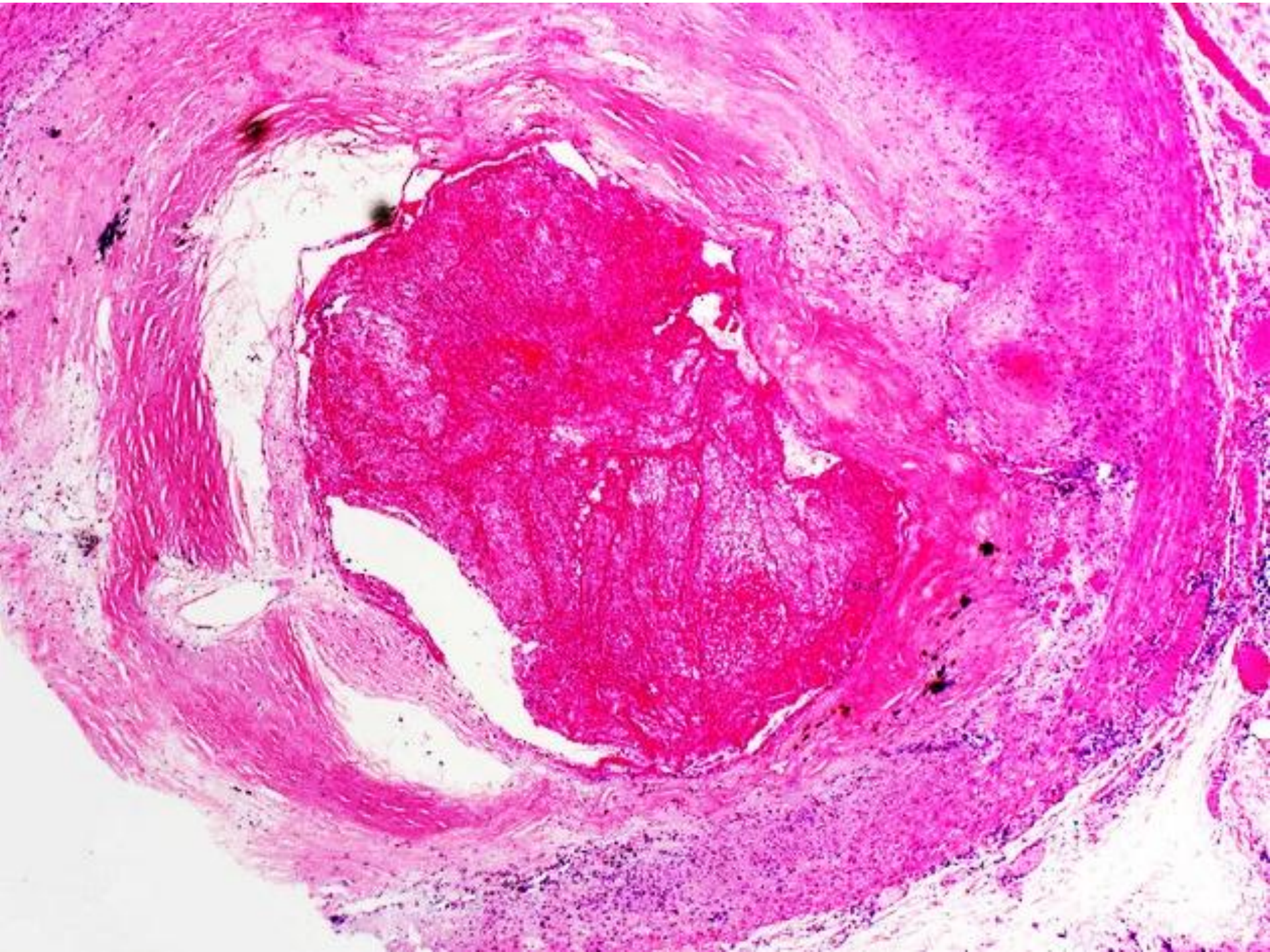
Microscopic picture

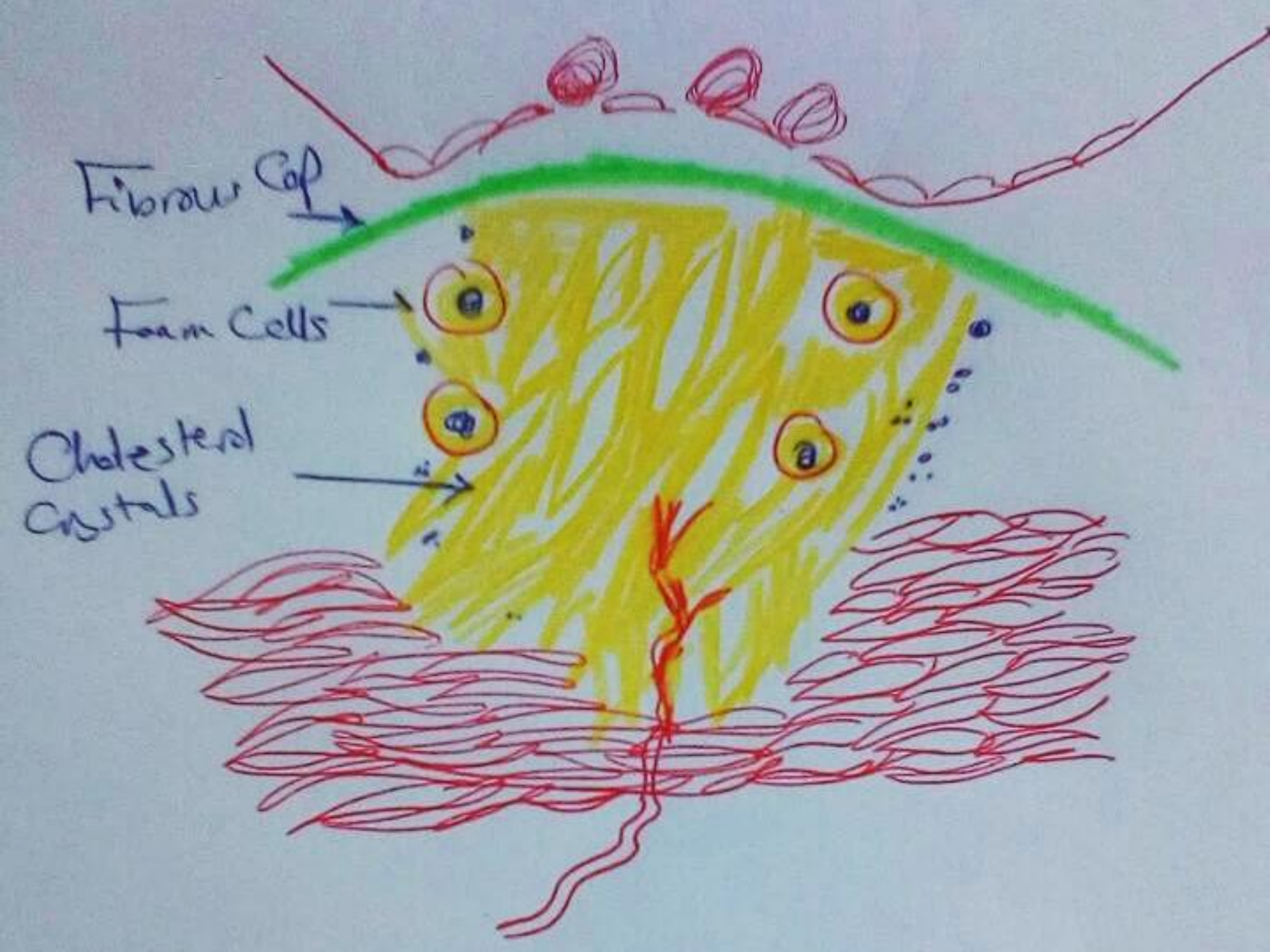
- Cholesterol and its esters are deposited in the subintimal connective tissue, they are found free, inside smooth muscle cells derived from the media and inside macrophages (foam cells). in paraffin sections; the free cholesterol crystals appear as needle shaped or rhombic shaped empty spaces (dissolved).
- Vascularization, fibrosis and hyalinosis of the subintimal connective tissue around the deposited lipids.
- Dark, blue stained calcium granules may be deposited in old lesions.
- Fragmentation of internal elastic lamina and atrophy of the media opposite the atheroma.





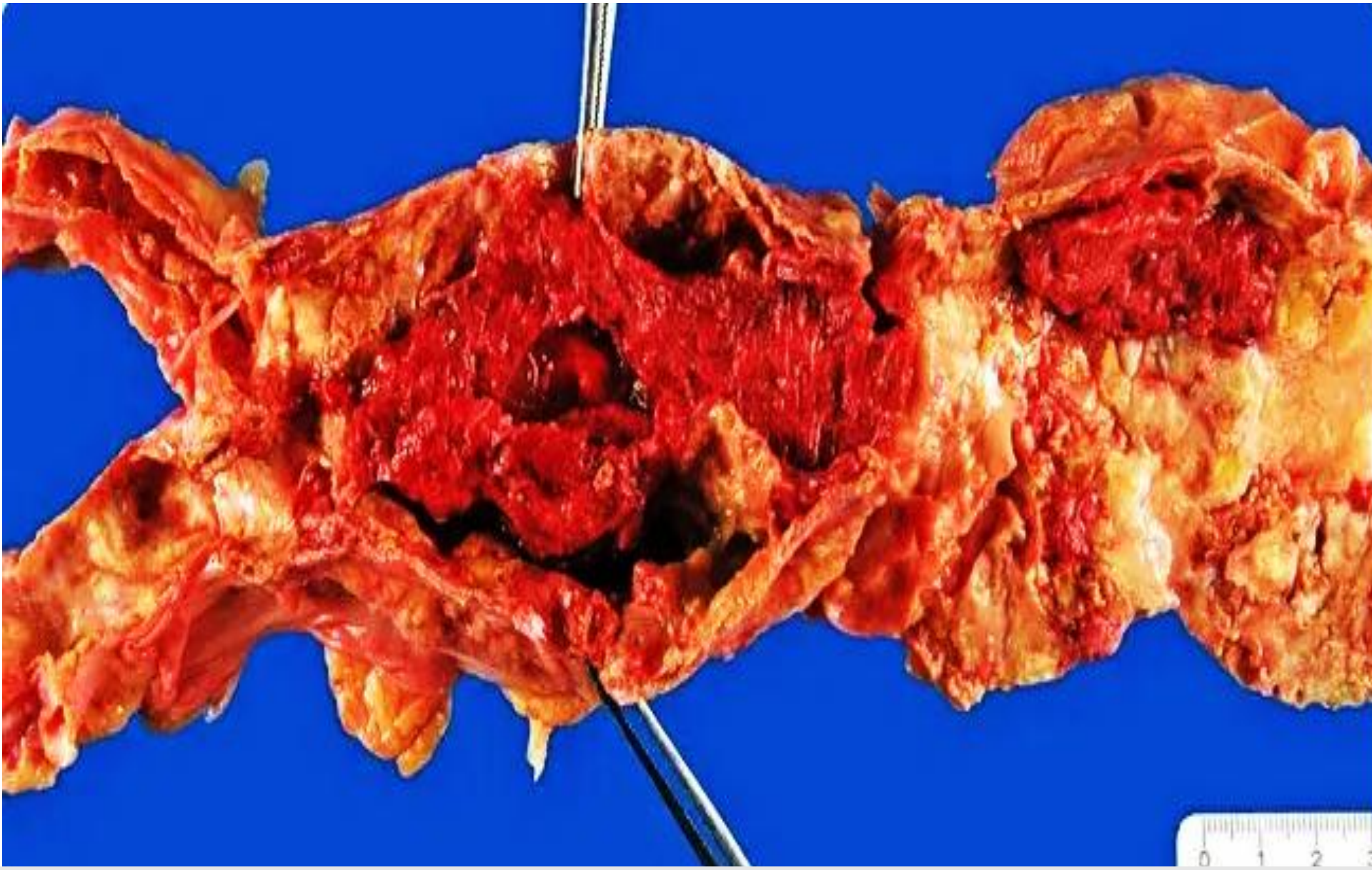





Fibrous Cap
Foam Cells
Cholesterol Crystals

Gross picture

- Yellow, slightly raised streaks and round patches on the intimal surface, caused by deposition of cholesterol and its esters in the subintimal connective tissue.
- Raised white plaques or nodules due to fibrosis around the deposited lipids.
- Superficial atheromatous ulcers due to necrosis of the endothelium which cover the lesions.
- Atheromatous nodules and ulcers may show calcification and appear chalky-white.
- Thrombi are formed over the ulcers and rough surfaces.
- The media that underlie the lesion is thin and atrophic.



The image shows severe atherosclerosis of the abdominal aorta and iliac vessels. Multiple calcified and atheromatous plaques are seen. **Image Copyright: pathorama.ch**.

Effects and complications of atherosclerosis:

In large arteries:

- Fusiform aneurysms results from loss of elasticity and atrophy of the media in severe cases.
- A thrombus over the atherosclerotic lesions gives rise to emboli causing infarcts in different organs.
- Dissecting aneurysms in the aorta.

In small arteries:

- Narrowing of the arteries causing ischaemia and fibrosis.
- Thrombosis of arteries causing infarctions.
- Atheromatous nodules in the cerebral arteries may cause pressure atrophy of the media resulting in small aneurysms or rupture and hemorrhage.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Dissecting Aortic Aneurysm


Thank You