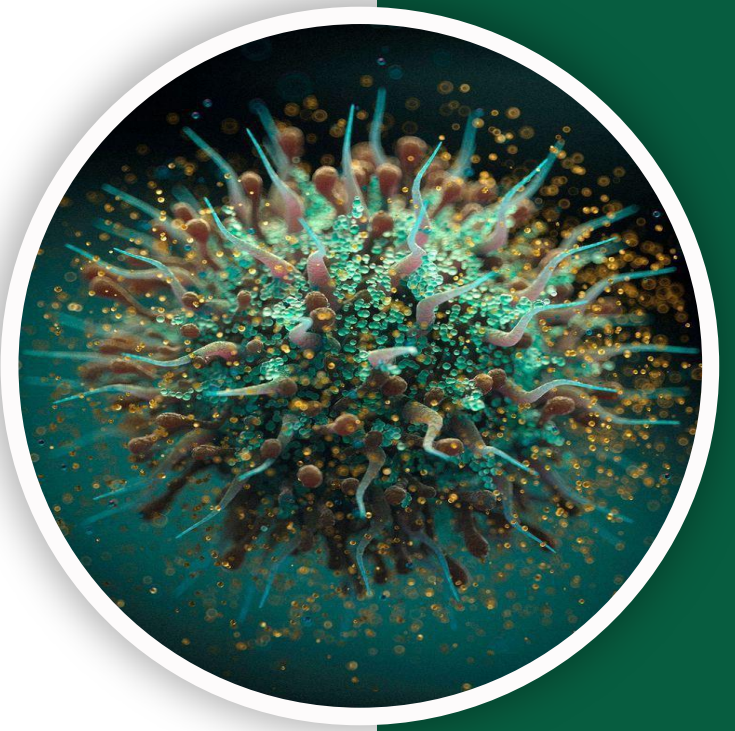
بسم الله الرحمـٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

CVS Pathology | MID 5

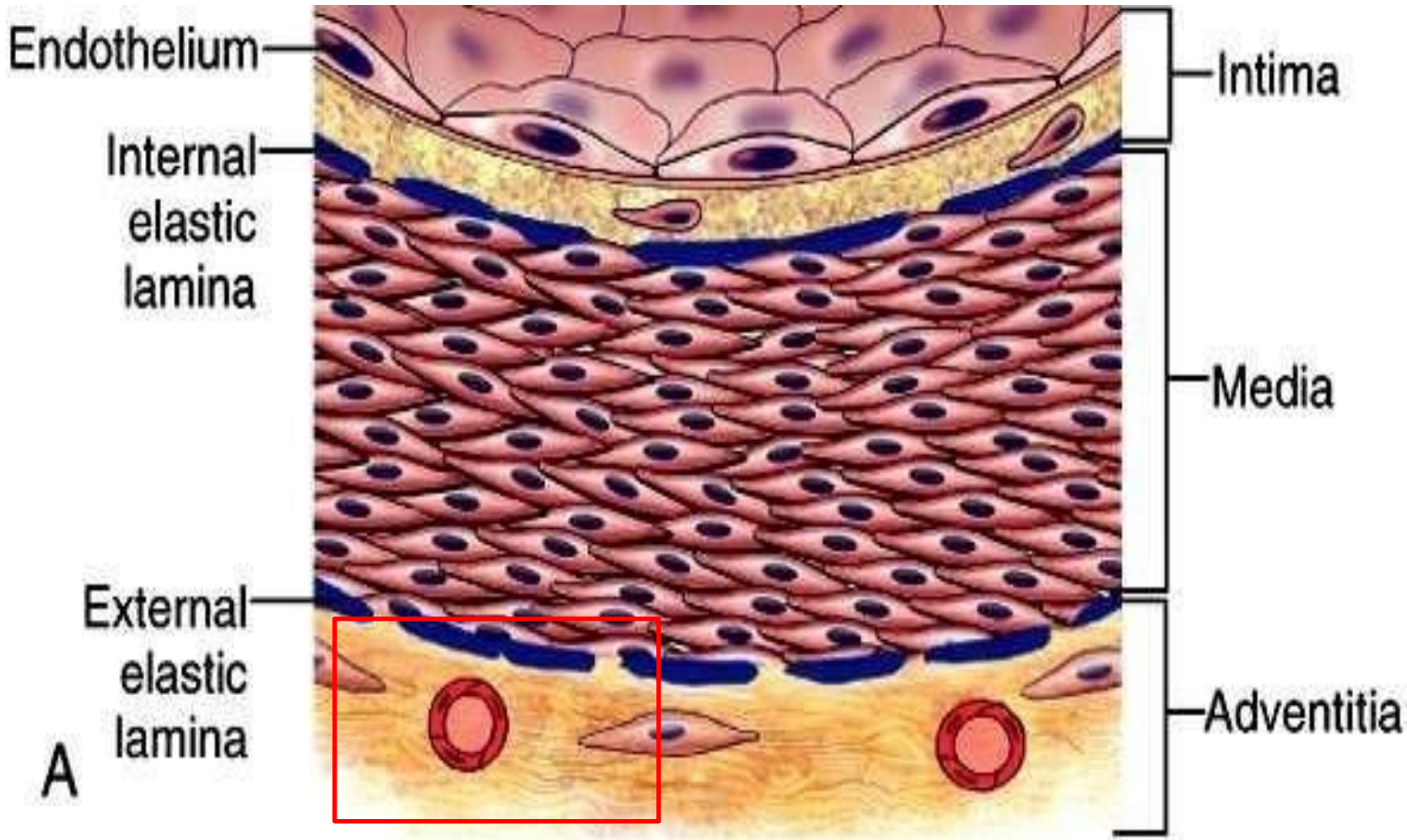
Arteriosclerosis



Written by : DST

NST

Reviewed by : NST



vasa vasorum

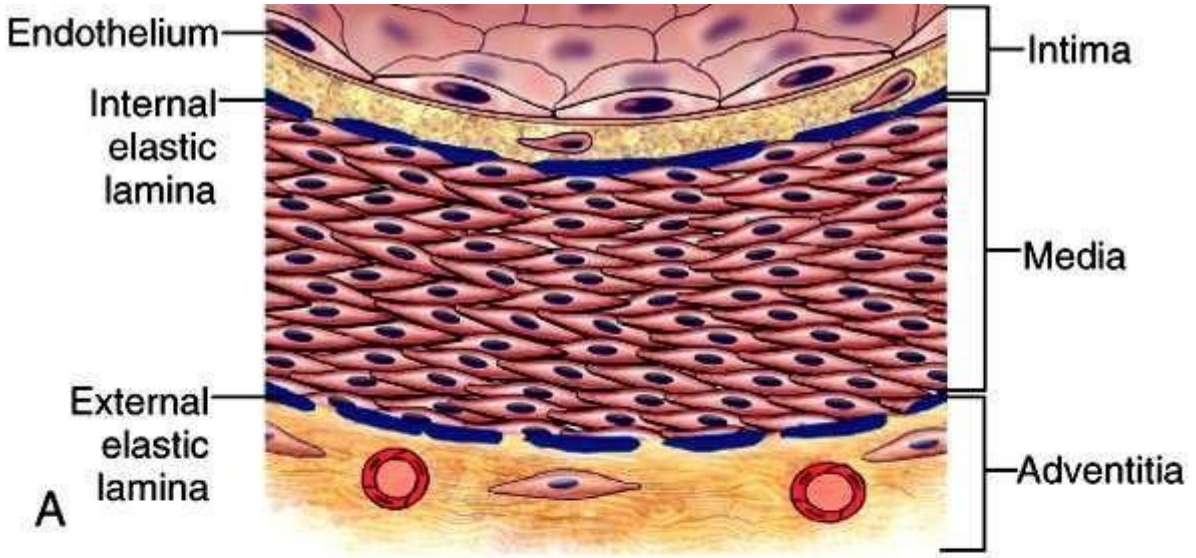
لَا إِلَهَ إِلَّا اللَّهُ
وَحْدَهُ لَا شَرِيكَ لَهُ، لَهُ
الْمُلْكُ وَلَهُ الْحَمْدُ، وَهُوَ عَلَى
كُلِّ شَيْءٍ قَدِيرٌ

1. Tunica Intima
The innermost layer of the blood vessel.
Consists mainly of endothelial cells and a thin layer of connective tissue.
Provides a smooth surface for blood flow.
Helps regulate vascular permeability and blood clotting.
2. Tunica Media
The middle layer of the blood vessel.
Mainly composed of smooth muscle cells and elastic fibers.
Responsible for vasoconstriction and vasodilation.
Regulates blood vessel diameter and blood pressure.
3. Tunica Adventitia
The outermost layer of the blood vessel.
Mainly composed of connective tissue, collagen, and elastic fibers.
Provides structural support and anchors the vessel to surrounding tissues.
Contains vasa vasorum, which nourish the walls of large blood vessels.

Normal blood vessels

A= Artery

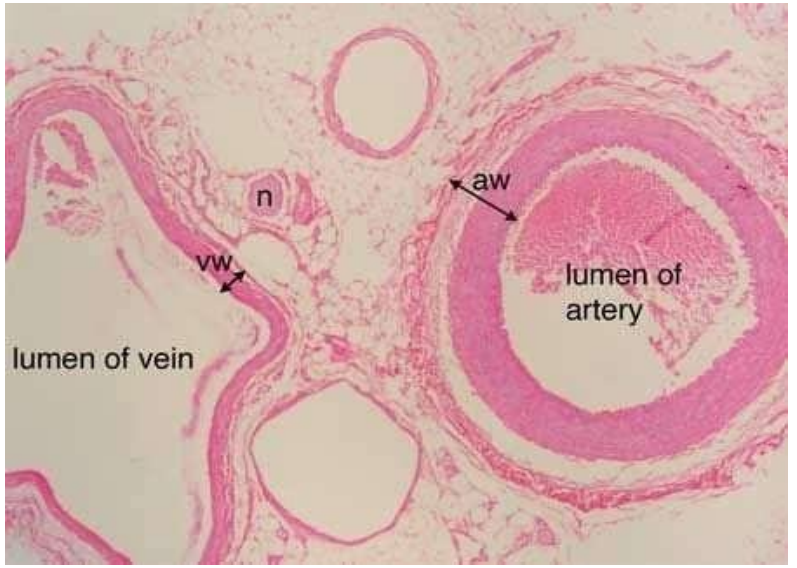
V= Vein



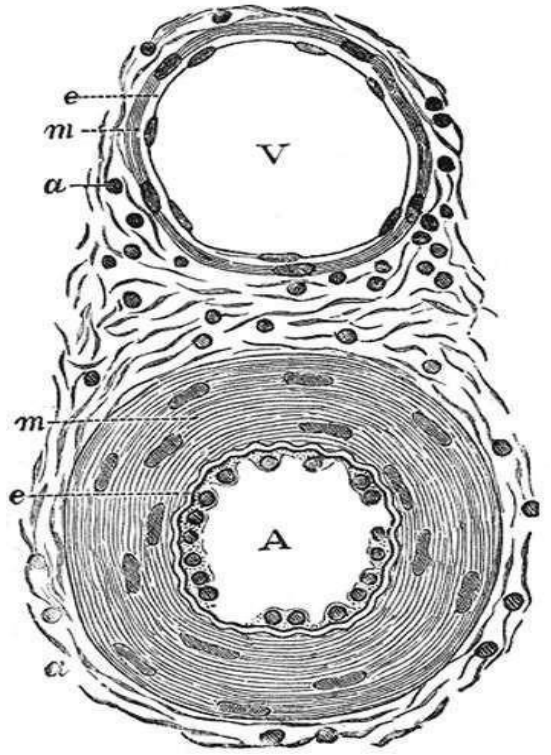


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Artery (A) versus Vein (V)



- The wall of an artery appears thicker, more rigid, and more fibrous, whereas the wall of a vein is thinner and tends to collapse. Why?
- Although both arteries and veins have three layers, the key difference lies in the thickness of the tunica media.
- The tunica media is much thicker and more developed in arteries, containing a greater amount of smooth muscle.
- This is essential for arterial function, as arteries require strong contractile ability and elastic recoil to regulate blood flow and pressure.



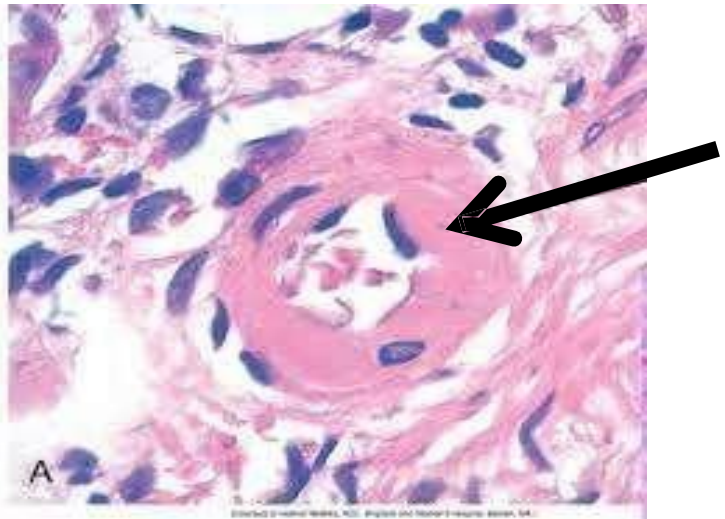
Arteriosclerosis

- Arteriosclerosis Definition: hardening of the arteries
- **Arterial** wall thickening and loss of elasticity.
- **Three** patterns are recognized, with different clinical and pathologic consequences:

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وَحْدَهُ لاَ شَرِيكَ لَهُ، لَهُ
المُلْكُ وَلَهُ الحَمْدُ، وَهُوَ عَلَى
كُلِّ شَيْءٍ قَدِيرٌ

1. Arteriolosclerosis

- Affects small arteries and arterioles
- Associated with hypertension and/or diabetes mellitus
- **Here we discuss arterioles, particularly in conditions such as hypertension, diabetes mellitus, and aging.**
- **In this image, the arteriolar wall is thickened due to the deposition ofabnormal material, leading to luminal narrowing.**



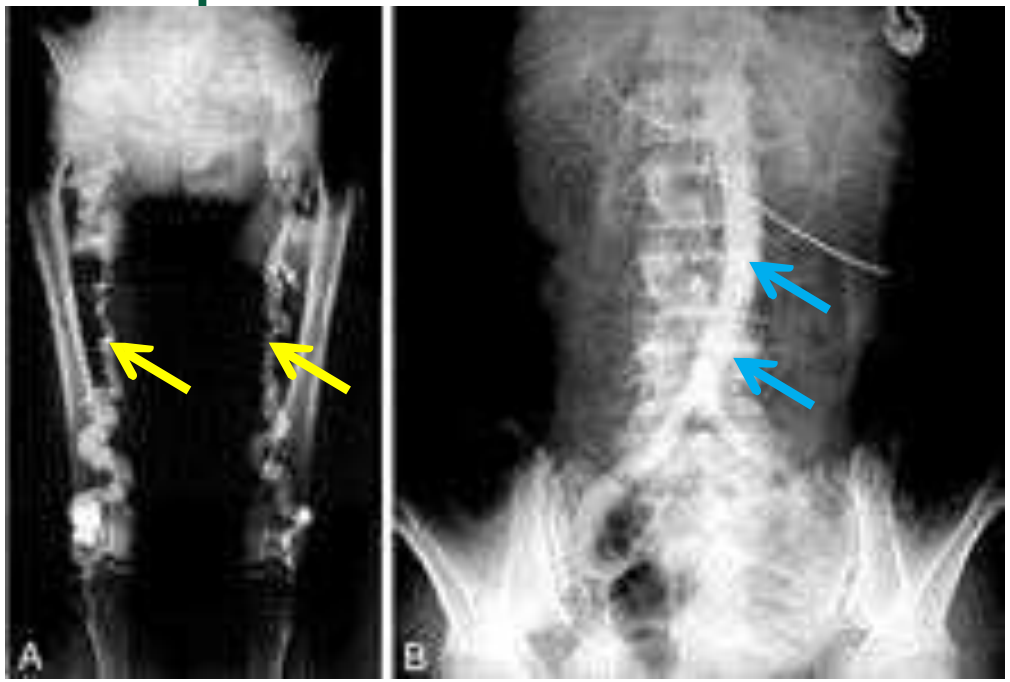
2. Mönckeberg Medial Calcific Sclerosis

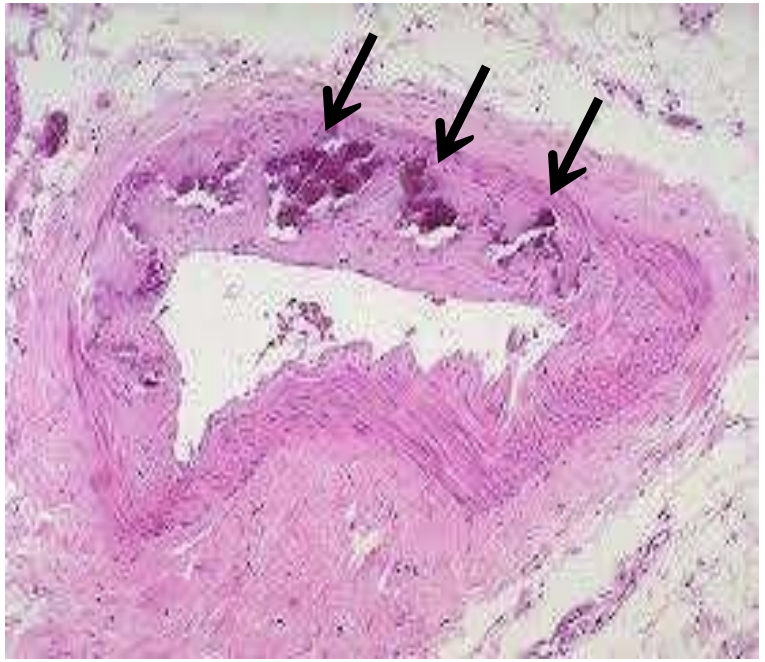
- The term “medial” refers to involvement of the tunica media
- Calcific: calcification the cause of disease
- Sclerosis: hardness
- **Calcific** deposits in **muscular** arteries
- Typically, in middle-aged persons >age 50.
- Because calcium is present, these legions are **Radiographically** visible (x-rays, etc.). On X-ray, these calcifications appear white
- Palpable hardened vessels walls, if the affected arteries are superficial
- Do **not** encroach on vessel lumen and are usually not clinically significant

2. Mönckeberg Medial Calcific Sclerosis

Here, the purple color in the slide represents calcium deposition within the media.

Why they are purple not white? Because of the stain

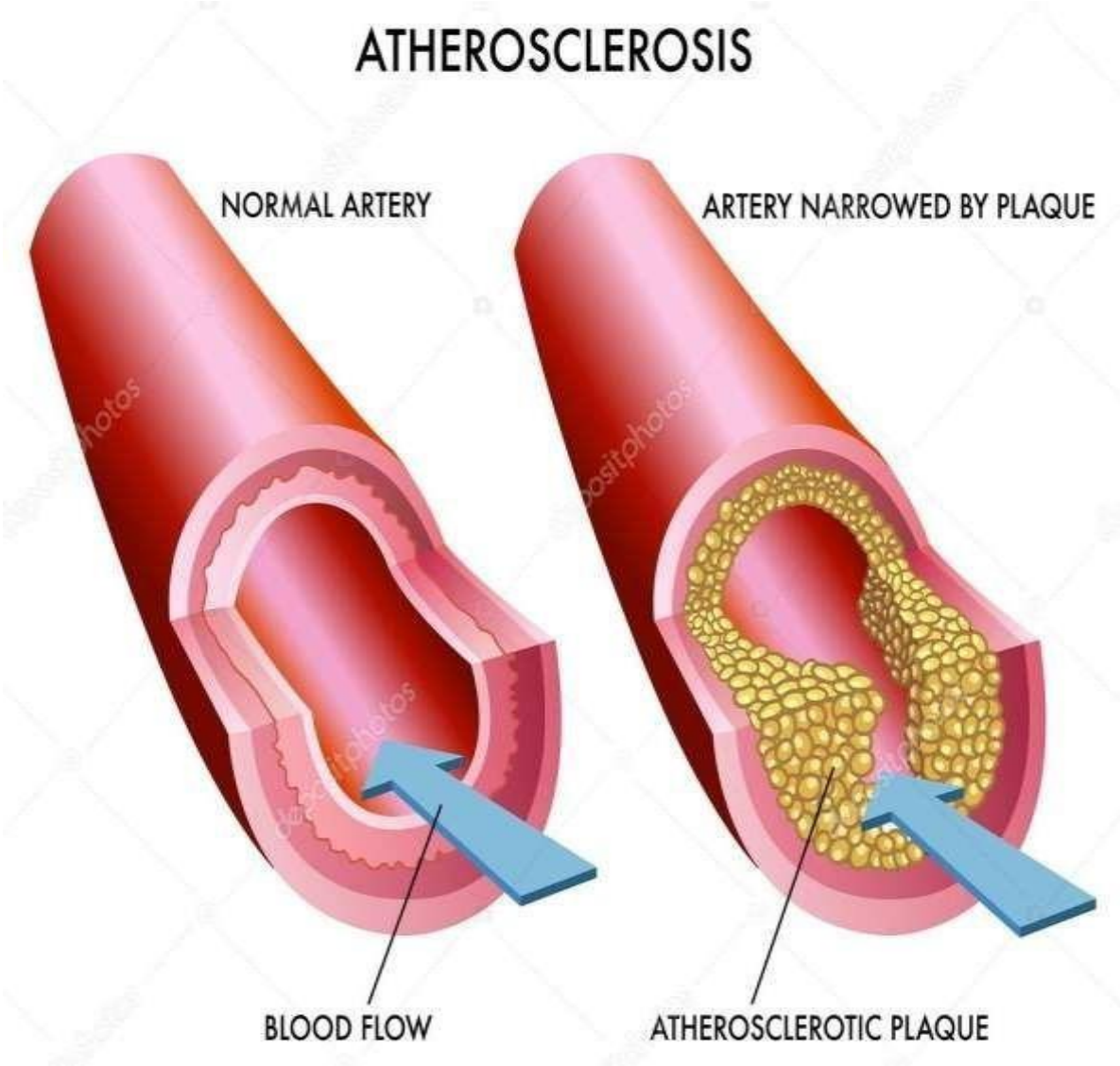




Importantly, if medial calcific sclerosis occurs without other vascular disease (such as atherosclerosis), the process does not encroach on the lumen, and therefore, does not cause narrowing and is usually not clinically significant.

Atherosclerosis

- Greek word "gruel", "hardening"
- Most **frequent** and **clinically important** pattern of arteriosclerosis
- Characterized by intimal lesions = **atheromas** (a.k.a. atherosclerotic plaques)
- Atheromatous plaque = **raised** lesion with a core of lipid (cholesterol and cholesterol esters) covered by a firm, white fibrous cap



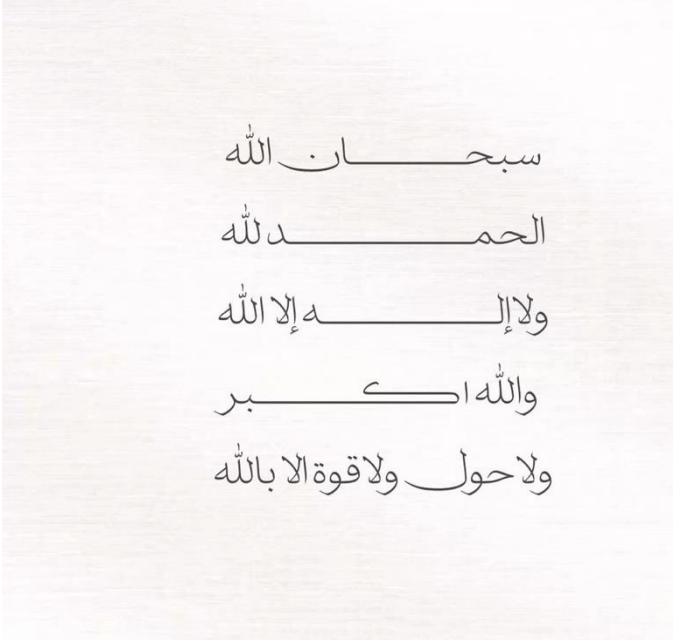
Atherosclerosis

- Atherosclerosis is a process in which lipid deposits accumulate within the tunica intima of arteries, causing:
  - Hardening and thickening of the vessel wall, and
  - Narrowing of the lumen.
- Because this occurs in arteries, the resulting luminal narrowing leads to ischemia, which is the most important clinical consequence of atherosclerosis.
- Two major events are required for atherosclerosis to develop:
  - Deposition of cholesterol (particularly LDL)
  - Inflammation
- Both are essential for the formation of atherosclerotic lesions.

Atherosclerosis – Pathogenesis

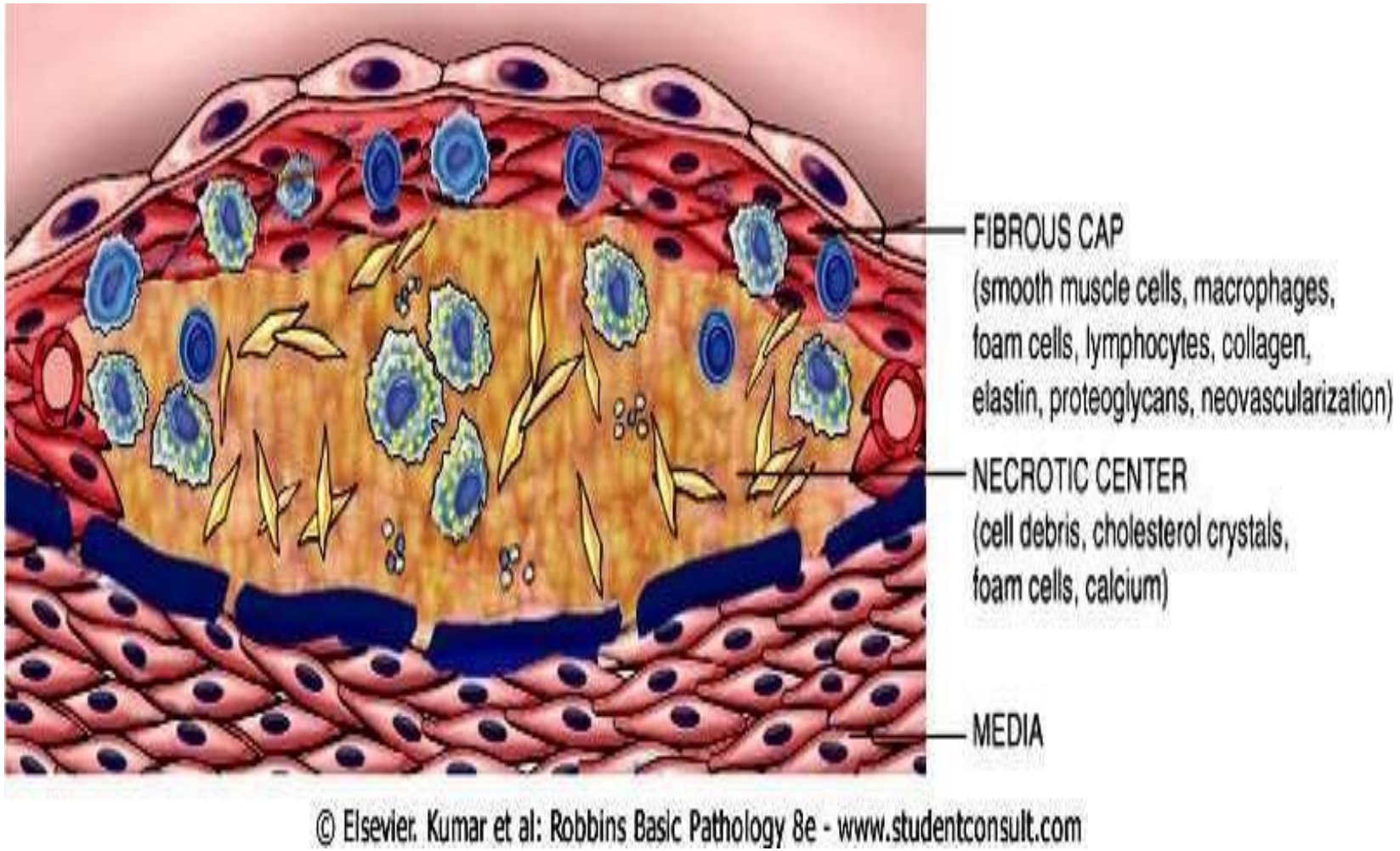
- Not fully understood
- ? Inflammatory process in endothelial cells of vessel wall associated with retained low-density lipoprotein (LDL) particles → a cause, an effect, or both, of underlying inflammatory process

Why LDL not HDL ?
LDL has a greater tendency to cause atherosclerosis, while HDL is considered the "good cholesterol



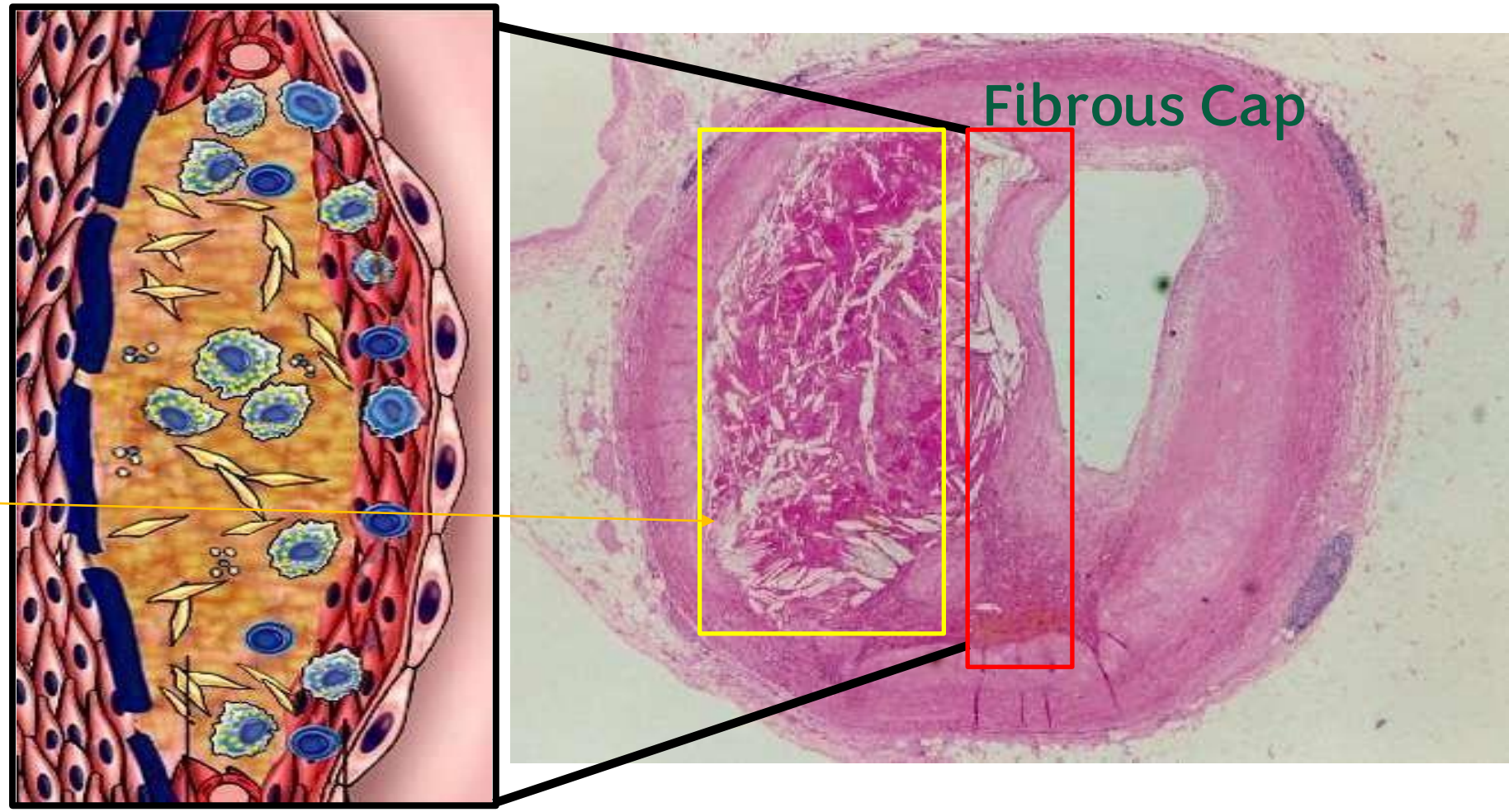
Underlined term is hyperlinked

The major components of a well-developed intimal atheromatous plaque

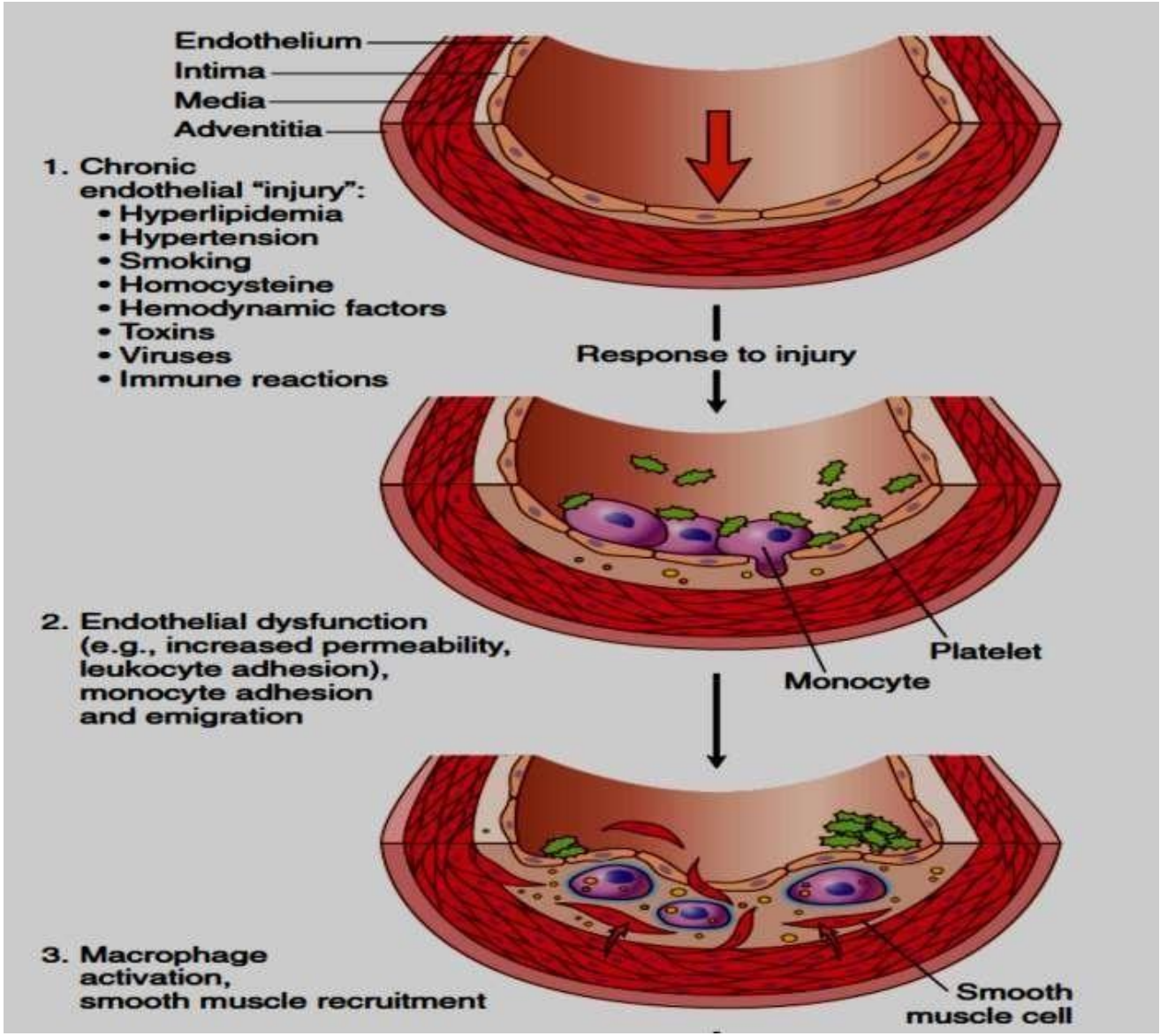


Atheromatous Plaque

Necrotic centre
It has a needle like appearance why ?
Dissolution of cholesterol crystals during tissue preparation.



Formation of Atheromatous Plaque



Macrophage Mechanism of Atherosclerosis Development

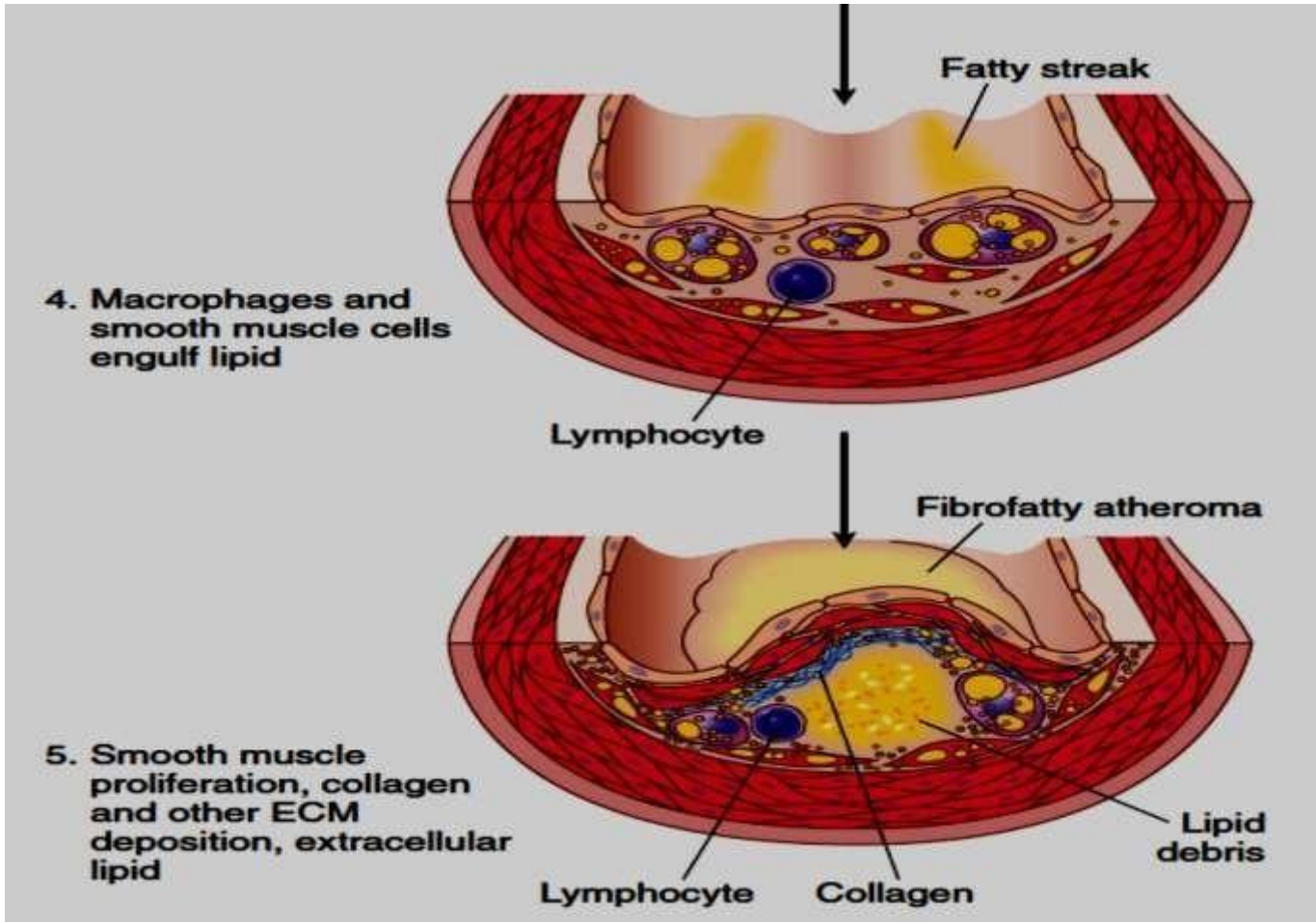
- A triggering event—endothelial injury or activation—occurs in the vessel wall. This stimulates:
  - Coagulation, and
  - Inflammation
- Monocytes from the blood migrate into the intima in response to these inflammatory and coagulation signals.
- Once they enter the tissue, they differentiate into macrophages.
- At the same time:
  - Cholesterol accumulates within the intima,
  - Platelet activation occurs, and
  - A vascular healing response begins.

A New Player then Appears: Smooth Muscle Cells.

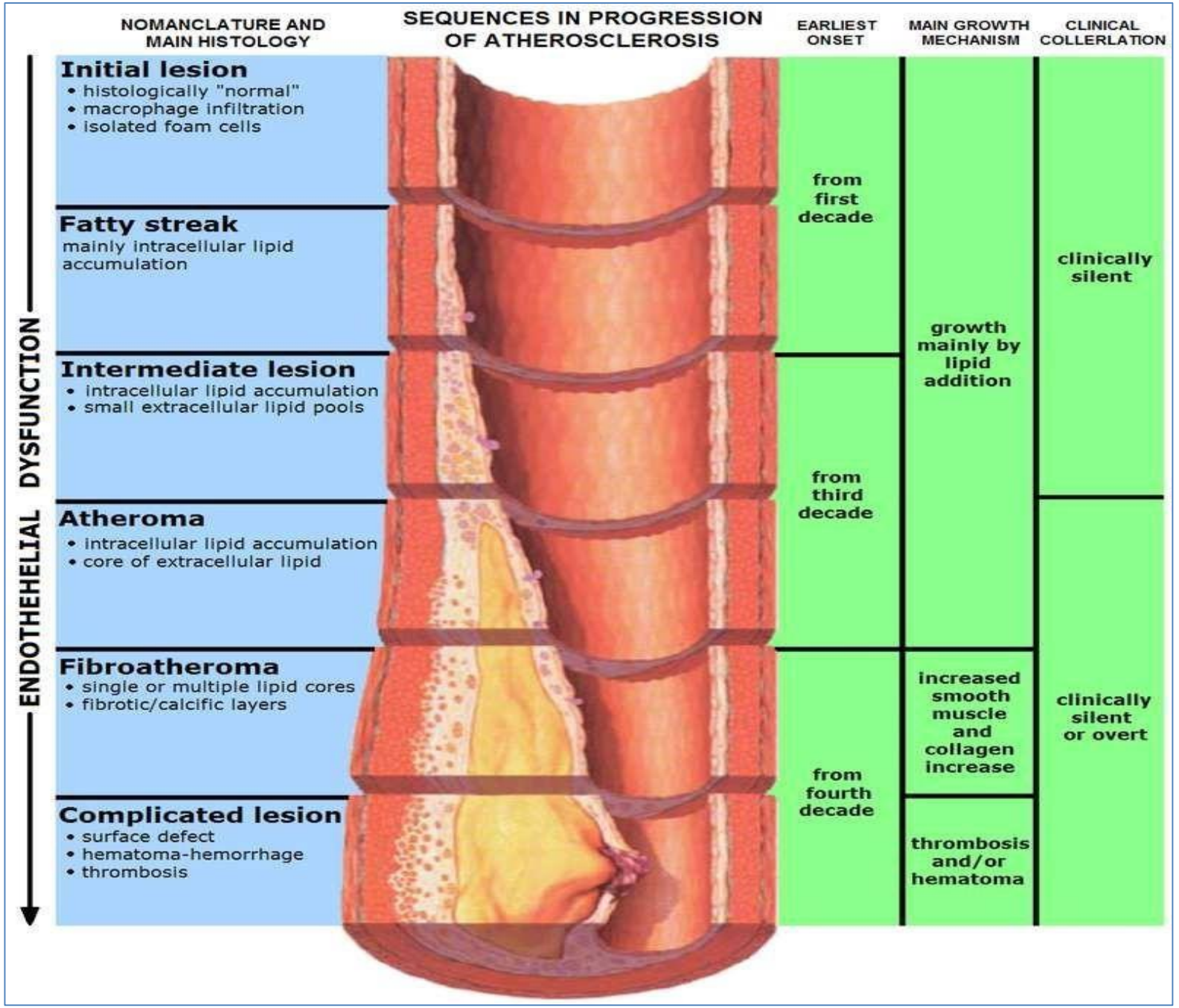
- Normally located in the tunica media, they migrate into the intima in response to inflammatory signaling.
- Inside the intima, they:
  - Differentiate,
  - Proliferate,
  - Produce extracellular matrix proteins, and
  - Participate in the inflammatory process.
- As a result, the intima thickens due to the accumulation of macrophages and smooth muscle cells.
- These cells engulf lipid and cellular debris, contributing to plaque growth.

Formation of Atheromatous Plaque

- In this stage, fat continues to accumulate inside the intima, and macrophages engulf lipids but are unable to control the increasing amount being deposited, leading to extracellular lipid accumulation.
- The intimal lesion becomes more developed and has two distinct parts: a lipid core (necrotic center) that contains cholesterol, and an overlying fibrous cap.



Atherosclerosis is a chronic, slowly progressive disease that usually develops over many years.



Atherosclerosis may begin in childhood, but its advanced and complicated stages develop over many years and may become more evident around the 4th decade of life.

Complications f Atherosclerosis

1. Thrombosis

Atherosclerotic plaque protrudes into the lumen, causing narrowing of the arterial diameter.

If the plaque ruptures or erodes, its thrombogenic contents become exposed to the blood.

This activates platelets and the coagulation cascade, leading to thrombus formation.

2. Embolism

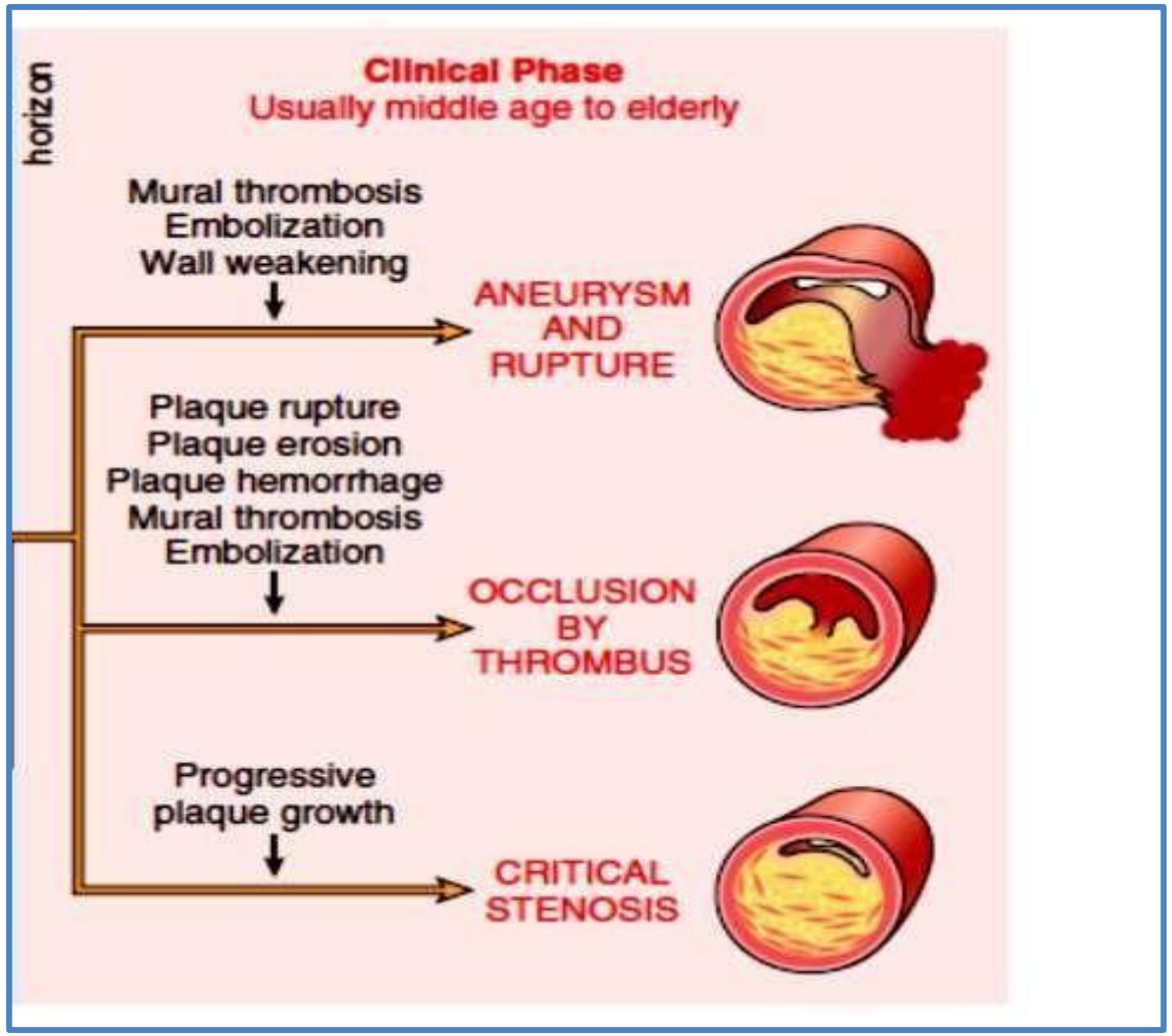
Part of the thrombus or plaque material may detach and travel through the bloodstream.

It becomes an embolus, which may occlude a smaller artery downstream.

3) Progressive stenosis and occlusion
The plaque gradually enlarges, progressively narrowing the arterial lumen.
If the obstruction becomes severe, blood flow to the tissue decreases, causing ischemia.
If blood supply becomes critically insufficient, it may lead to infarction (tissue necrosis due to ischemia).

4. Aneurysm formation
Atherosclerosis can weaken the arterial wall by damaging its underlying structural layers.
This may cause localized dilation of the artery, forming an aneurysm, which carries a risk of rupture.

Atherosclerosis: Progression



سبحـــــــان الله
الحمـــــــــد لله
ولا إلـــــــــه إلا الله
والله اكـــــــبر
ولا حول ولا قوة الا بالله

Critical stenosis is a severe narrowing of the arterial lumen due to atherosclerotic plaque, resulting in significant impairment of blood flow.
It is particularly important in ischemic heart disease, especially in the coronary arteries, because it reduces blood supply to the myocardium and may lead to myocardial ischemia.
Coronary artery stenosis ≥70%: Generally considered significant in major coronary arteries.
Left main coronary artery stenosis ≥50%: Generally considered significant.

why some patients with atherosclerosis develop complications while others don't, even if they both have atherosclerotic plaques.

The development of complications in atherosclerosis depends on both patient-related risk factors and the morphological characteristics of the atheromatous plaque.

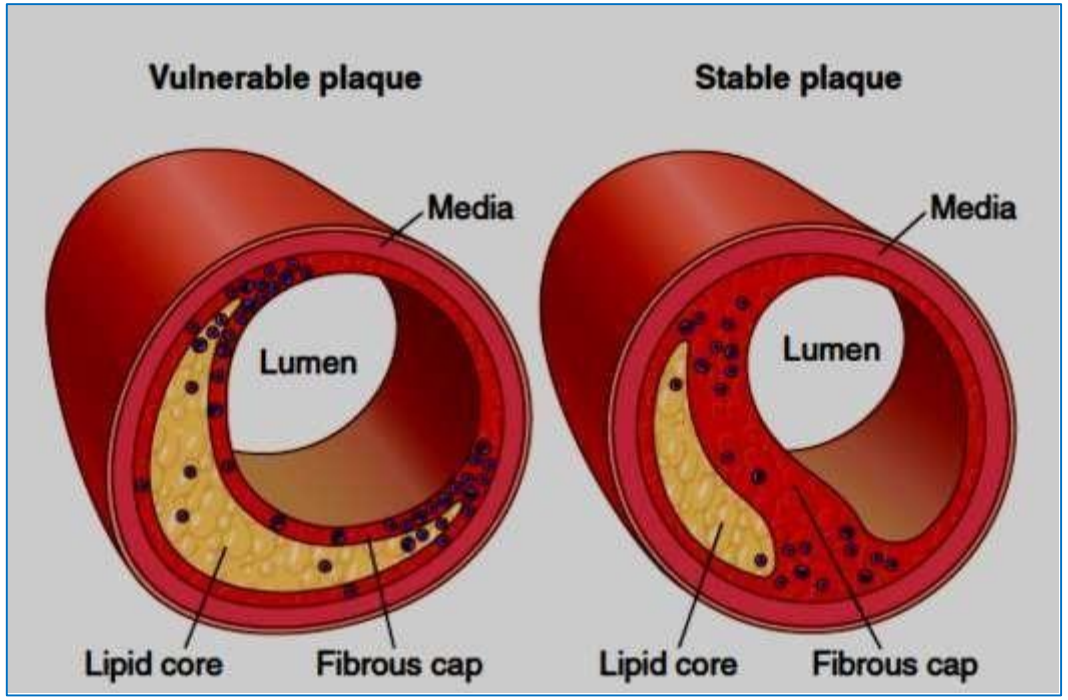
The characteristics of the atheroma itself play a major role in determining whether it becomes complicated. (Vulnerable vs stable)

A vulnerable plaque is more likely to rupture , exposing thrombogenic material and triggering thrombus formation. (Because of thin fibrous cap)

Vulnerable plaque	Stable plaque
Thin fibrous cap	Thick fibrous cap
Large lipid core	Smaller lipid core
High inflammation	Less inflammation
Prone to rupture	Less prone to rupture
Acute thrombosis / MI	Progressive stenosis / stable angina

Vulnerable vs Stable plaque

Vulnerable plaques are more sensitive to complications



Thick fat core
Thin fibrous cap
More inflammation

Thin fat core
Thick fibrous cap
less inflammation

Stable plaques are more resistance to complication

Risk Factors for Atherosclerosis

Major Risks	Lesser, Uncertain, or Non-quantitated Risks
Non-modifiable (non-controllable)	Obsesity
Increasing age	Physical inactivity
Male gender	Stress ("type A personality)
Family history	Postmenopausal estrogen deficiency
Genetic abnormalities	High carbohydrate intake
	Lipoprotein(a)
Potentially modifiable (Controllable)	Hardened (trans)unsaturated fat intake
Hyperlipidemia	
Hypertension	Chlamydia pneumoniae infection
Cigarette smoking	
Diabetes	
C-reactive protein (inflammation)	

Strong evidence

Lifestyle modification

CRP is a systemic inflammatory marker

Risk Factors for Atherosclerosis

1. **Age:** The major one
   - Ages 40 to 60, incidence of MI in men increases 5 x
   - Death rates from IHD rise with each decade
2. **Gender:**
   - Men are at higher risk because they lack the protective cardiovascular effects of estrogen.
   - Premenopausal* → protected against atherosclerosis compared with age-matched men.
   - After menopause → incidence of atherosclerosis- related diseases increases
   - *Unless they are otherwise predisposed by diabetes, hyperlipidemia, or severe hypertension.

Risk Factors for Atherosclerosis

3. Genetics

- Familial predisposition is **multifactorial**.
- Either :

1. Familial clustering of other risk factors
   - e.g., HTN or DM
2. Well-defined genetic derangements in lipoprotein metabolism
   - e.g., familial hypercholesterolemia

Additional Risk Factors for Atherosclerosis

- 20% of cardiovascular events occur in the **absence of identifiable risk factors**:
  - Hyperhomocystinemia
  - Metabolic syndrome
  - Lipoprotein-A levels
  - Factors Affecting Hemostasis (Elevated levels of procoagulants…)
- Others:
  - Lack of exercise
  - Competitive, stressful lifestyle ("type A" personality)
  - Obesity
  - High carbohydrate intake



PATHOLOGY QUIZ

LECTURE 4

رسالة من الفريق العلمي:

مارِس الرحمـــة قـــدر المُستـــطاع فكلـما
تلطّفـــت مـع خلق اللـه زاد اللـه لُطفه حولـك

Practice as much mercy as you can,
the kinder you are to Allah's creation,
the kinder Allah will be to you.

THEHQUOTES

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			