ARTERIOSCLEROSIS

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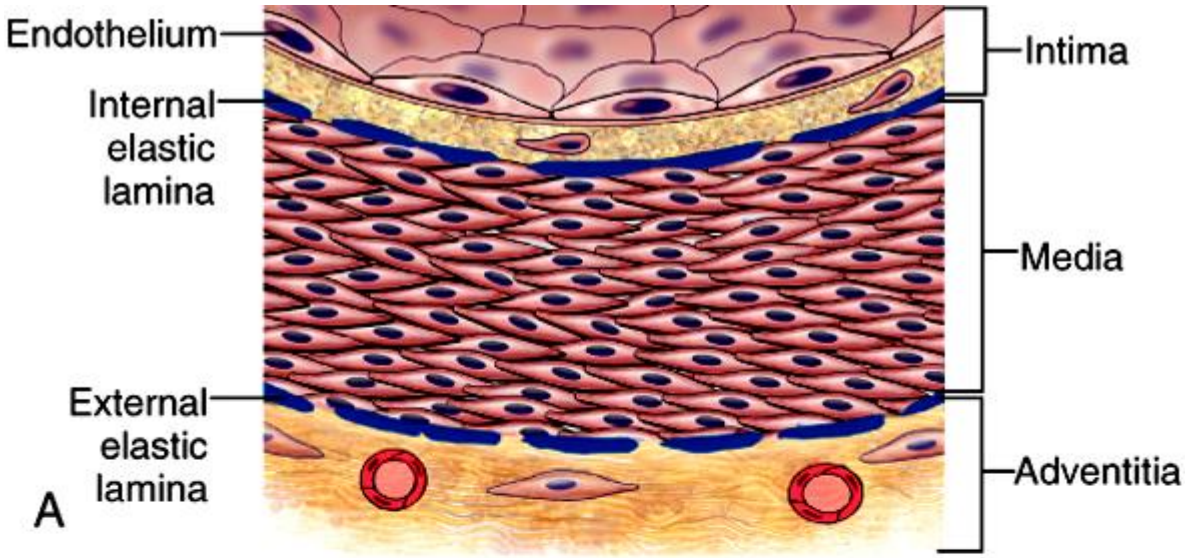
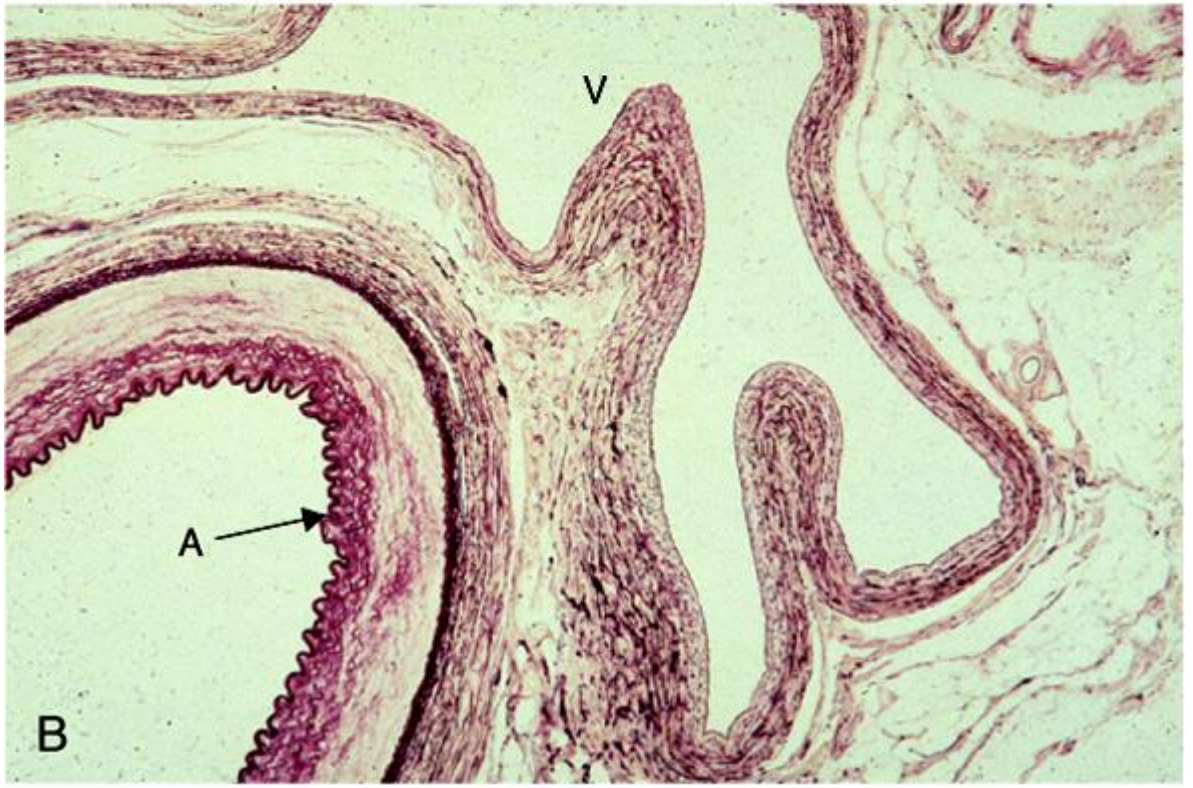
Normal blood vessels

A= artery

V= vein

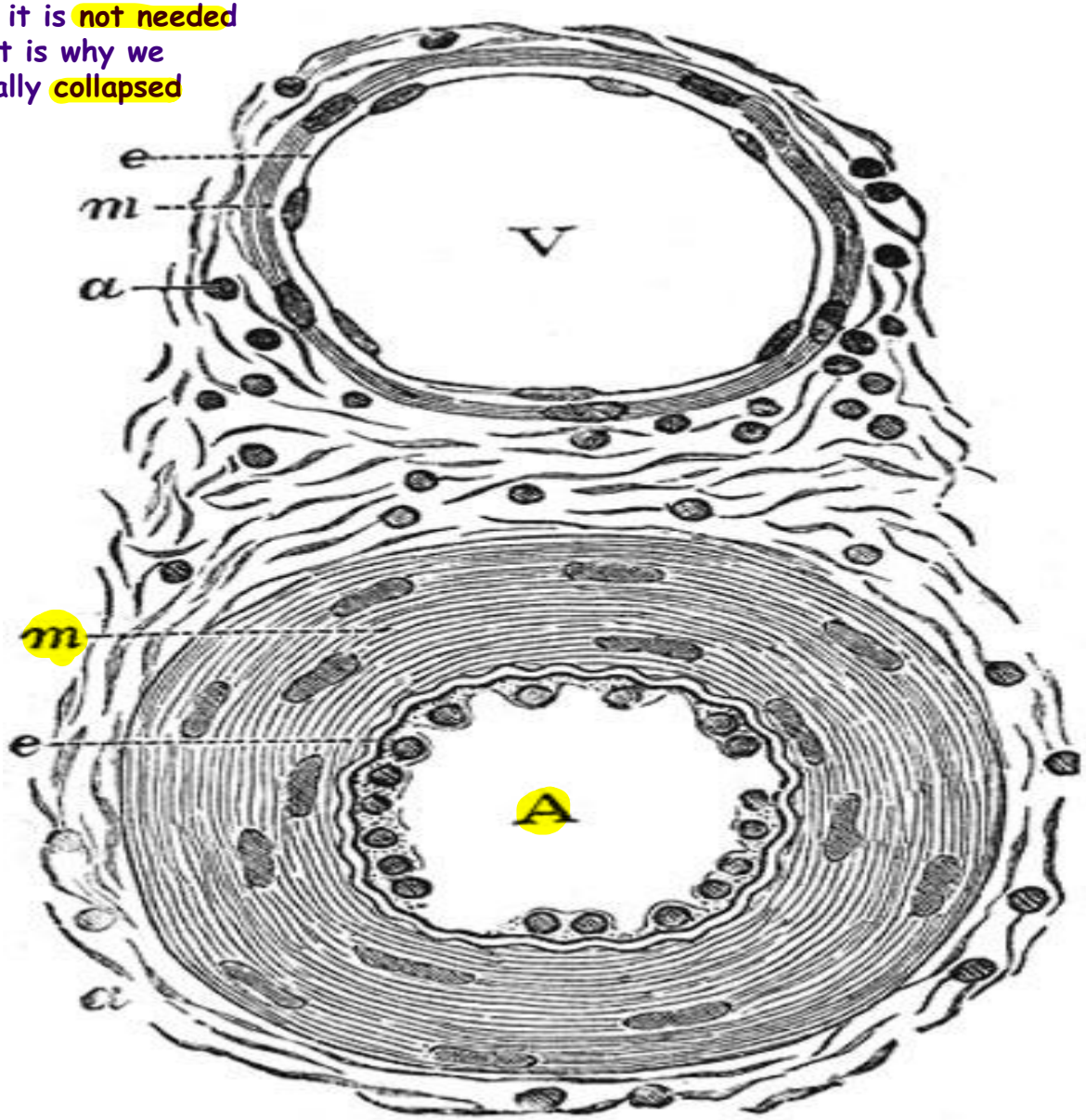
* the wall of the artery is much thicker than the vein and this is due to the second layer (media) , which contain more muscle fibers in case of artery and this is important
in the contractility of the artery .





Artery (A) versus vein (V)

*the contractility it is not needed in veins , and that is why we say the veins usually collapsed

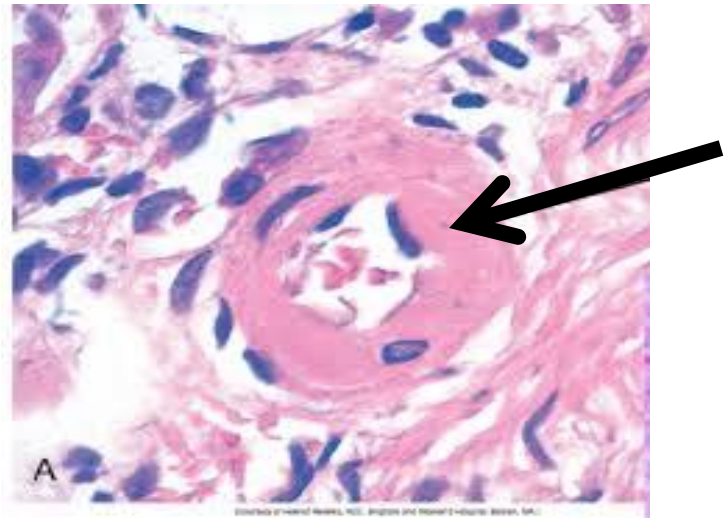


ARTERIOSCLEROSIS

- ***Arteriosclerosis*** **="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



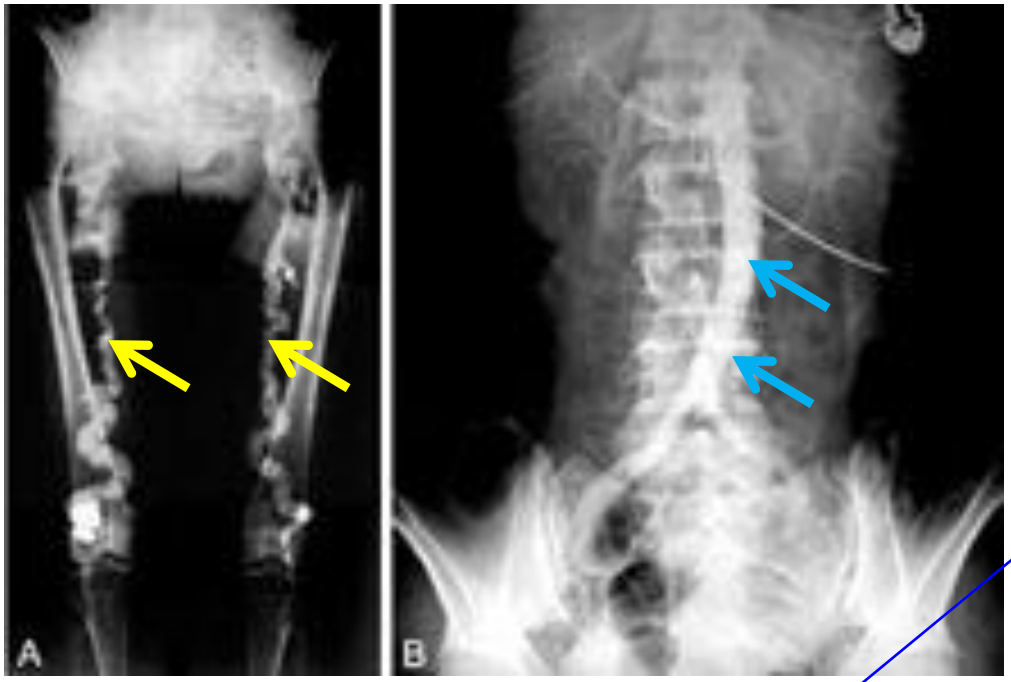
2- Mönckeberg medial calcific sclerosis

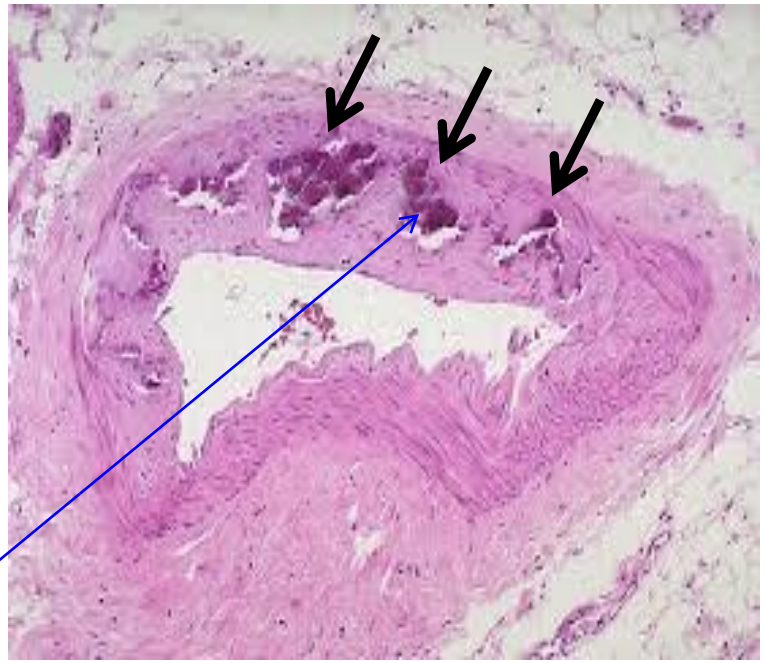
- **calcific deposits in muscular arteries**
- **typically in persons > age 50**
- **radiographically visible (x-rays, etc…)**
- **palpable vessels** if it is affect the subcutaneous vessels .
- **do not encroach on vessel lumen and are usually not clinically significant**

*this condition is not associated with any other pathology or disease in the artery .

2-Mönckeberg medial calcific sclerosis

it is visible in the X-ray





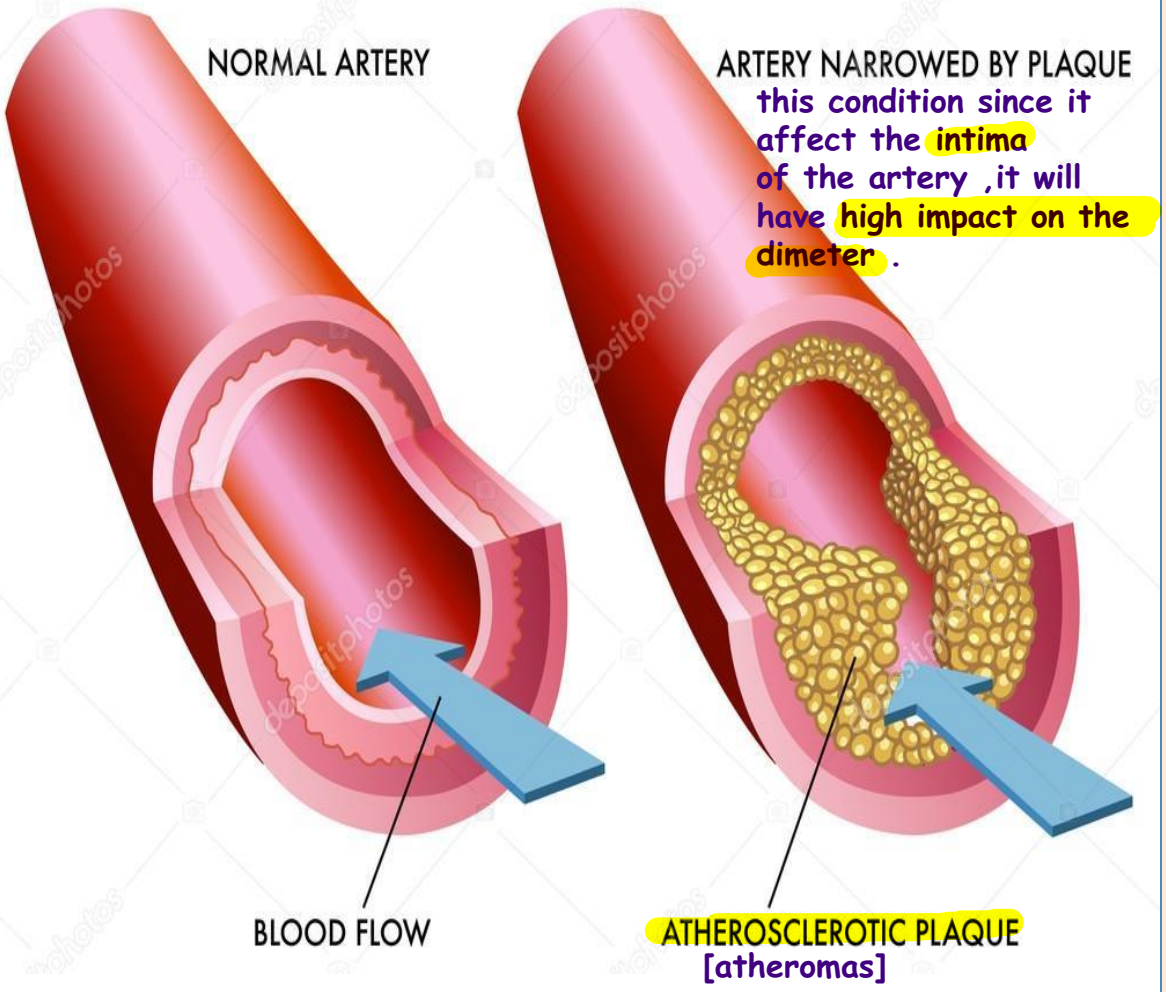
in the microscope the calcification will appear as a purple color deposits in the wall of the media.

if it is isolated it will not lead to abnormality in the lumen diameter .

*this process is a degenerative process as it is associated with the aging (affect >50 year) .

athero mean :

3- 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

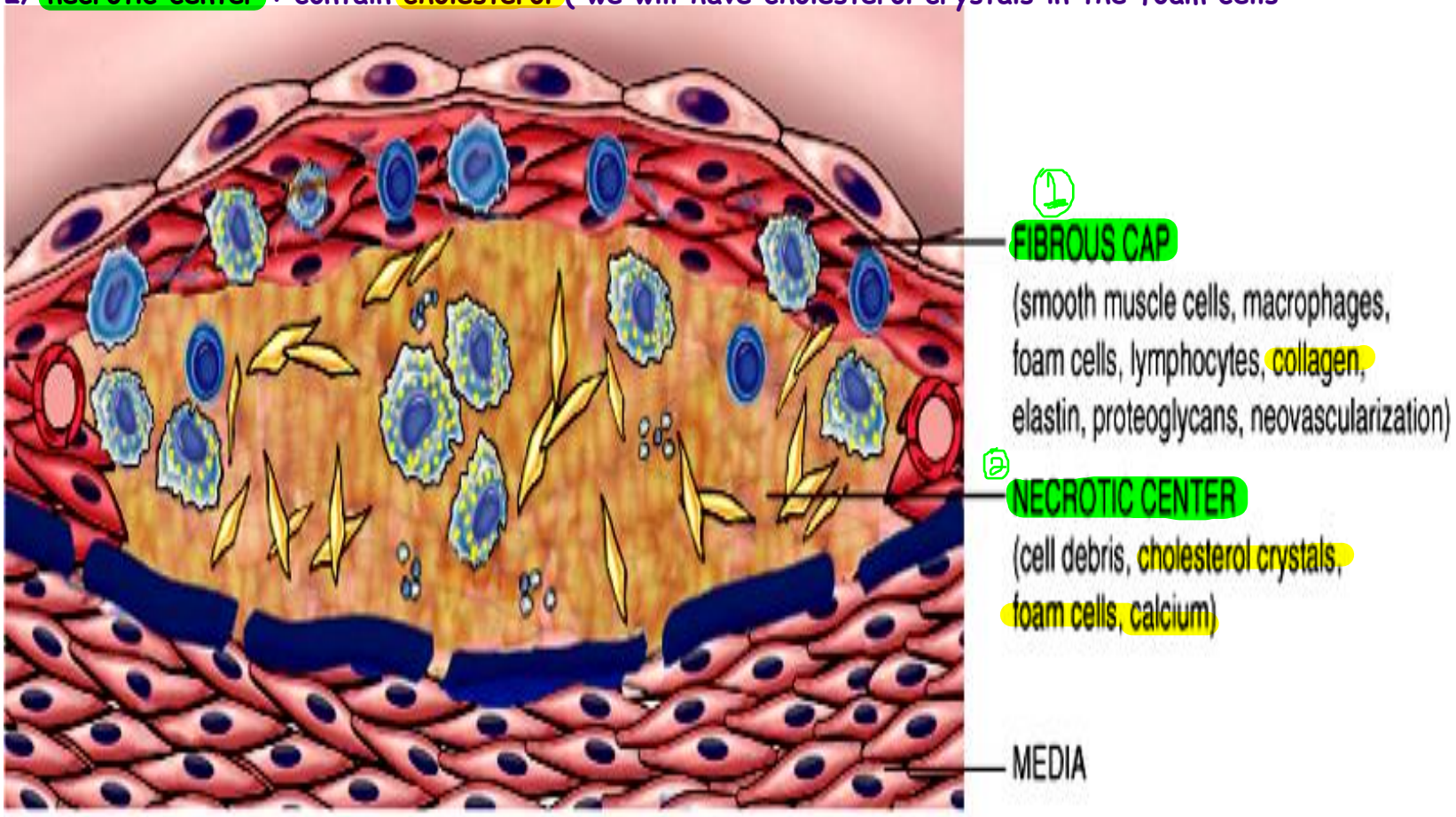
Atherosclerosis- Pathogenesis

- **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 pathogenesis of the atherosclerosis might occur due to : inflammation + deposition of the fat (LDL)>>> and this will lead to formation of atheroma >>> atherosclerosis.

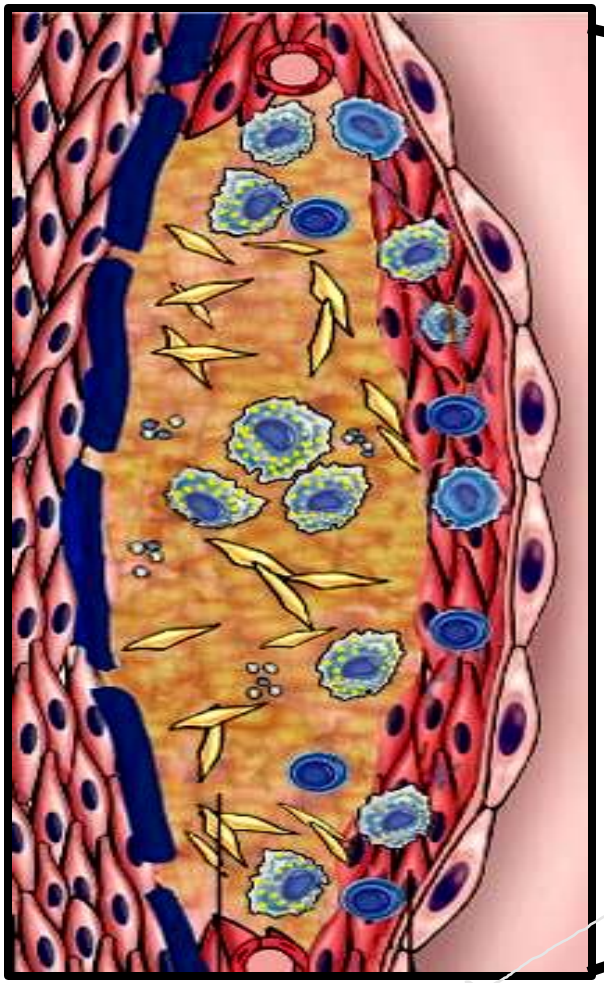
The major components of a well-developed intimal atheromatous plaque

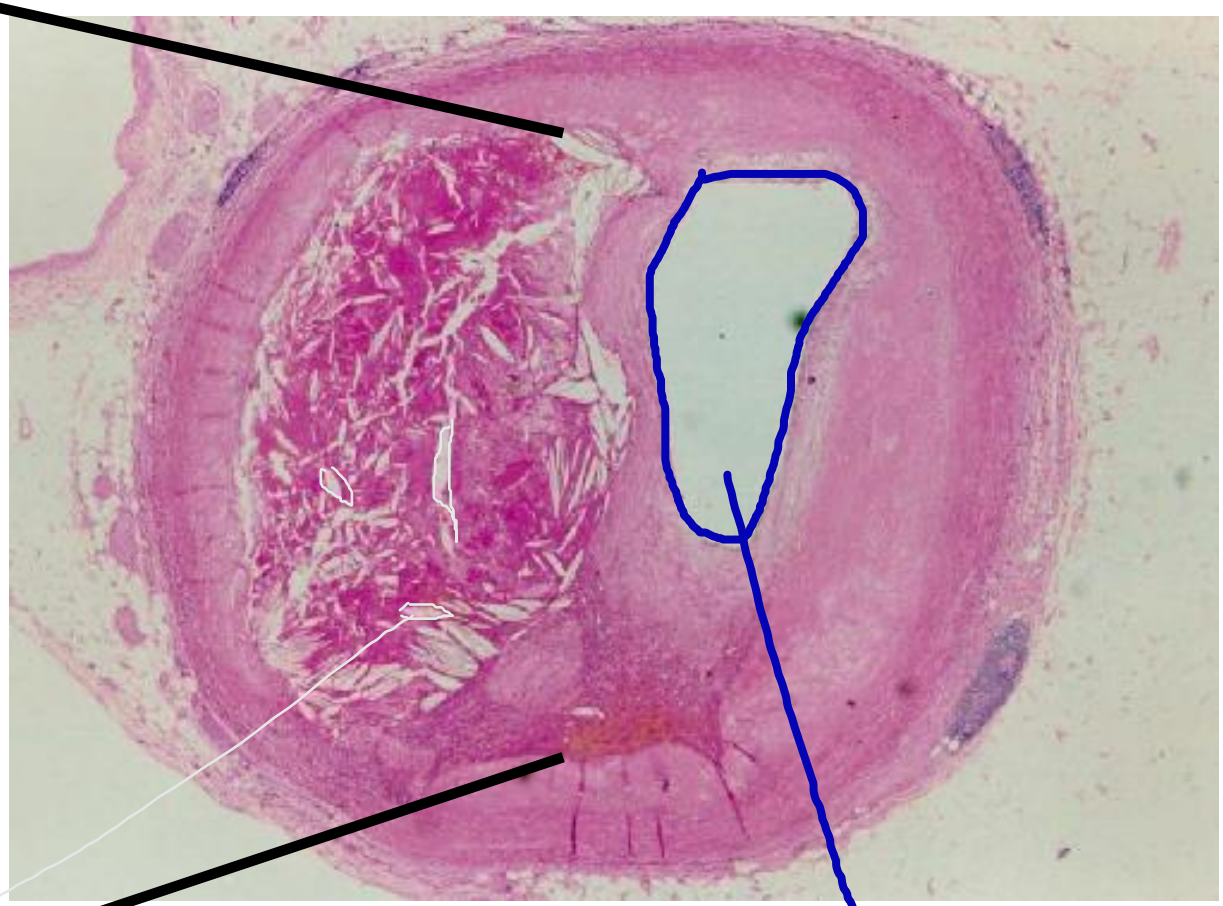
1/ fibrous cap : composed of protiens +certain types of cells
2/ necrotic center : contain cholesterol (we will have cholesterol crystals in the foam cells



Atheromatous plaque

* this picture represent [cross section in the artery that is affected by atherosclerosis].





-the needle shape whitish area inside the atheroma represent the necrotic center (which is the cholesterol crystals)

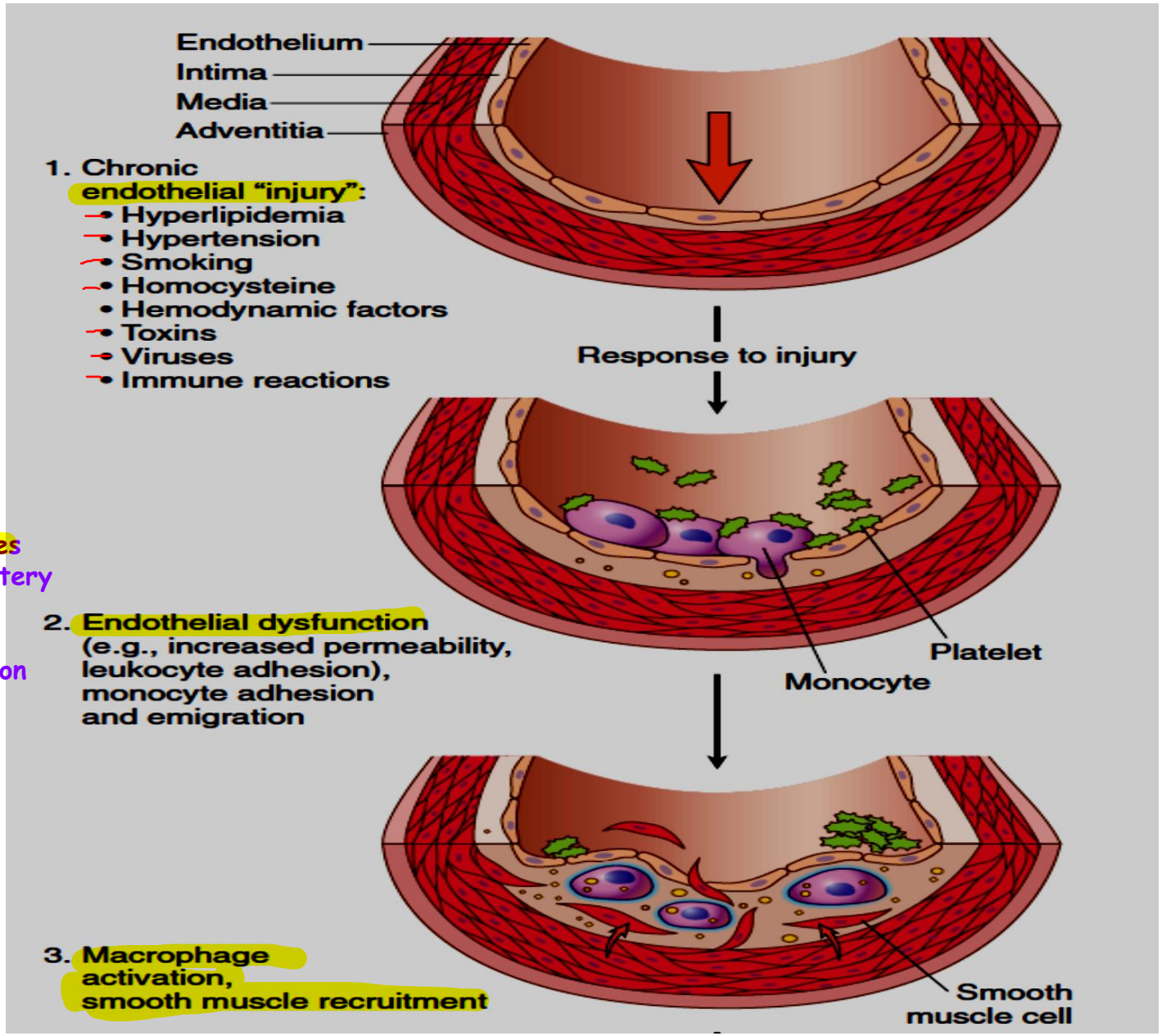
-we will have a significant impact on the luminal diameter (the lumen become very small) ,and this is the major important problem in the atherosclerosis

Formation of atheromatous plaque

needs 2 events :
1/ inflammation
2/ deposition of LDL .

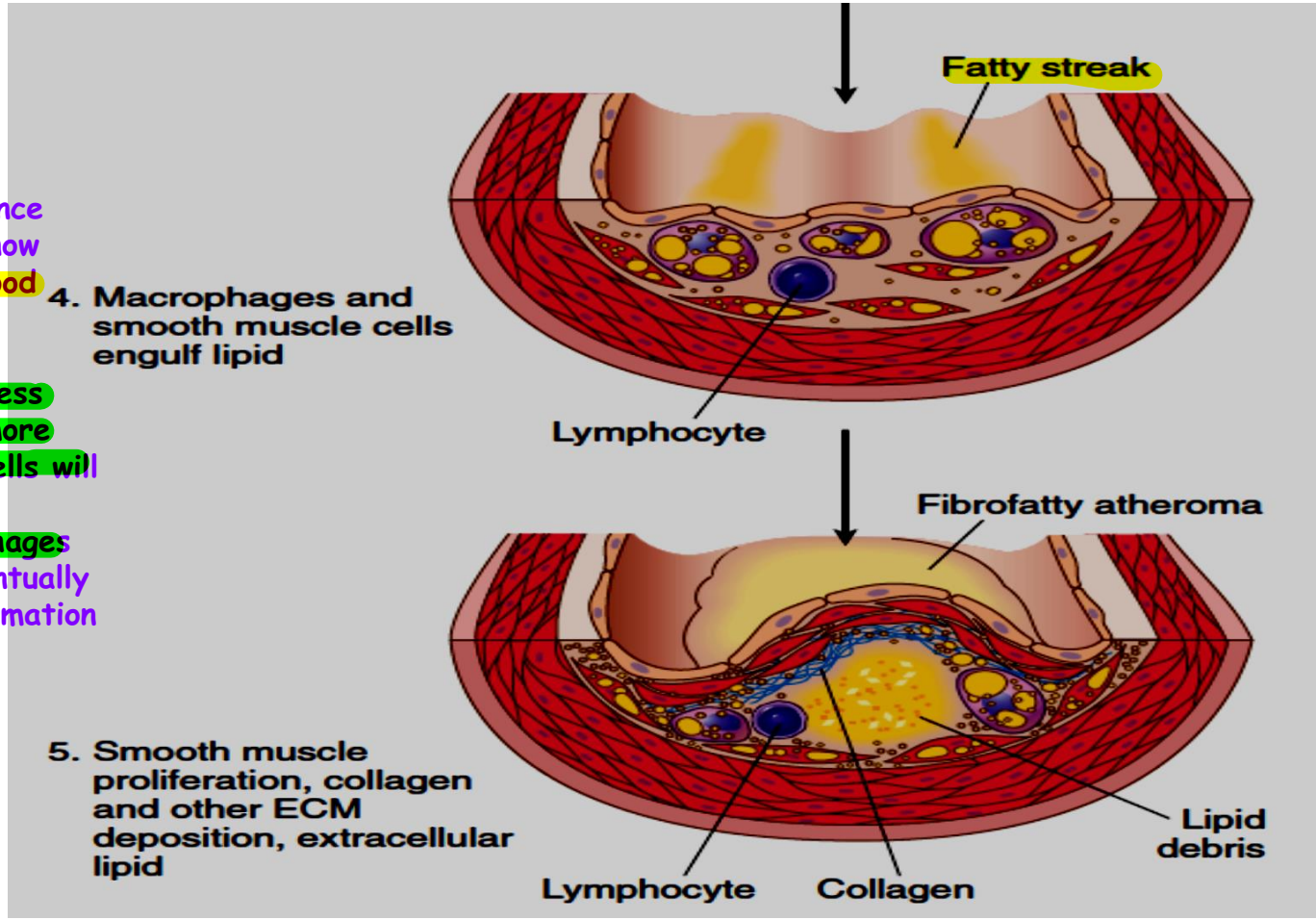
endothelial cells injury or dysfunction due to (immune rxn, smoking , viruses , smoking....) this will lead to cascade of inflammatory responses inside the wall of the artery including smooth muscle migration , macrophage activation , and production of extracellular matrix protiens

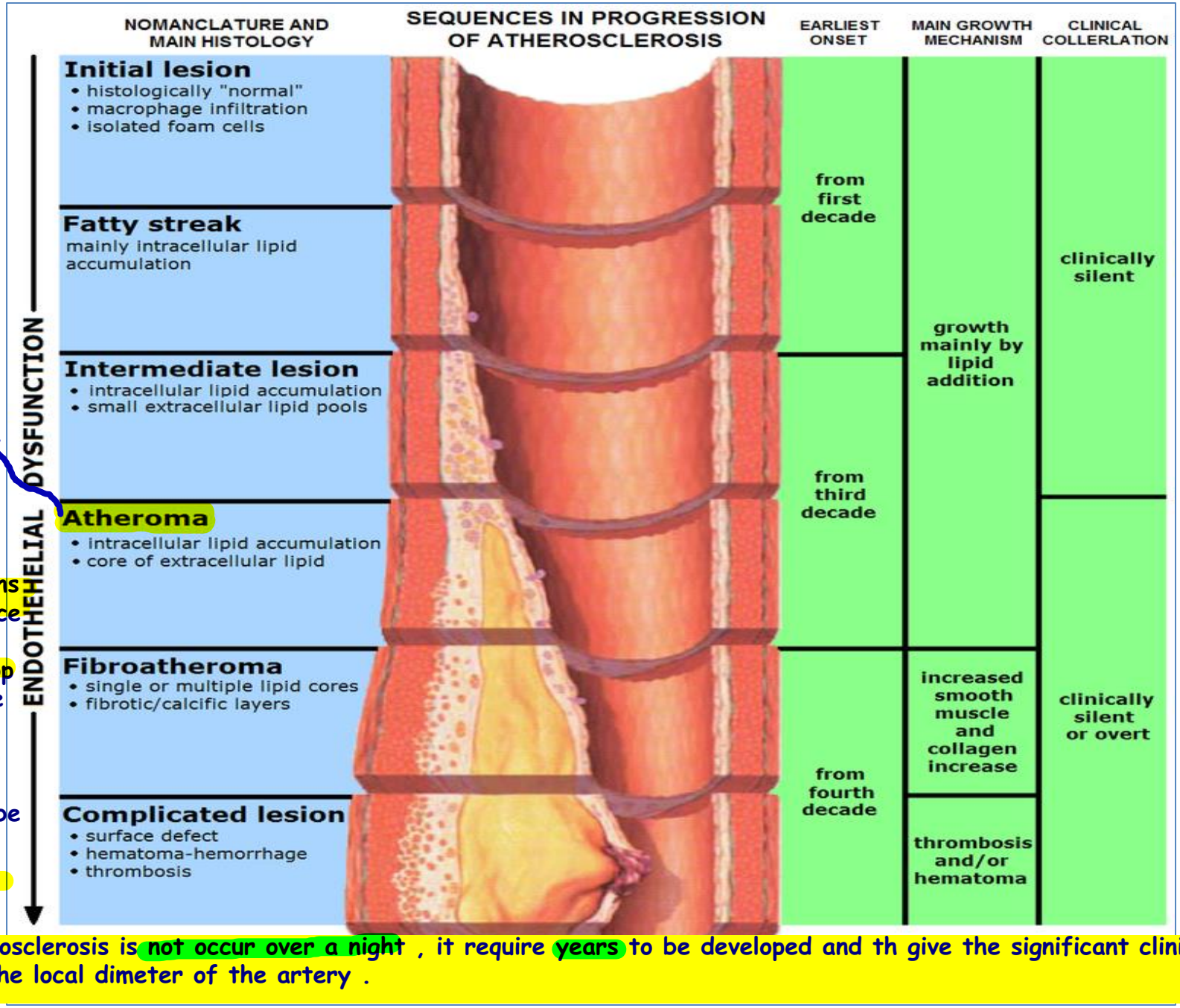
Cont



Formation of atheromatous plaque

*inflammation beside the presence of the LDL particles that are now deposited in the wall of the blood vessel specifically within the intima >> all these will also maintain the inflammatory process within the wall >>> more and more macrophages +smooth muscle cells will be recruited to the area >> the monocytes and the macrophages will engulf the lipid >> and eventually this will lead to lipid debris formation within the atheroma .



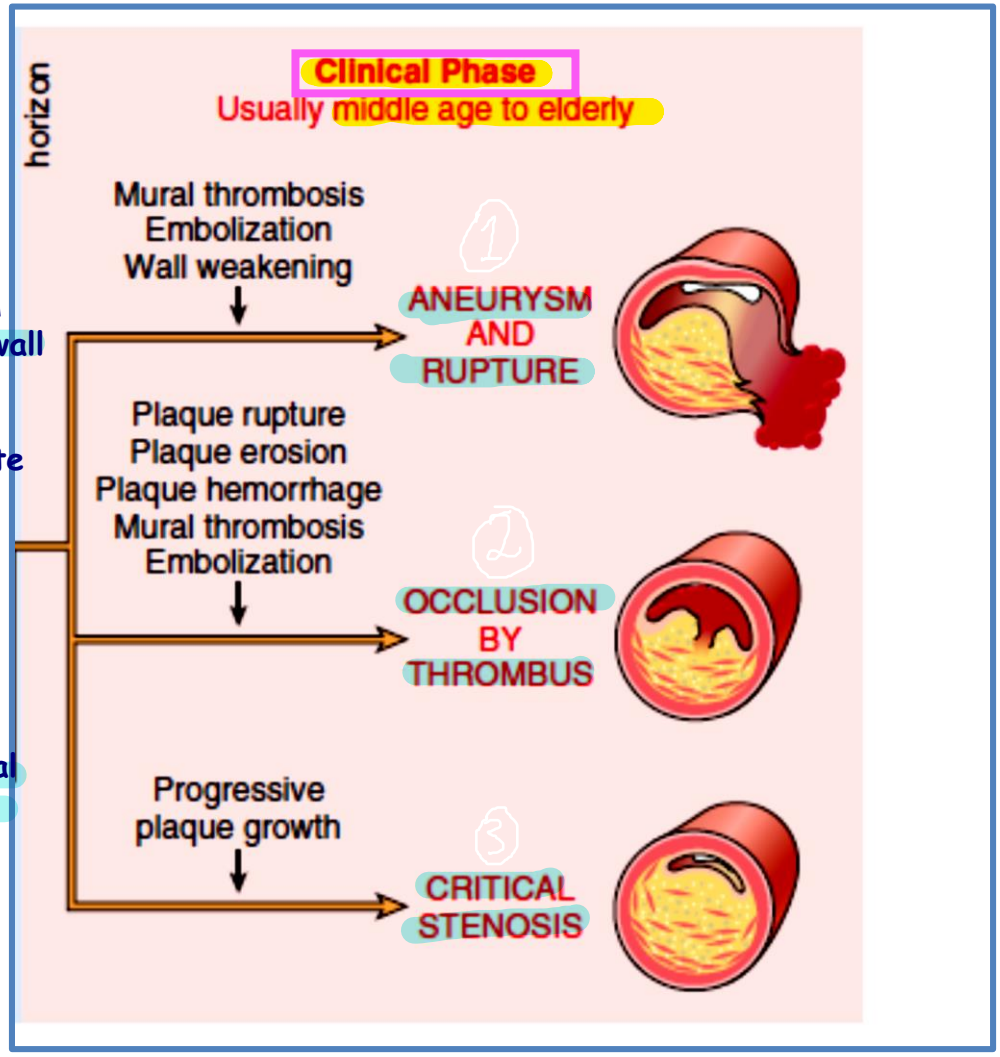


develops around the third decades of life and then the clinical complications and sequence of events that develop later in the artery also will develop later in life maybe in the 4th or 5th decade

* the atherosclerosis is not occur over a night , it require years to be developed and th give the significant clinical impact on the local dimeter of the artery .

Atherosclerosis: progression

-the clinical phase of the atherosclerosis is usually seen in the middle life , and these are related to progression and possible complications that develop in the wall of the artery , this could include [aneurysm formation +rupture of the wall of the artery +occlusion by superimposed thrombus] and this will lead to complete obstruction of the luminal area of the artery [critical stenosis meaning that more and more atherosclerosis and the atheromatous legion is now increasing in the size until reach very small luminal area that is left to get the blood supply .

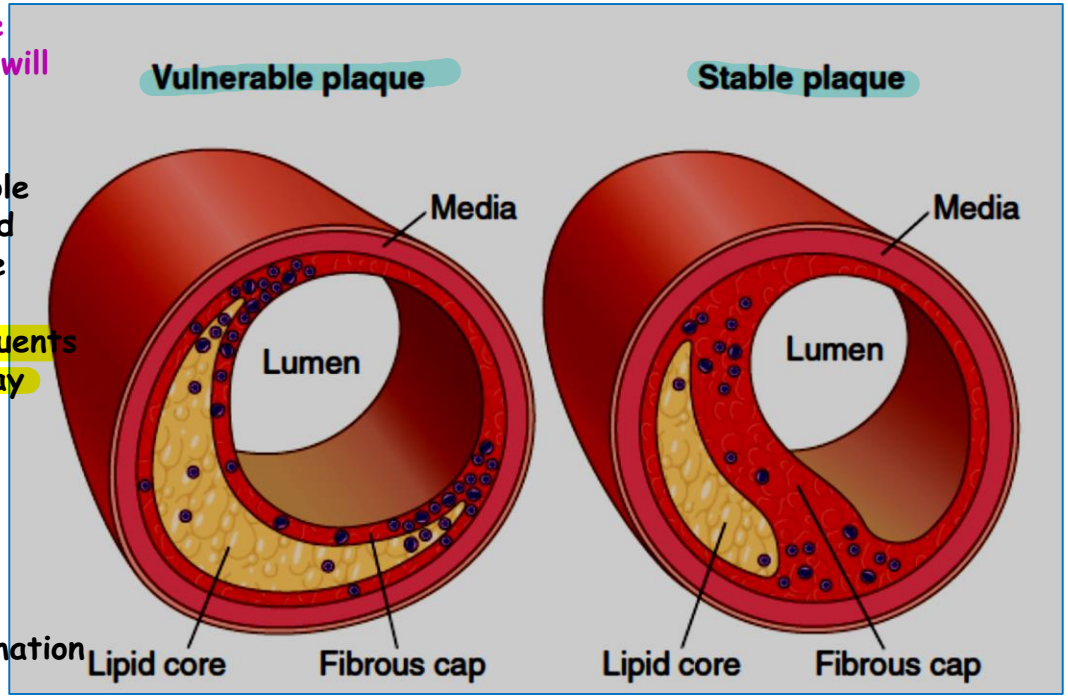


it mean vulnerable to develop complications and progression to complications of atherosclerosis .

Vulnerable vs stable plaque

*which determines which atheroma will have complication ??
+what determines the rate after which the atheroma will develop ??

many factors will play a role in this on of which is called (the concept of vulnerable vs stable atheroma)
in this concept the constituents of the plaque itself will play this role ...



so plaques that have:
thin fat core
and thick fibrous cap
and less amount of inflammation
[will be relatively stable]

the plaque that have:

Thick fat core
Thin fibrous cap
More inflammation
[it will be vulnerable]

Thick fat core
Thin fibrous cap
More inflammation

Thin fat core
Thick fibrous cap
less inflammation

can not modified by medication or life style modification

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 that involve the metabolism of the lipids	High carbohydrate intake
	Lipoprotein(a) abnormalities
Potentially modifiable (Controllable) it mean : it can be controlled by medications and lifestyle modifications	Hardened (trans)unsaturated fat intake
Hyperlipidemia	
Hypertension	Chlamydia pneumoniae infection
Cigarette smoking	
Diabetes	
C-reactive protein (inflammation)	

-Major / non-modifiable :

1-age

it is a complication of atherosclerosis

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

ischemic heart disease

2-Gender

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

-it was found that the pre-menopausal women if they don't have other associated risk factors [like hypertension/ hyperlipidemia/or diabetes] these women are relatively protected against atherosclerosis when they are compared with age matched men .

-After menopause the incidence of atherosclerosis will increase in women

- * 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

certain families are predisposed to have hypertension /DM /hyperlipidemia and all of this is considered major risk factors for atherosclerosis so this families are at higher risk to develop atherosclerosis

- e.g. HTN or DM

or :

2- well-defined genetic derangements in lipoprotein metabolism

- e.g. familial hypercholesterolemia

if a family is inheriting a certain well defined genetic abnormality regarding lipoprotein metabolism family members will develop higher risk to develop of atherosclerosis than the general population even if they don't have other risk factors and they are maintaining a healthy lifestyle

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