PATHOLOGY

بسم الله الرحمن الرحيم

FINAL | Lecture 4

# Arteriosclerosis

وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

اللهم إنّا نعوذ بك من شرور أنفسنا ومن سيئات أعمالنا


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**Reviewed by:** Laith Joudeh

# وَلِلَّهِ الْأَسْمَاءُ الْحُسْنَى فَادْعُوهُ بِهَا


**المعنى:** الذي لا يموت، وحياته – سبحانه – أكمل الحياة، تستلزم جميع صفات الكمال، وتنفي أضدادها من جميع الوجوه، وكمال حياته يستلزم أن لا تأخذه سِنةٌ ولانومٌ.

**الورود:** ورد في القرآن (٥) مرات.

**الشاهد:** ﴿ٱللَّهُ لَآ إِلَٰهَ إِلَّا هُوَ ٱلۡحَيُّ ٱلۡقَيُّومُۚ﴾ [البقرة:٢٥٥].

١٣

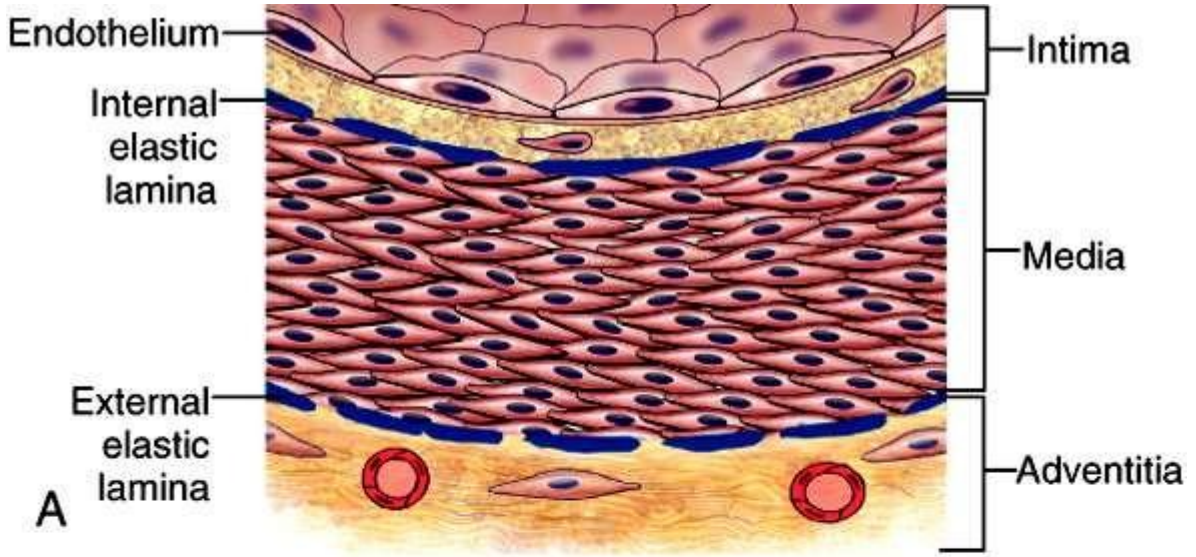
*اضغط هنا لشرحٍ أكثر تفصيلًا*

- 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.

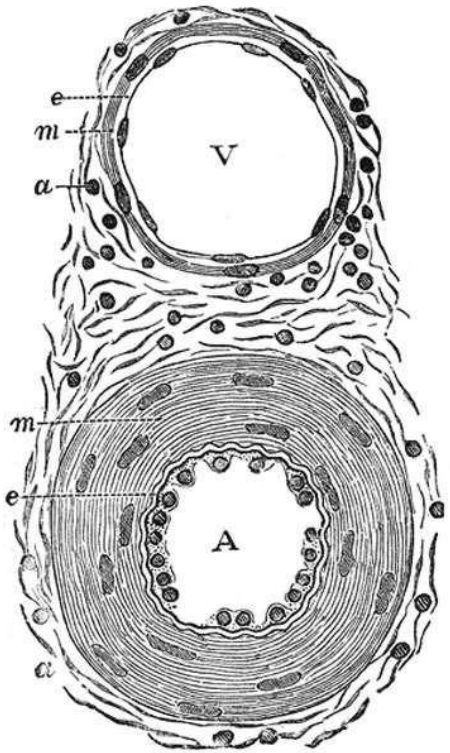
Normal blood vessels

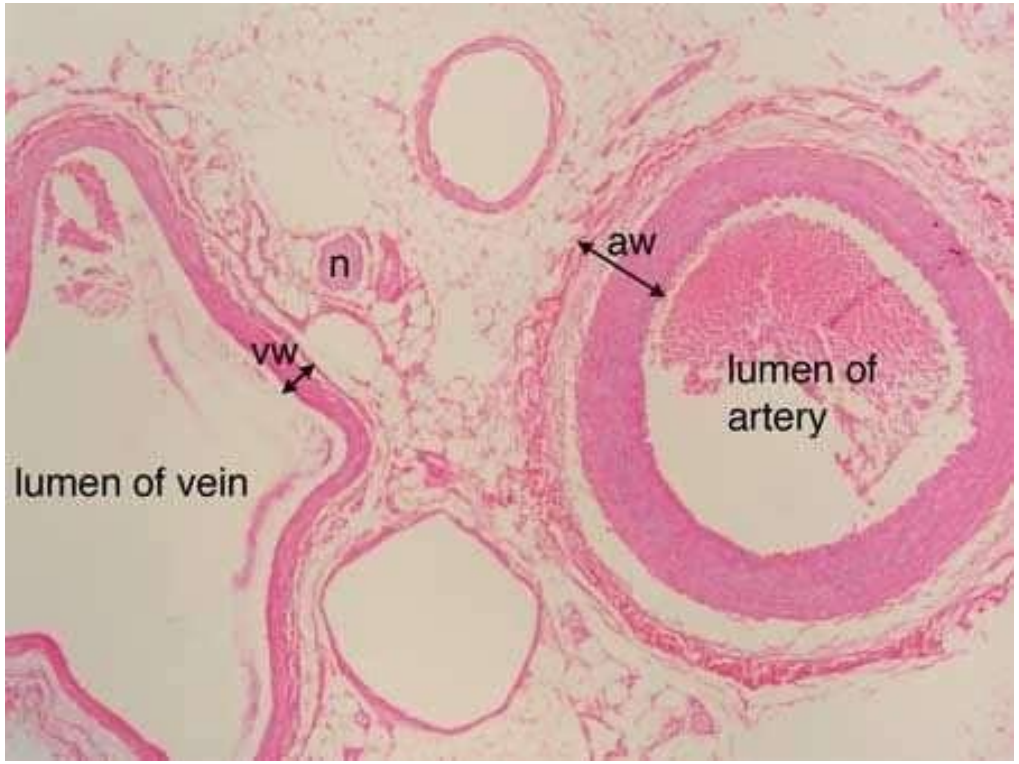
A= Artery

V= Vein




# Artery (A) versus Vein (V)



# Arteriosclerosis

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

# 1. Arteriolosclerosis

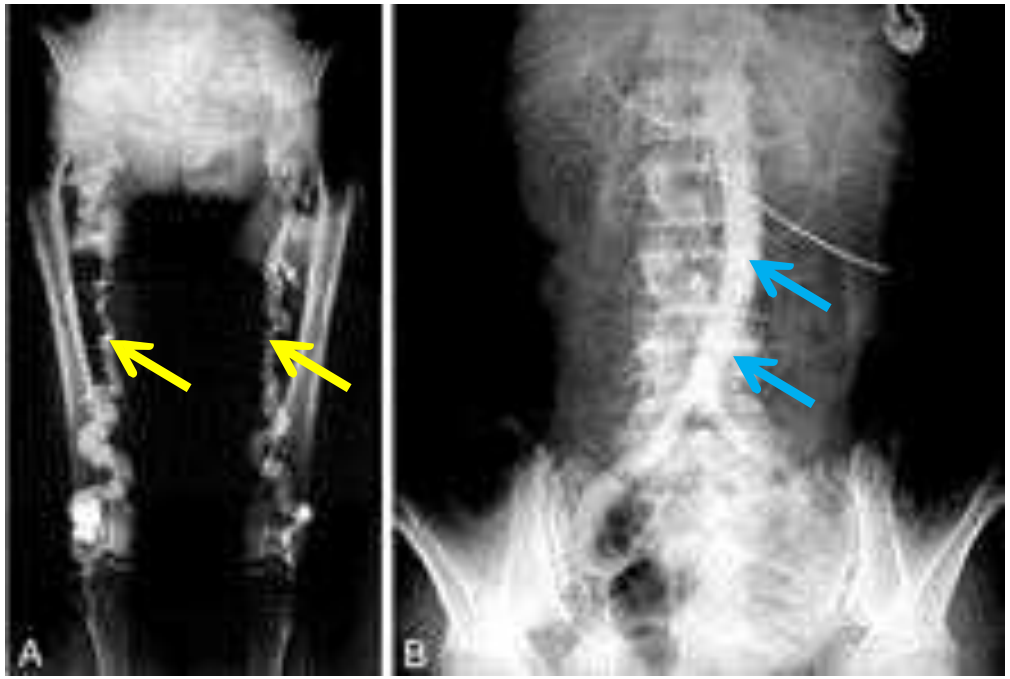

- Affects small arteries and arterioles
- Associated with hypertension and/or diabetes mellitus
- Here we discuss arterioles, **particularly in conditions such as hypertension, diabetes mellitus, and aging**.
- In this image, the arteriolar wall is **thickened due to the deposition of abnormal material,** leading to **luminal narrowing**.
- For example, when arteriolosclerosis affects the kidneys, **prolonged ischemia develops**, and over time this chronic ischemia results in:
  - →**Loss of kidney function**,
  - →**Renal impairment**, and eventually
  - →**Chronic renal failure**.

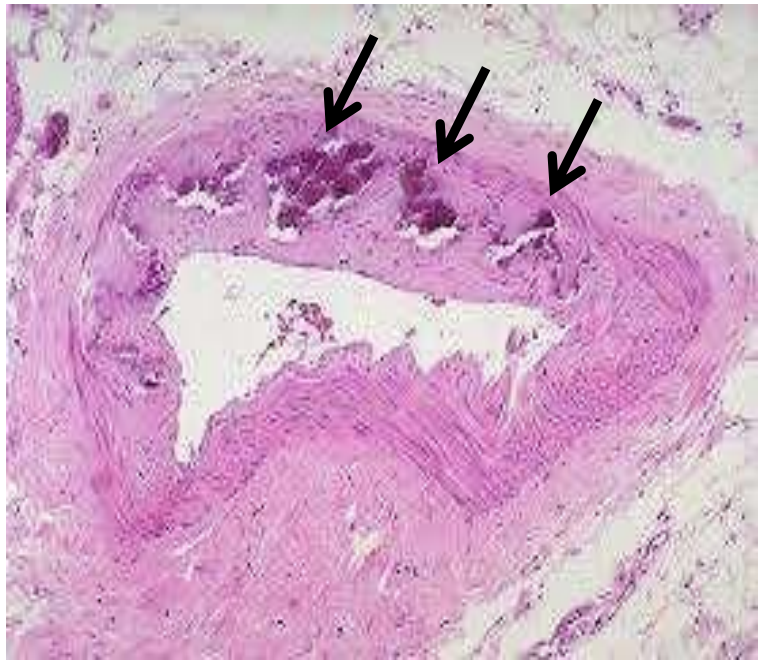
# 2. Mönckeberg Medial Calcific Sclerosis

- Named after Mönckeberg, the scientist who first described the condition.
- The term "medial" refers to involvement of the **tunica media**
- **Calcific** deposits in **muscular** arteries
- Typically, in middle-aged persons >age 50
- They may affect multiple arteries and are usually **patchy, occurring in scattered segments rather than continuously**.
- 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
  - 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**.

# 2. Mönckeberg Medial Calcific Sclerosis

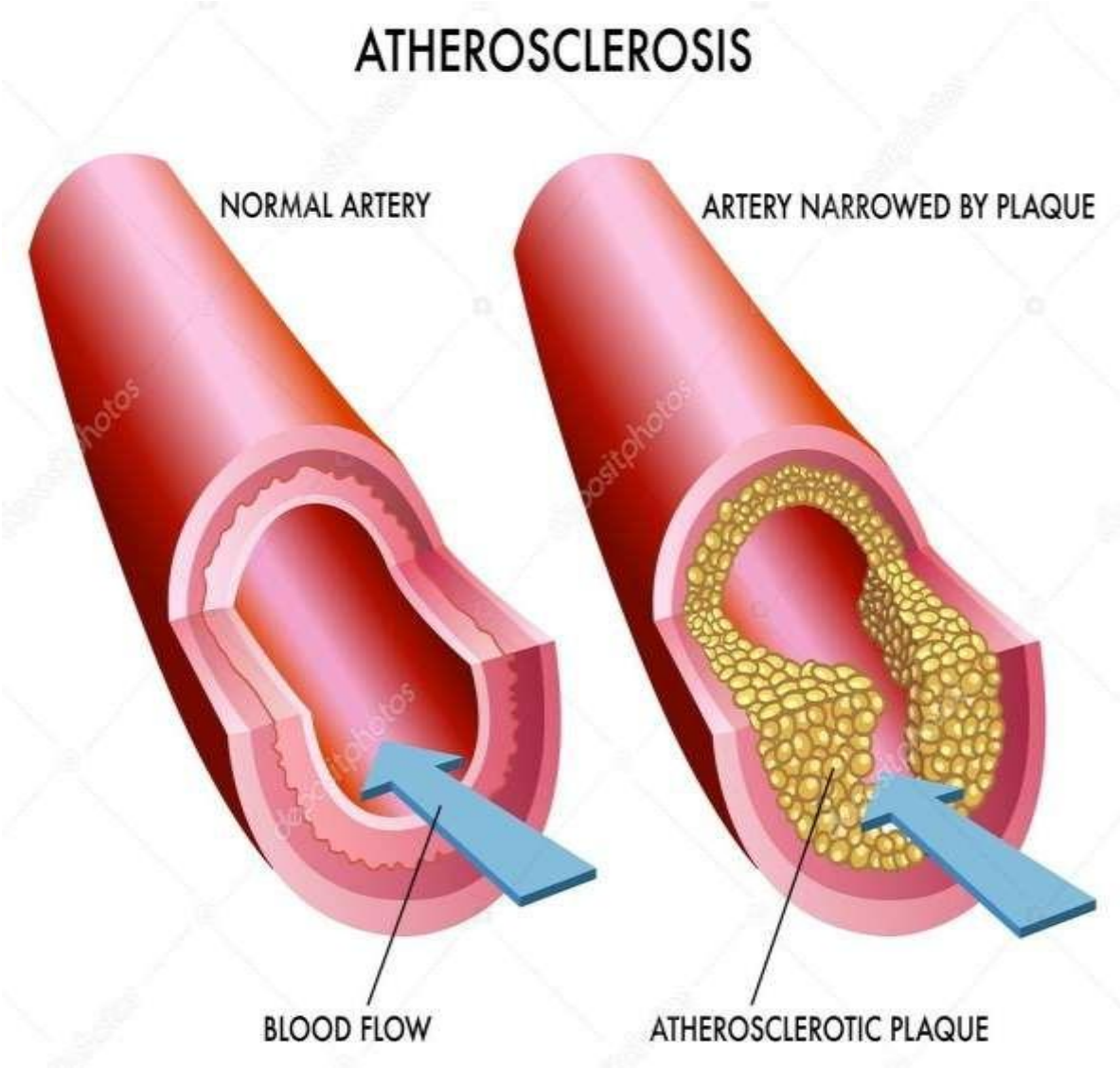
Here, the purple color in the slide represents **calcium deposition within the media.**



# 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

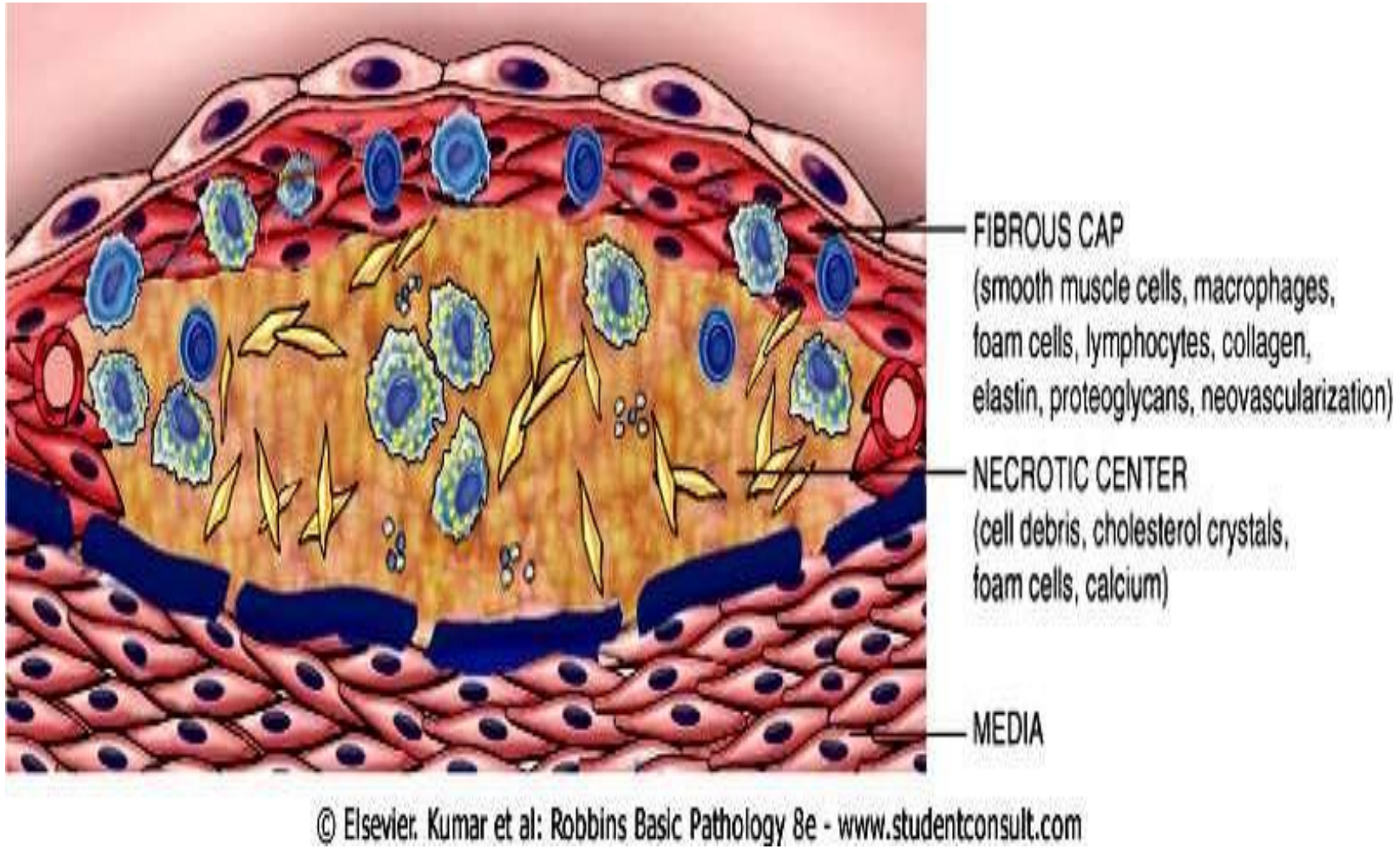
- Atherosclerosis is a process in which **lipid deposits accumulate within the tunica intima** of arteries, causing:
  - Hardening and thickening of the vessel wall, and
  - Narrowing of the lumen.
- Because this occurs in arteries, **the resulting luminal narrowing leads to ischemia**, which is the 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

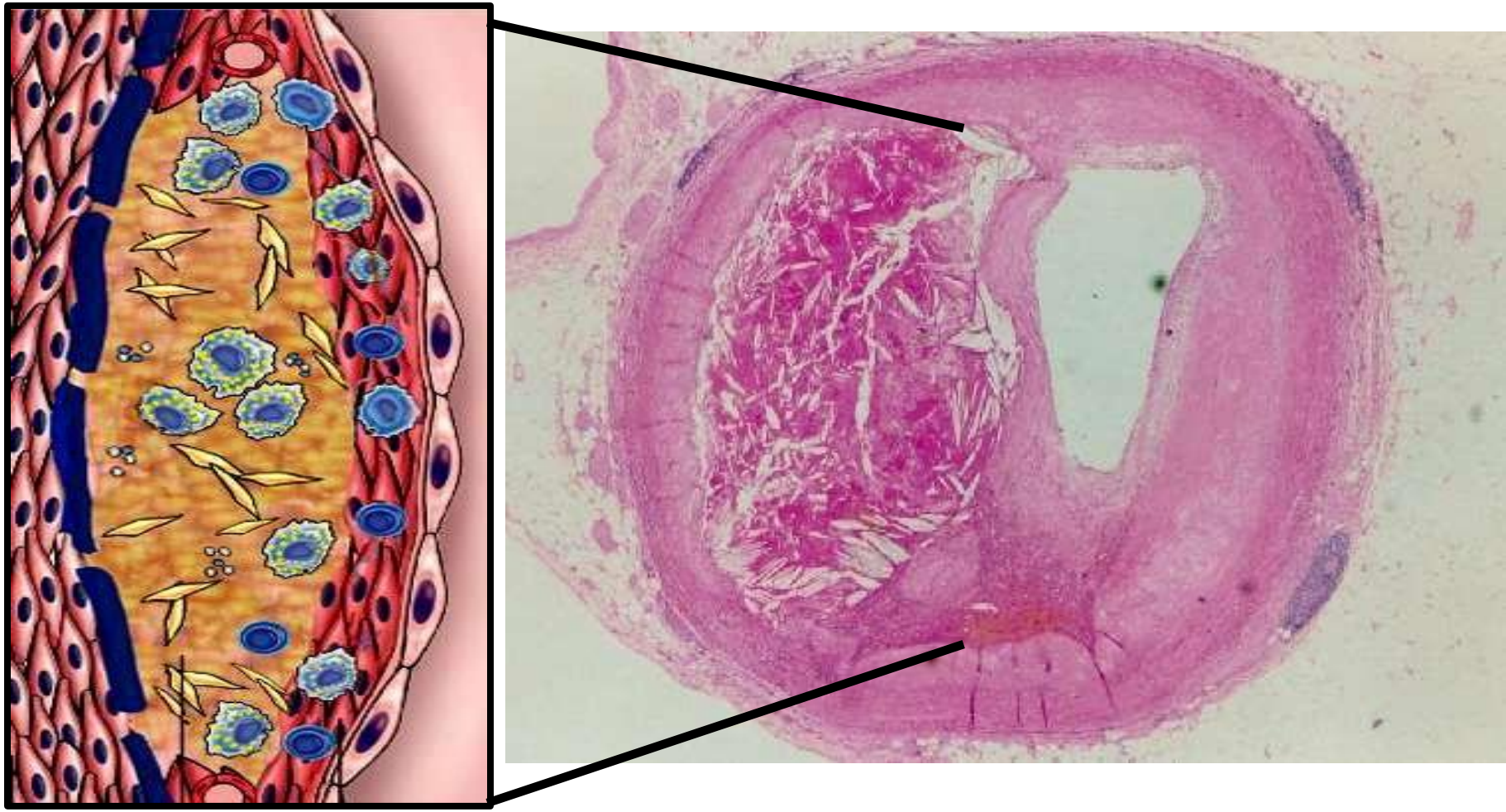
# The major components of a well-developed intimal atheromatous plaque

The labelled components illustrate the constituents of an atheromatous plaque.

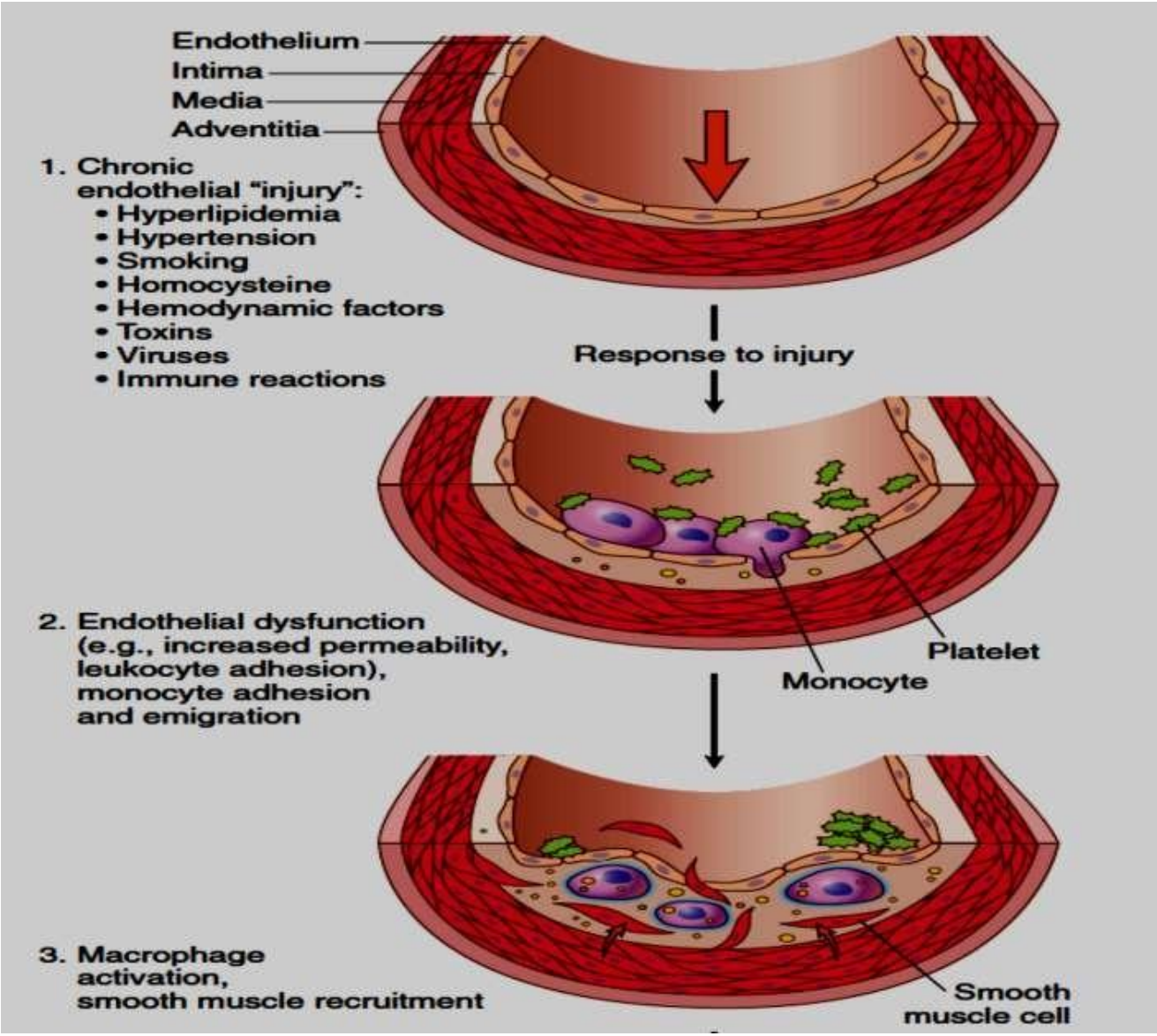


# Atheromatous Plaque

Atheroma Appearance
This image shows an atheroma after it has formed.



# Formation of Atheromatous Plaque



# Macrophage Mechanism of Atherosclerosis Development

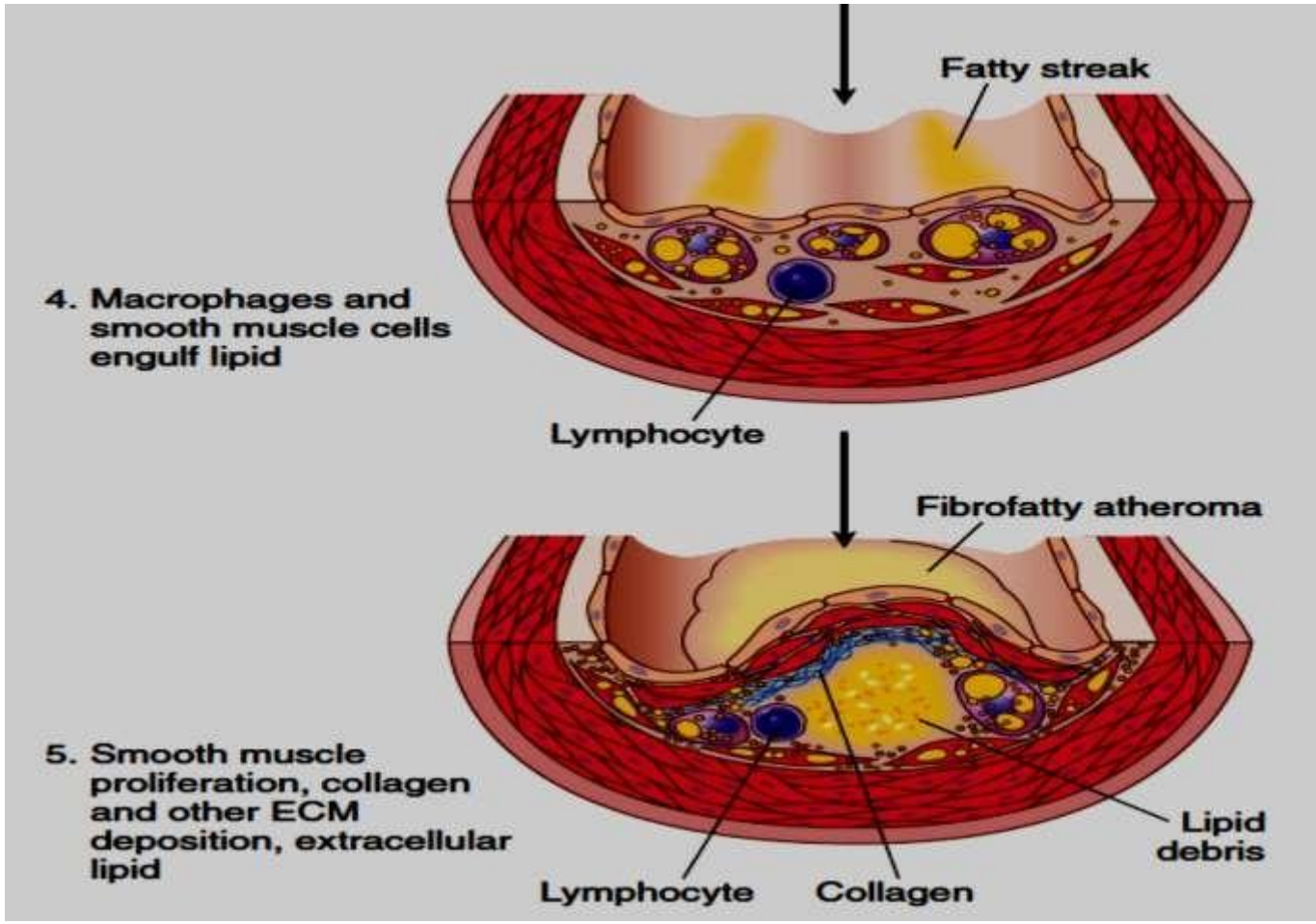
- A triggering event—**endothelial injury or activation**—occurs in the vessel wall. This stimulates:
  - **Coagulation**, and
  - **Inflammation**
- Monocytes from the blood **migrate into the intima in response to these inflammatory and coagulation signals.**
- Once they enter the tissue, they **differentiate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

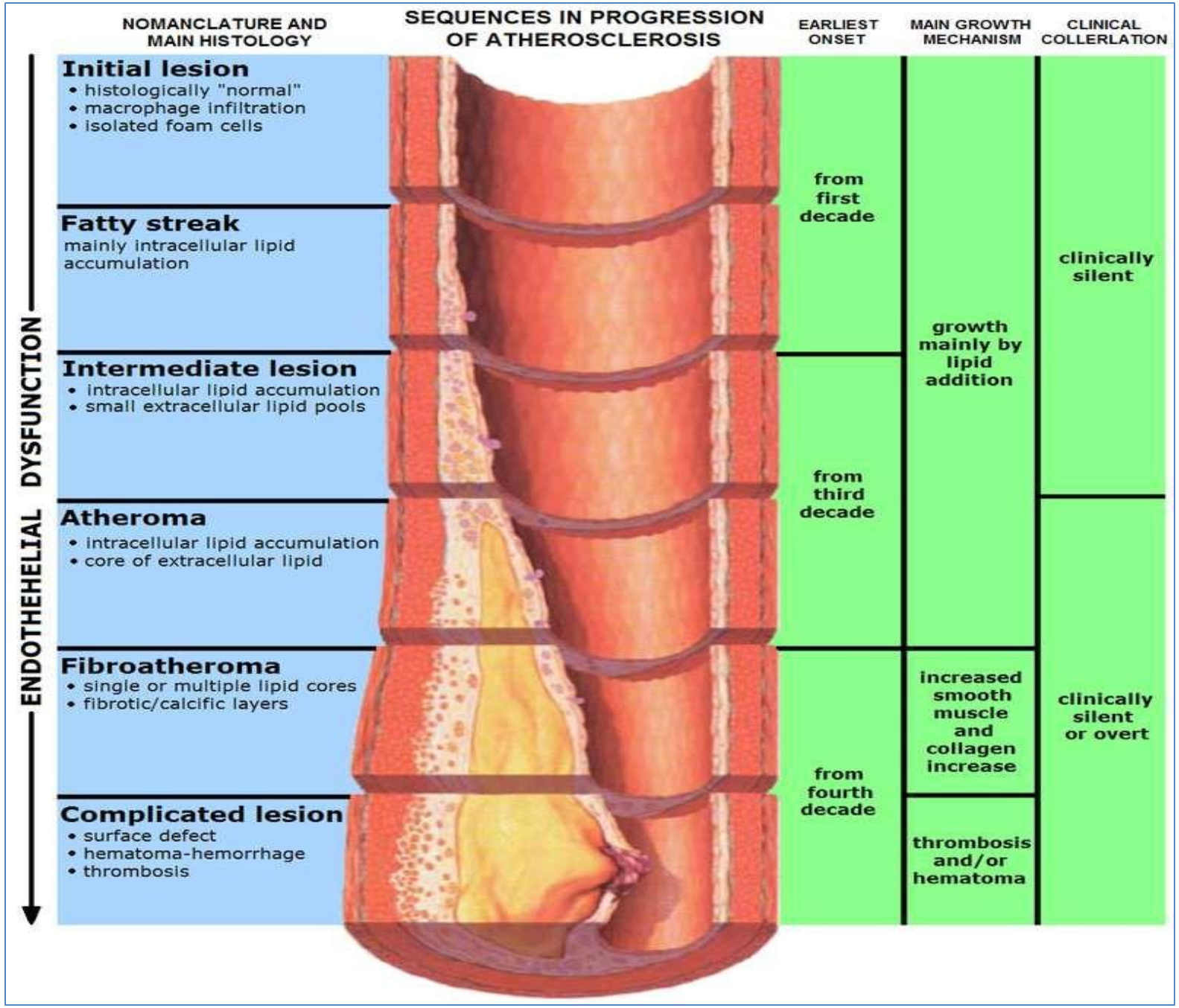
# A New Player then Appears: Smooth Muscle Cells.

- 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**.

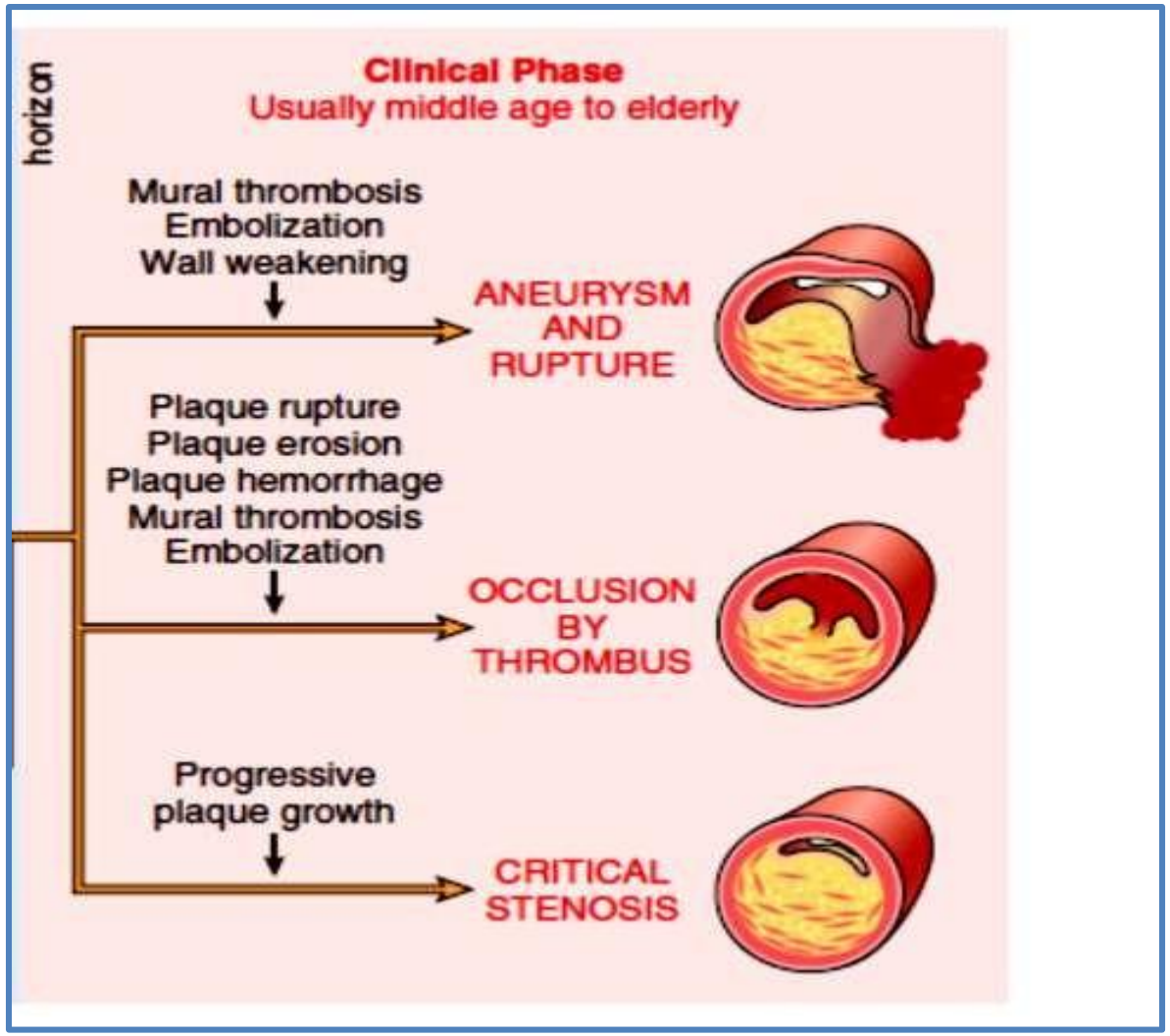
# Formation of Atheromatous Plaque

- 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.**



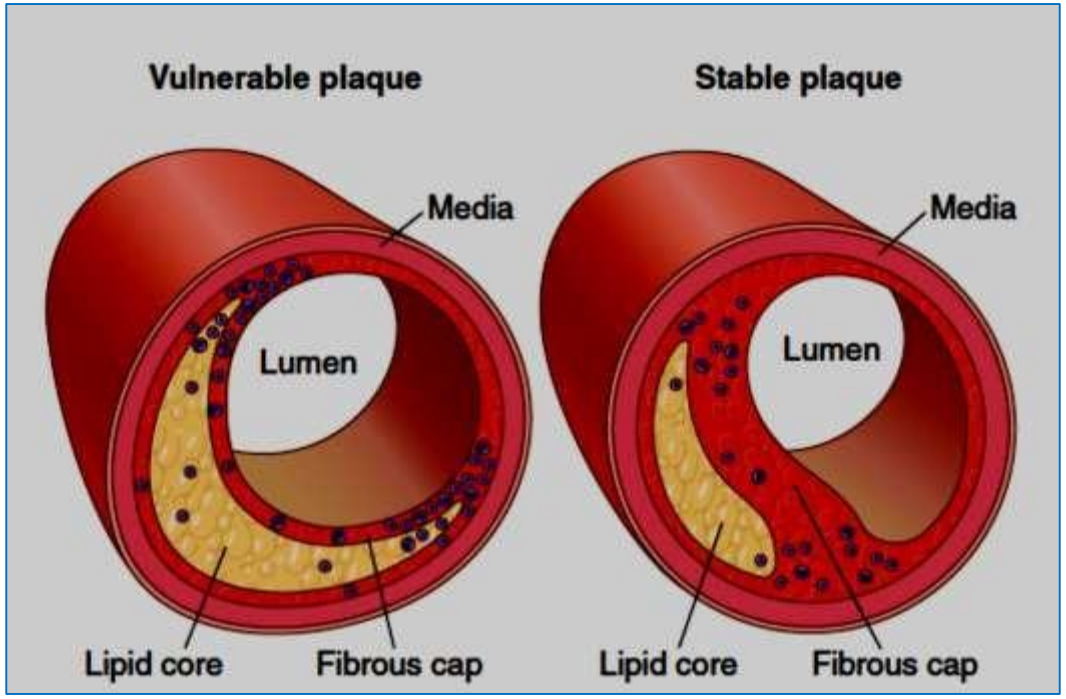

NOMANCLATURE AND MAIN HISTOLOGY
SEQUENCES IN PROGRESSION OF ATHEROSCLEROSIS
EARLIEST ONSET
MAIN GROWTH MECHANISM
CLINICAL COLLERLATION
ENDOTHEHELIAL DYSFUNCTION
Initial lesion
• histologically "normal"
• macrophage infiltration
• isolated foam cells
Fatty streak
mainly intracellular lipid accumulation
Intermediate lesion
• intracellular lipid accumulation
• small extracellular lipid pools
Atheroma
• intracellular lipid accumulation
• core of extracellular lipid
Fibroatheroma
• single or multiple lipid cores
• fibrotic/calcific layers
Complicated lesion
• surface defect
• hematoma-hemorrhage
• thrombosis
from first decade
from third decade
from fourth decade
growth mainly by lipid addition
increased smooth muscle and collagen increase
thrombosis and/or hematoma
clinically silent
clinically silent or overt

# Atherosclerosis: Progression



# Vulnerable vs Stable plaque

Vulnerable plaques are more sensitive to complications




Stable plaques are more resistance to complication

Thick fat core
Thin fibrous cap
More inflammation

Thin fat core
Thick fibrous cap
less inflammation

# 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) | |

# Risk Factors for Atherosclerosis

1. **Age:**
   - 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

# Scan the QR code or click it for FEEDBACK

Corrections from previous versions:

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