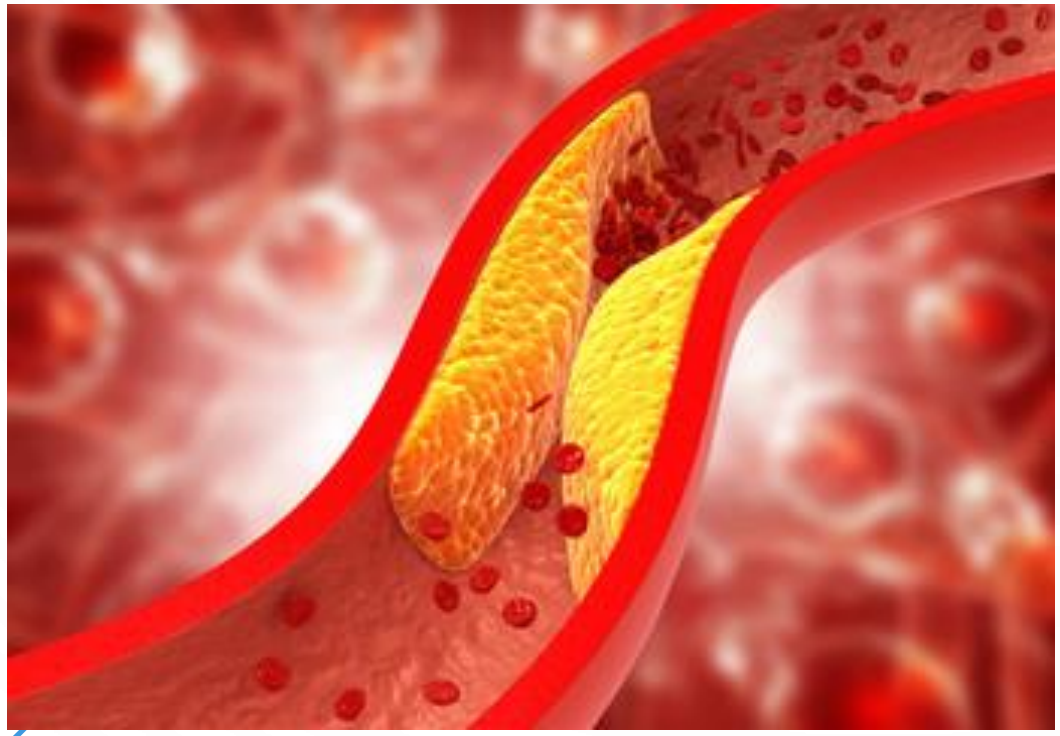
CVS MODULE – 2. ARTERIOSCLEROSIS AND ATHEROSCLEROSIS



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12-11-2023.

ARTERIOSCLEROSIS

- Arteriosclerosis is vascular disease characterized by thickening, hardening and remodeling of the arterial wall.

- Classified into the following three categories:

❖ Atherosclerosis.

❖ Mönckeberg's medial calcific sclerosis.

❖ Arteriolosclerosis.

- 1. Arteriolosclerosis:

- Arteriolosclerosis affects small arteries and arterioles and may cause downstream ischemic injury due to thickening of the vessel walls that narrows the lumen.

- Risk factors:

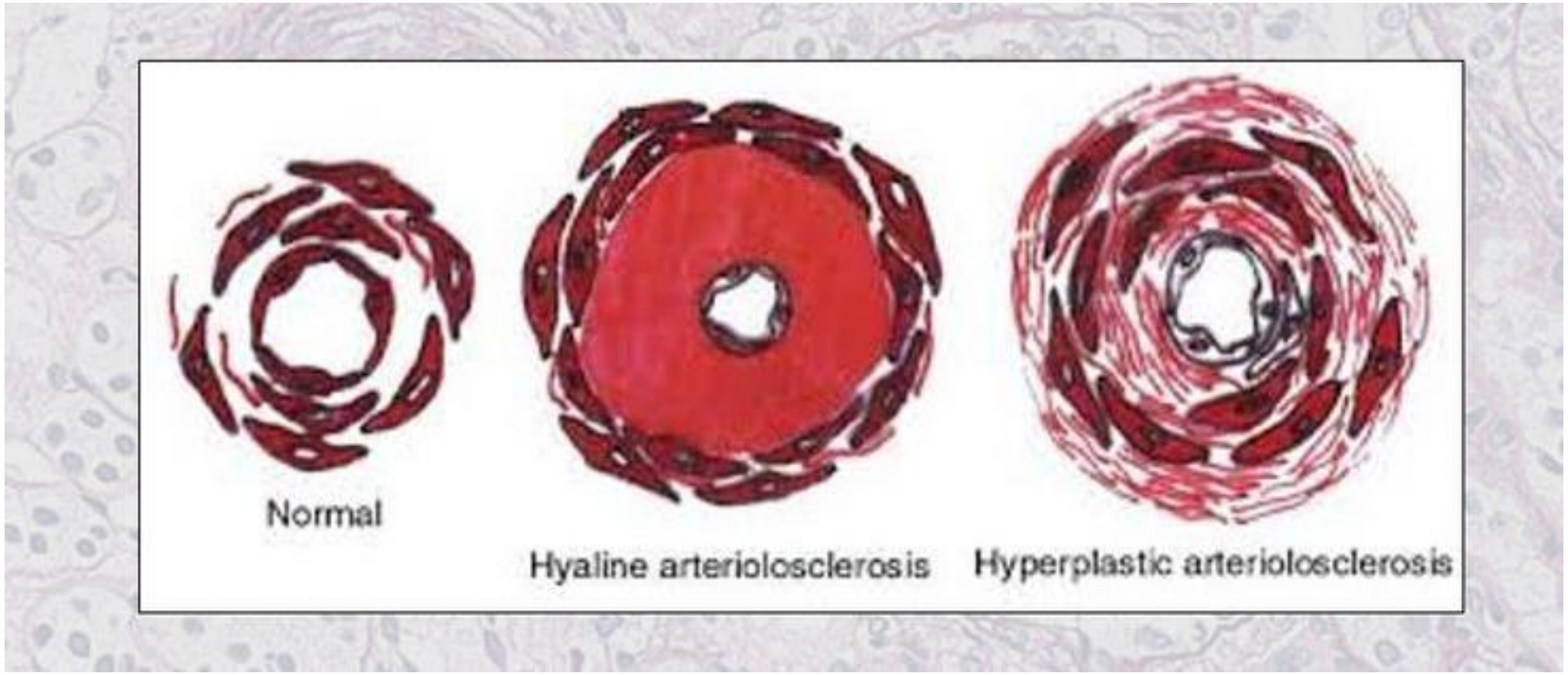
❖ diabetes mellitus.

❖ high blood pressure.

❖ normal part of aging.

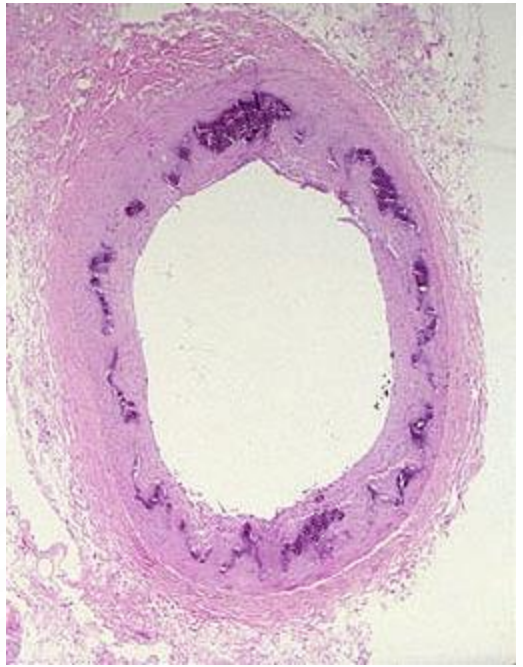
*Hyaline arteriolosclerosis:
it is characterized by thickening of the arteriolar wall due to the accumulation of homogeneous material.

*Hyperplastic arteriolosclerosis:
it is characterized by thickening of the arteriolar wall due to the concentric proliferation of smooth muscle cells.



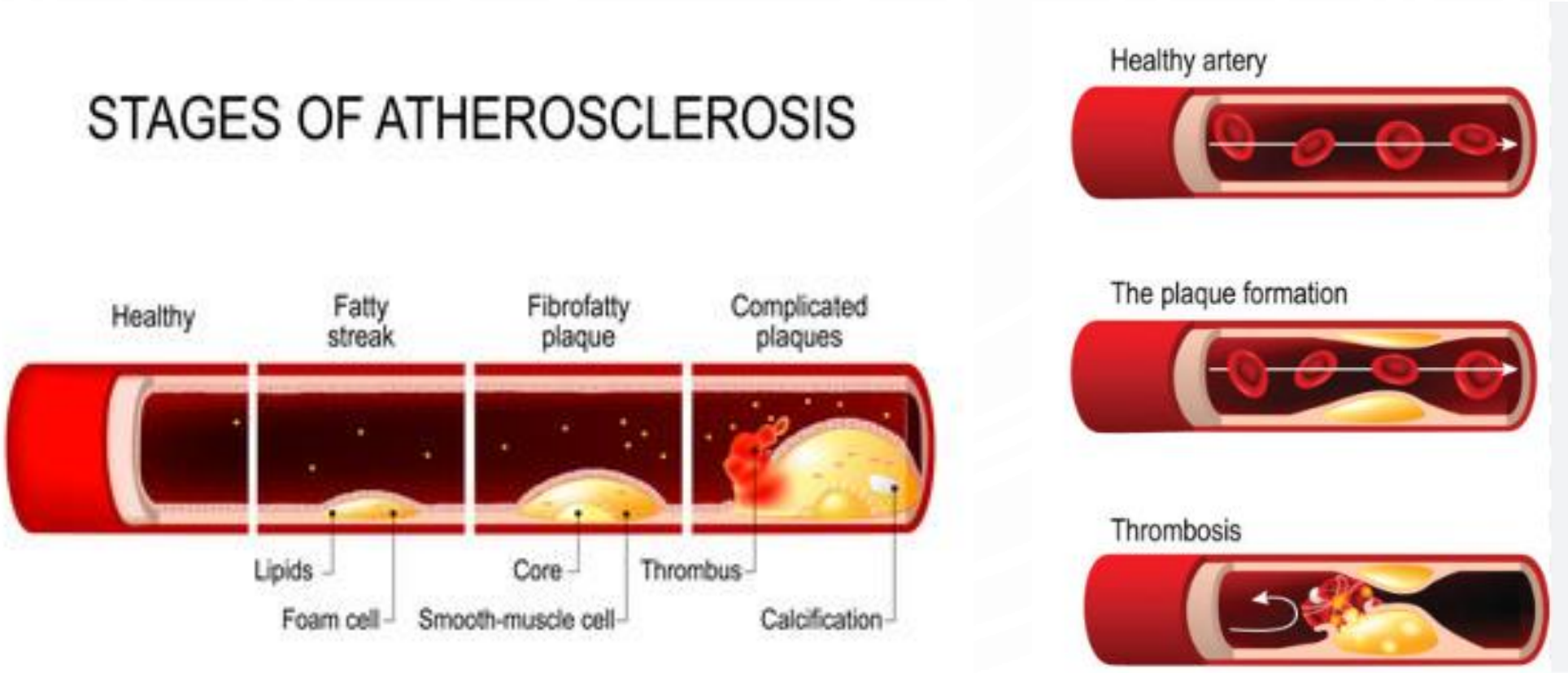
2. MÖNCKEBERG'S MEDIAL CALCIFIC SCLEROSIS.

- Its characterized by the presence of calcific deposits in muscular arteries, usually centered on the internal elastic lamina, and typically in individuals older than 50 years of age.
- The lesions do not encroach on the vessel lumen and usually are not clinically significant.

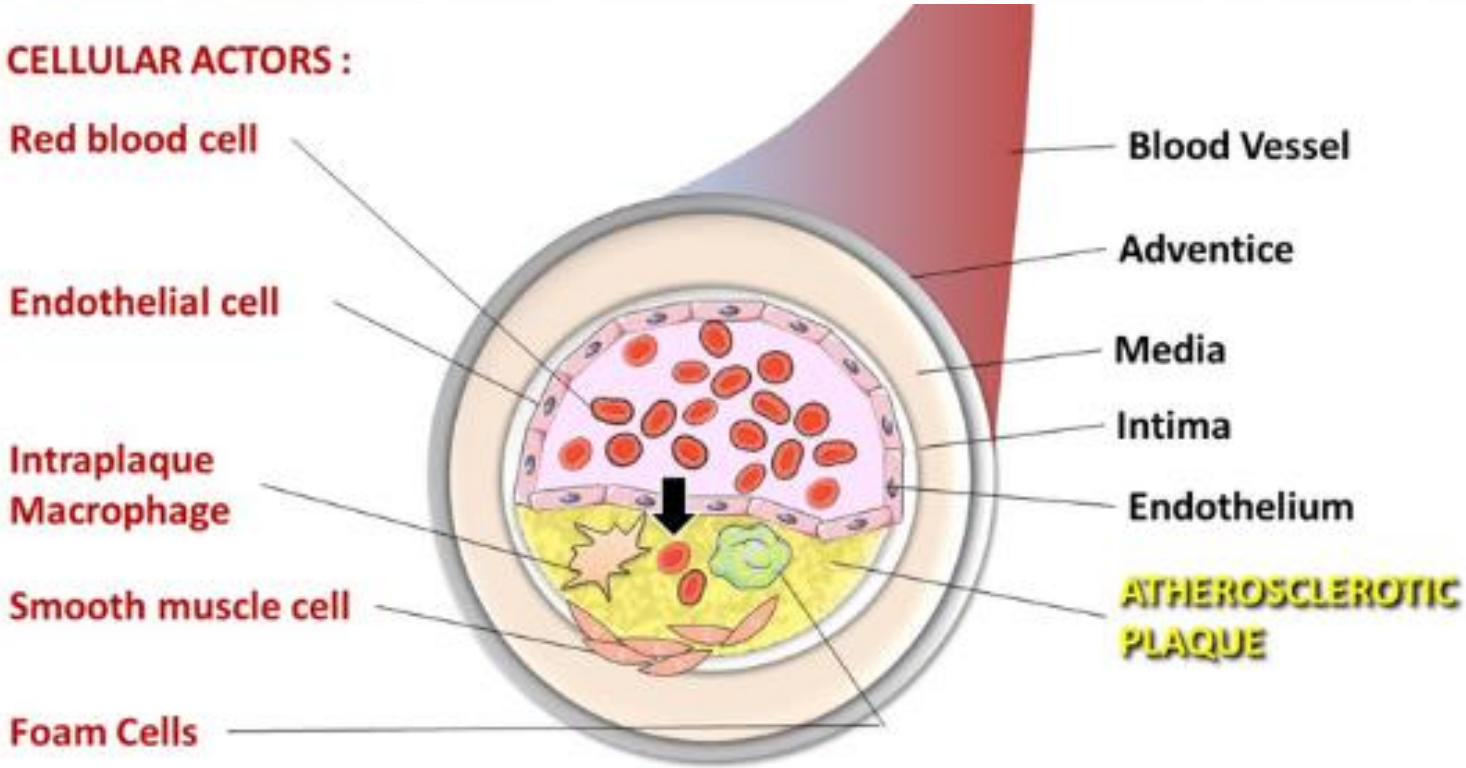


3. ATHEROSCLEROSIS.

- Its characterized by intimal lesions called atheromas (or atheromatous or atherosclerotic plaques) that impinge on the vascular lumen and can rupture to cause sudden occlusion.

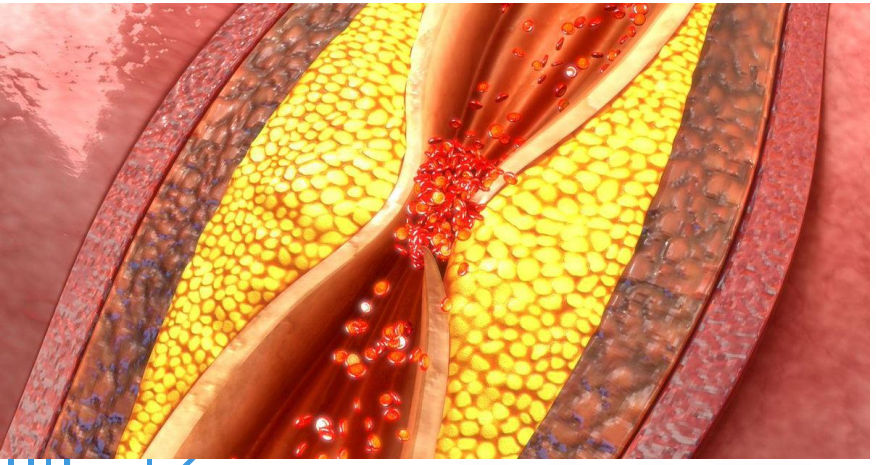


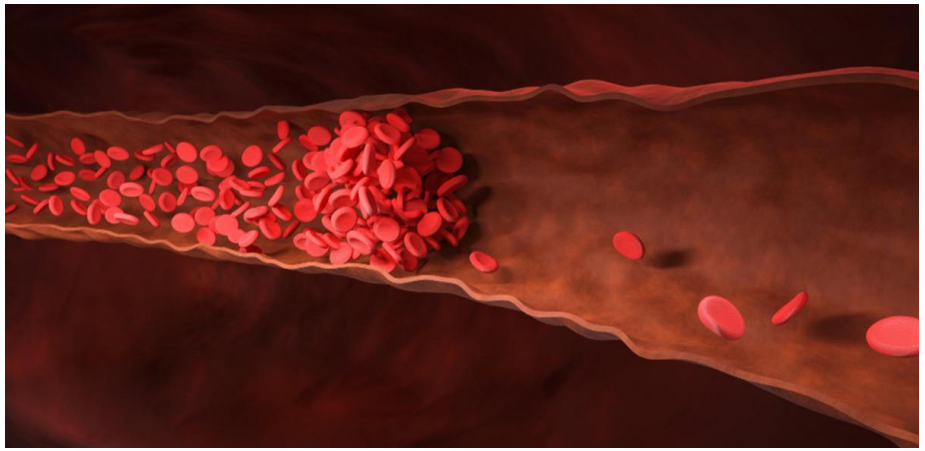
- Atheromatous plaques are raised lesions composed of soft lipid cores (mainly cholesterol and cholesterol esters, with necrotic debris) covered by fibrous caps.



THEN?

- If they enlarged, atherosclerotic plaques may mechanically obstruct vascular lumina, leading to stenosis.
- Atherosclerotic plaques are prone to rupture that may result in thrombosis and sudden occlusion of the vessel.
- Ischemia and inflammation of the underlying media that result in aneurysms.





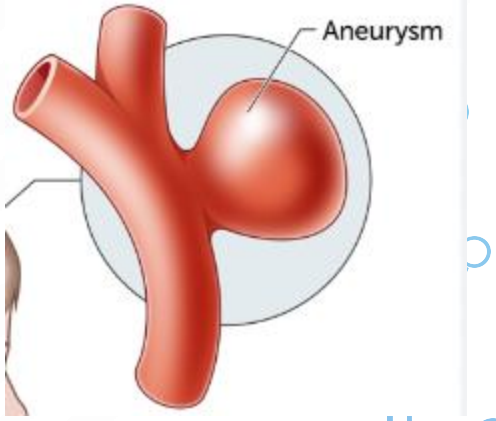


Table 10.3 Major Risk Factors for Atherosclerosis

Nonmodifiable (Constitutional)
Genetic abnormalities
Family history
Increasing age
Male gender
Modifiable
Hyperlipidemia
Hypertension
Cigarette smoking
Diabetes
Inflammation

RISK FACTORS

- Genetics: e.g., familial hypercholesterolemia.
- Gender: premenopausal women are relatively protected against atherosclerosis compared with age-matched men?
- Hyperlipidemia: main cholesterol component:

✓ Low-density lipoprotein (LDL) cholesterol ("bad cholesterol"); LDL distributes cholesterol to peripheral tissues.

✓ High-density lipoprotein (HDL) cholesterol ("good cholesterol") mobilizes cholesterol from developing and existing vascular plaques and transports it to the liver for biliary excretion

- Metabolic syndrome: Clinical entity characterized by:

✓ central obesity

✓ insulin resistance.

✓ Hypertension.

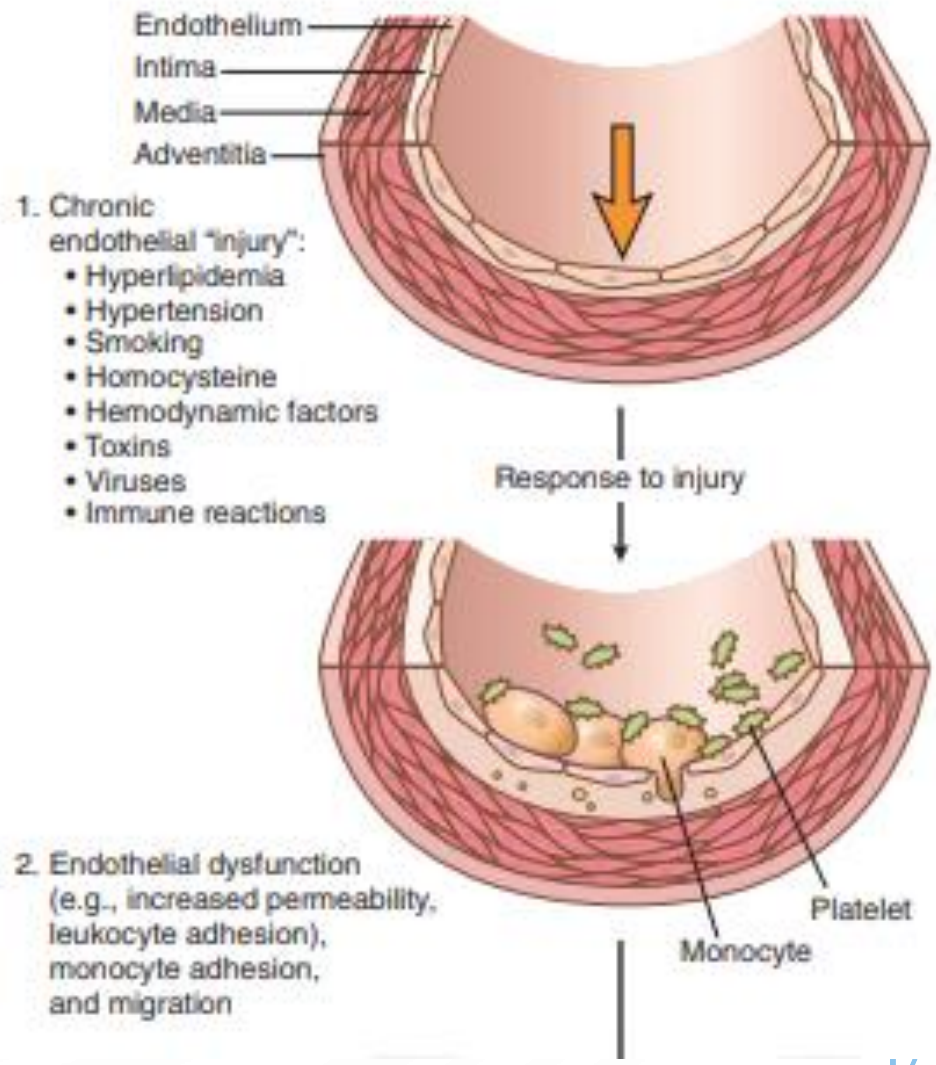
✓ dyslipidemia (elevated triglycerides and depressed HDL).

✓ hypercoagulability.

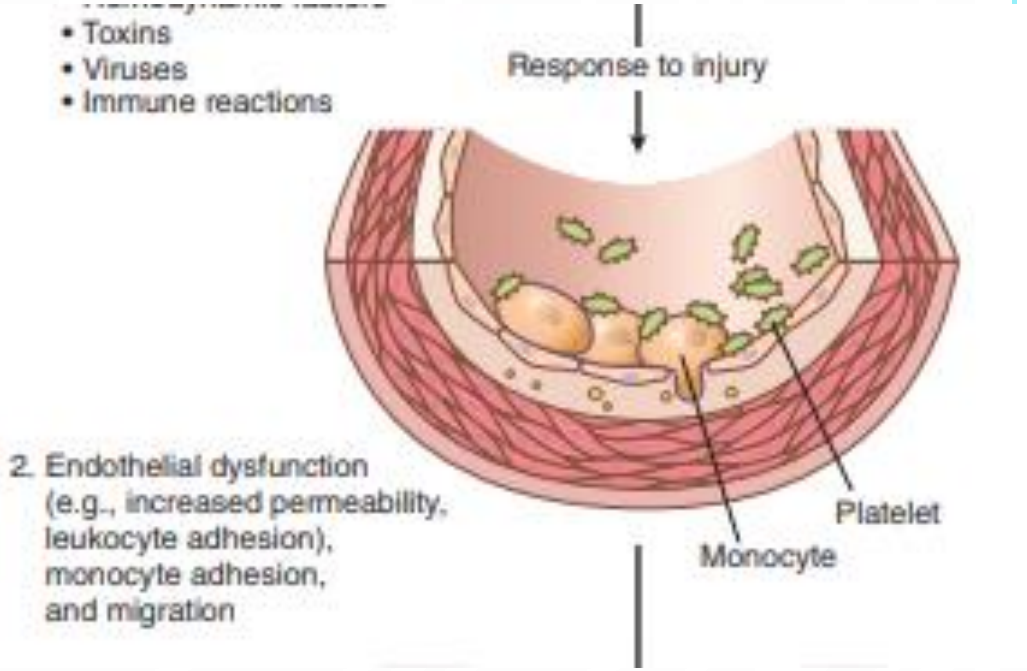
✓ pro-inflammatory state, which may be triggered by cytokines released from adipocytes.

PATHOGENESIS

1. EC injury and resultant endothelial dysfunction leading to increased permeability, leukocyte adhesion, and thrombosis



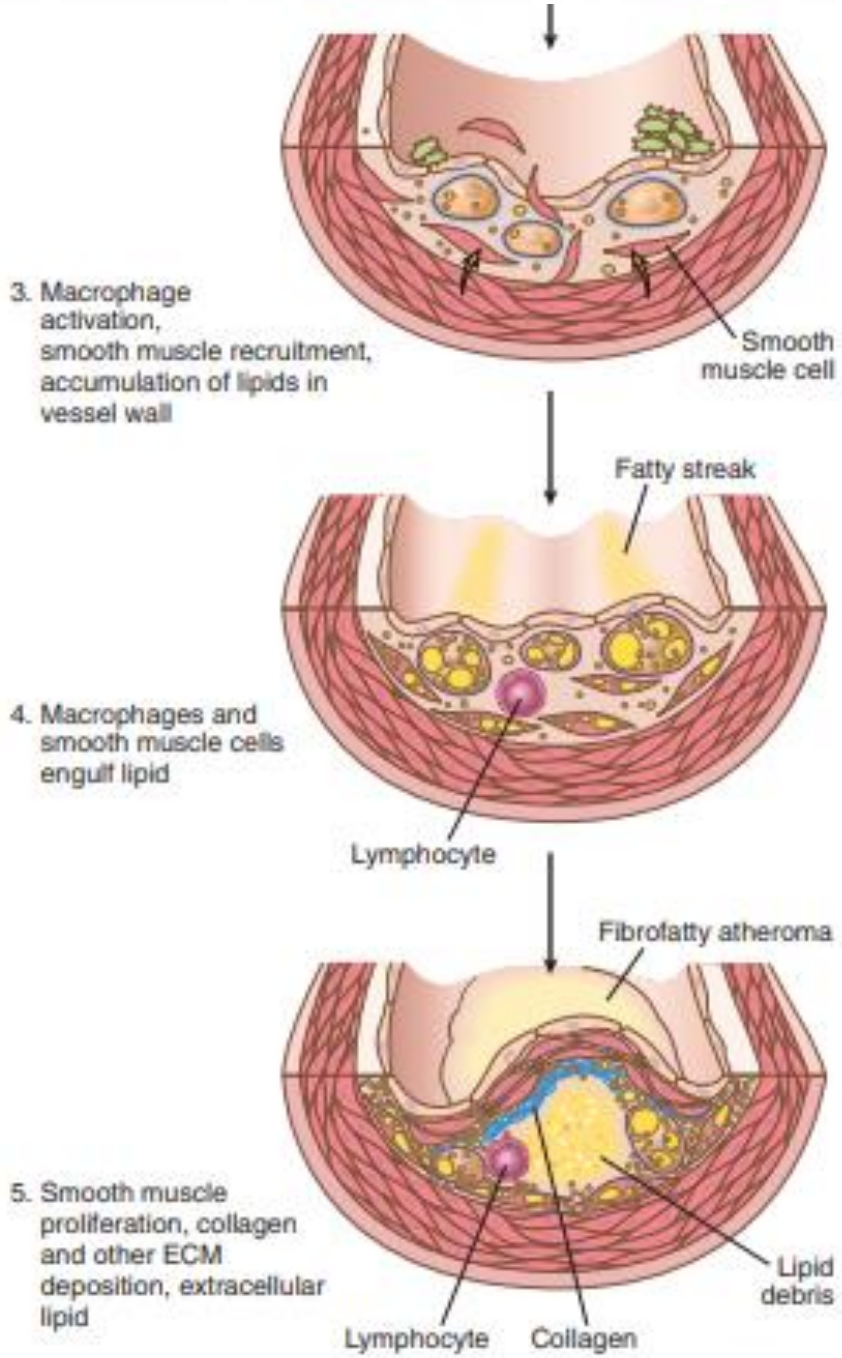
- Accumulation of lipoproteins (mainly oxidized LDL and cholesterol crystals) in the vessel wall .
- Platelet adhesion .
- Monocyte adhesion to the endothelium, migration into the intima, and differentiation into macrophages and foam cells.



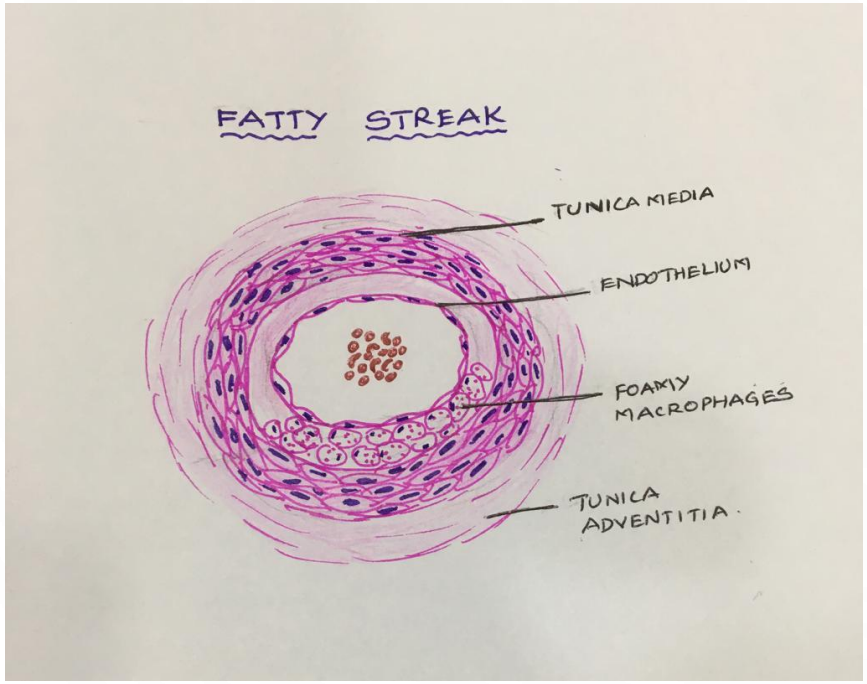
- Inflammation contributes to the initiation, progression, and complications of atherosclerotic lesions.

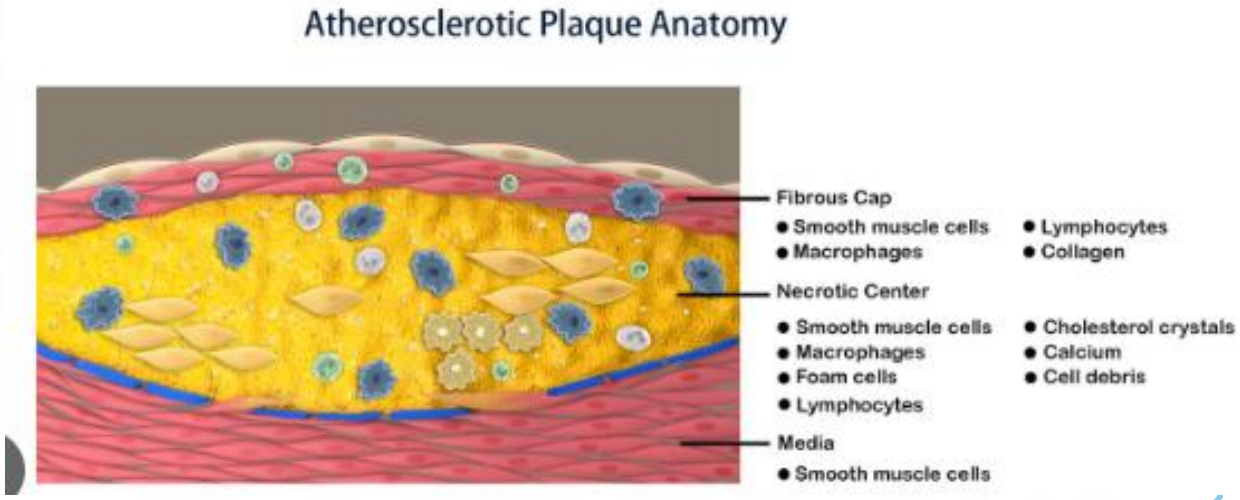
- Normal vessels do not bind inflammatory cells.
- Early in atherogenesis, however, dysfunctional ECs express adhesion molecules that promote leukocyte adhesion, in particular, monocytes and T cells which migrate into the intima under the influence of locally produced chemokines.
- Monocytes differentiate into macrophages and avidly engulf lipoproteins, including oxidized LDL and small cholesterol crystals.

- Lipid accumulation within macrophages, which respond by releasing inflammatory cytokines
- SMC recruitment due to factors released from activated platelets, macrophages, and vascular wall cells
- SMC proliferation and ECM production

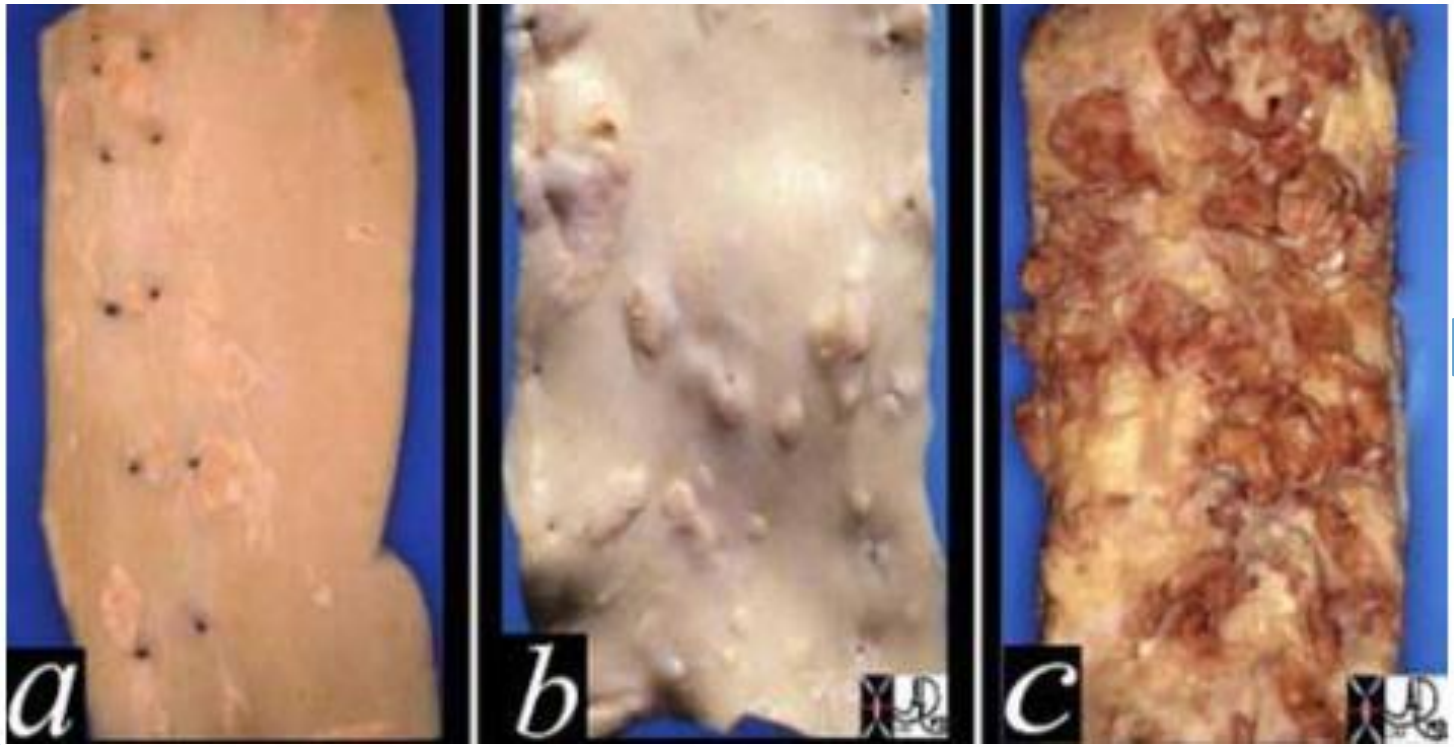


- intimal SMC proliferation and ECM deposition lead to conversion of the earliest lesion, a fatty streak, into a mature atheroma, thus contributing to the progressive growth of atherosclerotic lesions and rupture.





GROSSING



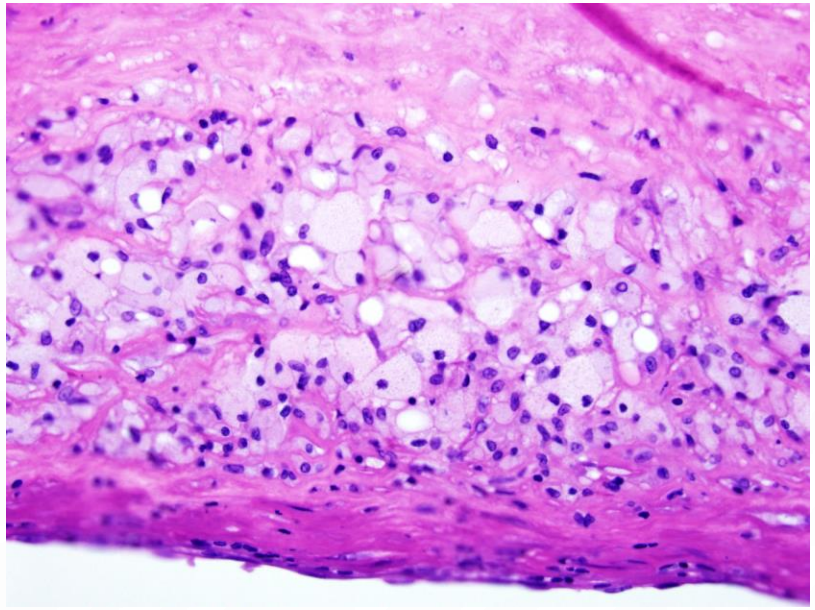
a. raised fatty streaks.

b. raised fibrofatty nodules

c. Rupture plaque

HISTOLOGY

* The earliest lesion is the fatty streak: They consist of many lipid-laden foam cells that contain cholesteryl esters and a variable amount of extracellular lipid



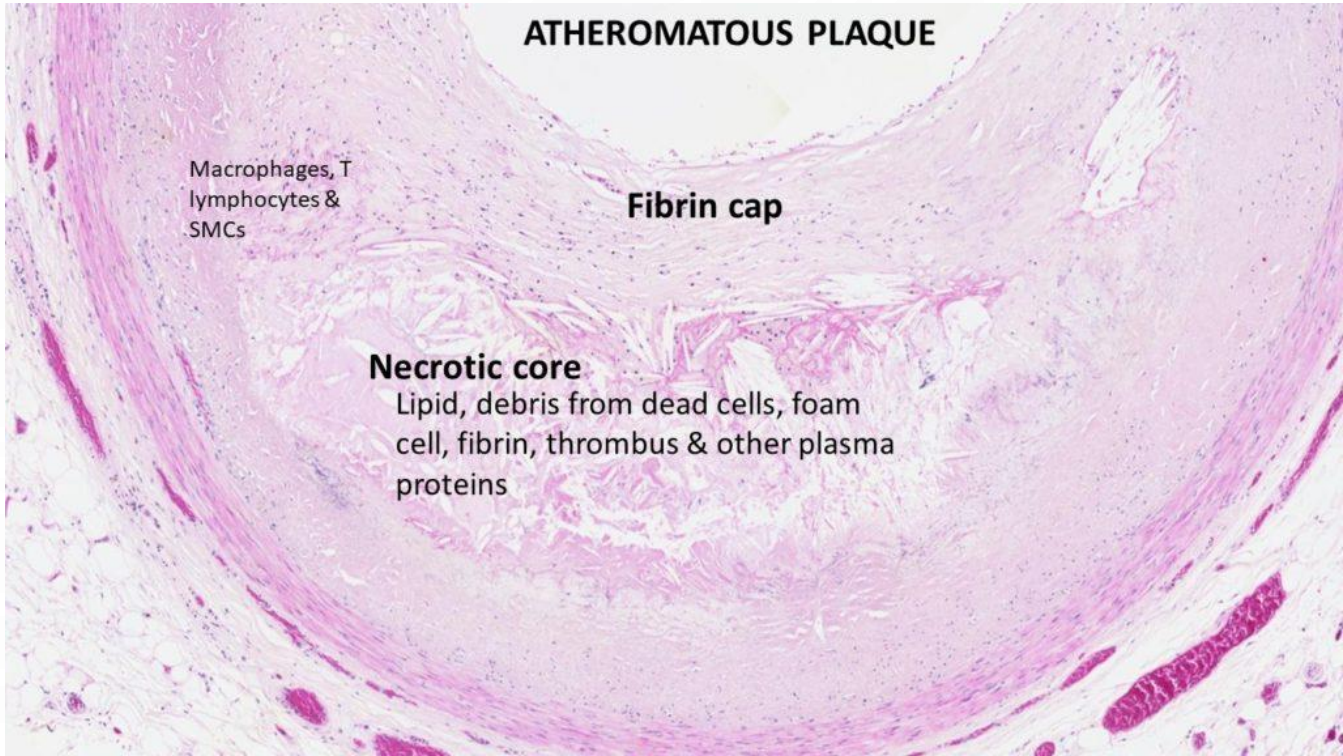
HISTOLOGY CONT.

- Atherosclerotic plaques: have three principal components:

❖cells, including SMCs, macrophages, and T cells.

❖ECM, including collagen, elastic fibers, and proteoglycans.

❖intracellular and extracellular lipid.



CLINICAL FEATURES

- The focal nature of atherosclerotic lesions may be related to the vascular hemodynamics.
- local flow disturbances, such as turbulence at branch points, make certain parts of a vessel wall especially susceptible to plaque formation.
- in descending order of severity, atherosclerosis involves the;

○ infrarenal abdominal aorta.

○coronary arteries.

○ popliteal arteries.

○ internal carotid arteries.

○The vessels of the circle of willis.

ATHEROSCLEROTIC PLAQUES ARE SUSCEPTIBLE TO SEVERAL CLINICALLY IMPORTANT CHANGES:

1. Rupture, ulceration, thrombus formation.
2. Hemorrhage into a plaque.
3. Atheroembolism.
4. Aneurysm formation.

clinical consequences

- Myocardial infarction (heart attack).
- Cerebral infarction (stroke),
- Aortic aneurysm.
- Peripheral vascular disease (gangrene of extremities)

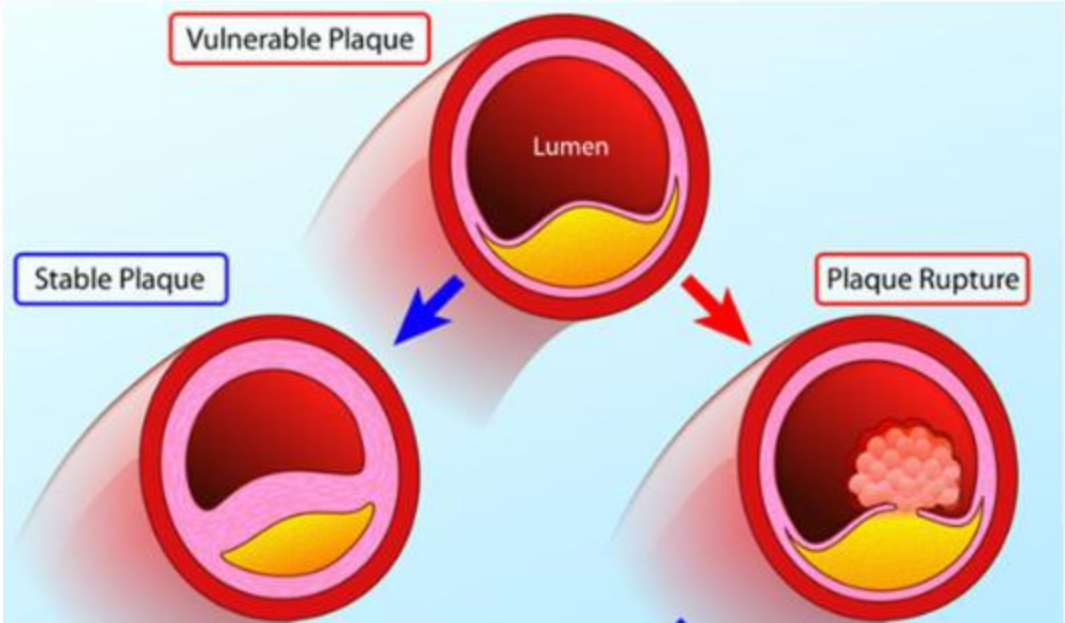
VULNERABLE PLAQUES

- Plaques at high risk for rupture, These include :

✓ plaques that contain large numbers of foam cells and abundant extracellular lipid.

✓ plaques that have thin fibrous caps containing few SMCs.

✓ plaques that contain clusters of inflammatory cells.



EXTRINSIC FACTORS MAY LEAD TO PLAQUES RUPTURE

- adrenergic stimulation, e.g:

➢ With intense emotions: can increase systemic blood pressure or induce local vasoconstriction, thereby increasing the mechanical stress on a given plaque.

➢ adrenergic surge associated with waking and rising (circadian periodicity), sufficient to cause blood pressure spikes and heightened platelet reactivity.