Pathology team 441

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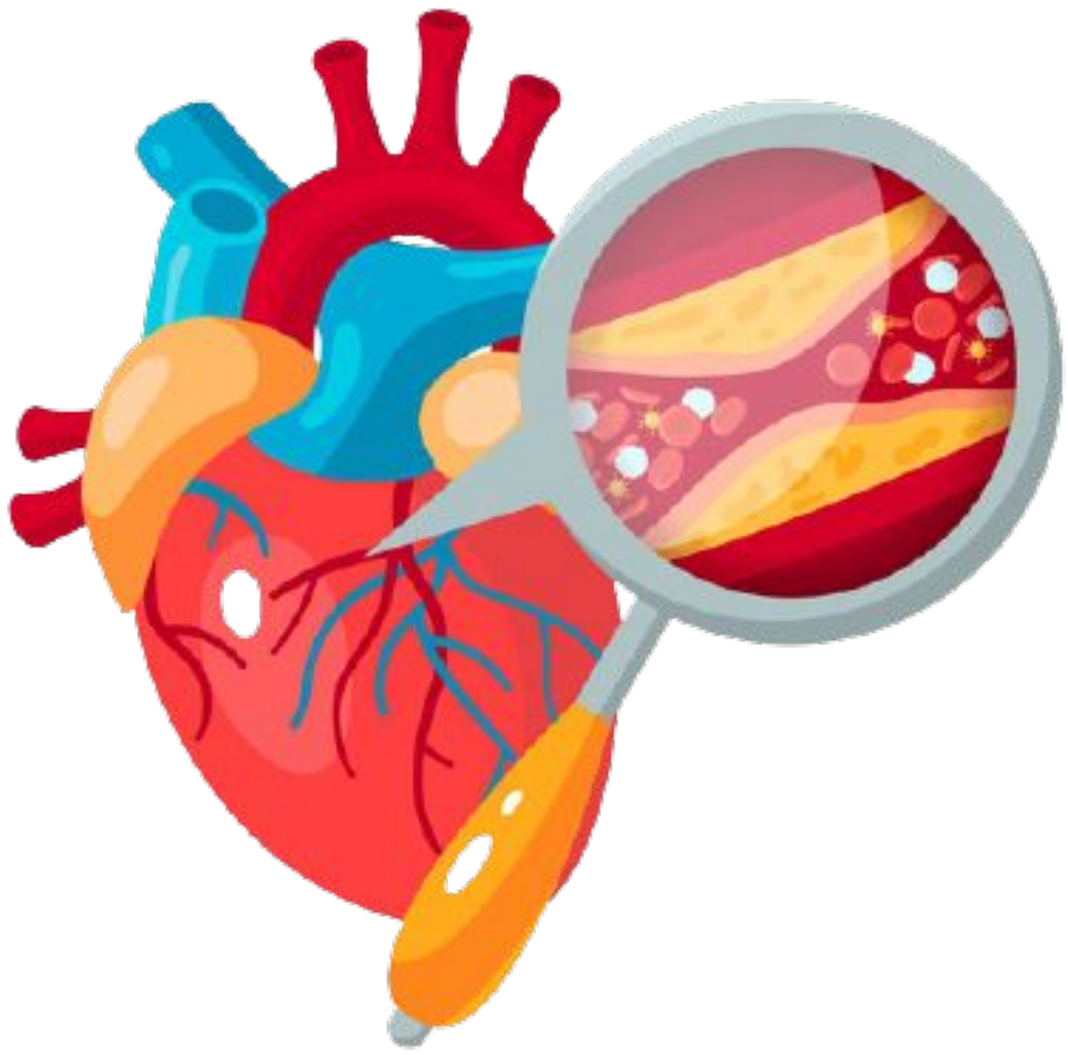
MED441
KING SAUD UNIVERSITY

Atherosclerosis



Editing File

Color Index:

- Main text
- Important
- Boys slides
- Girls slides
- Dr's notes
- Extra

Objectives

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

Normal Blood Vessels

Girls slides only

Arteries

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

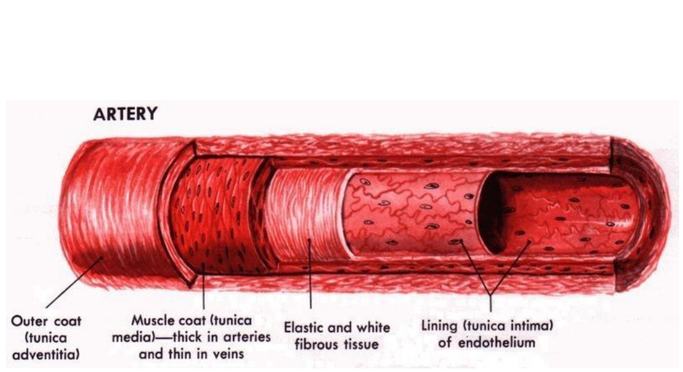
Venules/veins

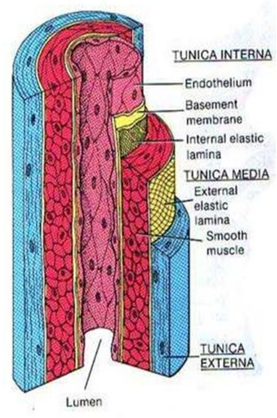
- large diameter, thin walls
- compressible, penetrable by tumor
- Have valves

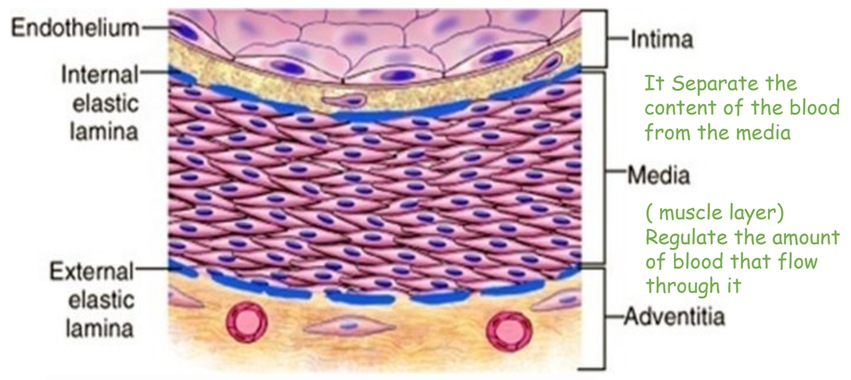
Lymphatics

- drain excess interstitial fluid from the interstitial tissue.
- pass through nodes
- End in the superior vena cava.

Artery



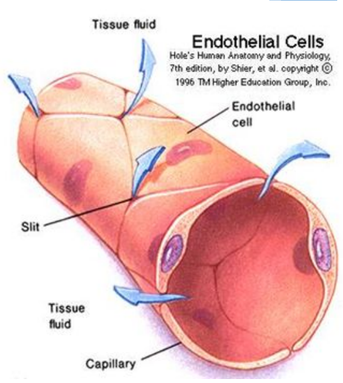




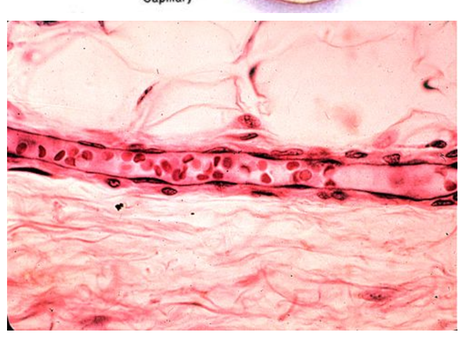
Endothelial Cell

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 covers the basement membrane completely.)



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.

If the endothelial cell gets injured, the basement membrane gets exposed. This exposure is a source of trouble and diseases.
- Intact endothelial cells are very important for normal physiology.

Normal Blood Vessels

Girls slides only

Smooth muscle cells (SMC)

- SMCs are present in the media of blood vessels
- SMCs are responsible for:
  - vasoconstriction of blood vessel
  - vasodilation of blood vessel

  to regulate the amount of the blood in the vessel

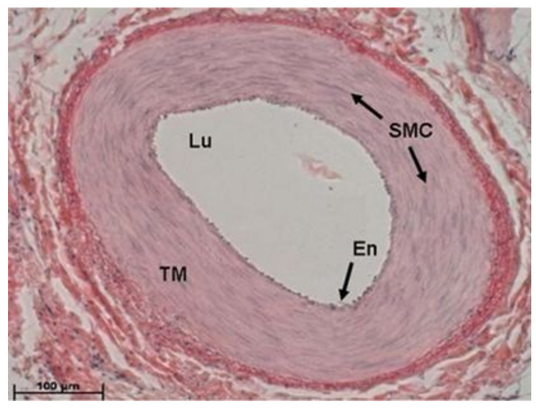
Any vascular injury or dysfunction stimulates SMCs.

On stimulation the SMCs:

1- Migrate from the media to the intima

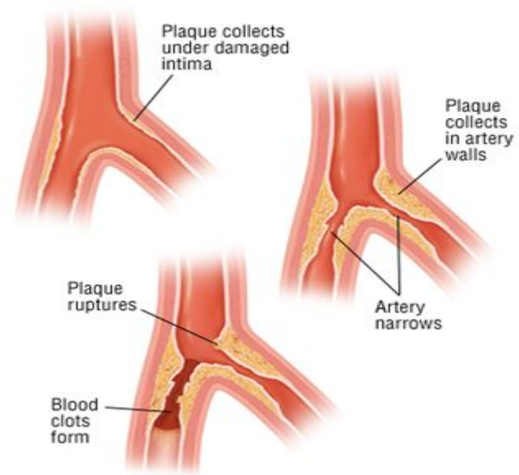
2- In the intima the SMCs lose the capacity to contract and gain the capacity to divide. So they proliferate as intimal SMCs.
(SMCs changed completely)

3- They synthesize collagen, elastin etc and deposit extracellular matrix (ECM).



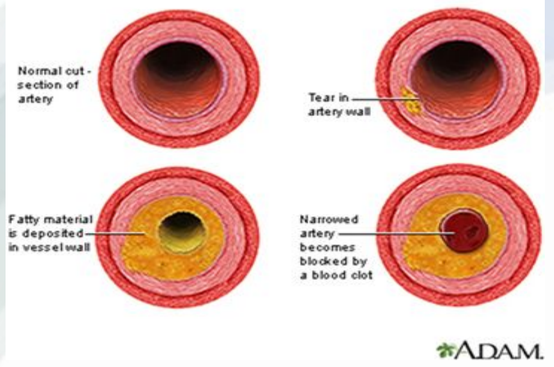
Atherosclerosis (AS)

- **Atherosclerosis** (a type of arteriosclerosis, a build-up of fat (cholestrol)) 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.as the Atheroma grows the vessel became narrower and the blood flow decrease leading to atherosclerosis.
- 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 (3 arteries come together and meet to form a circle)



AS plaque grow leading to serious complications (depends on the location of AS)

- In Coronary artery disease (angina & MI)
- Carotid atherosclerotic disease (stroke)



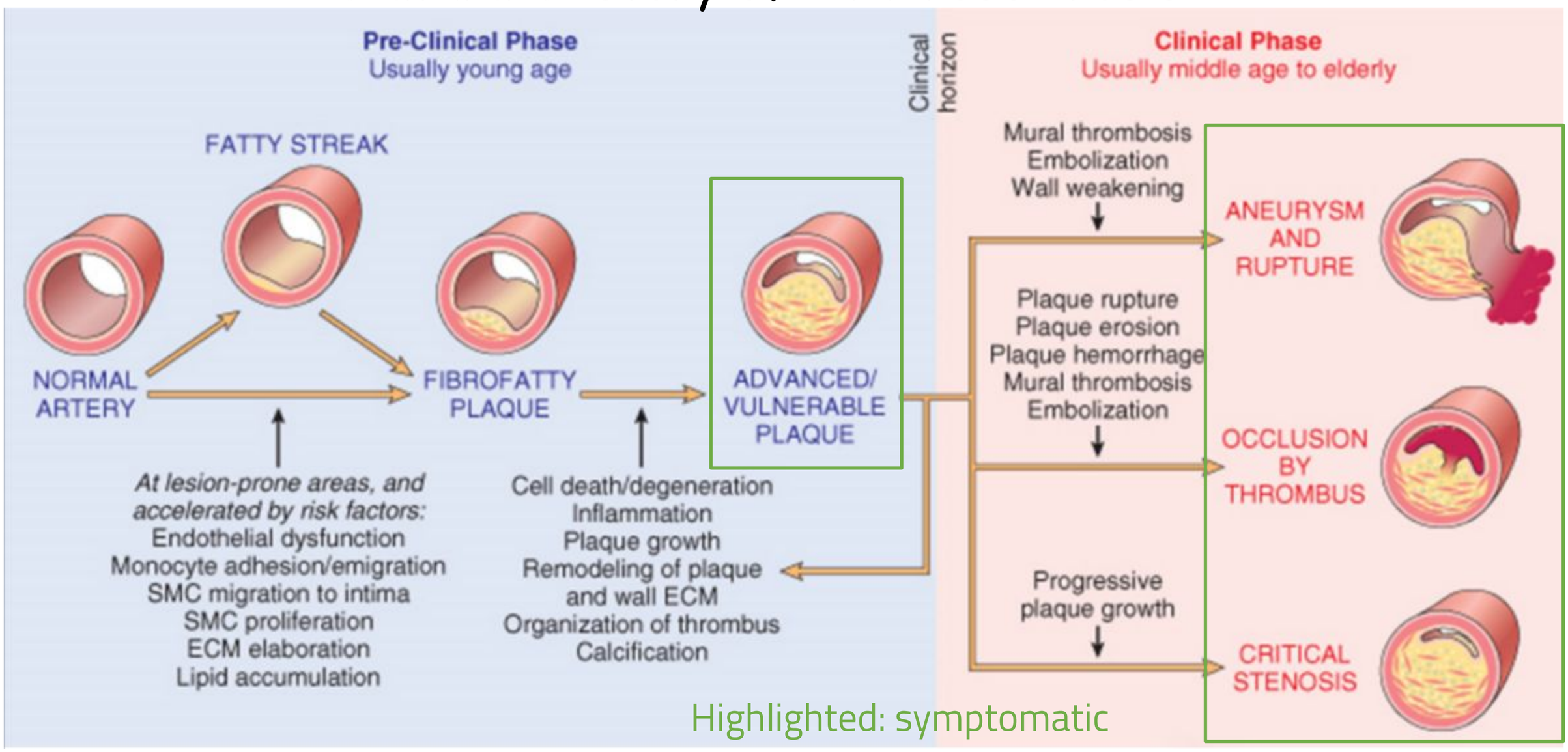
Arteriosclerosis (hardening of the arteries) is a generic term for thickening and loss of elasticity of arterial walls.

1. Arteriosclerosis
2. Hypertension
3. calcific sclerosis , Mönckeberg medial
4. Atherosclerosis
5. Old age

#439
What is atheroma? An atheroma, or atheromatous plaque ("plaque"), is an abnormal accumulation of material in the inner layer of the wall of an artery. The material consists of mostly macrophage cells, or debris, containing lipids, calcium and a variable amount of fibrous connective tissue. Atheroma is shown in the below gross pathological picture

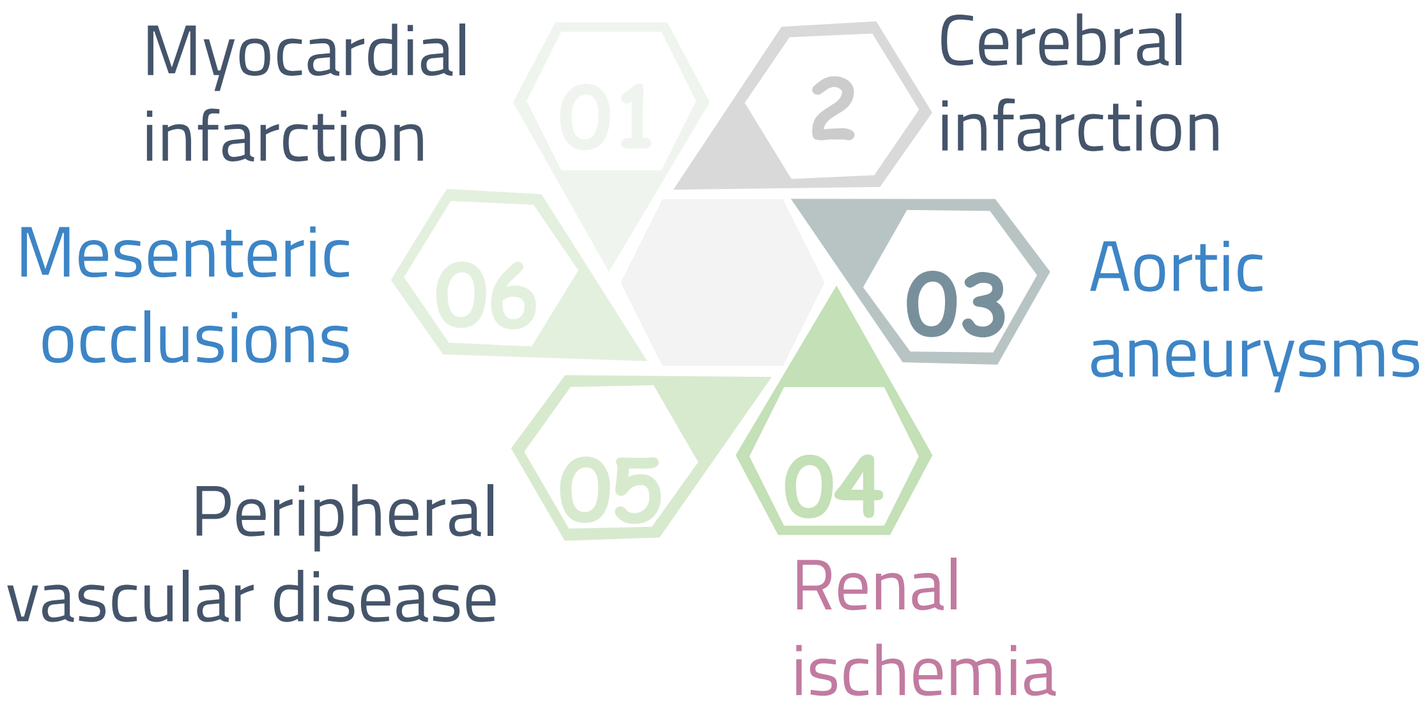
Atherosclerosis and CVD

Natural History of Atherosclerosis



Highlighted: symptomatic

Complications



- Ill effects of atherosclerosis
1. Chest pain (angina)
2. May lead to heart attack
3. May lead to stroke

AS can cause:

Coronary heart disease

- Angina
- Heart disease
- Heart attack

Peripheral arterial disease

- Leg blood clot (gangrene)
- Intermittent claudication (pain on walking)

Cerebrovascular stroke

Atherosclerosis Risk Factors

(Should be aware of them)

Major

Non-modifiable
(cannot be changed)

1. Increasing age
2. Male gender
3. Family history
4. Genetic defects i.e: hypercholesterolemia

Potentially modifiable
(can be managed)

Via medication, weight loss, etc

1. Hyperlipidemia
2. Hypertension
3. Smoking
4. Diabetes

Minor/ Uncertain

Associated with lifestyle

1. High CHO intake
2. Alcohol
3. Trans fat intake
4. Physical inactivity

Other

1. Obesity
2. Stress (type A personality)
3. Post-menopause estrogen deficiency
4. LipoproteinA (high levels)
5. Chlamydia pneumoniae

Estrogen protects against AS

Importance of lipoprotein types in hyperlipidemia

(High levels)

*High cholesterol markers in blood tests

"Bad"
(promote AS)

- *Low-density (LPLs) "bad cholesterol"
- *Very-low-density (VLDPs)
- Chylomicrons

If you know the *bad* guy Loki, remember Low densities

"Good"
(protect against heart attack)

- High-density (HDLs) "good cholesterol"

High levels of HDL protect, **low levels increase risk**. HDL helps reverse the effects of high cholesterol.

Pathogenesis of AS

The hypothesis is that AS is a response to injury

Video at 1:14

1 **LP Accumulation**

Mainly LDL with its high cholesterol content in the vessel wall and **subtle chronic endothelial injury**

2 Increased permeability and leukocyte (monocyte) adhesion

3 **Adhesion of blood leukocytes to the endothelium**

Then leukocytes **migrate** into intima & transform into macrophages & foam cells

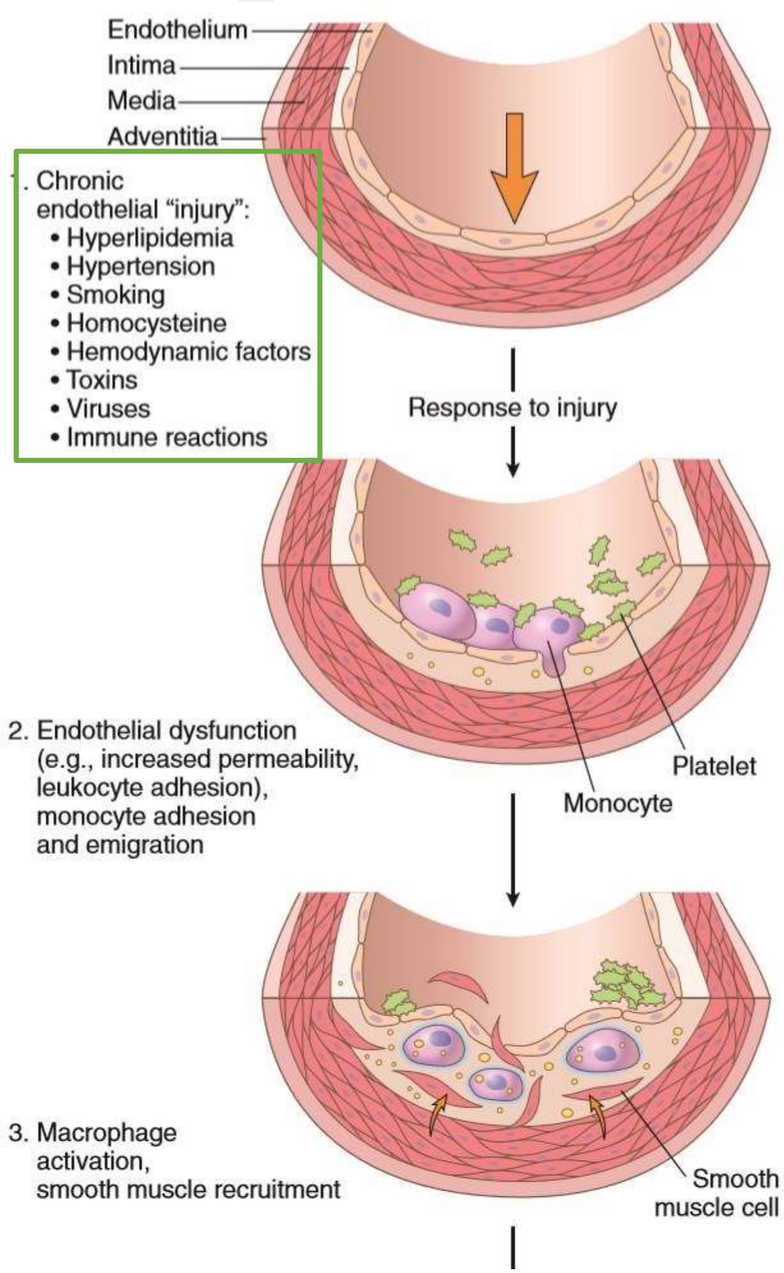
4 **Adhesion of Platelets**

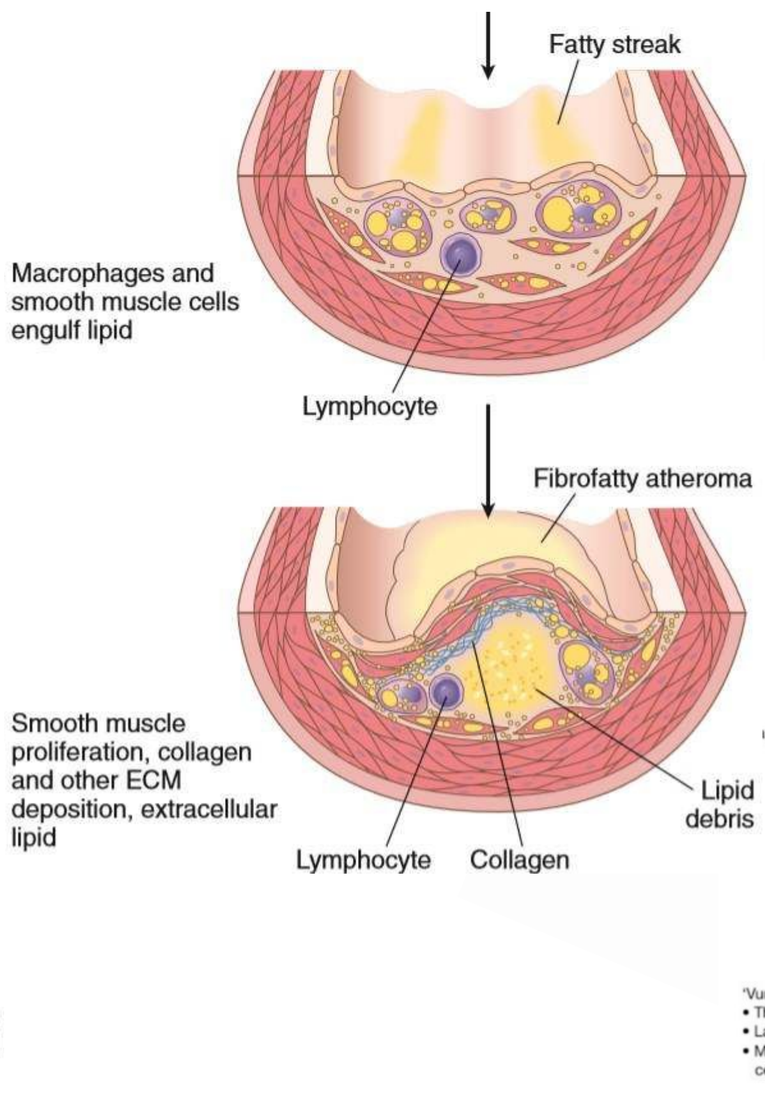
5 **Release of Factors**

From activated platelets, macrophages, or vascular cells to cause migration of SMCs from media into the intima.

6 **Proliferation of smooth muscle cells in intima, and production of EC matrix** (collagen & proteoglycans). Produces proper atheroma

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





Endothelial injury

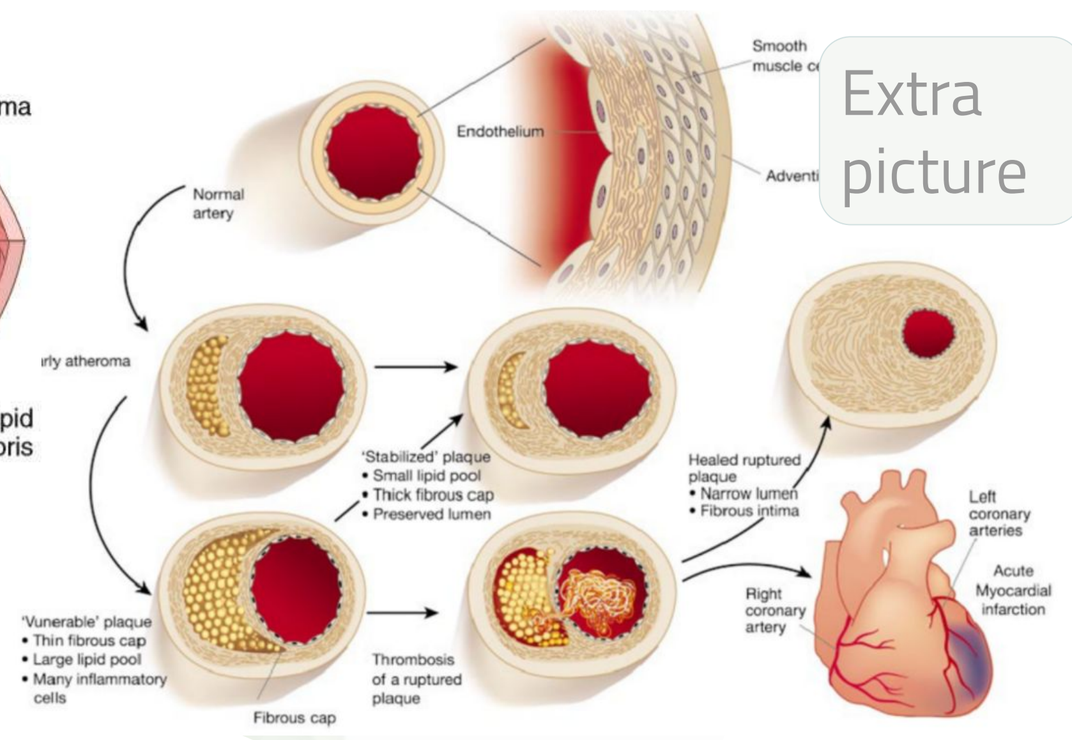
– Not completely understood

– Two most important causes of endothelial dysfunction are:

- Hemodynamic disturbances
- Hypercholesterolemia

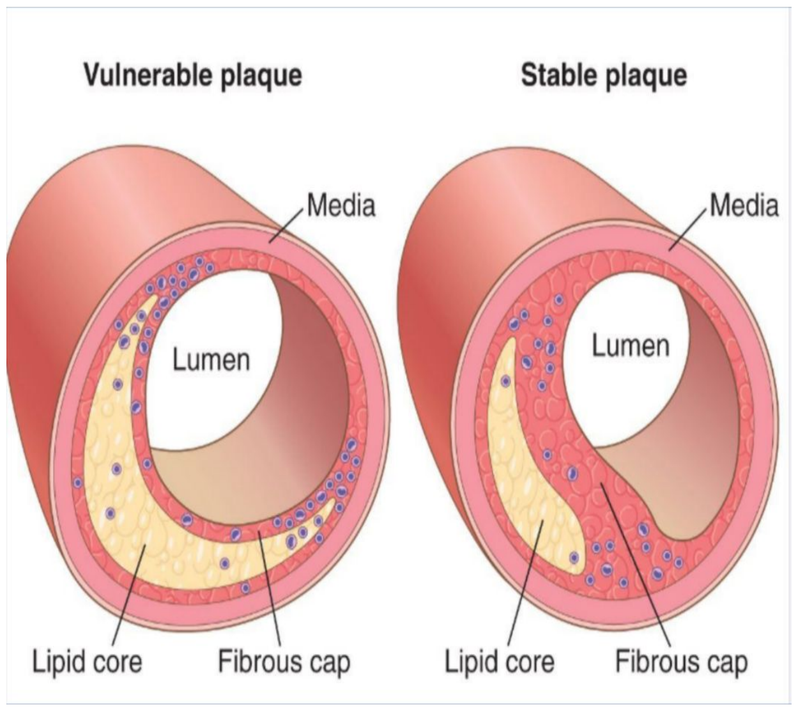
– Inflammation is also an important contributor.

- Smooth muscle cell proliferation



Extra picture

Vulnerable and Stable plaque

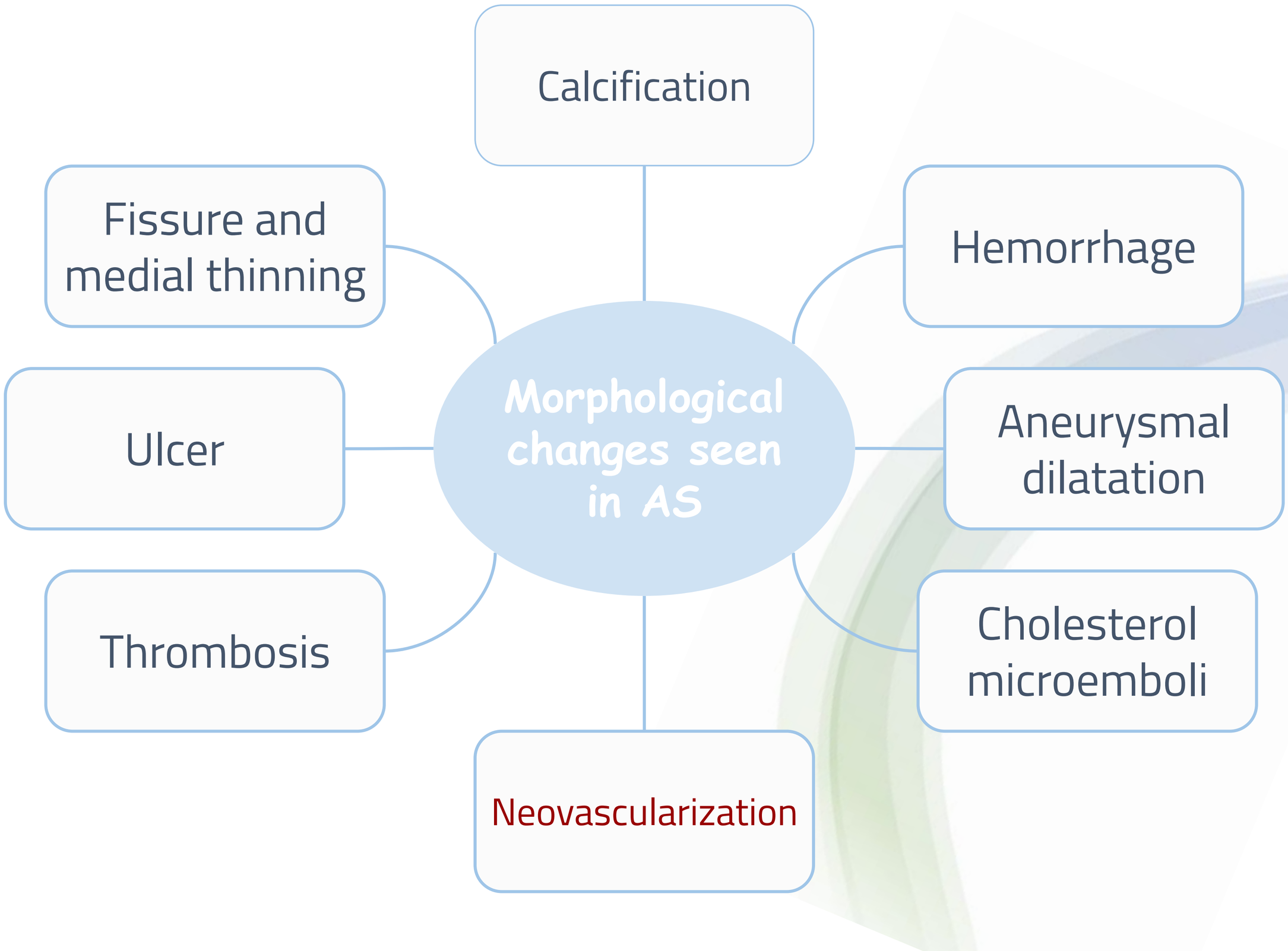


Male's slides only

Vulnerable plaque	Stable plaque
More Lymphocytes	Less lymphocytes
Bigger lipid core	Smaller lipid core
Thinner fibrous cap	Thicker fibrous cap

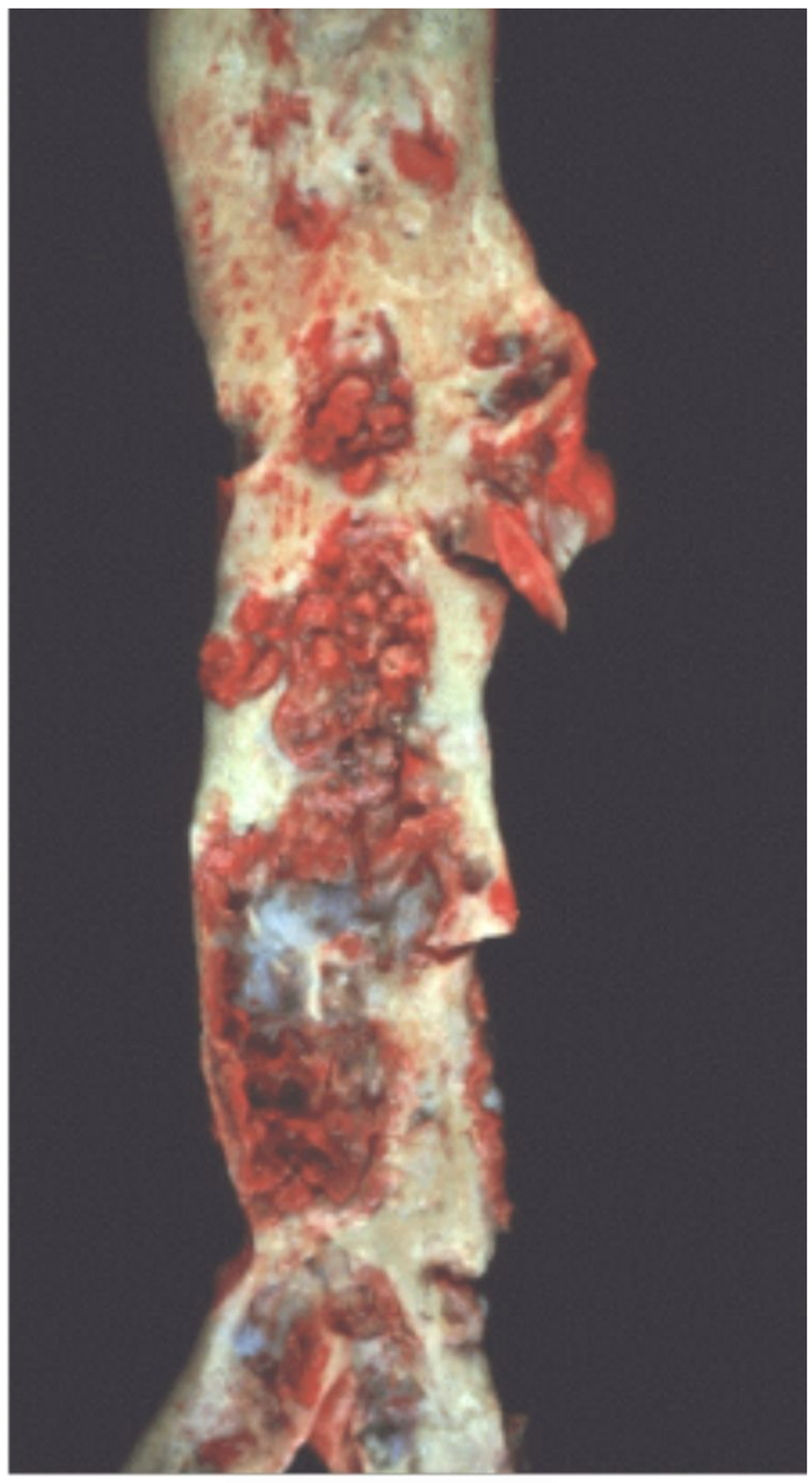
Table from doctor's notes

Morphological changes in AS



Gross morphology of atheroma

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



Picture of Abdominal Aorta cut open

Microscopic morphology of atheroma

- **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:**

Cells: SMCs, Macrophages, Lymphocytes and foam cells

Extracellular matrix: collagen, elastic fibers and proteoglycans

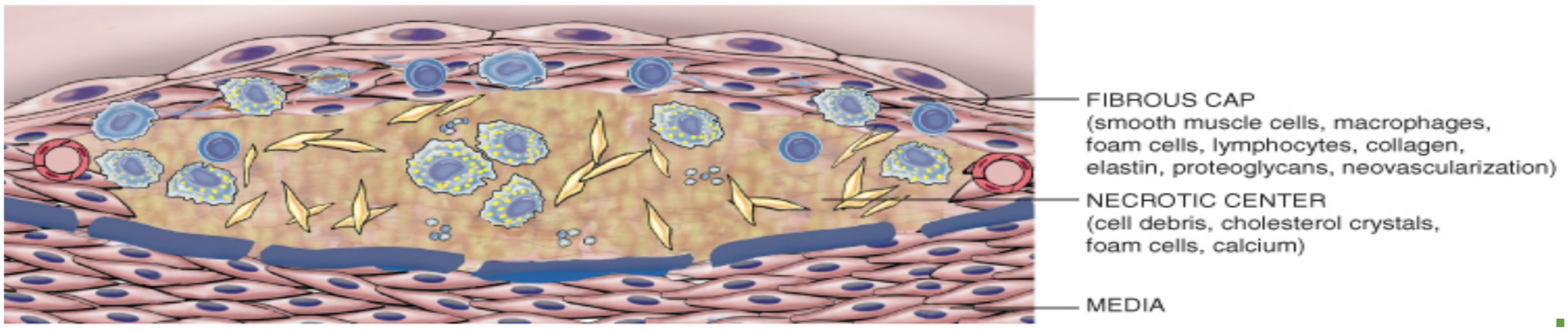
Lipid: typical atheromas contain relatively abundant lipid both extracellular and intracellular lipid

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

Cont.

Typically, the superficial fibrous cap is composed of SMCs and extracellular matrix. With some macrophages and T lymphocytes.

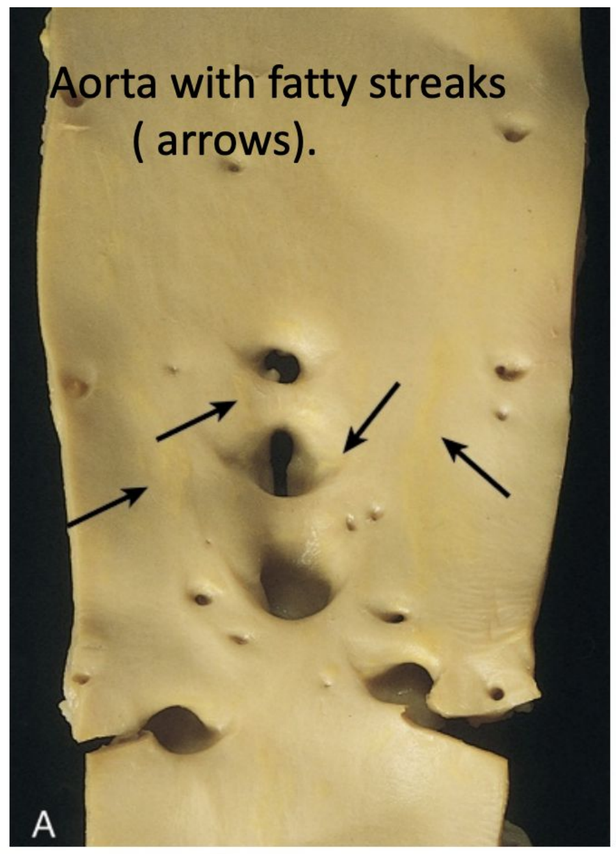
Below the fibrous cap is a necrotic core, containing lipid deposits (primarily cholesterol and cholesterol esters), cholesterol clefts, debris from dead cells, foam cells, fibrin



Fatty streaks

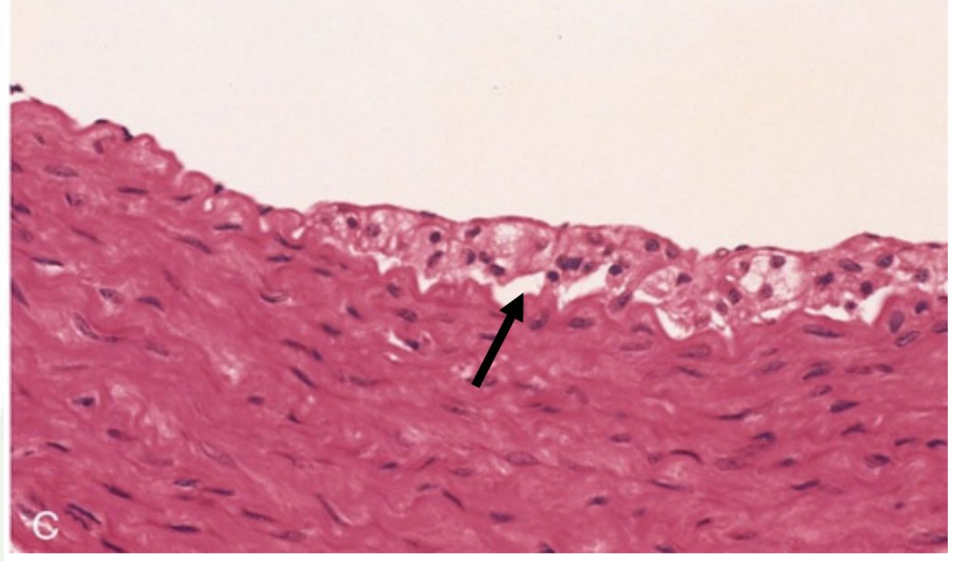
1. **Fatty streaks are the earliest lesion of AS they are a collection of lipid and lipid laden foam cells* in the intima**

2. **They do not cause disturbance in blood flow**



3. **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.**

4. **We all have fatty streaks and they are completely harmless, they only become harmful once they develop into atheromas**



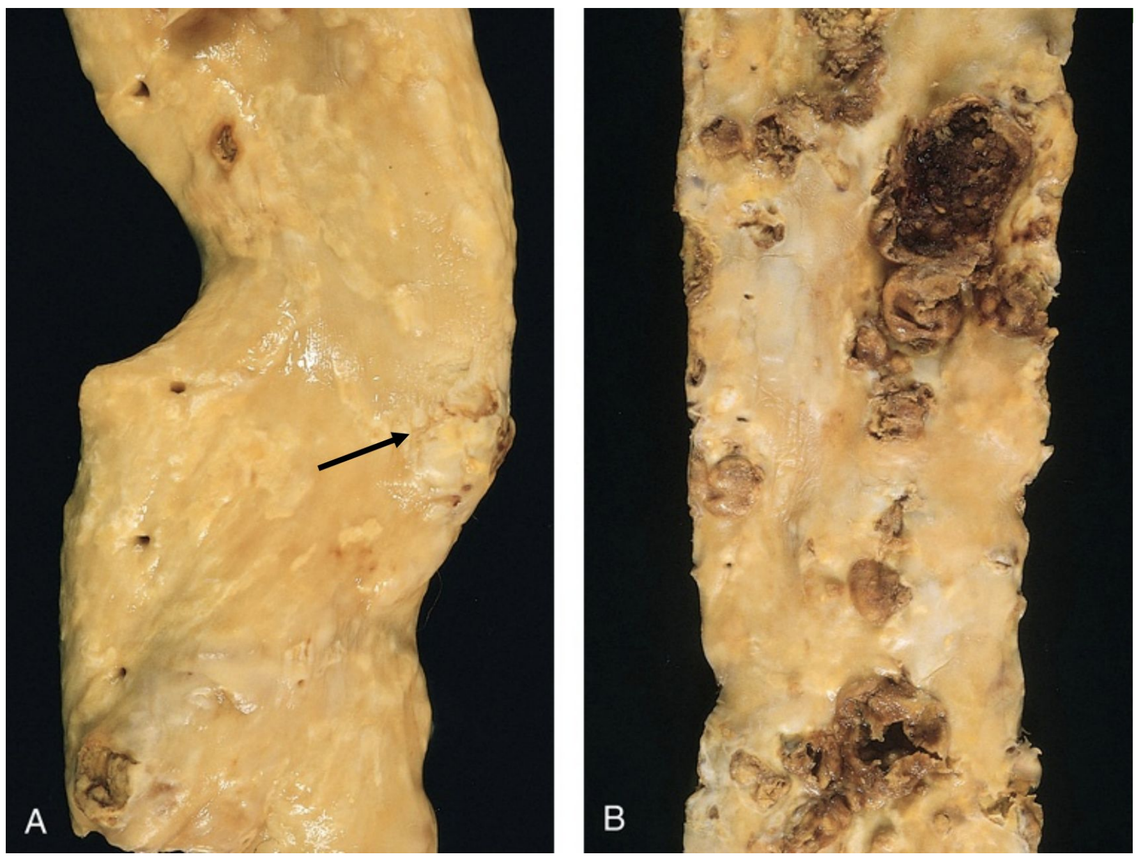
Photomicrograph of fatty streak in an experimental hypercholesterolemic rabbit demonstrating intimal macrophage-derived foam cells

*Foam cells are macrophages that contain lipid in their cytoplasm

Morphology of AS

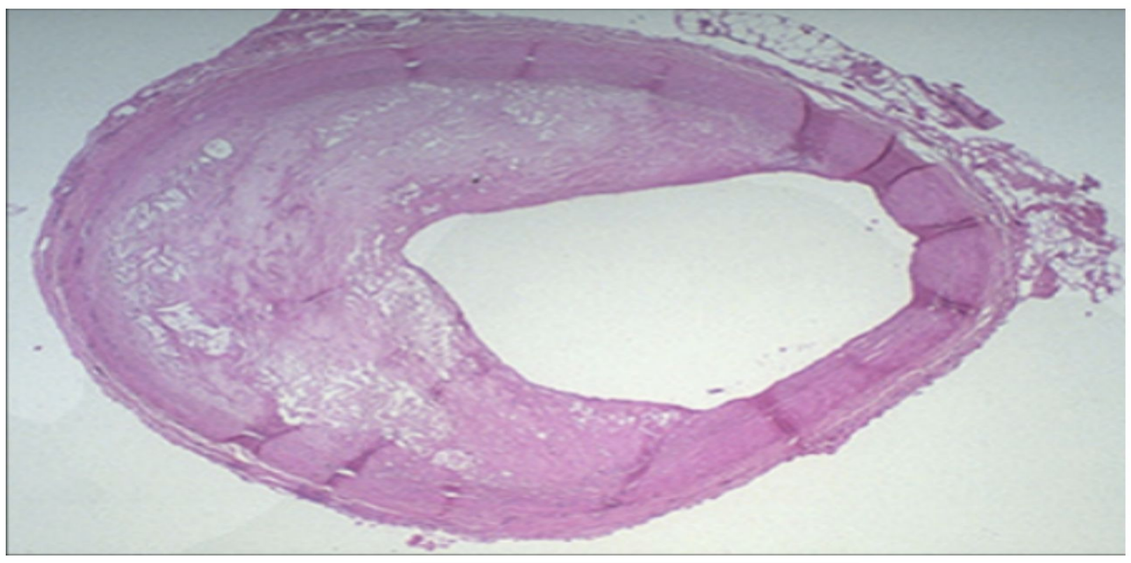
1. **Mild atherosclerosis composed of fibrous plaques, one of which is denoted by the arrow**

2. **Severe disease with diffuse and complicated lesions**



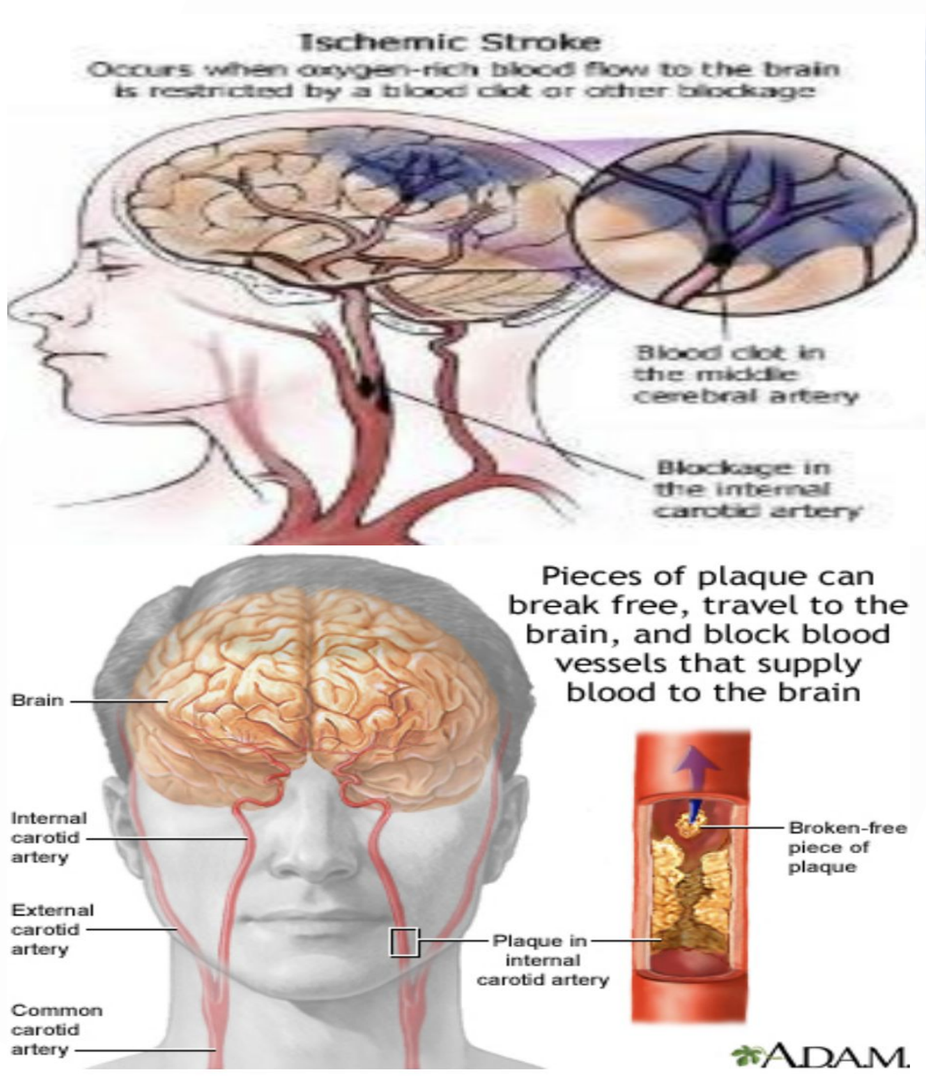
Gross view of AS in the aorta

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



Stroke / cerebrovascular accident

Ischemic stroke occurs when oxygen-rich blood flow to the brain is restricted, the type of the stroke depends on the site involved. 439



Pathological complications of AS

Calcifications: Atheromas often undergo calcification

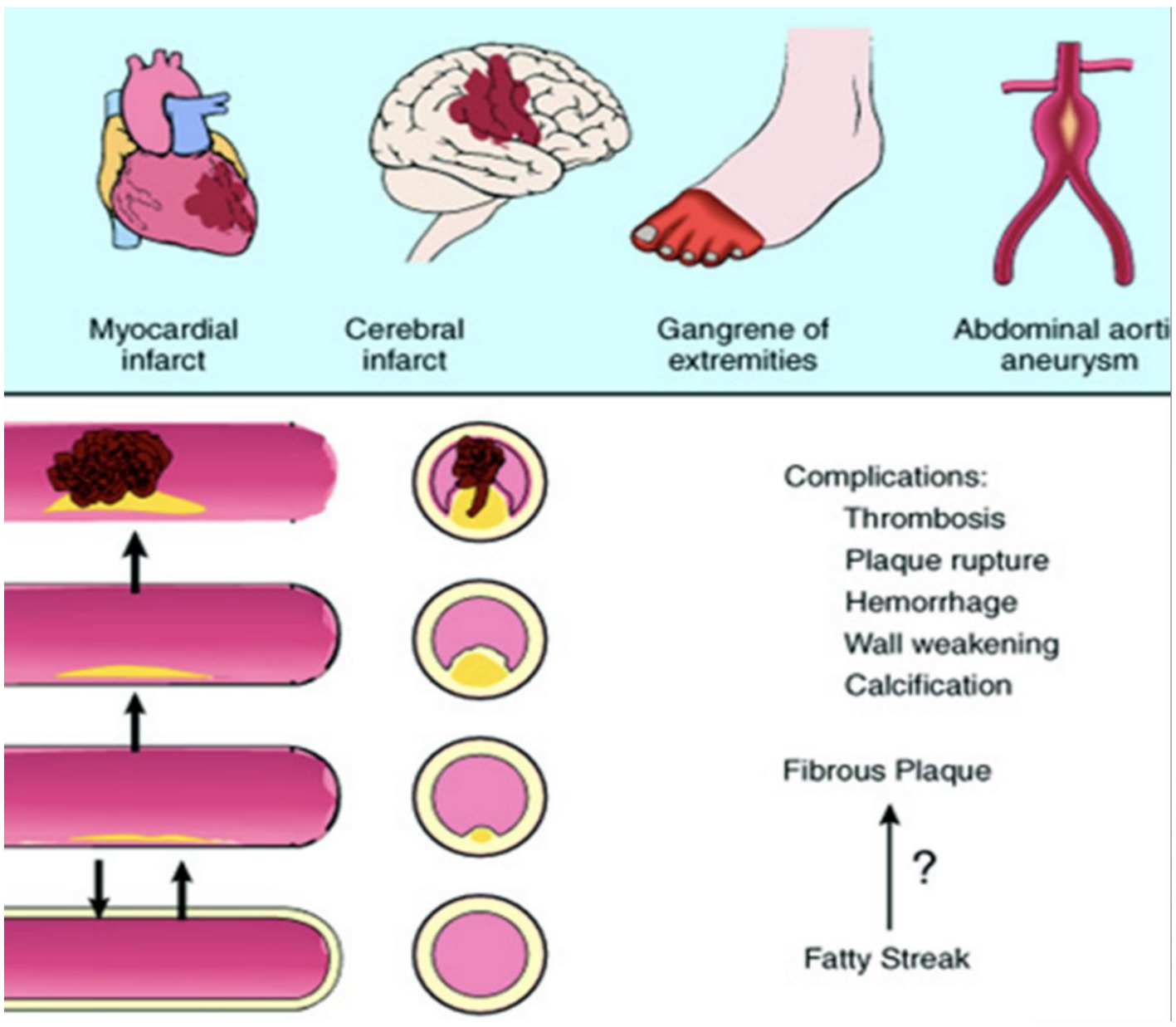
Plaque **rupture/ ulceration/ erosion** (same meaning) of the AS plaques may induce **thrombus formation** OR the AS plaque may discharge debris into the bloodstream, producing **microemboli** composed of plaque lipid (cholesterol emboli or atheroemboli).

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

Advanced lesion of AS is at risk of the following

Hemorrhage into the 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

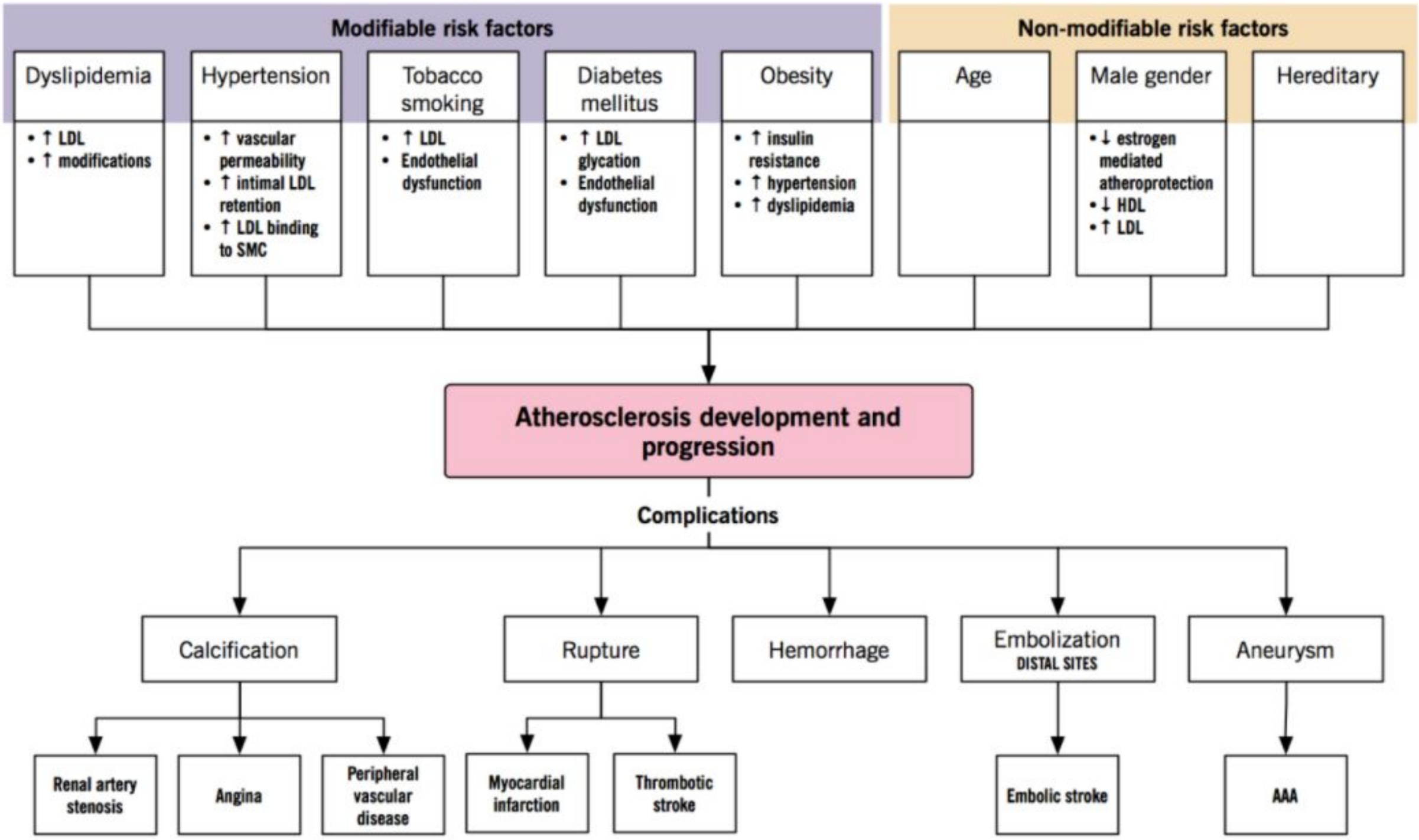
Weakening of the blood vessel wall with **aneurysmal dilation****. Atheroma can induce atrophy of the underlying media, causing weakness, aneurysm and potential rupture



**An aneurysm is a dilatation of the blood vessel wall due to its weakness so it bulges outwards and is more likely to rupture

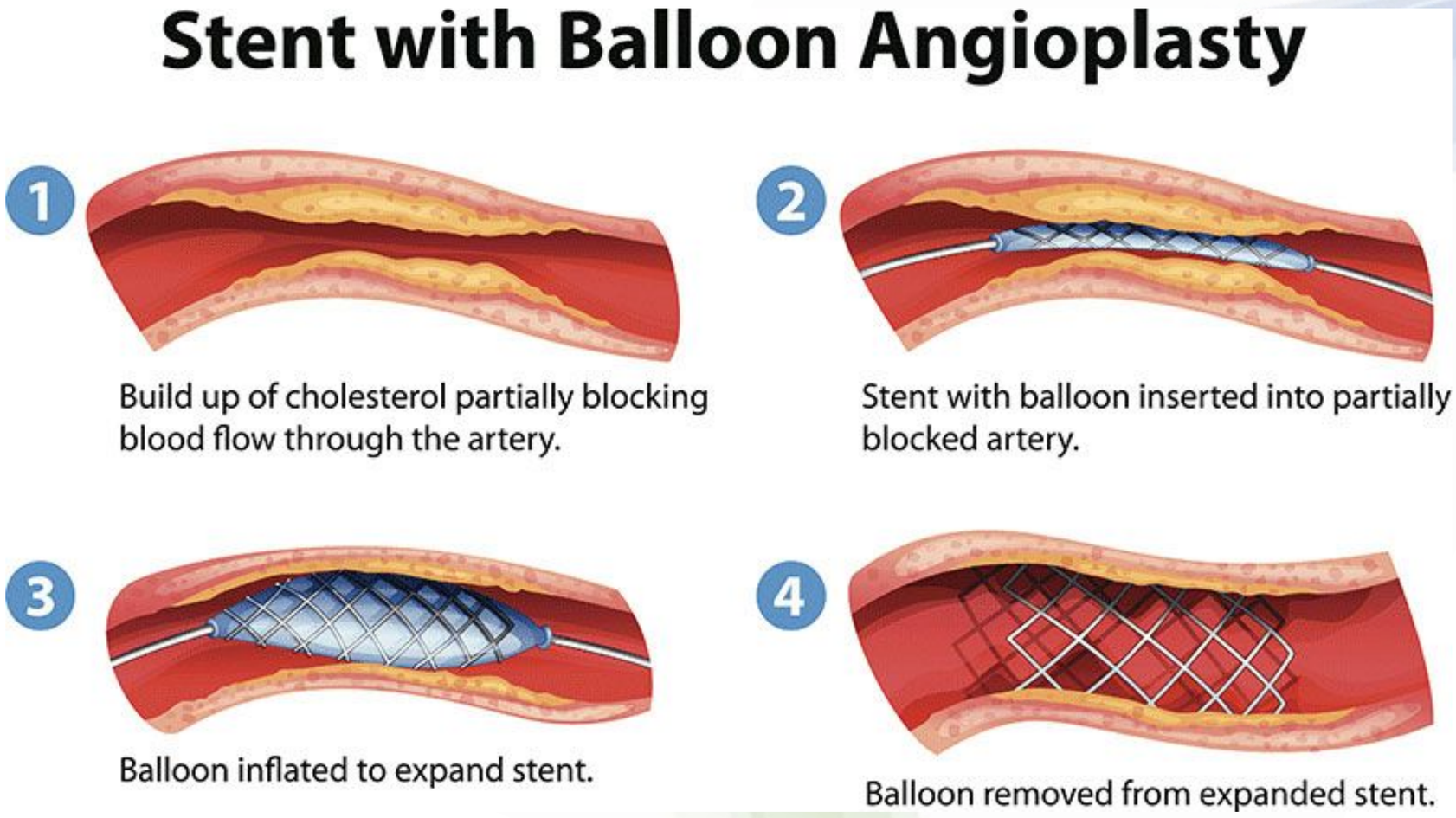
*Due to blood contact with thrombogenic basement membrane

Summary and Angioplasty(extra)



Mainly in abdominal aorta

[Angioplasty video starts at 1:57]



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