look!

V2 : Slide 16 above the boxes Stable ↔ unstable

THE UNIVERSITY OF JORDAN

Condition affect arteries

hardening usually results from thickining

ARTERIOSCLEROSIS

modified by Lynn Alhamaideh

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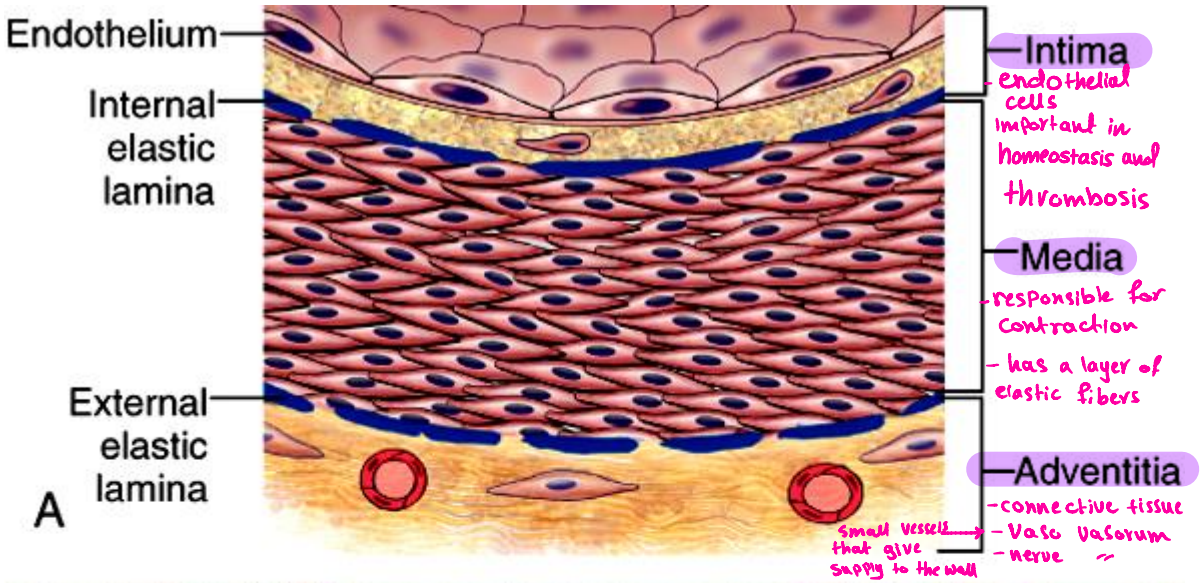
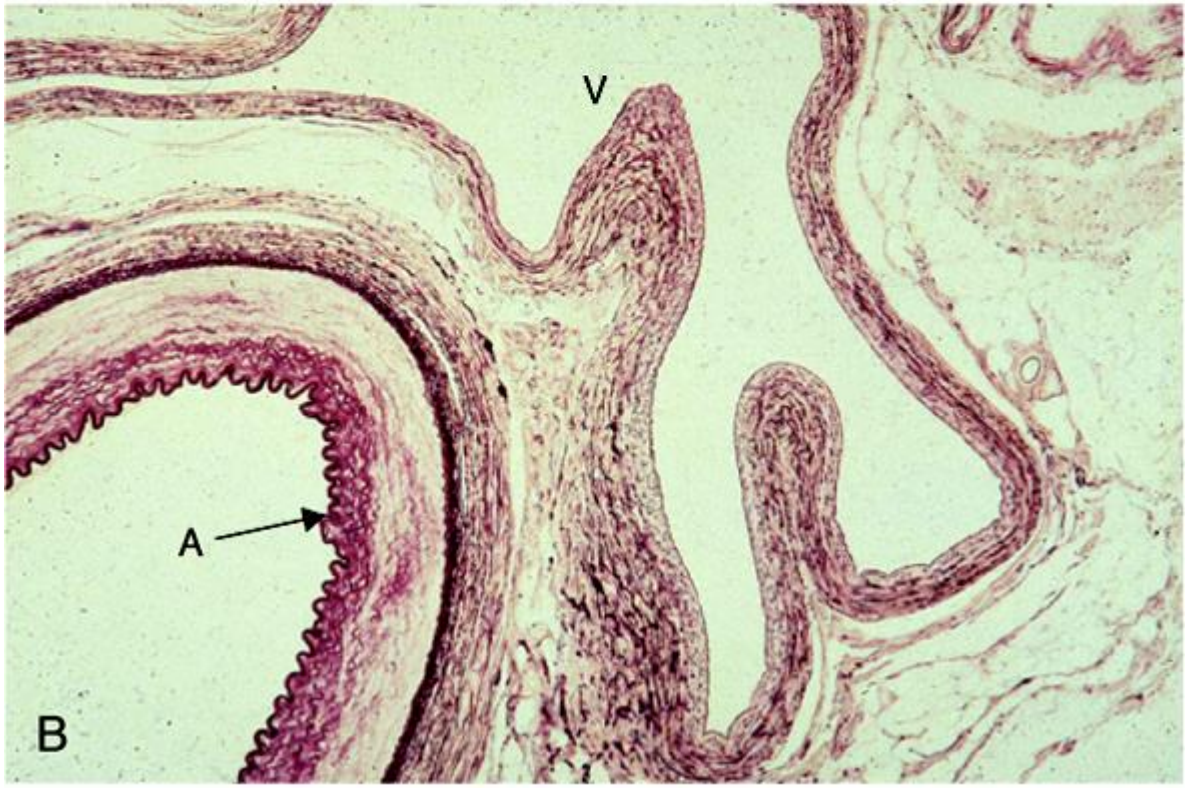
Normal blood vessels

A= artery

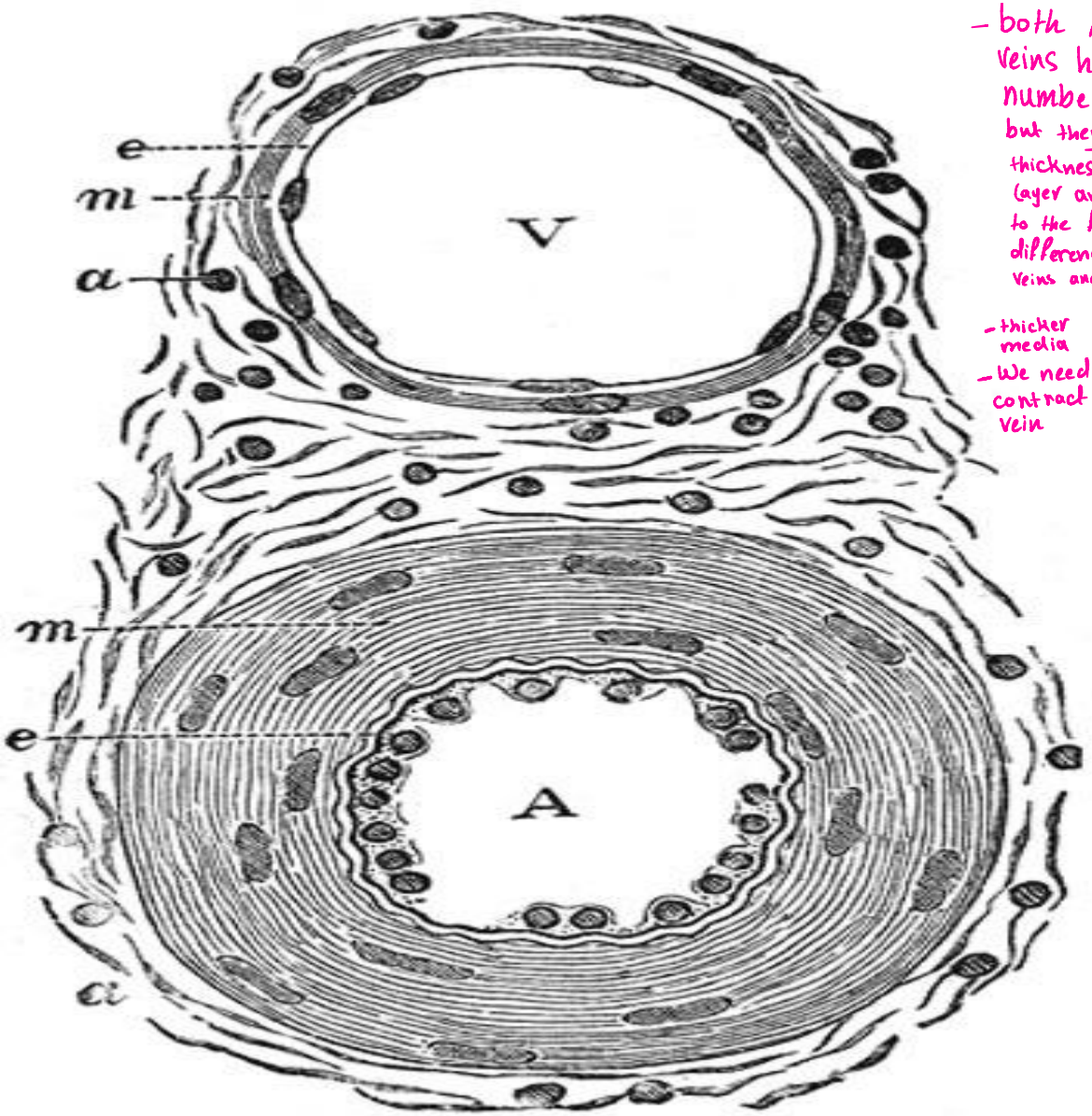
V= vein

These histology info. are mentioned by the doctor to undrstand the lecture well but aren't required for the exam. (you'll not be asked about them in patho questions)





Artery (A) versus vein (V)



- both Arteries and veins has the same numbers of layers but they differ in thickness of the media layer and this is due to the functional differences between veins and arteries
  - thicker media
  - We need the ability to contract more than the vein

ARTERIOSCLEROSIS

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

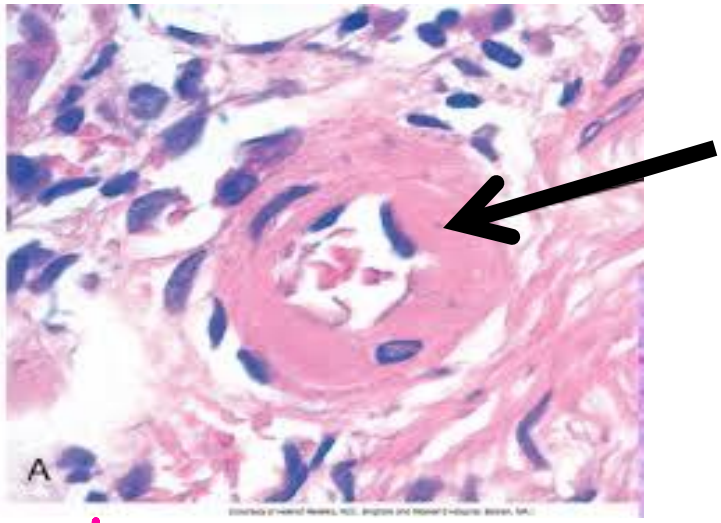
not a single disease

difference between this type name and the main name.

1-Arteriolosclerosis

- affects small arteries and arterioles (smalleset artries)
- associated with hypertension and/or diabetes mellitus

Thickening of the wall as a result of depositing of a certain material.



* Thickening of the wall → narrowing of the vessels → ischemia of the supplied tissue.

We will take more about this type in the recorded lecture

2- Mönckeberg medial calcific sclerosis

Involve media layer

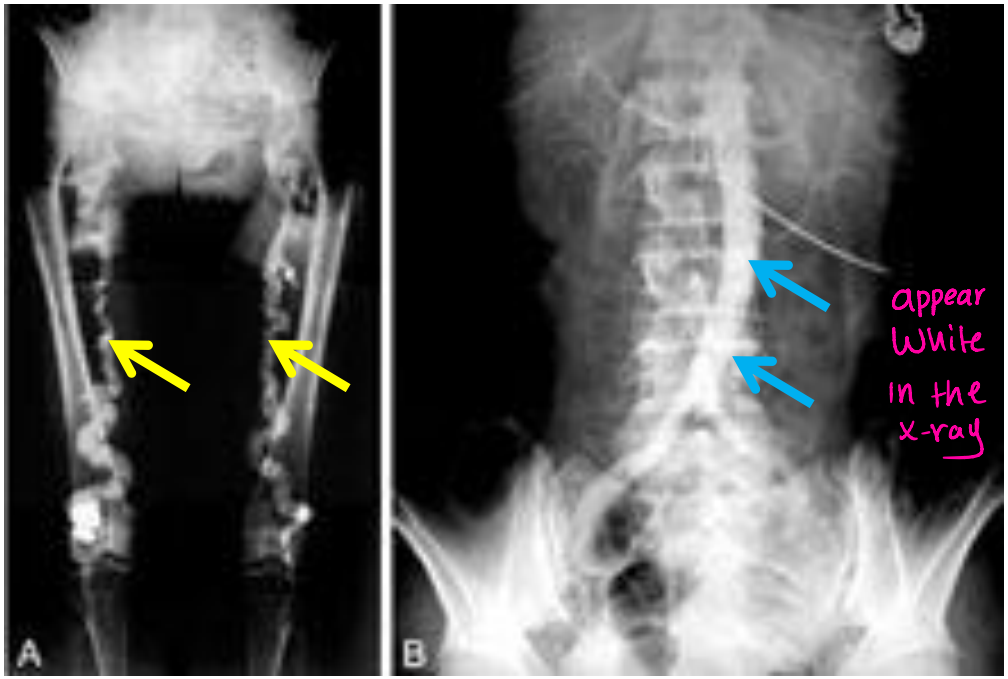
Type of deposited material

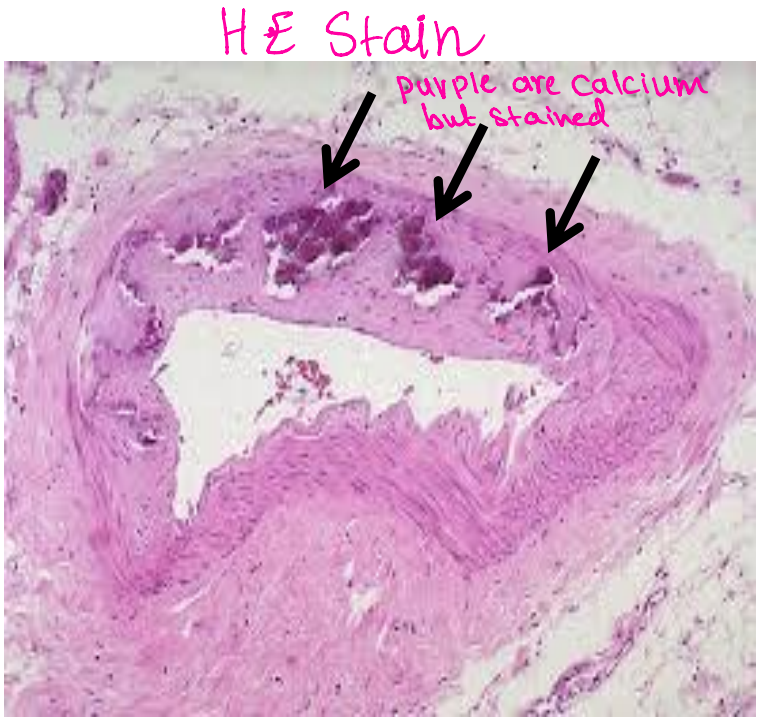
- **calcific deposits in muscular arteries**
- **typically in persons > age 50**
- **radiographically visible (x-rays, etc…)**
- **palpable vessels**
- **do not encroach on vessel lumen and are usually not clinically significant**

alone can't cause ischemia or narrowing of the lumen

- It happens due to aging and because it happens in the media not intima it can't cause narrowing or ischemia

2-Mönckeberg medial calcific sclerosis





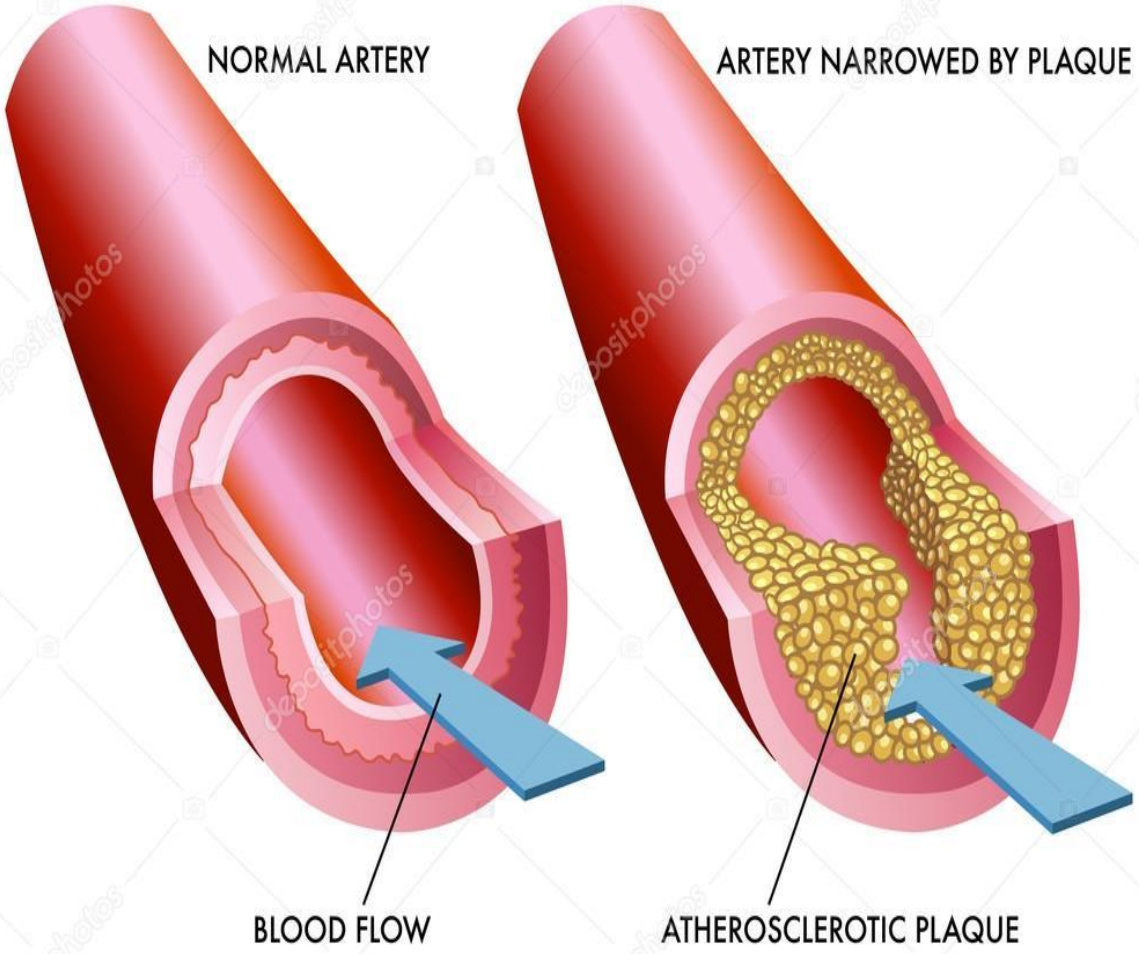
3rd type

تصلب الشرايين

ATHEROSCLEROSIS

diabetes, HBP, obesity = المحاتسبب في الاصابة

MI, ↑ LDL , ↓ HDL



- Greek word "gruel" (fatty) ,"hardening,"
- most frequent and clinically important pattern of arteriosclerosis — it causes narrowing of the lumen + ischemia
- characterized by intimal lesions =*atheromas* (a.k.a. *atherosclerotic plaques*)
  - or fibroatheroma or atheroma plaque all refer to the same word
- atheromatous plaque = raised lesion with a core of lipid (cholesterol and cholesterol esters) covered by a firm, white fibrous cap
  - bad cholesterol LDL

- It affects intima → LDL deposition → تقرحات او خلل → endothelial injury = thrombosis + → narrowing of the lumen.
  - changes in smooth muscle in the media which travel to the intima and produce ECM proteins + Chemical mediators ... مثل كرات الدم البيض « inflammation.

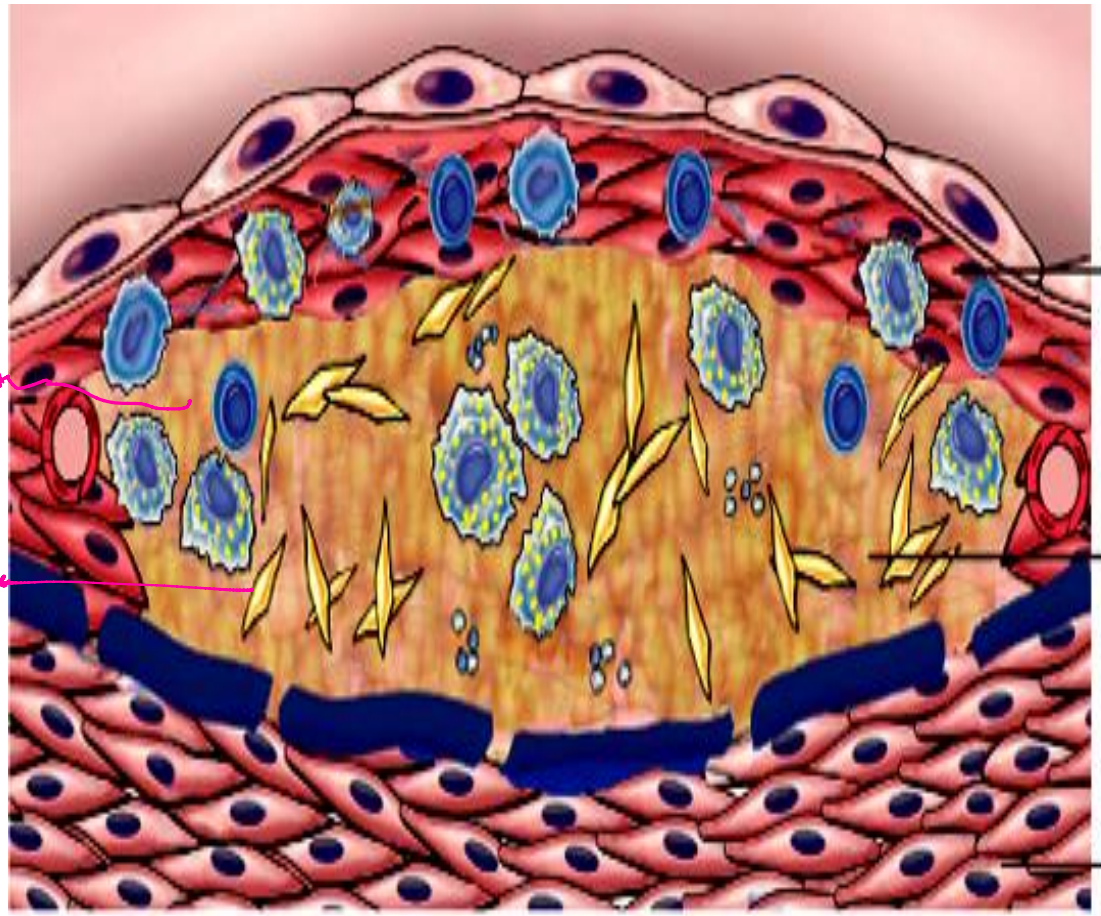
So, in this type narrowing of the lumen is due to 1. LDL deposition 2. Inflammation process highlighted

We don't know which one happens first LDL accumulation or inflammation.

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



Intima is expanding due to LDL accumulation and inflammatory response

FIBROUS CAP
(smooth muscle cells, macrophages, foam cells, lymphocytes, collagen, elastin, proteoglycans, neovascularization)
+the ECM

NECROTIC CENTER
(cell debris, cholesterol crystals, foam cells, calcium)

And macrophages that are there to engulf the cholesterol deposits

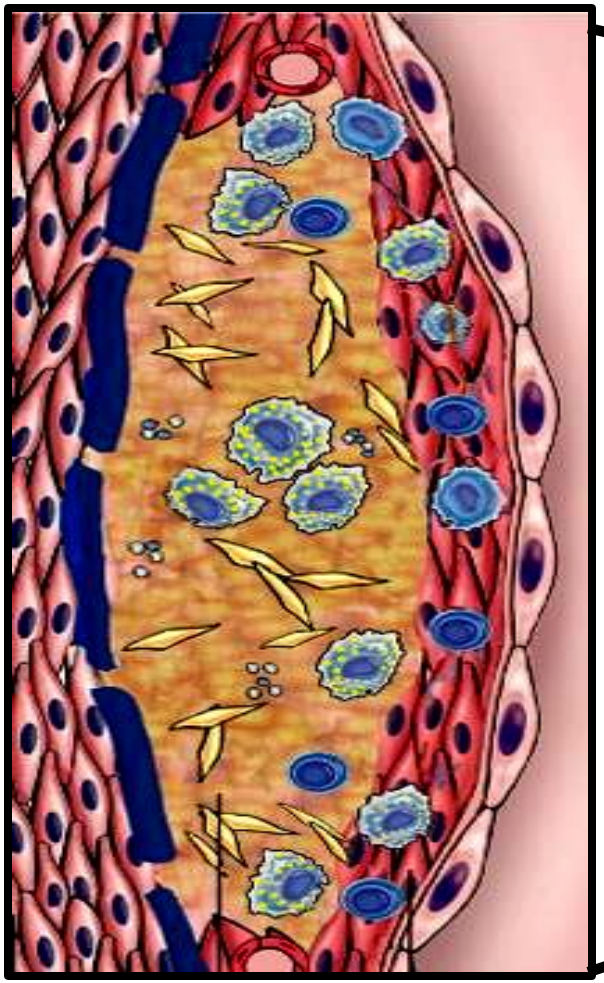
MEDIA

cholestrol

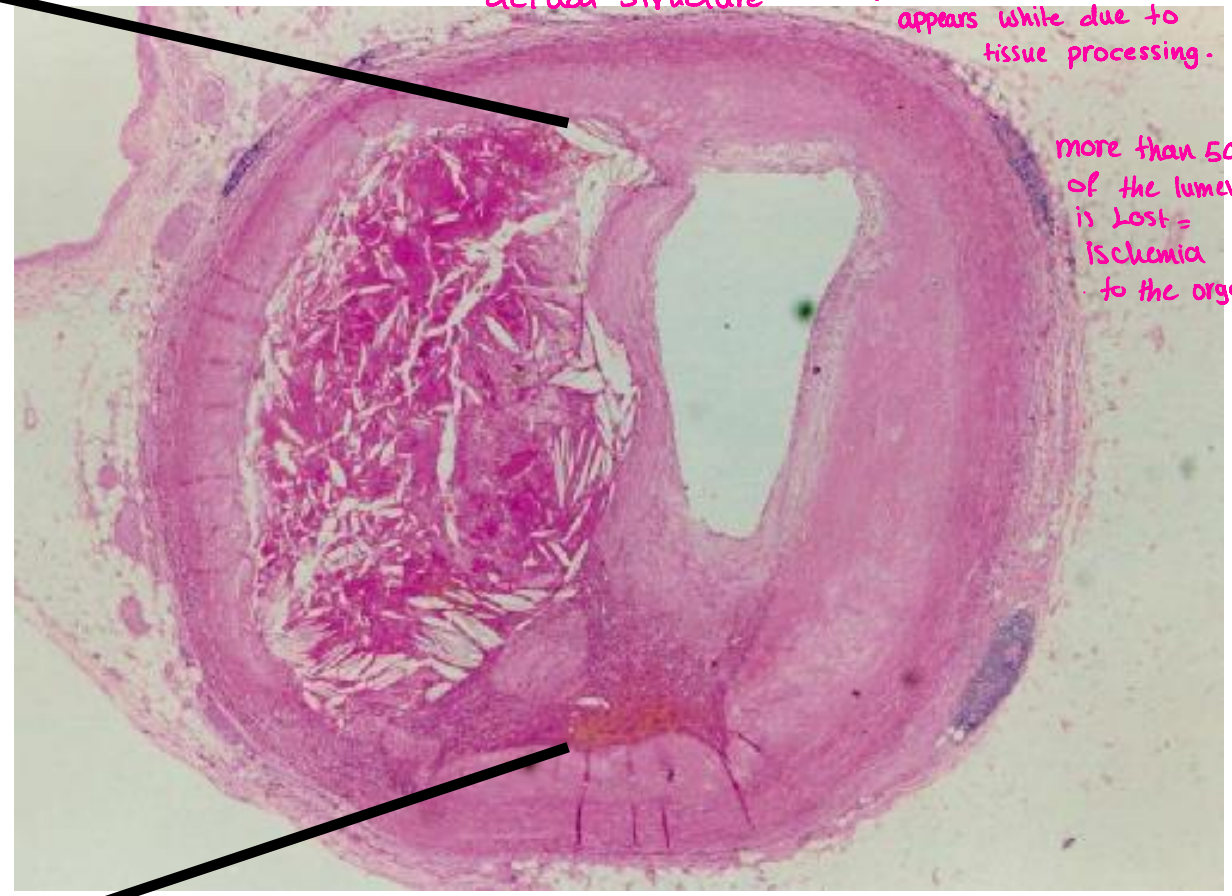
cholestrol crystals

With time atheroma will get mature and divide to 2 well distinguished parts 1. Necrotic (fat) center 2 fiber cap that covers the center

Atheromatous plaque



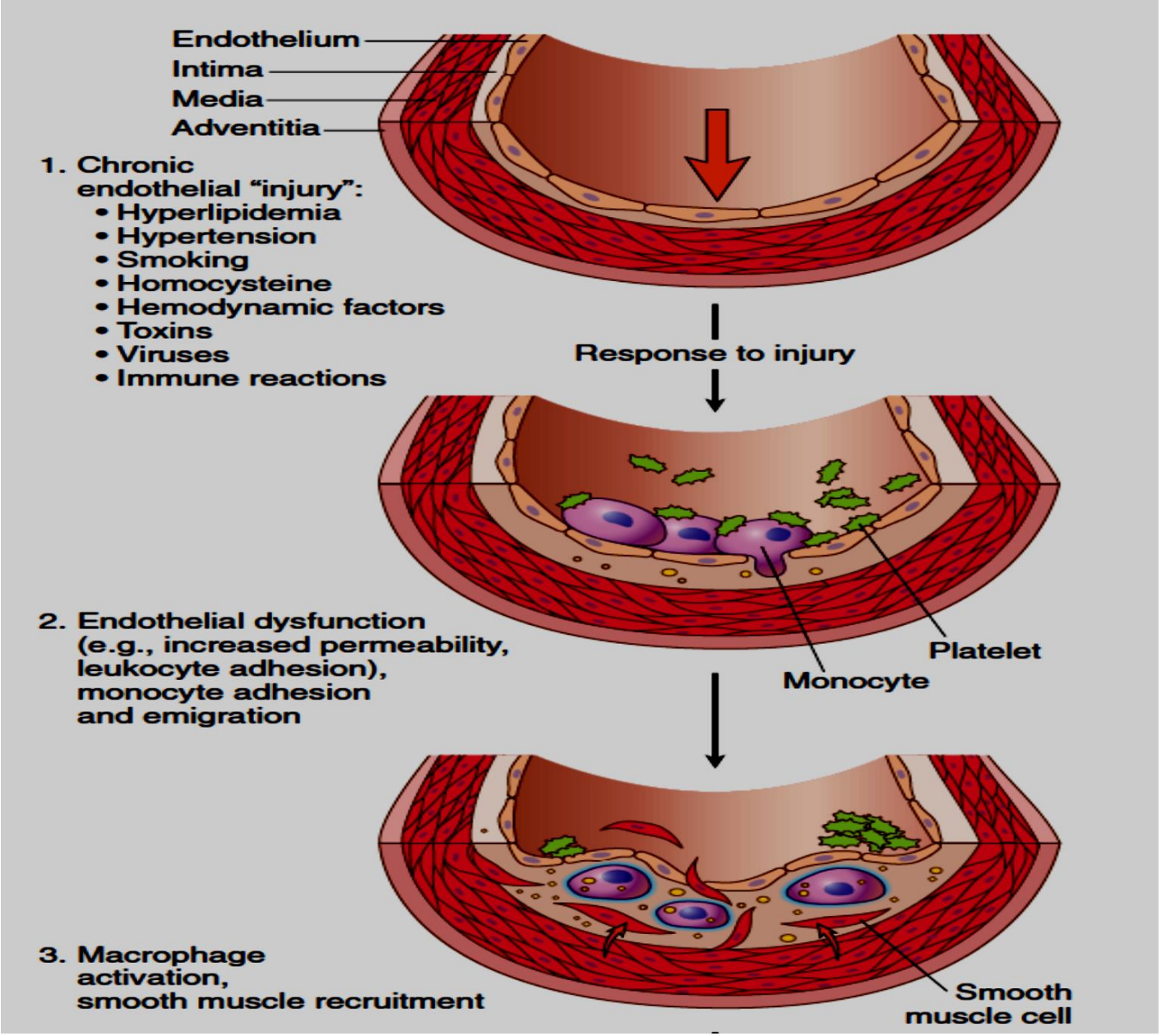
actual structure



Yellowish needles (crystals) appears while due to tissue processing.

more than 50% of the lumen is lost = Ischemia to the organ.

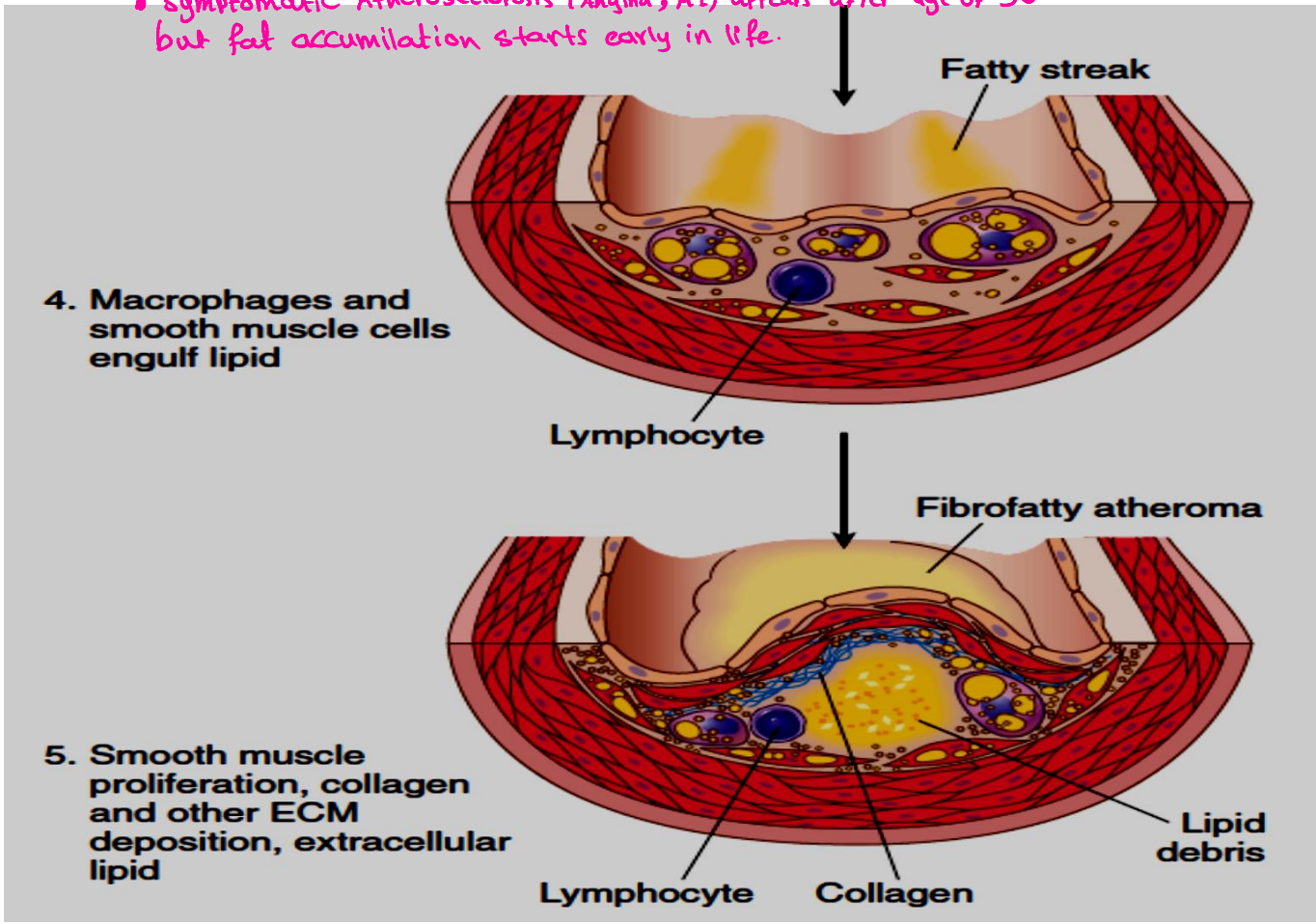
Formation of atheromatous plaque

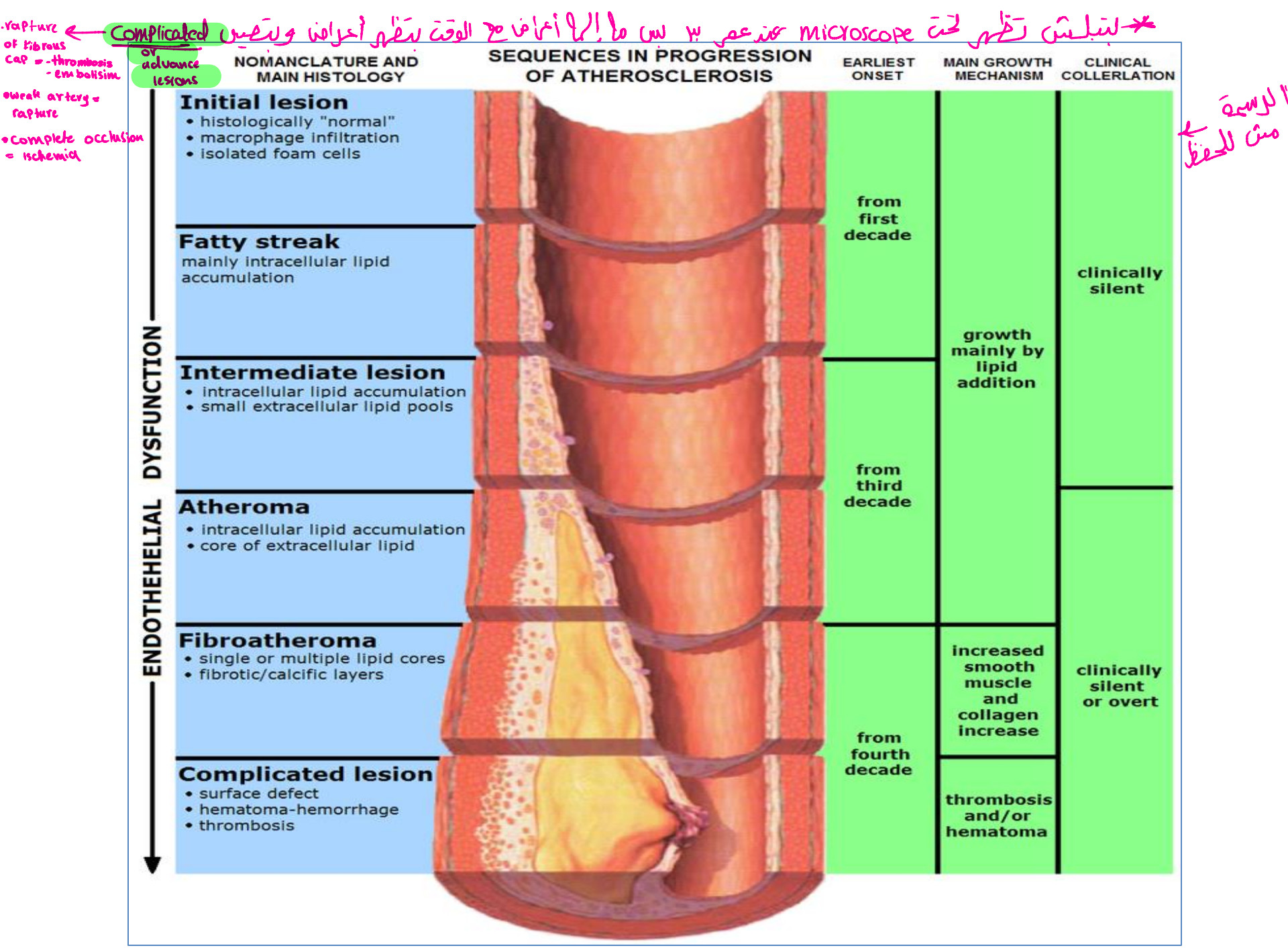


Formation of atheromatous plaque

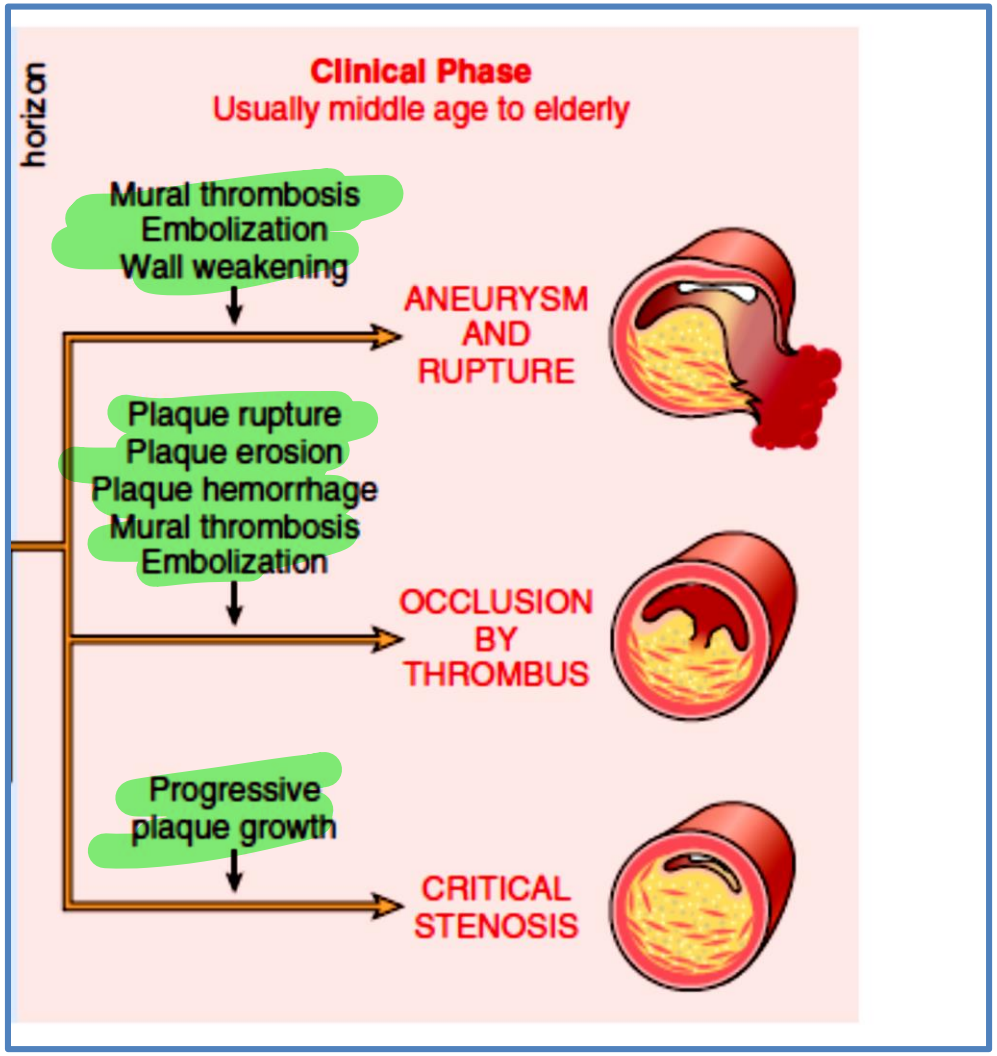
- Is this process limited to a single tissue or systemic?
  Systemic because if the patient has ↑ LDL it will affect most of the arteries

- This condition happens gradually, it's a disease of old age.
- symptomatic Atherosclerosis (Angina, MI) appears after age of 50. but fat accumulation starts early in life.



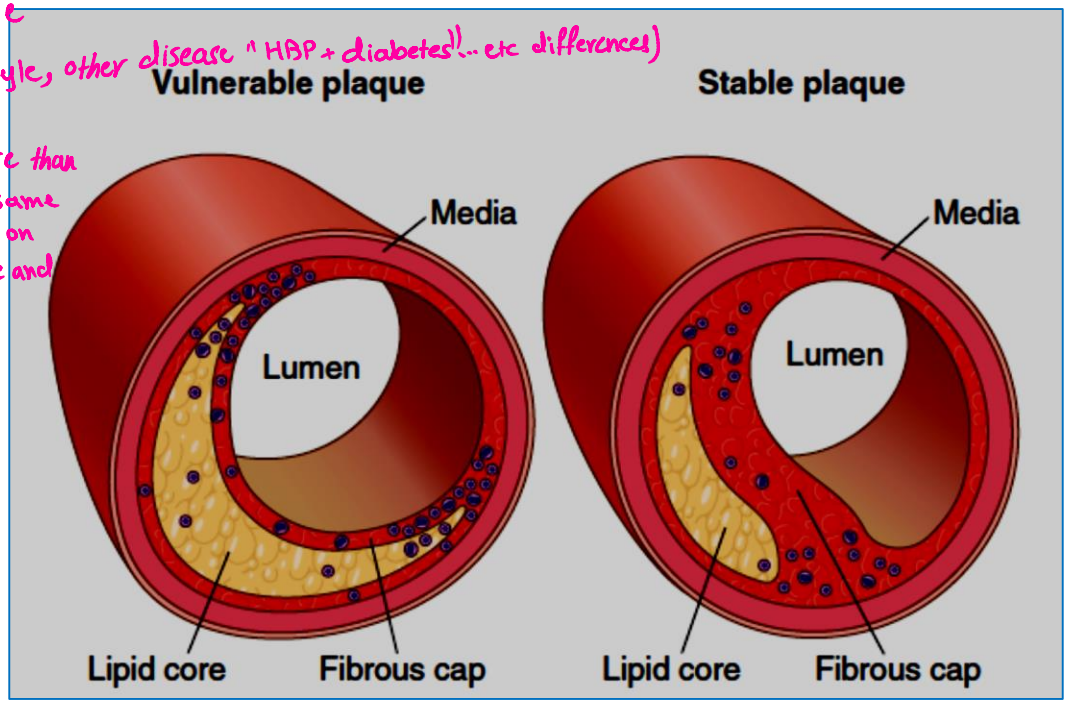

Complicated or advance lesions
NOMANCLATURE AND MAIN HISTOLOGY
SEQUENCES IN PROGRESSION OF ATHEROSCLEROSIS
EARLIEST ONSET
MAIN GROWTH MECHANISM
CLINICAL COLLERLATION
ENDOTHEHELIAL DYSFUNCTION
Initial lesion
• histologically "normal"
• macrophage infiltration
• isolated foam cells
Fatty streak
mainly 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

- Not all patient will develop same risks. (genetics, age, lifestyle, other disease "HBP + diabetes!"... etc differences)
- Single patient with more than one lesion will not develop same risks in all lesions, it depend on artery size, atheroma size, type and location of artery.



- atheroma components will differ from lesion to lesion. [تختلف المكونات بختلف]

Vulnerable / Unstable plaque

Thick fat core
Thin fibrous cap
More inflammation

more complications

Stable plaque

Thin fat core
Thick fibrous cap
less inflammation

less complication

* according to many studies

Risk Factors for Atherosclerosis

Major Risks (علاقة قوية)	Lesser, Uncertain, or Non-quantitated Risks (علاقة ضعيفة)
Non-modifiable (non-controllable) (ما نقدر نغيره)	Obesity
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) (نقدر نغيره ونتحكم فيه)	Hardened (trans)unsaturated fat intake
Hyperlipidemia	
Hypertension	Chlamydia pneumoniae infection
Cigarette smoking	
Diabetes	
C-reactive protein (inflammation) → indicator of inflammation	

1-age

- **ages 40 to 60, incidence of MI in men increases 5 x**
- **Death rates from IHD rise with each decade**

2-Gender → male gender are more succistable.

- **Premenopausal* → protected against atherosclerosis compared with age-matched men.**
- **After menopause→ incidence of atherosclerosis-related diseases increases**

*females before menopause are protected by estrogen.

- *** unless they are otherwise predisposed by diabetes, hyperlipidemia, or severe hypertension.**

3-Genetics

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

1- familial clustering of other risk factors

- e.g. HTN or DM

or :

2- well-defined genetic derangements in lipoprotein metabolism

- e.g. familial hypercholesterolemia

Doctor didn't read this slide

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; Clonal hematopoiesis)*
- **Others:**

-lack of exercise

-competitive, stressful lifestyle ("type A" personality)

-obesity

-High carbohydrate intake