ATHEROSCLEROSIS

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PATHOLOGY.
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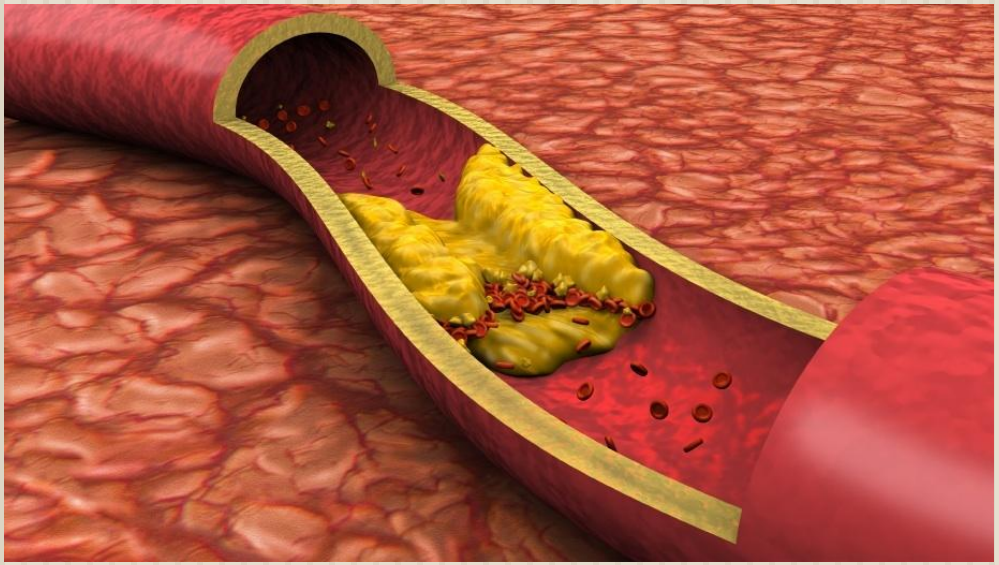


Objectives for Atherosclerosis, ischemic heart diseases (angina and myocardial infarction) 2 lectures

- Understand the pathogenesis and clinical consequences of atherosclerosis.
- Be able to discuss pathology and complications of ischemic heart diseases with special emphasis on myocardial infarction.
- Know how lifestyle modifications can reduce the risk of ischemic heart diseases.

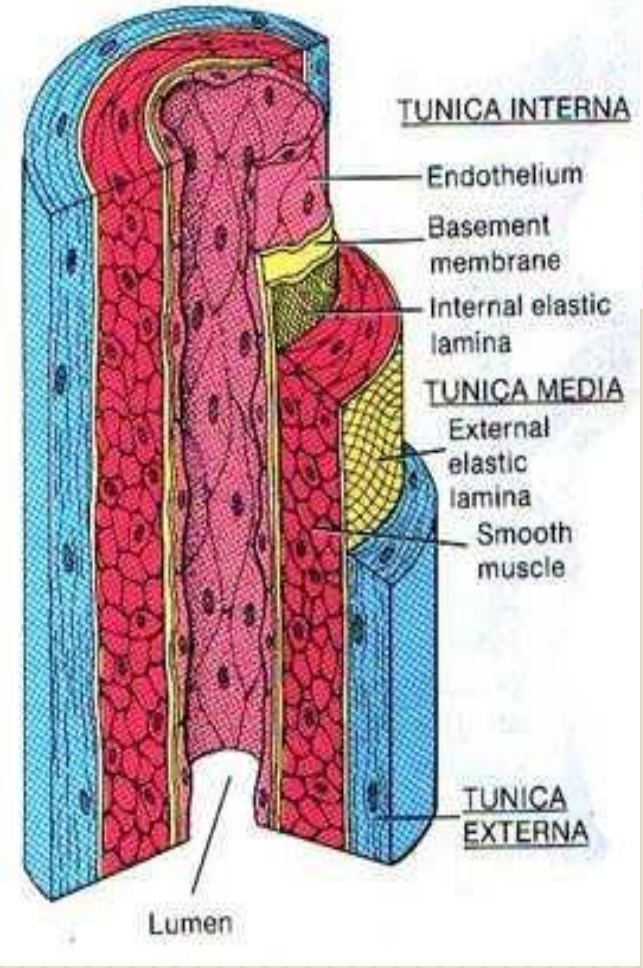
Key principles to be discussed:

- Risk factors of atherosclerosis.
- Pathogenesis of the fibro lipid atherosclerotic plaque.
- Clinical complications of atherosclerosis.
- Commonest sites for the clinically significant coronary atherosclerosis.
- Macroscopic and microscopic changes in myocardial infarction.
- Biochemical markers of myocardial infarction.
- Complications of myocardial infarction: immediate and late.

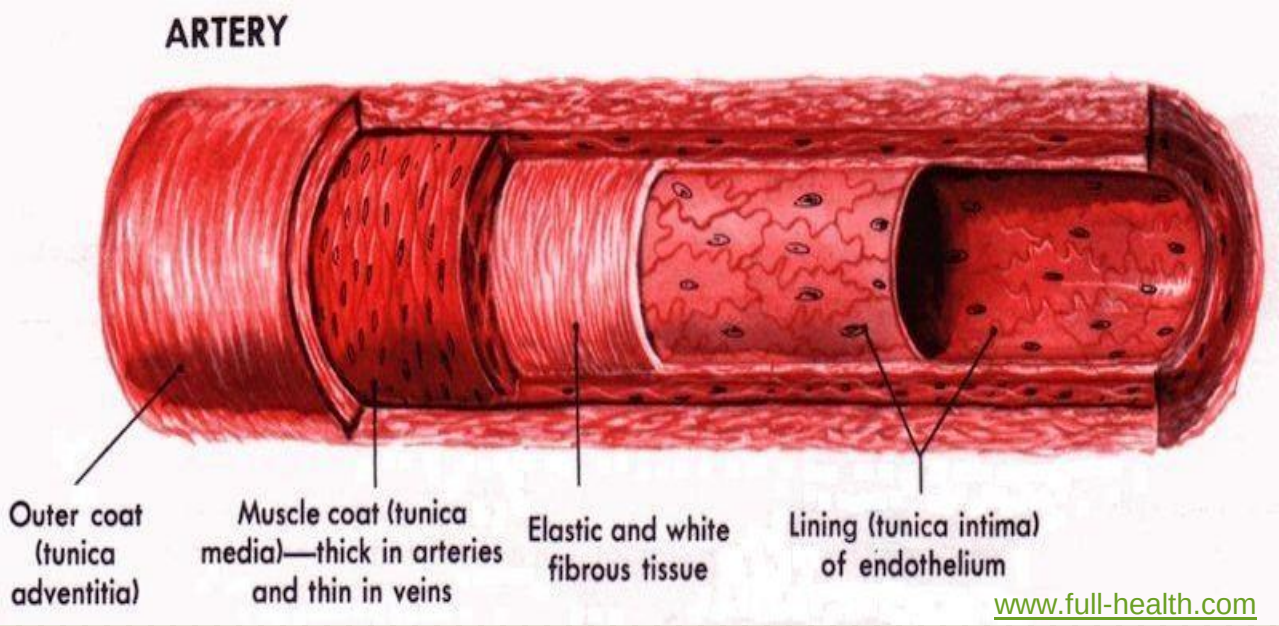
Normal Blood Vessels

- Large (elastic) arteries
  - aorta, common carotid, iliac
  - lots of elastic fibers
- Medium (muscular) arteries
  - coronary, renal arteries
  - mostly smooth muscle cells
- Small arteries/arterioles
  - all smooth muscle cells
  - blood pressure controlled here
- Capillaries
  - diameter of RBC
  - thin walls, slow flow
  - great for exchanging oxygen, nutrients
- Venules/veins
  - large diameter, thin walls
  - compressible, penetrable by tumor
  - Have valves
- Lymphatics
  - drain excess interstitial fluid
  - pass through nodes

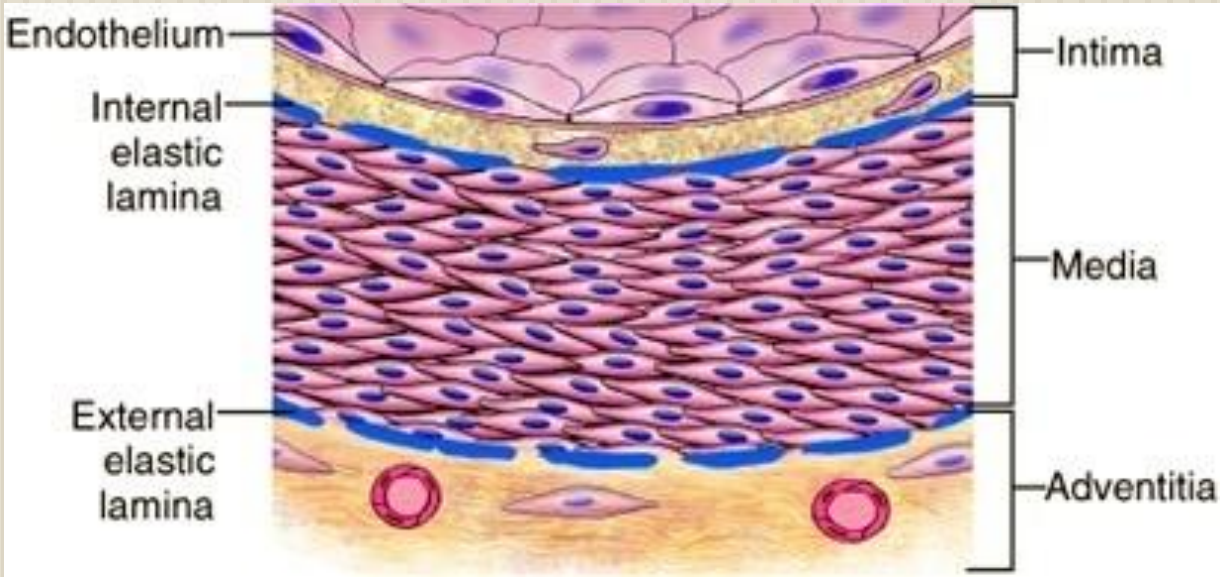
Artery



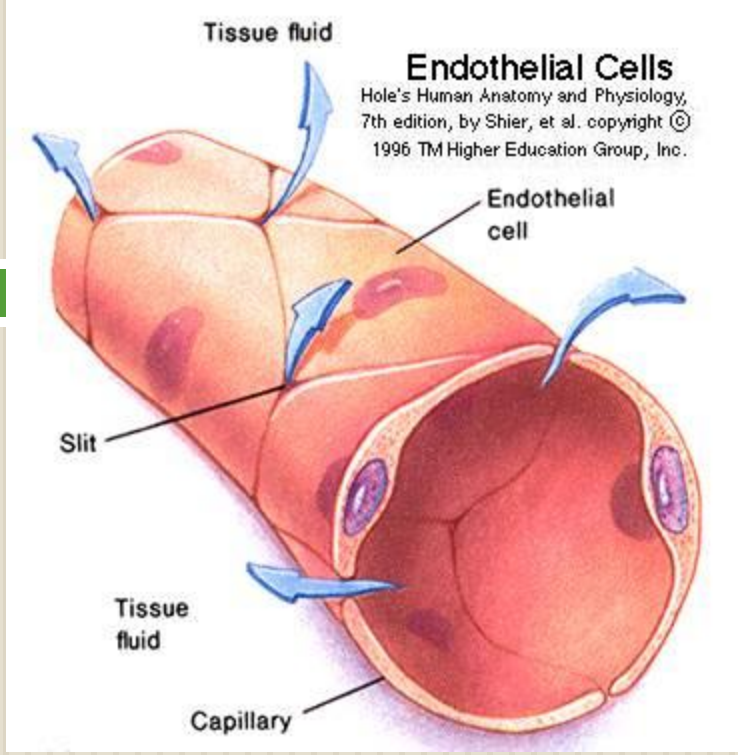
www.mananatomy.com



www.full-health.com



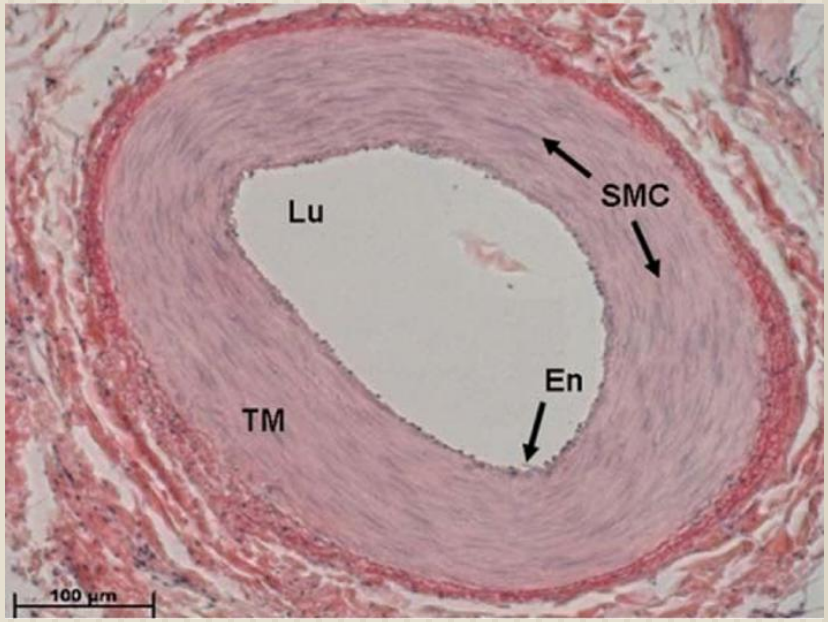
ENDOTHELIAL CELLS



- The endothelium is a single cell thick lining of endothelial cells and it is the inner lining of the entire cardiovascular system (arteries, veins and capillaries) and the lymphatic system.
- It is in direct contact with the blood/lymph and the cells circulating in it.
- A normal structure and function of endothelium is essential for the maintenance of vessel wall homeostasis and normal circulatory function.

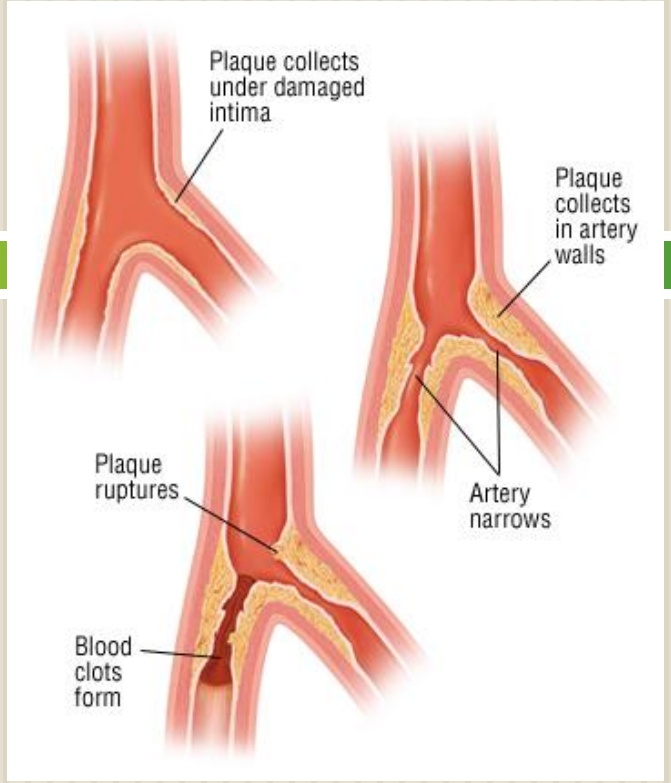
www.udel.edu

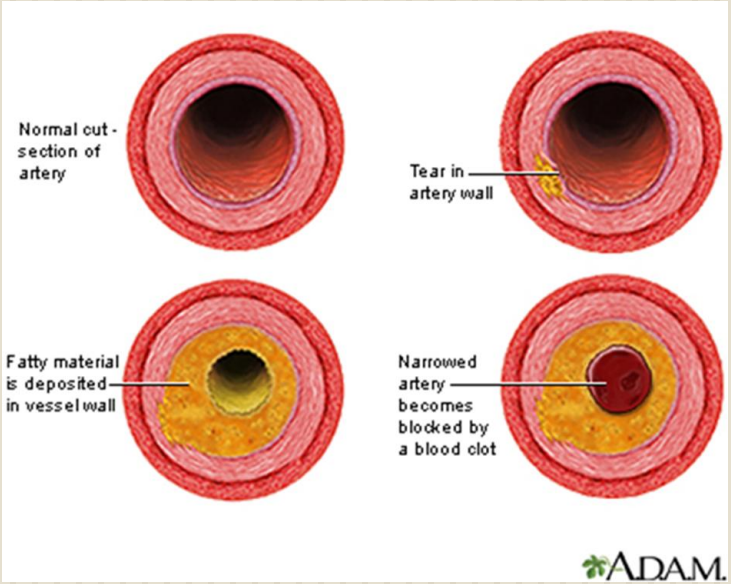
Smooth muscle cells (SMC)



- SMCs are present in the media of blood vessels
- SMCs are responsible for vasoconstriction and vasodilation of blood vessel.
- Any vascular injury or dysfunction stimulates SMCs. On stimulation the SMCs:
  1. Migrate from the media to the intima.
  2. In the intima the SMCs lose the capacity to contract and gain the capacity to divide. So they proliferate as intimal SMCs.
  3. They synthesize collagen, elastin etc and deposit extracellular matrix (ECM).

Atherosclerosis (AS)

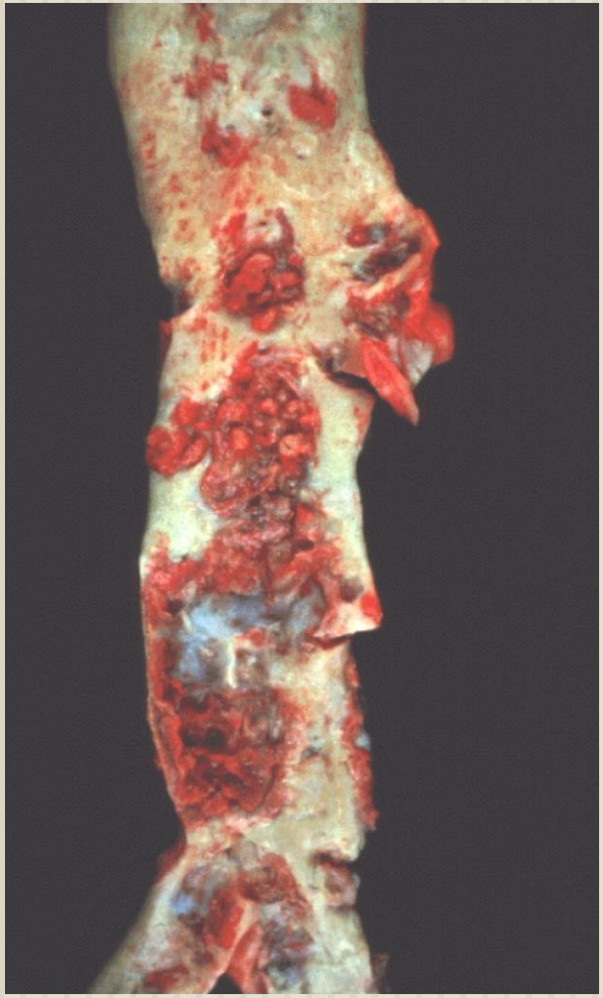




- Atherosclerosis is characterized by intimal lesions called **atheromas (also known as atheromatous plaque or fibrofatty plaque)**, which protrude into and obstruct vascular lumens and weaken the underlying media.
- The most commonly involved vessels are the abdominal aorta then coronary arteries, the popliteal arteries, the internal carotid arteries, and the vessels of the circle of Willis.
- AS can → serious complications like Coronary artery disease (angina & MI) and Carotid atherosclerotic disease (stroke)

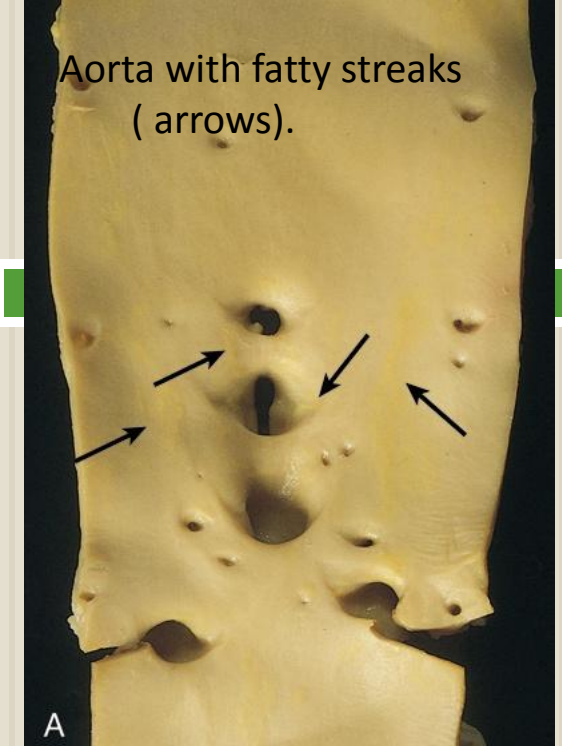
Gross morphology of atheroma/atheromatous (AS) plaque

- The key processes in AS is intimal thickening and lipid accumulation.
- AS plaques impinge on the lumen of the artery.
- AS plaques vary in size.
- AS plaques usually involve only a partial circumference of the arterial wall ("eccentric" lesions) and are patchy and variable along the vessel length.



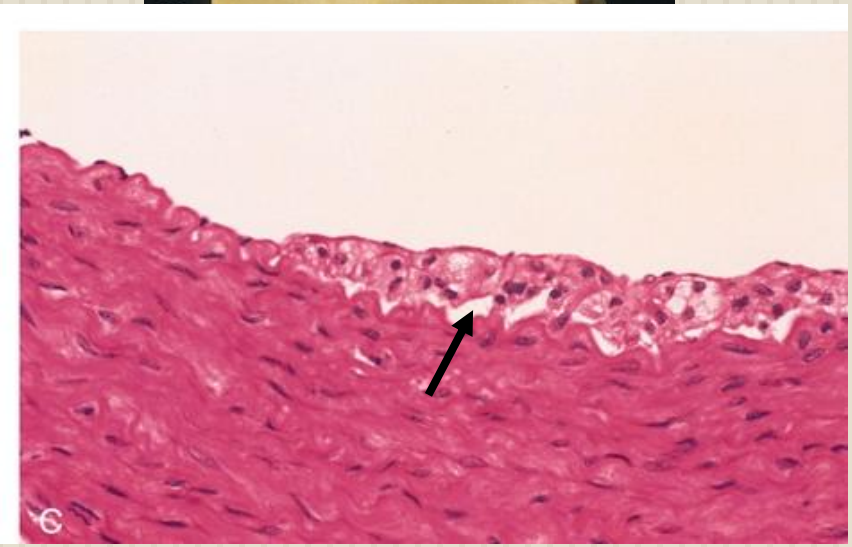
www.med.uottawa.ca

Atherosclerosis:



Aorta with fatty streaks (arrows).

- *Fatty streaks* are the earliest lesion of atherosclerosis they are a collection of **lipid and lipid laden foam cells in the intima.**
- They do not cause any disturbance in blood flow.
- Fatty streaks begin as multiple yellow, flat spots less than 1 mm in diameter that coalesce into elongated streaks, 1 cm long or longer. They contain T lymphocytes, extracellular lipid in smaller amounts and rare lipid laden foam cells than in plaques.



Photomicrograph of fatty streak in an experimental hypercholesterolemic rabbit, demonstrating intimal macrophage-derived foam cells (arrow).

Atherosclerosis: Microscopic morphology

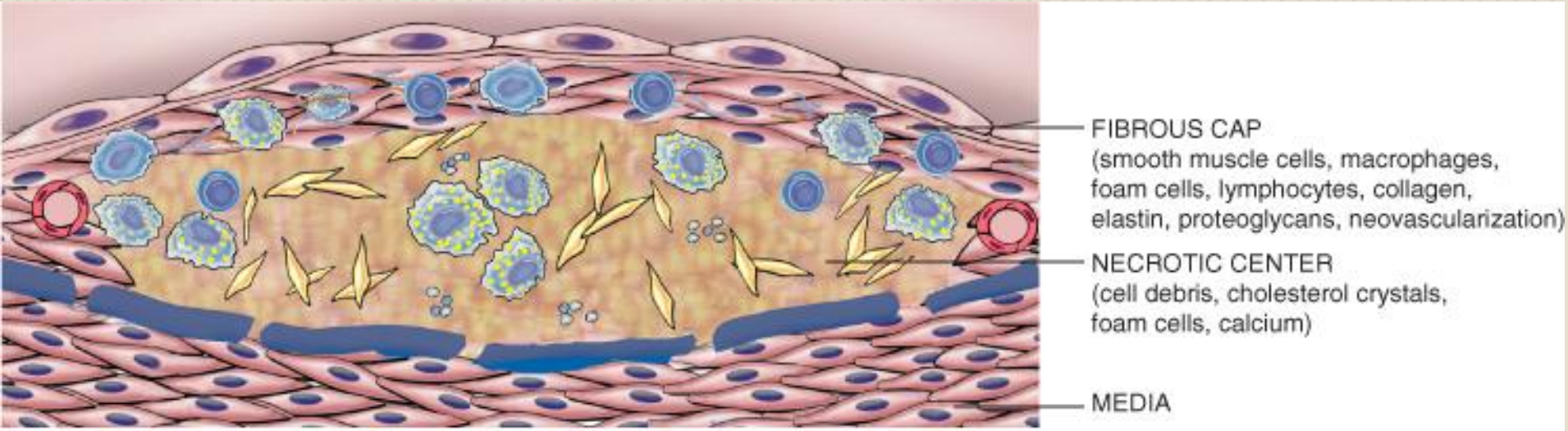
A well established atheroma/AS plaque consists of a raised focal lesion in the intima, with a soft, yellow, grumous/granular core of lipid (mainly cholesterol and cholesterol esters), covered by a firm, white fibrous cap. Atherosclerotic plaques have three principal components:

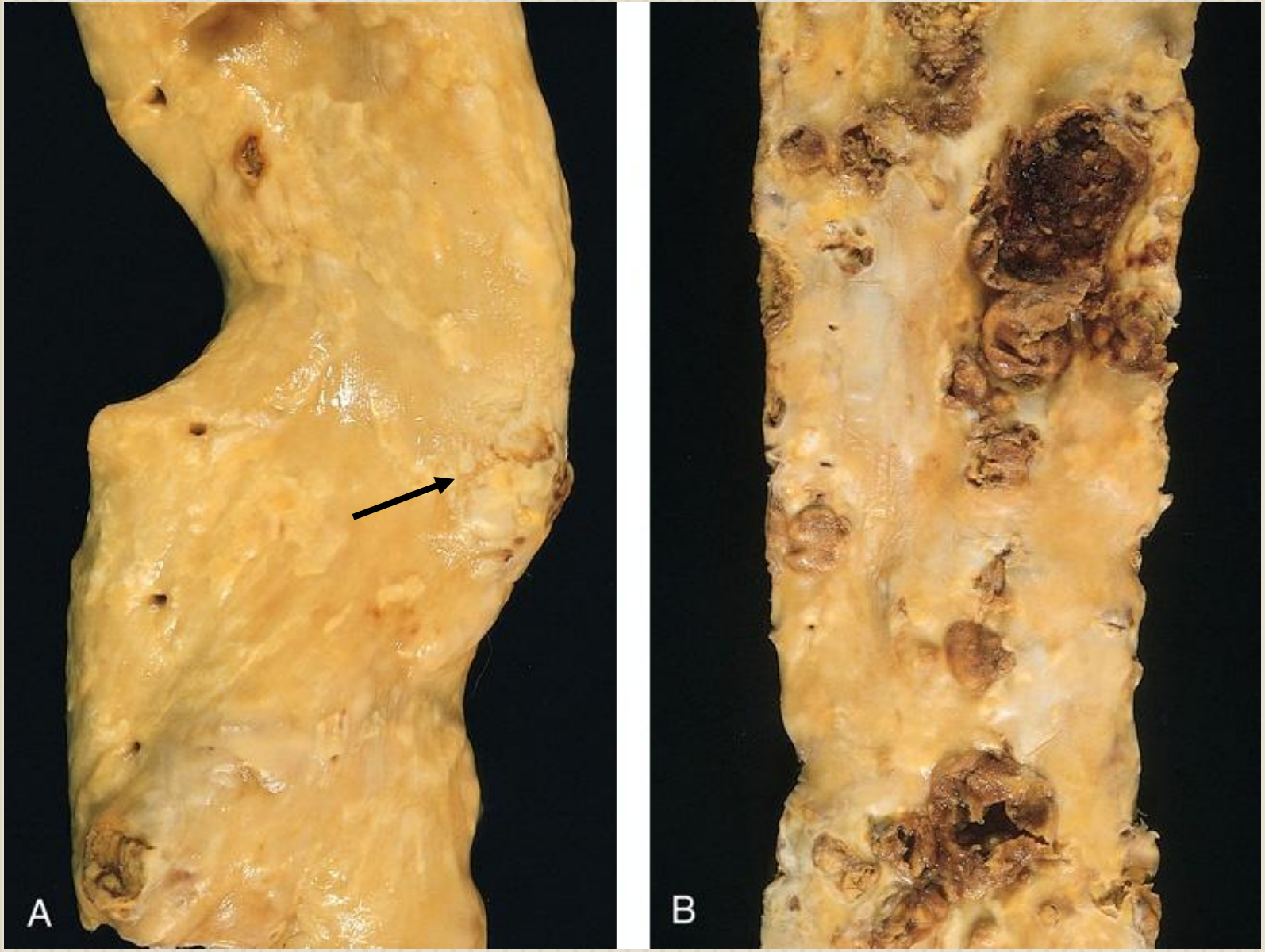
1. **Cells**: SMCs, macrophages, lymphocytes and foam cell
2. **Extracellular matrix**: including collagen, elastic fibers, and proteoglycans
3. **Lipid**: Typical atheromas contain relatively abundant lipid both intracellular and extracellular lipid .

NOTE: Foam cells are large, lipid-laden macrophages derived from blood monocytes, but SMCs can also imbibe lipid to become foam cells.

Atherosclerosis: microscopic morphology

- Typically, the superficial fibrous cap is composed of SMCs and extracellular matrix. With some macrophages and T lymphocytes.
- Below the fibrous cap is a necrotic core, containing a lipid deposits (primarily cholesterol and cholesterol esters), cholesterol clefts, debris from dead cells, foam cells, fibrin.

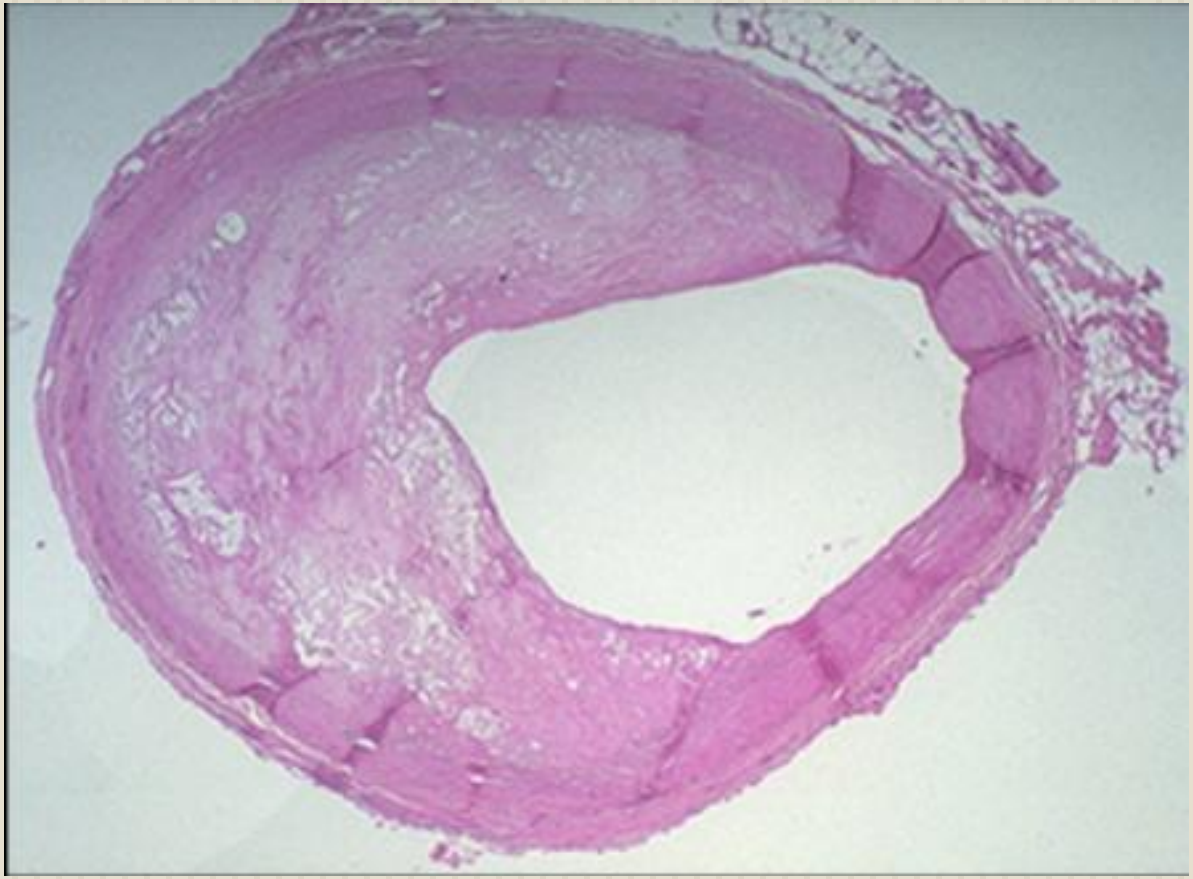




Gross views of atherosclerosis in the aorta.

A. Mild atherosclerosis composed of fibrous plaques, one of which is denoted by the arrow.

B. Severe disease with diffuse and complicated lesions.



http://sphweb.bumc.bu.edu/otlt/MPH-Modules/PH/PH709_Heart/PH709_Heart3.html

Overall architecture demonstrating an eccentric lesion with a fibrous cap and a central lipid core with typical cholesterol clefts. The lumen is moderately narrowed.

PATHOLOGICAL COMPLICATIONS OF AS: advanced lesion
of AS is at risk for the following

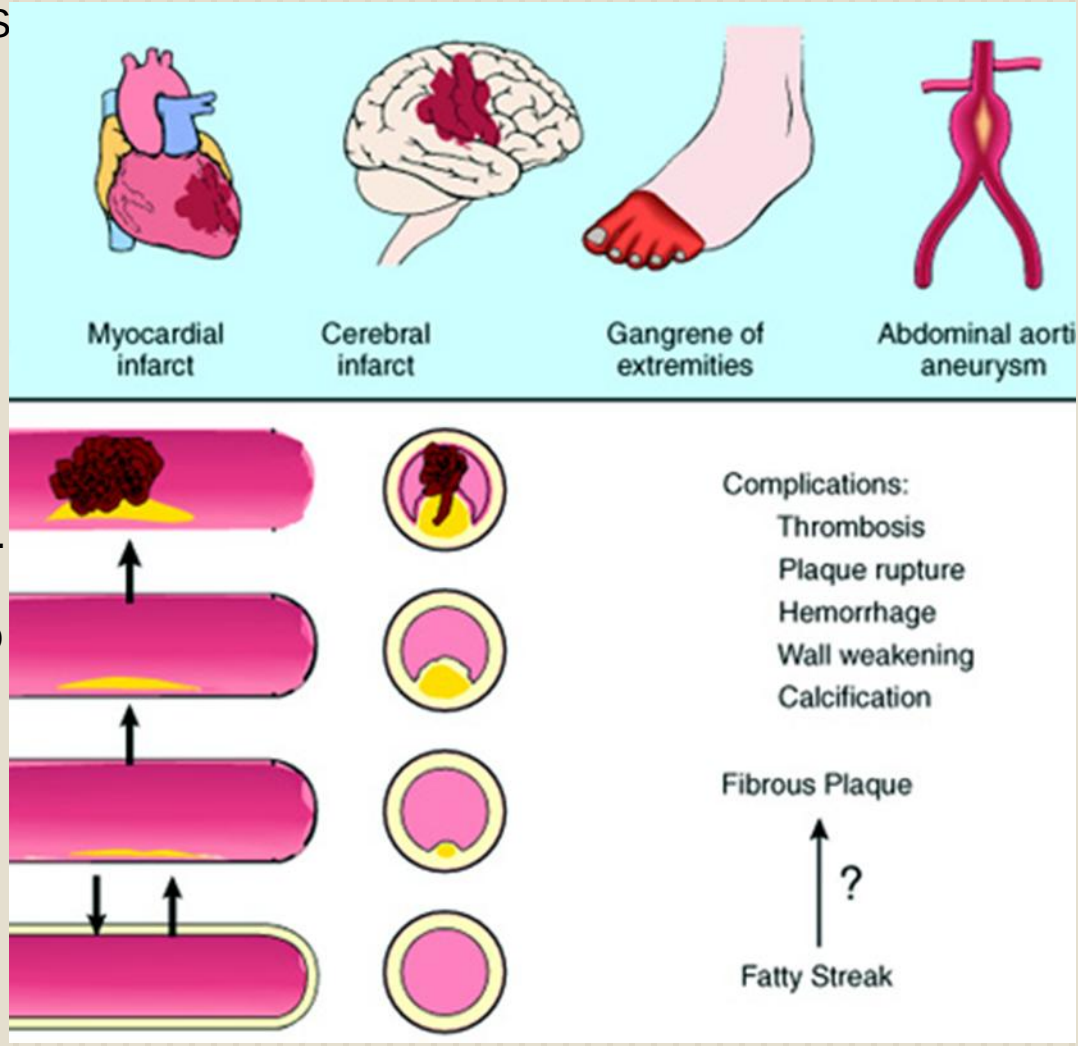
Plaque rupture/ ulceration/ erosion of the AS plaques → induce thrombus formation OR the AS plaque may discharge debris into the bloodstream, producing microemboli composed of plaque lipid **(cholesterol emboli or atheroemboli)**.

Hemorrhage into a plaque due to rupture of the overlying fibrous cap or the capillaries in the plaque. The hematoma may expand the plaque or induce plaque rupture

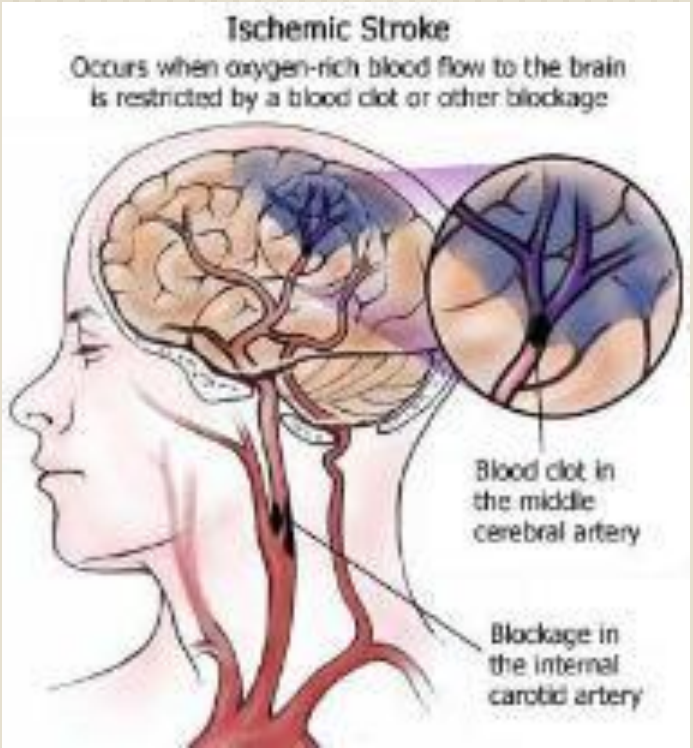
Superimposed thrombosis, which usually occurs on top of ruptured or ulcerated plaques. It is the most feared complication. The thrombus can lead to partial or complete occlusion of the lumen. The thrombus can also embolize.

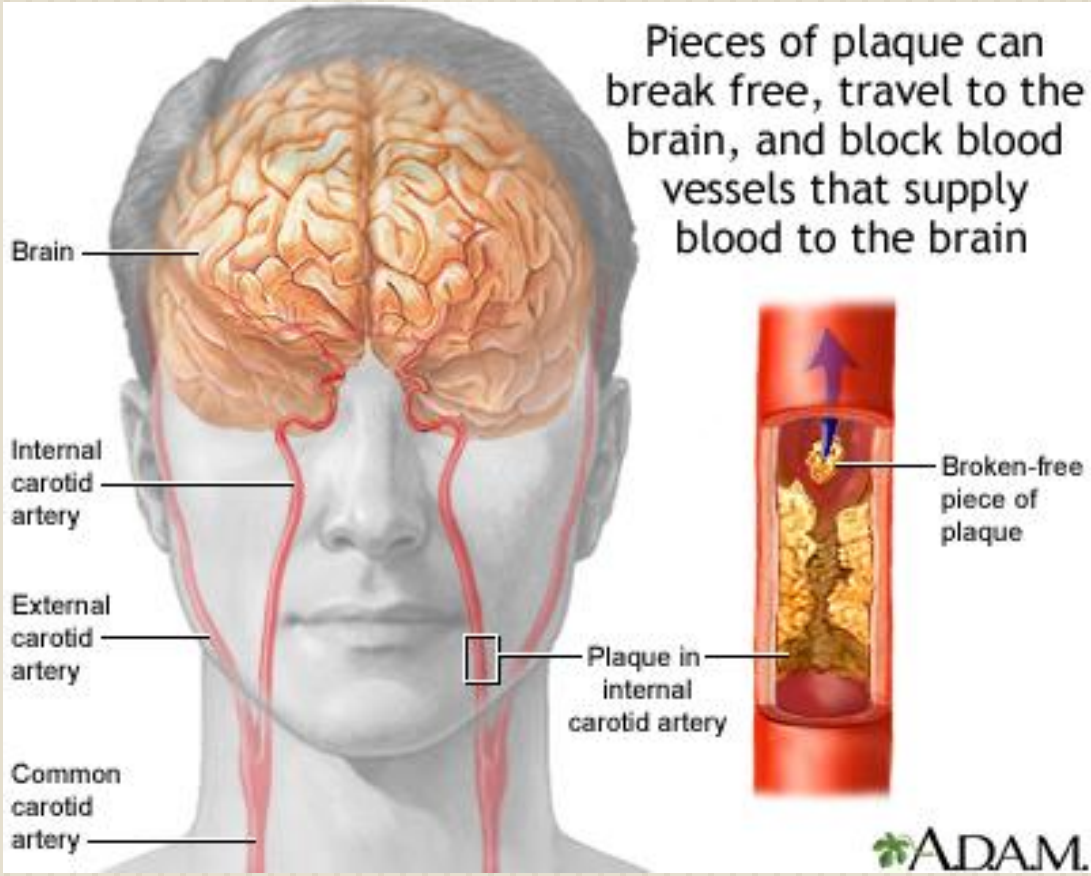
Weakening of the blood vessel wall with aneurysmal dilation. Atheroma can induce atrophy of the underlying media, causing weakness, aneurysm and potential rupture.

Calcifications: Atheromas often undergo calcification.



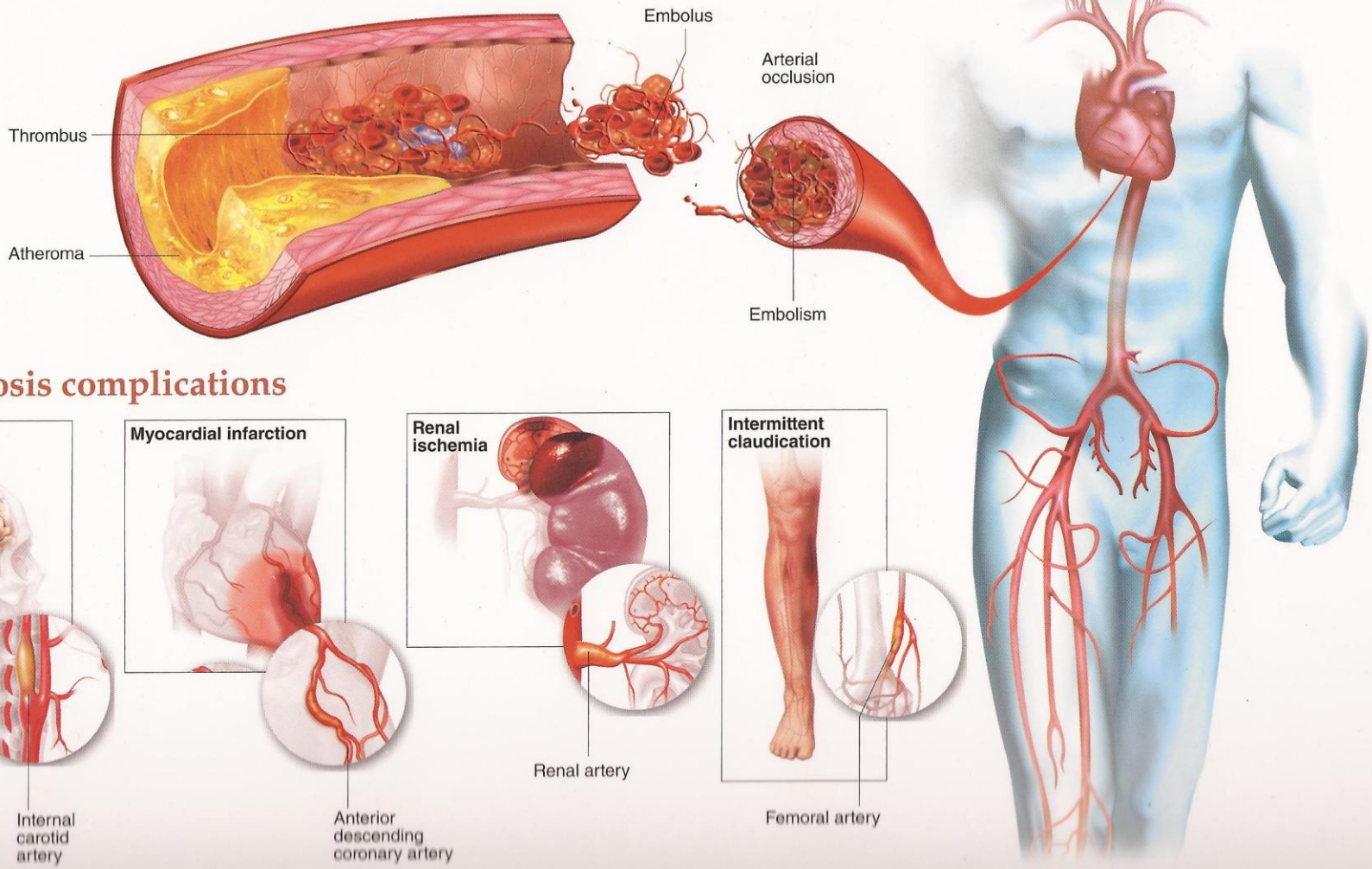
Stroke/ cerebrovascular accident



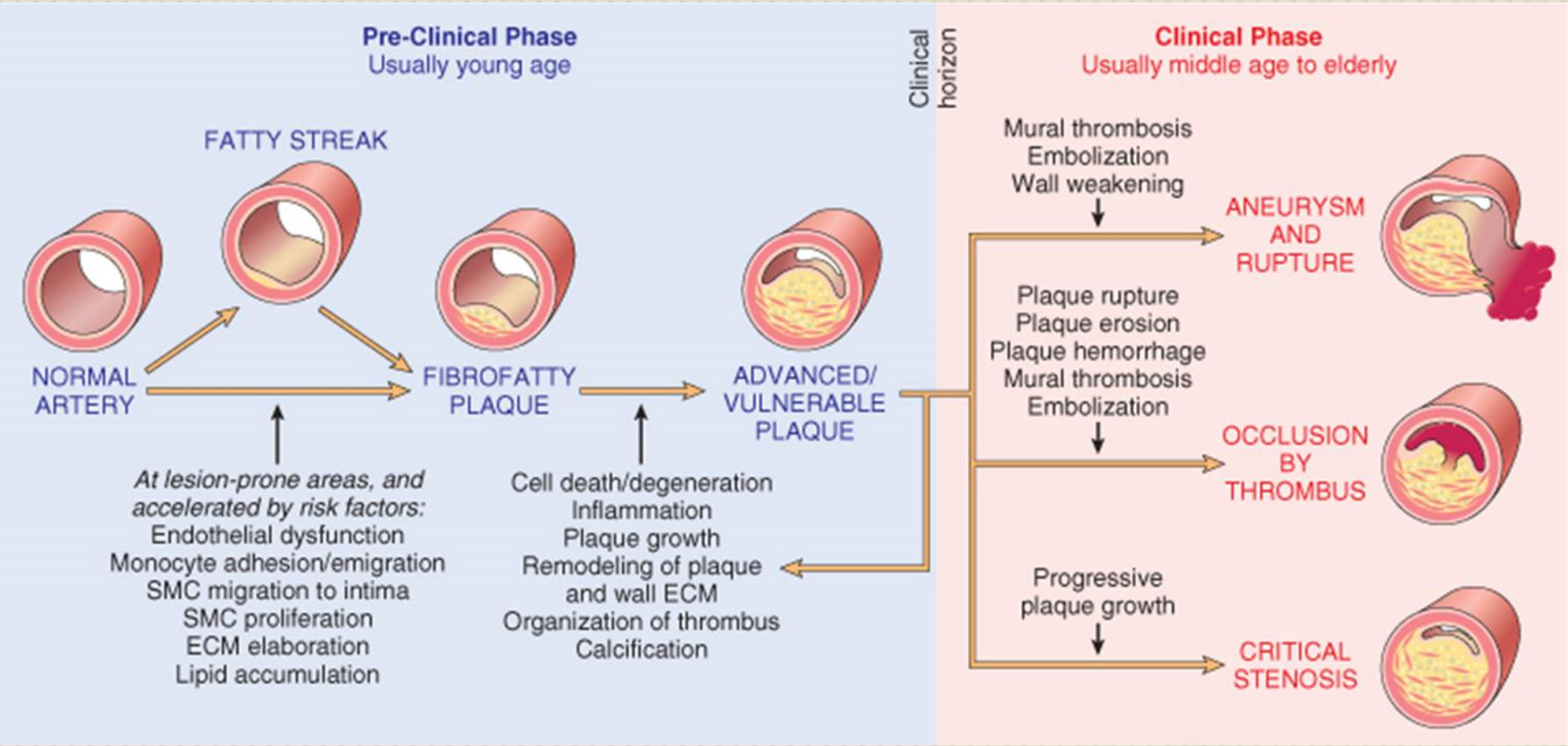


healthcaredir.com -

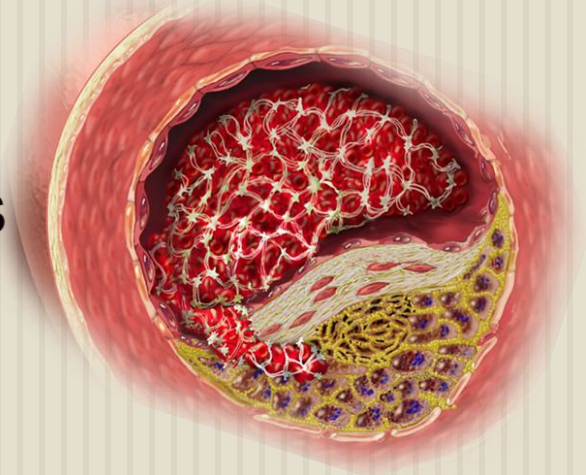
Atherosclerosis and cardiovascular disease



cardiologydoc.wordpress.com



Natural history of atherosclerosis



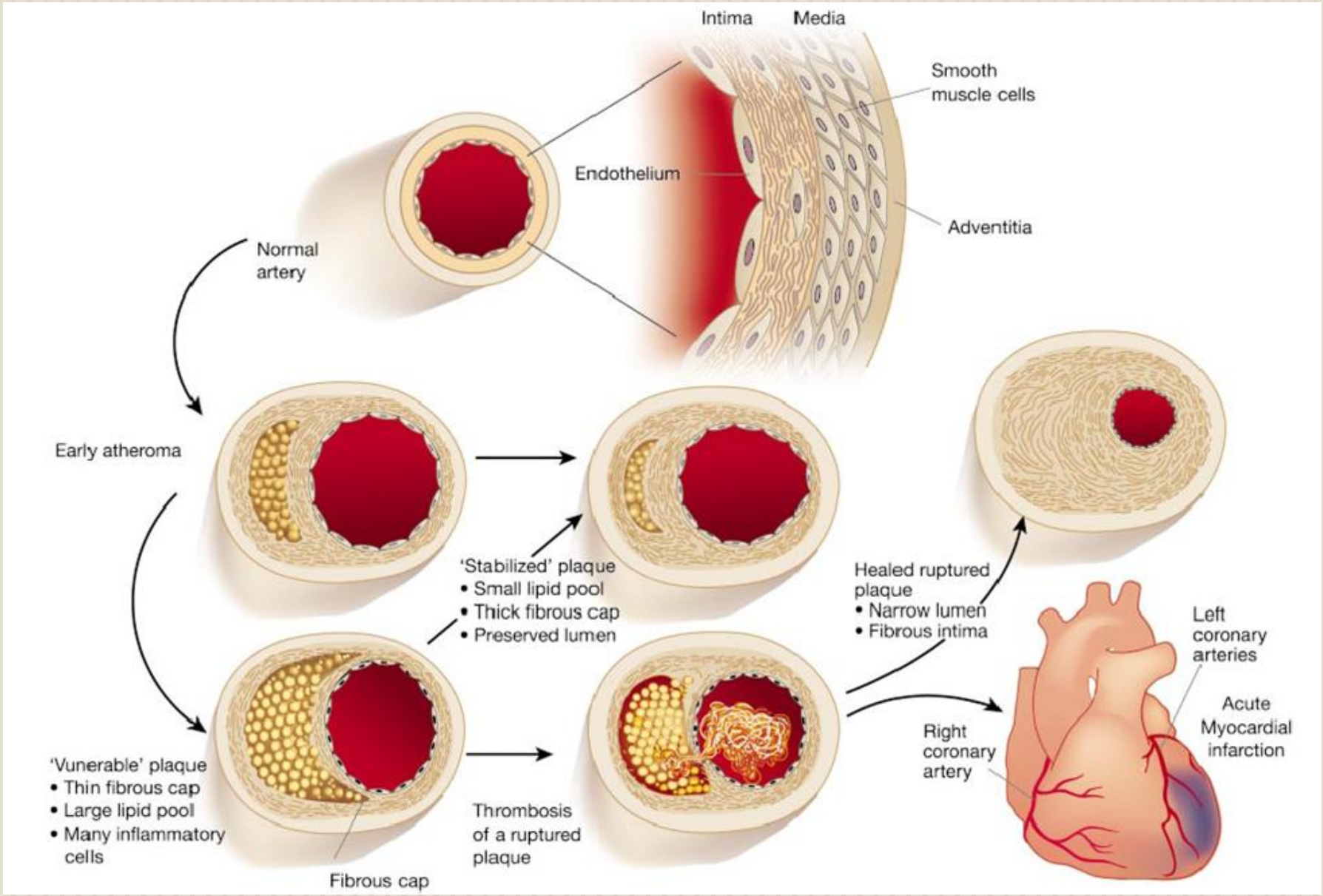
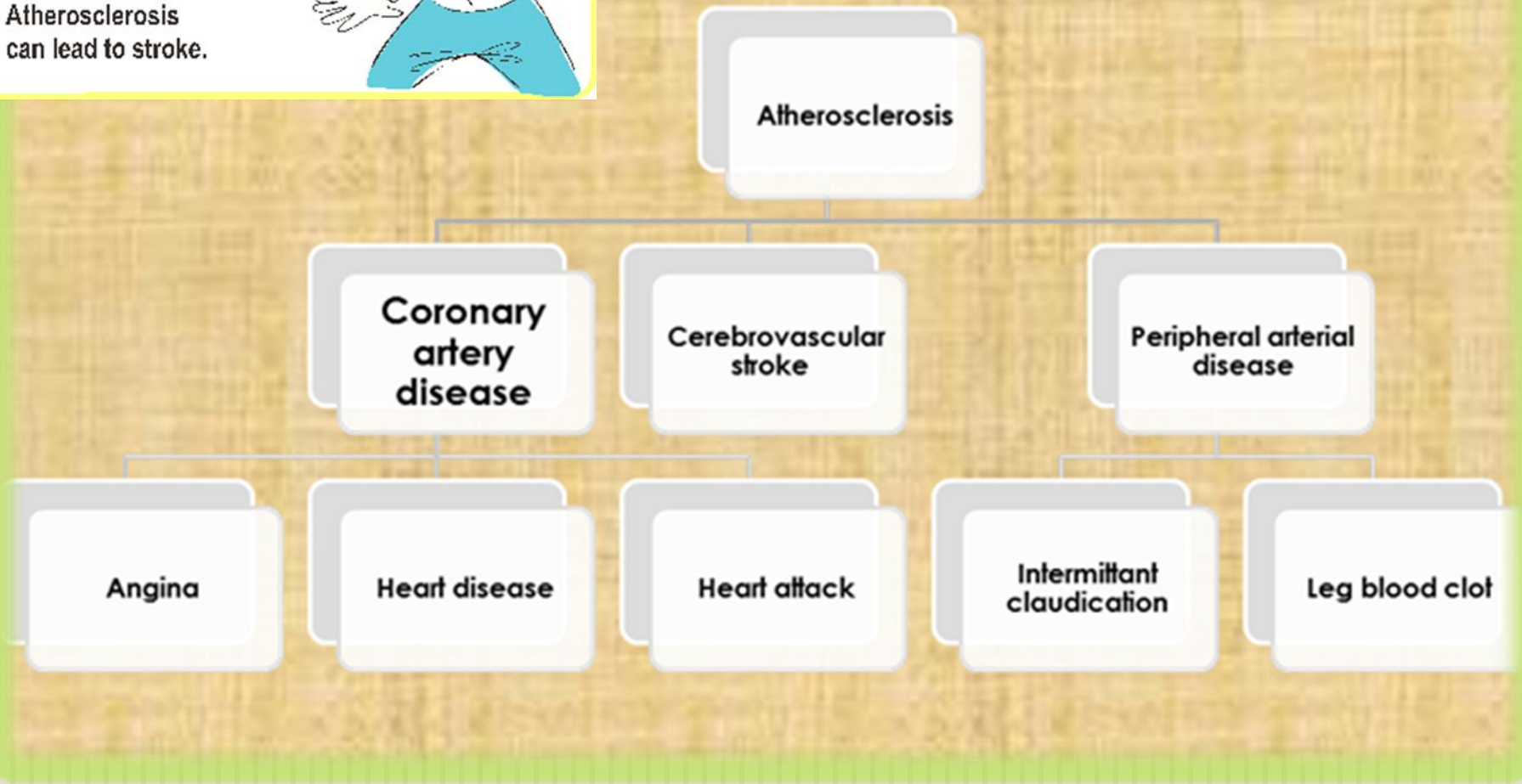


Illustration from from Libby P: Inflammation in Atherosclerosis. Nature 202;420:868

What are the ill effects of Atherosclerosis ?

- Atherosclerosis can lead to pain in the chest known as angina.
- Atherosclerosis can lead to heart attack.
- Atherosclerosis can lead to stroke.



Risk Factors for Atherosclerosis

MAJOR RISK FACTORS
NON-MODIFIABLE FACTORS
1. Increasing age
2. Male gender
3. Family history
4. Genetic abnormalities
POTENTIALLY MODIFIABLE FACTORS
1. Hyperlipidemia
2. Hypertension
3. Cigarette smoking
4. Diabetes

MINOR/ UNCERTAIN RISK FACTORS
Obesity
Physical inactivity
Stress ("type A" personality)
Postmenopausal estrogen deficiency
High carbohydrate intake
Alcohol
Lipoprotein Lp(a)
Hardened (trans)unsaturated fat intake
Chlamydia pneumoniae

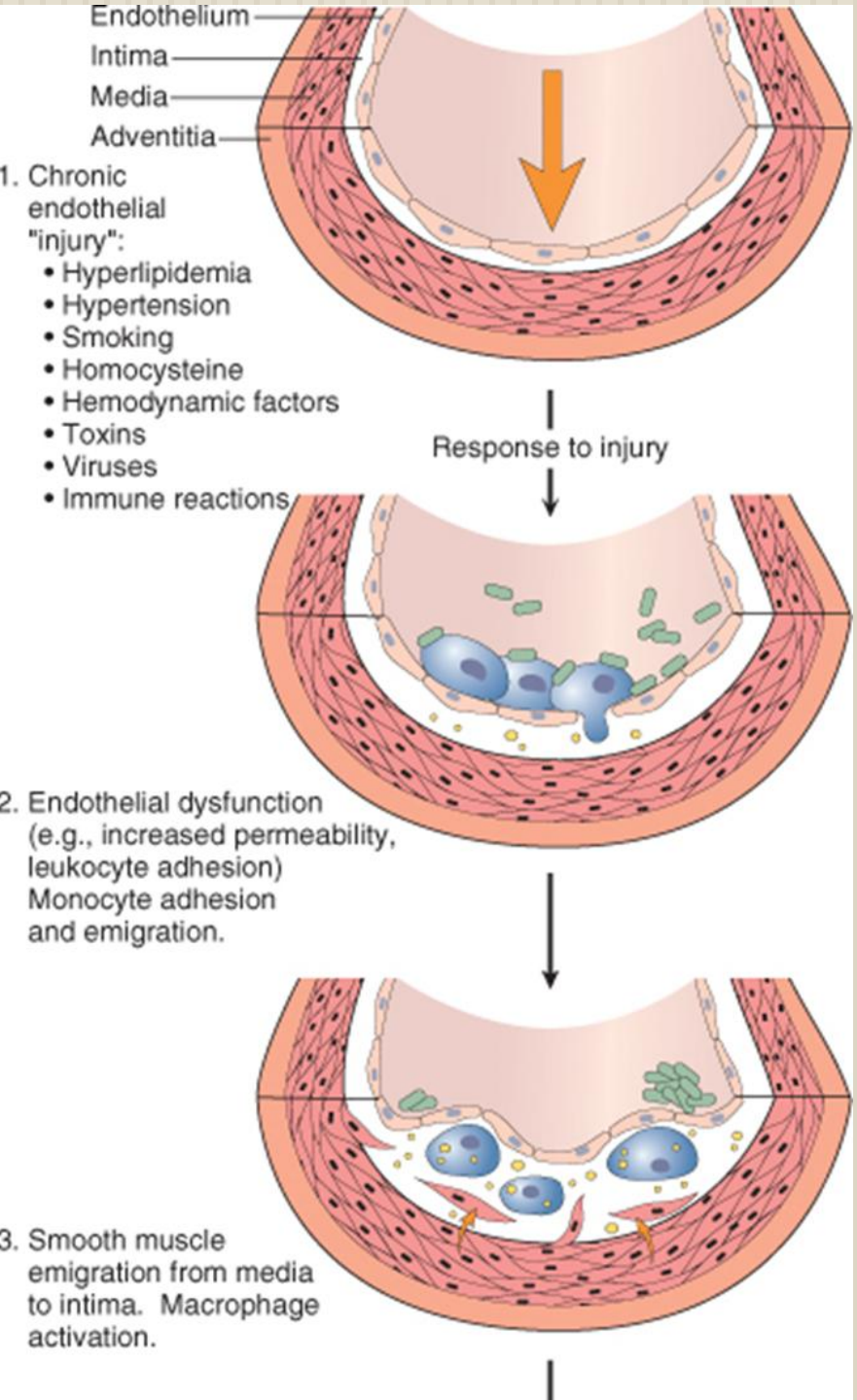
IMPORTANCE OF TYPES OF LIPOPROTEINS IN HYPERLIPIDEMIA

High blood levels of the following promotes AS and therefore heart disease:

- **Low-density lipoproteins (LDLs):** It is "bad cholesterol".
- **Very-low-density lipoproteins (VLDLs)**
- **Chylomicrons**

Good cholesterol:

- **High-density lipoproteins (HDLs):** is known as "good" cholesterol. High levels of HDL protects against heart attack. Low levels of HDL also increase the risk of heart disease. HDLs help to reverse the effects of high cholesterol.



PATHOGENESIS: the hypothesis is that AS is a response to injury

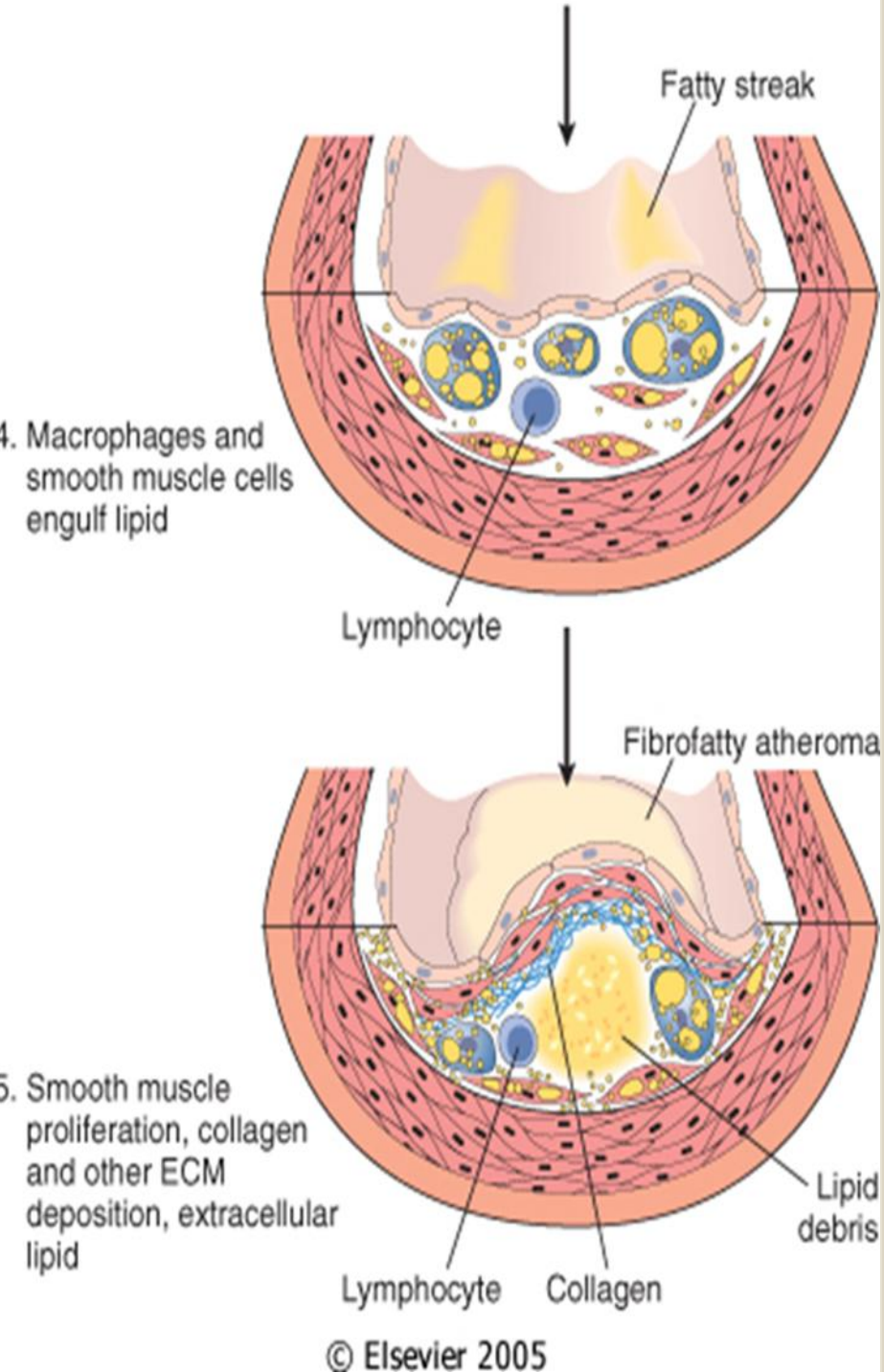
The steps are as follows:

a. Accumulation of lipoproteins (mainly LDL with its high cholesterol content) in the vessel wall and **subtle chronic endothelial injury**

b. Increased permeability, leukocyte adhesion, and thrombotic potential.

c. **Adhesion** of blood monocytes and leukocytes **to the endothelium, followed by migration** of monocytes into the intima and transformation into macrophages and foam cells

d. **Adhesion of platelets**



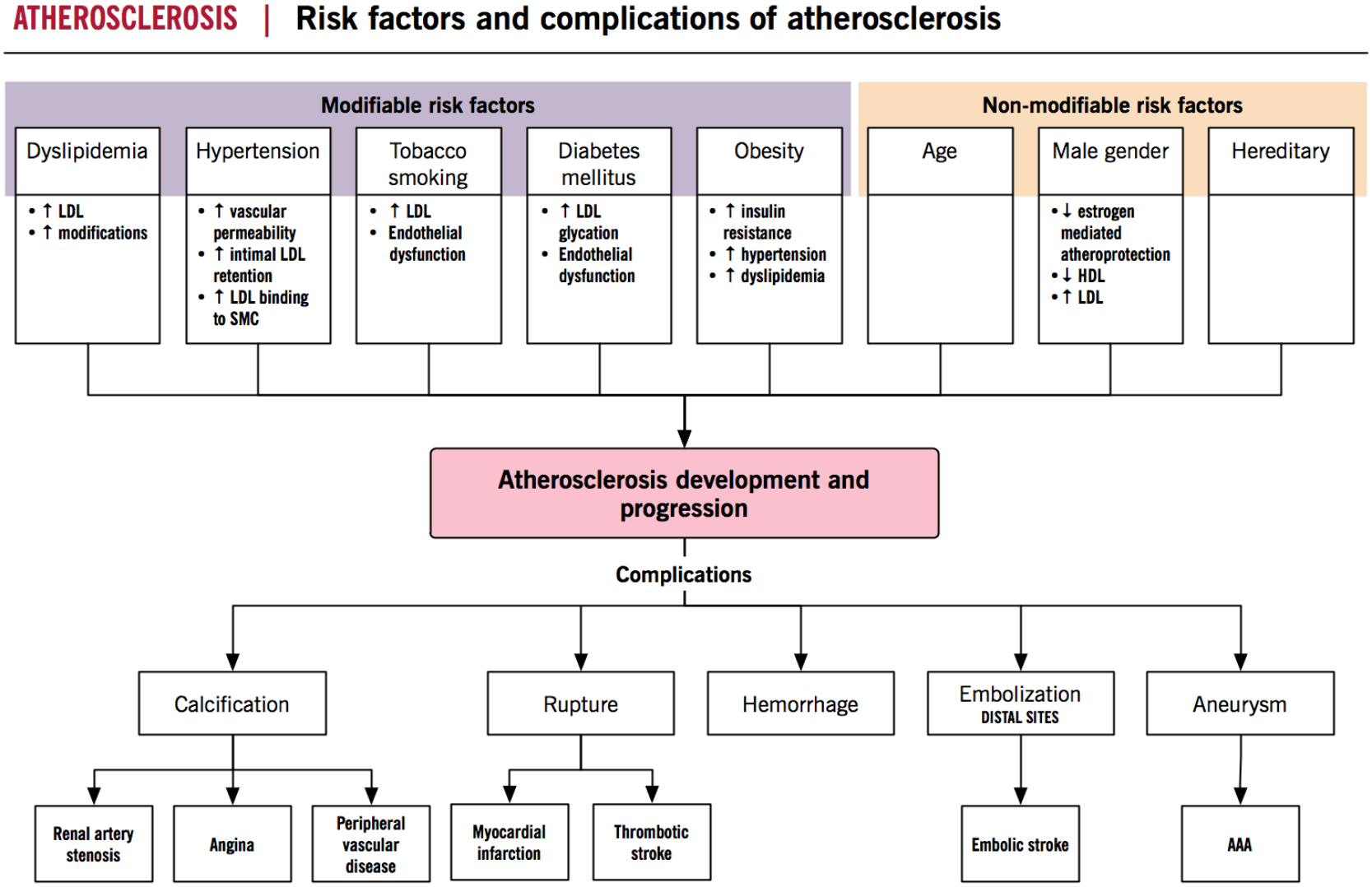
PATHOGENESIS:

f. Release of factors from activated platelets, macrophages, or vascular cells that cause **migration of SMCs from m**edia into the intima.

g. **Proliferation of smooth muscle cells in the intima, and production of extracellular matrix** (e.g. collagen & proteoglycans).

h. Enhanced accumulation of intracellular (macrophages and SMCs) and extracellularly lipids.

SUMMARY



http://www.pathophys.org/

Angioplasty