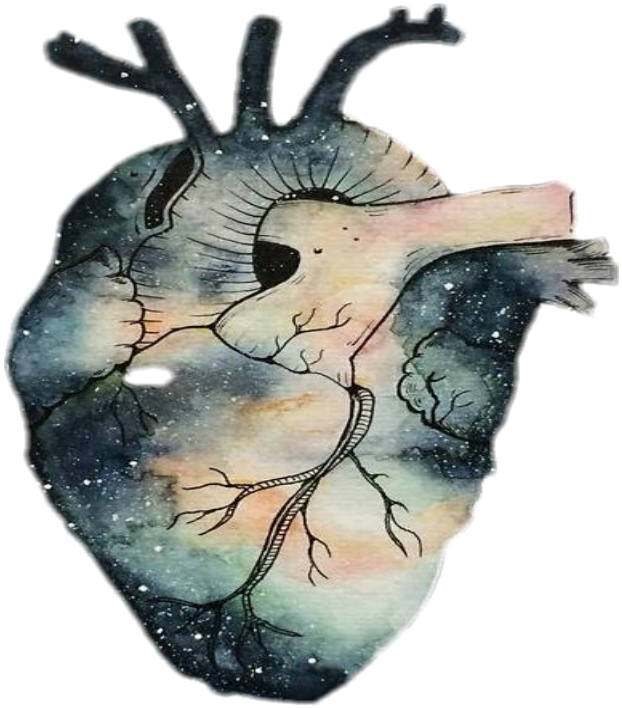
PATHOLOGY TEAM 436

MEDICINE
KING SAUD UNIVERSITY

Atherosclerosis



Revised by
شوق الأحمري & طراد الوكيل

Objectives:

1- Understand the pathogenesis and clinical consequences of atherosclerosis.

Key principles to be discussed:

1- Risk factors of atherosclerosis.
2- Pathogenesis of the fibrolipid atherosclerotic plaque.
3- Clinical complications of atherosclerosis.
4- Commonest sites for the clinically significant coronary atherosclerosis.

Black: Doctor's slides.

Red: important!

Green: Doctor's notes.

Grey: Extra.

Bold black: New terminology.

Purple: Female's slides.

Blue: Male's slides.

Normal Blood Vessels & Capillaries:

https://www.youtube.com/watch?v=MjC1-odNY5k

Arteries:

- **Large (elastic) arteries:** (E.g. aorta, common carotid, iliac). The media has lots of elastic fibers.
- **Medium (muscular) arteries:** (E.g. coronary, renal arteries). Most the media consist mostly of smooth muscle cells.
- **Small arteries/arterioles:** All the media here consist of smooth muscle cells, the size of lumen have effect on blood pressure control.

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 & Pass through nodes.

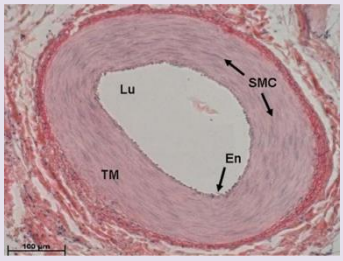
Endothelial cells:

- 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 is in direct contact with the blood/lymph and the cells circulating in it.
- Endothelial structural and functional integrity is fundamental[1] to the maintenance of vessel wall homeostasis and normal circulatory function.

[1] أساسي

Smooth muscle cells (SMC):

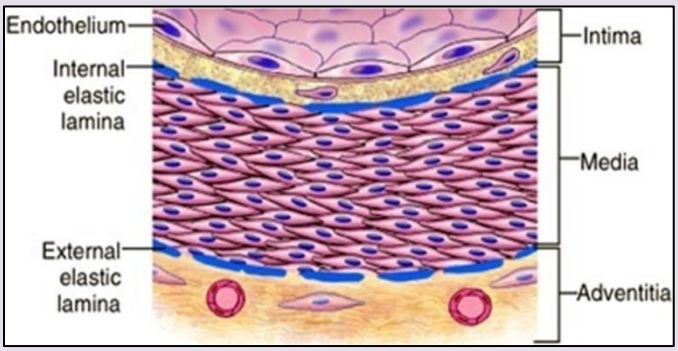
SMCs are present in the vascular media. They are also responsible for vasoconstriction and dilation in response to normal or pharmacologic stimuli. Smooth muscle cells participate in both normal vascular repair and pathologic processes such as atherosclerosis.



- Any vascular injury or dysfunction stimulates SMCs, on stimulation they:

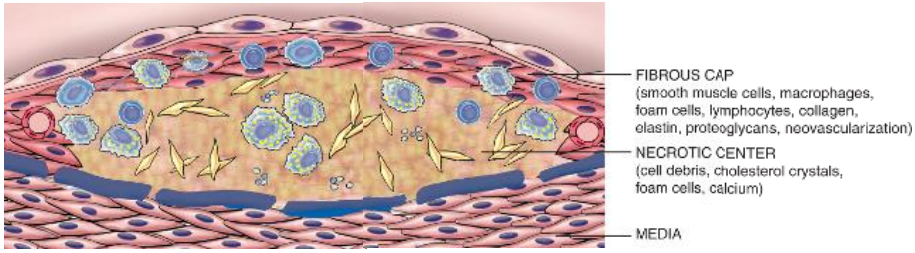
1. They migrate[2] from the media to the intima.
2. In the intima, they lose the capacity to contract and gain the capacity to divide. So they multiply/proliferate as intimal SMCs.
3. They synthesize collagen, elastin etc.. And deposit extracellular matrix (ECM).

Intima not supposed to have SMC.
When it has SMC they proliferate in it and thickened the wall of blood vessel.



AS ↓

Atherosclerosis (AS):



Atherosclerosis is characterized by intimal lesions called ***Atheroma / Atheromatous[3] / Fibrofatty*** plaques, which protrude[4] into and obstruct vascular lumens and weaken the underlying media.

They may lead to serious complications like ***Coronary artery disease (angina & MI[5])*** and ***Carotid atherosclerotic[6]*** disease (stroke).

The most heavily involved vessels are (common sites):
The Abdominal Aorta then, *the Coronary Arteries*, *The Popliteal Arteries*, *the Internal Carotid Arteries*, and The vessels of The Circle of Willis[7].

[2] تُهاجر
[3] Atheromatous plaques are raised lesions composed of soft grumous (thick, clotted) lipid cores (mainly 2 cholesterol and Cholesterol esters, with necrotic debris) covered by fibrous caps
[4] تبرُز
[5] Myocardial Infraction
[6] Blood supply to the brain
[5] Circle Supplies blood to the brain and surrounding structures. هي دائرة شرايين تزوّد الدماغ بالدم

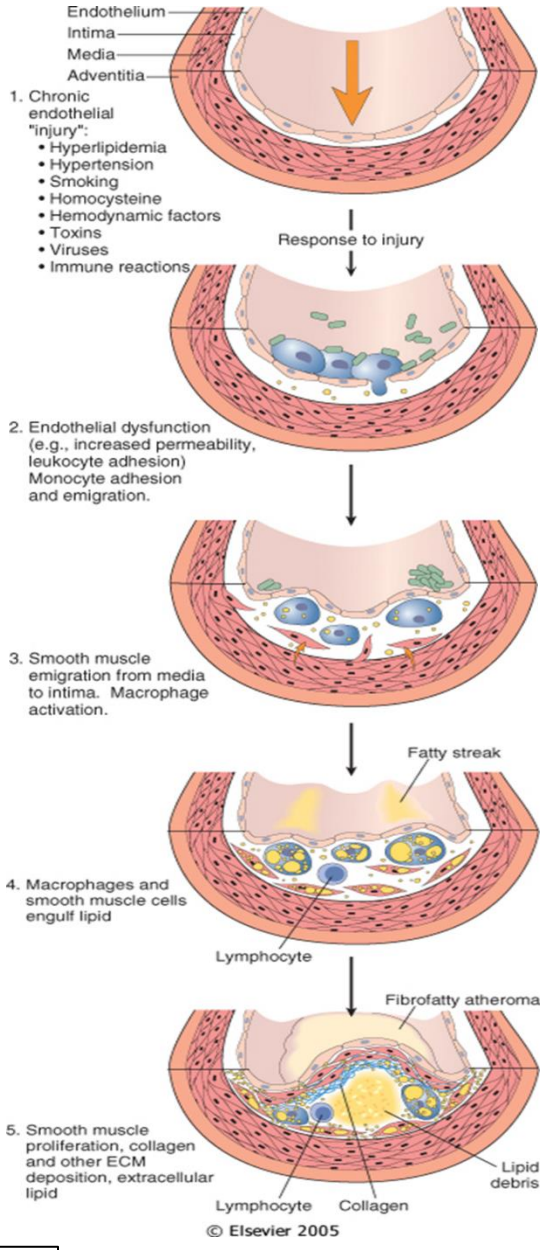
PATHOGENESIS: response to injury hypothesis

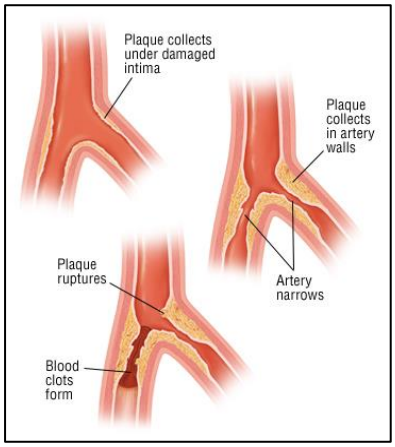
https://www.youtube.com/watch?v=R6QTiBfzULE

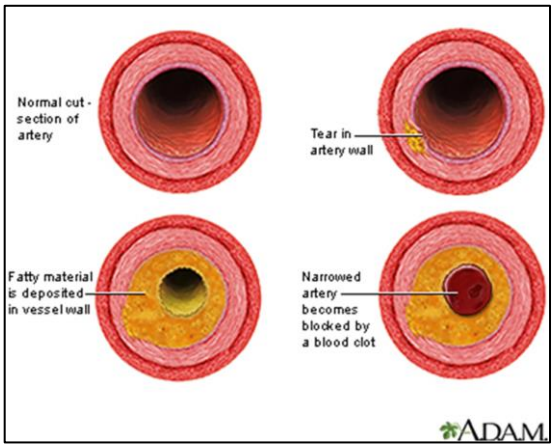
اتبعنا ترتيب روبنز هنا

Central to this hypothesis are the following:

- Subtle Chronic **endothelial injury** _and resultant endothelial dysfunction_ Leading to Increased permeability, leukocyte adhesion and thrombosis.
- **Accumulation of lipoproteins** (mainly LDL with its high cholesterol content) in the vessel wall.
- **Adhesion of platelets.**
- **Adhesion** of blood **monocytes** (and other leukocytes) **to the endothelium**, followed by migration of monocytes into the intima and transformation 'differentiation' into **macrophages** and **foam cells.**
- **Lipid accumulation** within macrophage, which release inflammatory cytokines.
- **Release** of **factors** from activated platelets, macrophages, or vascular cells that cause migration '**recruitment'** of **SMCs** from media into the intima
- **Proliferation of smooth muscle cells** in the intima, and elaboration of extracellular matrix **(ECM),** leading to the accumulation of collagen and proteoglycans
- Enhanced accumulation of lipids both within cells (macrophages and SMCs) and extracellularly.







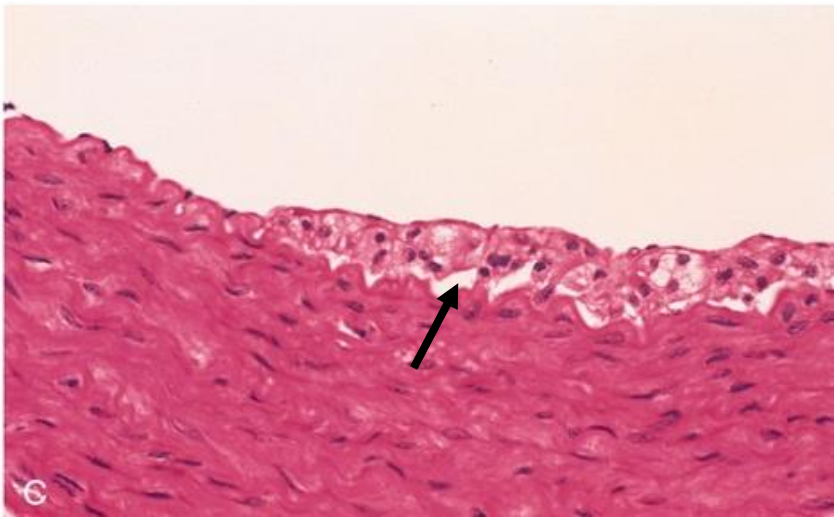
Morphology

Gross Morphology:

- ***Fatty streaks*** are the earliest lesion of atherosclerosis they are a collection of lipid laden **foam cells**[8] in the intima. They do not cause any disturbance in blood flow.

  Fatty streaks begin as multiple yellow, flat spots less than 1 mm in diameter that **coalesce**[9] into elongated streaks[10], 1 cm long or longer. They contain T lymphocytes and extracellular lipid in smaller amounts than in plaques.

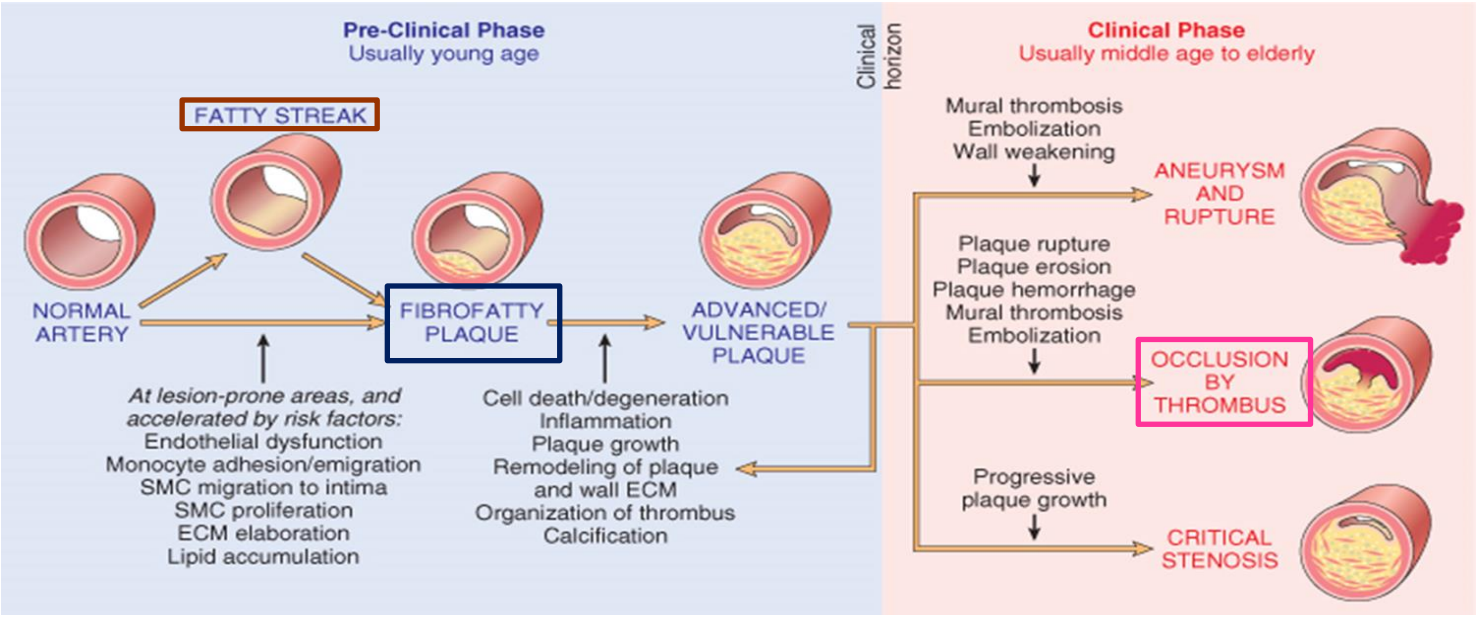
- **Atheromatous plaques**[11]: The key features in AS, it is intimal thickening + lipid accumulation. The atheromatous plaques impinge[12] on the lumen of the artery. They vary in size.
  Usually involve only a partial circumference[13] of the arterial wall ("**eccentric" lesions**)[14] and are patchy and variable along the vessel length.

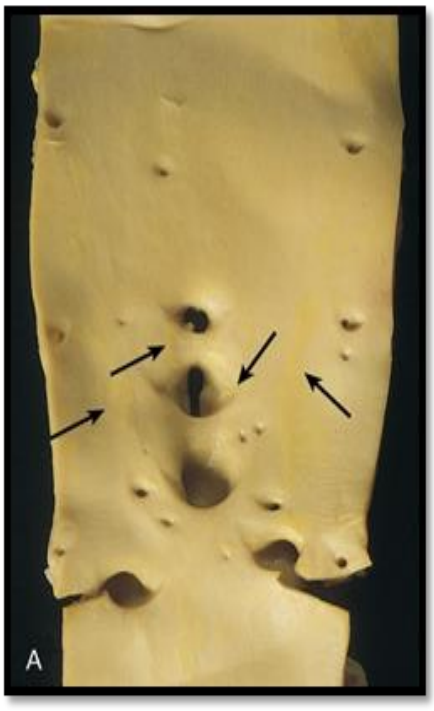


Photomicrograph of fatty streak in an experimental hypercholesterolemic rabbit, demonstrating intimal macrophage-derived foam cells (arrow).

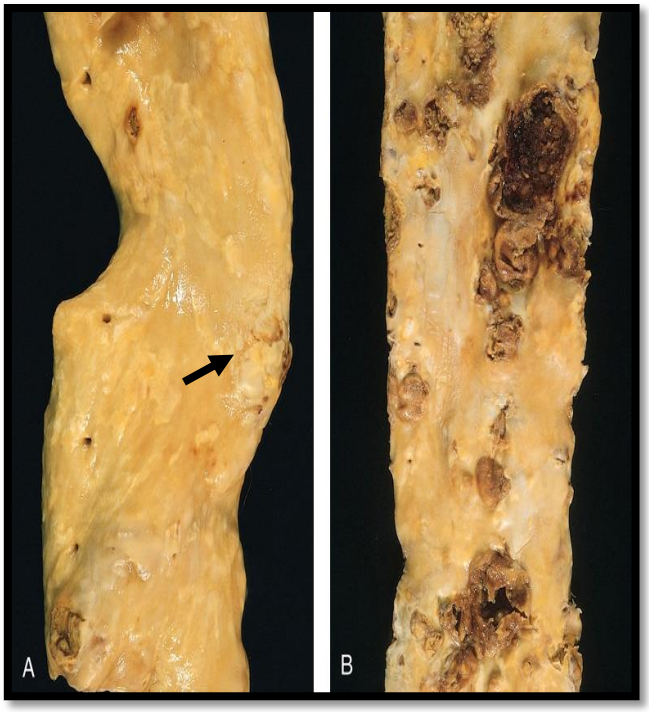
[8] خلايا رغوية مُحمّلة الدهون
[9] تلتئم أو تلتحم
[10] خيوط/شرائط
[11] ترسبات
[12] مصطدمة/تؤثر على
[13] محيط
[14] Strange pathological features 'not placed centrally or not having its axis' آفة غريبة الأطوار

Important





Aorta with fatty streaks[15] (arrows)



Fibrous plaques Complicated lesions

*إلى ما قبل 75% من الإنسداد يكون ما في أعراض.

[15] Macrophage-derived foam cells

Microscopic Morphology:

- **An atheroma** consists of a raised focal lesion in the intima, with a soft, yellow, grumous core of lipid (mainly cholesterol and cholesterol esters), covered by a firm, white fibrous cap.
- **Atherosclerotic plaques** have three principal components:

1. **Cells:** SMCs, macrophages, lymphocytes and foam cell.

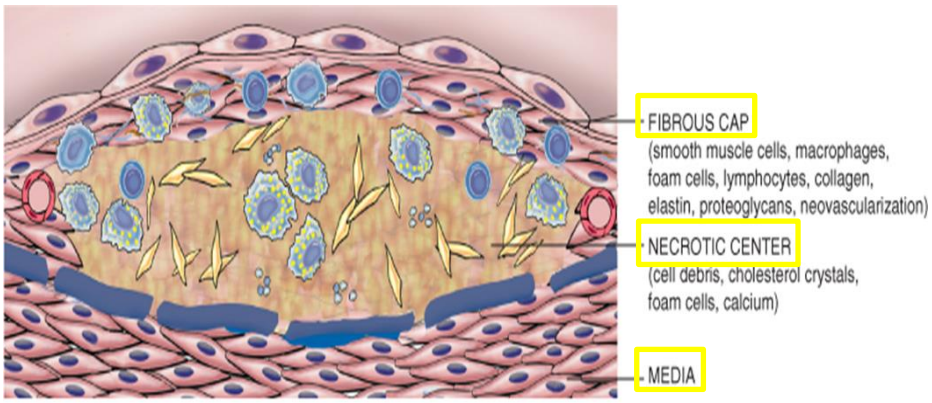
2. **Extracellular matrix:** including collagen, elastic fibers, and proteoglycans.

3. **Lipid:** Typical atheromas contain relatively abundant lipid both intracellular and extracellular lipid.

- **Foam cells**[16]**:** are large, lipid-laden macrophages derived from blood monocytes, but SMCs can also imbibe[17] lipid to become foam cells.

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 a lipid deposits (primarily cholesterol and cholesterol esters), cholesterol clefts, debris from dead cells, foam cells, fibrin.



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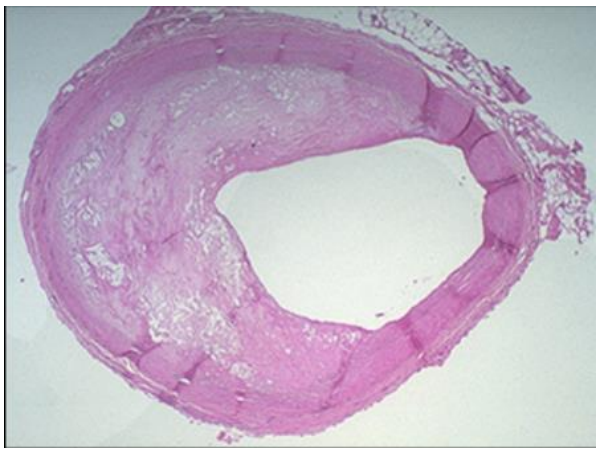


1. Eccentric lesion with a fibrous cap
2. Central lipid core with cholesterol clefts
3. The lumen is narrowed

[16] خلايا رغوية
[17] متشربة

Clinical complications of atherosclerosis

*Everything in **red** you should not skip it, it mentioned by the both **doctors***

The advanced lesion of AS[18] is at risk to developing these complications that have clinical significance:

1- **Focal rupture**, **ulceration**, or **erosion** of the luminal surface of the atheromatous plaques, which may induce thrombus formation,[19] or discharge of debris into the bloodstream, producing microemboli composed of lesion contents (cholesterol emboli or atheroemboli)[20].

2- **Hemorrhage** into a plaque (especially when atheroma[21] in the coronary arteries) due to the rupture of the overlying fibrous cap or the capillaries in the plaque. The hematoma may expand the plaque or induce plaque rupture.

3- Superimposed **thrombosis** (most serious complication), usually occurs on disrupted lesions (those with Rupture, ulceration, erosion, or hemorrhage) the thrombus can lead to partial or complete occlusion of the lumen. The thrombus can also (embolize)[22] .

4- **Wall weakening with aneurysmal[23] dilation**. Atheroma can induce atrophy of the underlying media, with loss of elastic tissue, causing weakness, aneurysm and potential rupture.

5- Calcification[24]: Atheromas often undergo calcification.

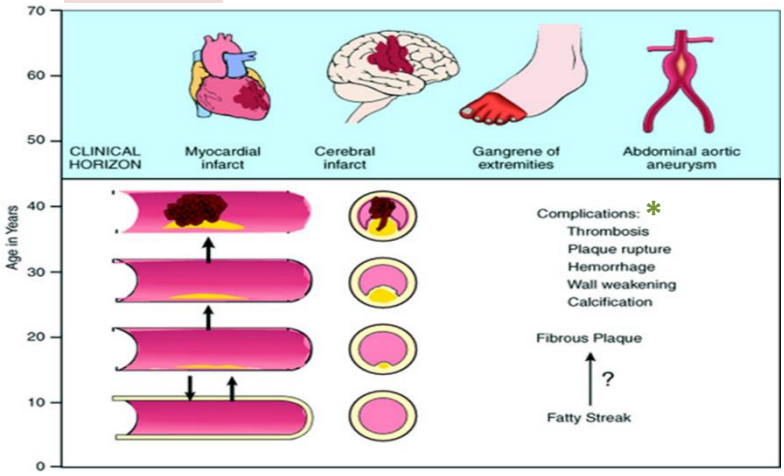
6- May lead to coronary artery disease (myocardial infraction and angina[25]), carotid atherosclerotic disease (stroke)[26], gangrenous extremities, renal ischemia, intermittent claudication[27] and cerebral infraction.

Natural history of atherosclerosis: not that important

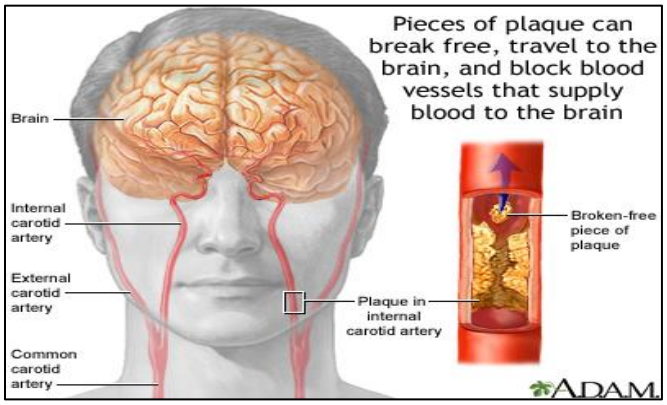
Plaques usually develop slowly and insidiously over many years, beginning in childhood or shortly thereafter. As described in the text, they may progress from a fatty streak to a fibrous plaque and then to a complicated plaque that is likely to lead to clinical effects.

Complications depend on the affected organ.

Important



[18] Atherosclerosis.
[19] The rupture of the plaques will discharge the components into the bloodstream which lead to thrombus formation 'blood clot'.
[20] They are the same.
[21] Is also known as atherosclerosis = deposit of fatty material on the inner wall of a vessel.
[22] Embolize means 'to cause embolism in the blood vessel' = to obstruct. انسداد للوعاء الدموي.
[23] Weakening and dilatation of blood vessels due to the atrophy with loss of elastic tissue.
[24] Accumulation of calcium salt in the wall of the blood vessels
[25] الذبحة الصدرية
[26] Occur when the oxygenated blood flow to the brain is stopped by plaque
[27] عَرَج متقطّع



Stroke / cerebrovascular accident.

*Because they don't have Estrogen. So, after menopause both males and females are at risk.

**(i) anti-C. pneumoniae antibodies. (ii) detection of the organism within atherosclerotic lesions.

Risk factor of atherosclerosis:

MAJOR RISK FACTORS (*Important*)
- NON-MODIFIABLE FACTORS
1. Increasing age
2. Male gender*
3. Family history
4. Genetic abnormalities
- POTENTIALLY MODIFIABLE FACTORS *It's more Important because we can change it*
1. Hyperlipidemia
2. Hypertension
3. Cigarette smoking
4. **Diabetes** أهم عامل

MINOR/ UNCERTAIN RISK FACTORS (*not important*)
Obesity
Physical inactivity
Stress ("type A" personality)
Postmenopausal estrogen deficiency
High carbohydrate intake
Alcohol
Lipoprotein Lp(a)
Hardened (trans) unsaturated fat intake
Chlamydia pneumonia**

Importance of lipoproteins in hyperlipidemia

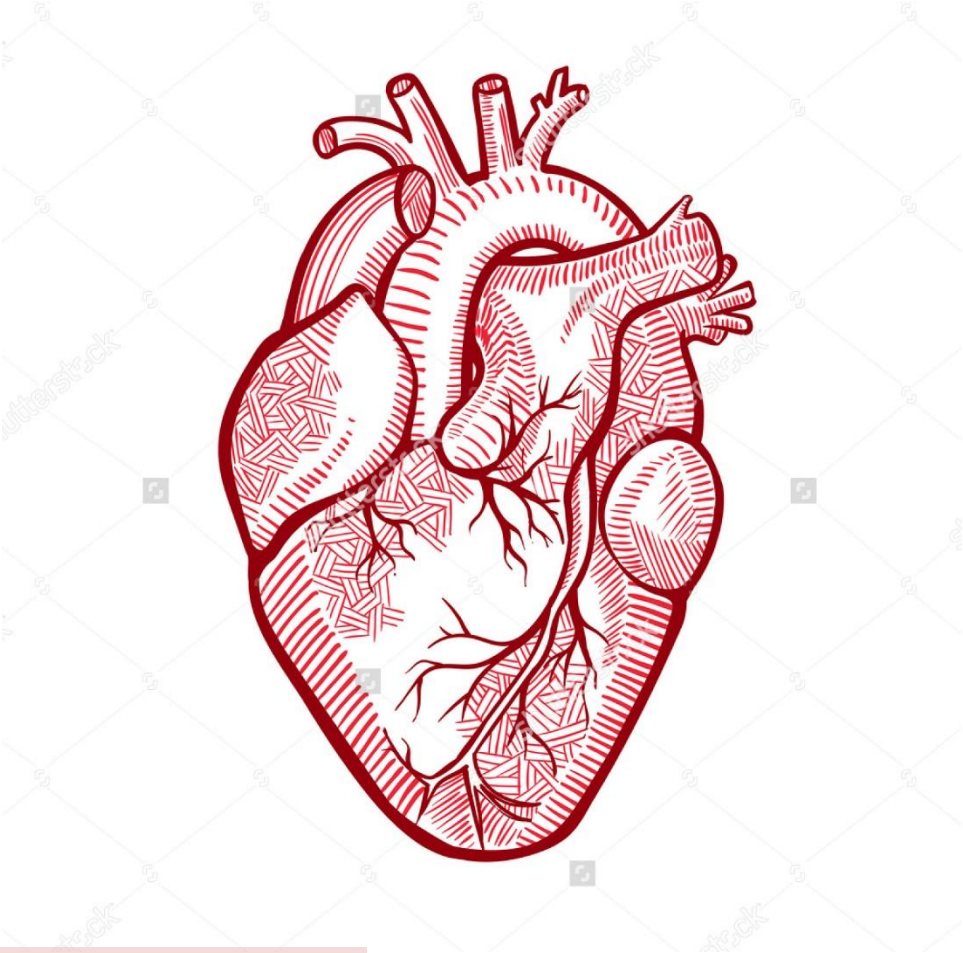
- Very low-density lipoproteins (VLDLs).
  - Is also considered to be a type of bad cholesterol and it promote atherosclerosis.
- High density lipoproteins (HDLs).
  - Is known as "good" cholesterol, because high levels of HDL protects against heart attack. Low levels of HDL also increase the risk of heart disease. HDLs help to reverse the effects of high cholesterol.
- Low density lipoproteins (LDLs).
  - When too much LDL (bad) cholesterol circulates in the blood, it promotes atherosclerosis and therefore contributes to heart disease.
- Chylomicrons
  - Also promote atherosclerosis

Treatment:

Angioplasty.

مو مطلوب منكم أي تريتمنت

"اللهم لا سهل إلا ما جعلته سهلًا و أنت تجعل الحزن إذا شئت سهلًا"



MCQs

Editing File

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