Cardio-Vascular System

4

Pathology

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00:00

In this lecture we will be talking about one of the diseases that affect arteries; ***arteriosclerosis.***

Quick revision of the histology of blood vessels and the major difference between arteries and veins histologically:

We all know that the normal blood vessel is composed of **three layers:** tunica intima (innermost), tunica media and tunica adventitia (outermost), and the difference between arteries and veins is in terms of **the thickness of the wall;** arteries have a **thicker wall** than that of the veins mainly due to the second layer which is **tunica media;** it contains smooth muscle fibers and is needed for the elasticity and contractility of the artery—that is; it's so essential for the function of the artery which needs good contractility DESPITE the high intraluminal pressure. This contractility is not needed in veins (that's why we usually see veins as "collapsed" adjacent to arteries). Notice figure (1).

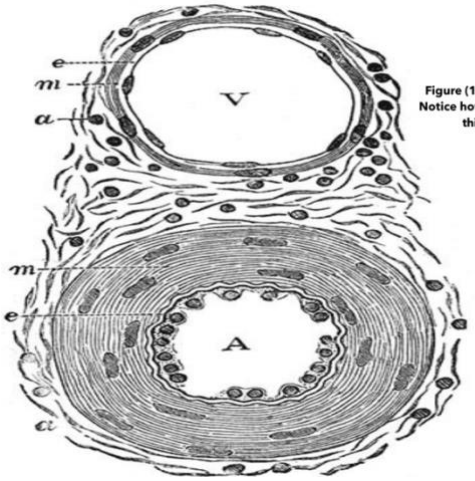


Figure (1): Artery vs. Vein
Notice how the artery has a thicker wall.

Arteriosclerosis:

Arterio = artery, sclerosis = hardening and thickening. **Arteriosclerosis is arterial wall thickening and loss of elasticity.**

There are actually three patterns of arteriosclerosis, each with different pathological and clinical consequences:

1- Arterio**lo**sclerosis.
2- Mönckeberg Medial Calcific Sclerosis (MCS).
3- Atherosclerosis.

The first pattern: Arteriolosclerosis **(pay attention to the extra 2 letters)**

This condition affects very small arteries and arterioles. It's associated with hypertension and/or DM. Notice figure (2).

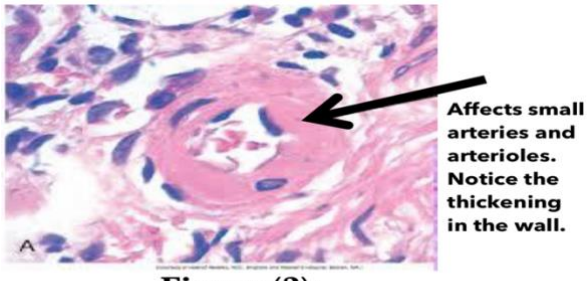


Figure (2): Arteriolosclerosis.

The second pattern: Mönckeberg Medial Calcific Sclerosis

Affects muscular arteries: the presence of calcific deposits in muscular arteries and these calcific deposits are visible radiographically (x-ray and other imaging studies). This process is a degenerative process that might be associated with aging, so it's seen in people of age > 50 years. If it affects subcutaneous vessels, then these vessels will be palpable.

This condition, if isolated and not associated with any other pathology in the artery (i.e. there's no evidence of any other problem like atherosclerosis), would not affect the vessel lumen (no effect on the diameter) thus would not be clinically significant.

Notice figures (3) and (4).

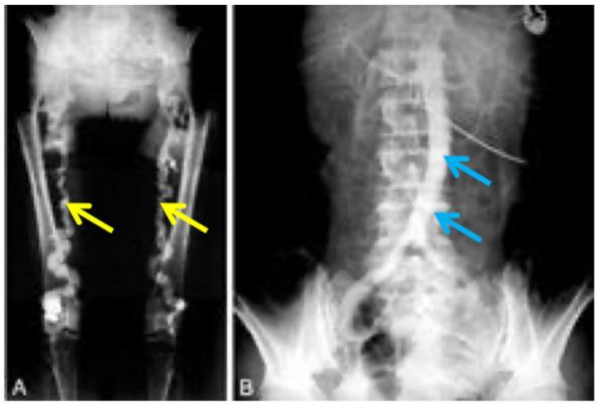


Figure (3): calcifications visible on x-ray and another imaging study

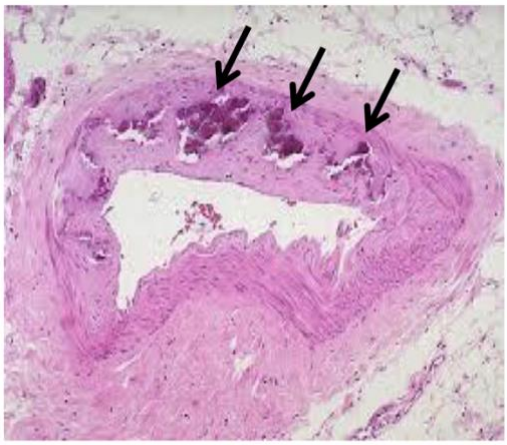


Figure (4): LM Deposits (purple) within the media

The third pattern: Atherosclerosis

Atherosclerosis is the most important and frequently encountered pattern of arteriosclerosis. Athero = gruel (Greek) = hardening.

This condition affects the intima of arteries, it's characterised by intimal lesions (atheromas) = (atherosclerotic plaque) thus it has a significant impact on the luminal diameter. An **atheromatous plaque or atheroma** is a raised lesion that contains **lipids**, mainly cholesterol and cholesterol esters. These lipids are covered by a firm white fibrous cap.

Pathogenesis:

The pathogenesis of atherosclerosis has been extensively studied yet is not fully understood, but it's said that two events happen inside the blood vessel: **inflammation** and **deposition of cholesterol (LDL particles)**.

It's quite important to understand that **inflammatory processes** in the endothelial cells of the vascular wall that are associated with **retained (deposited) LDL particles** will have an impact on the formation of atheroma and then the progression of atherosclerosis.

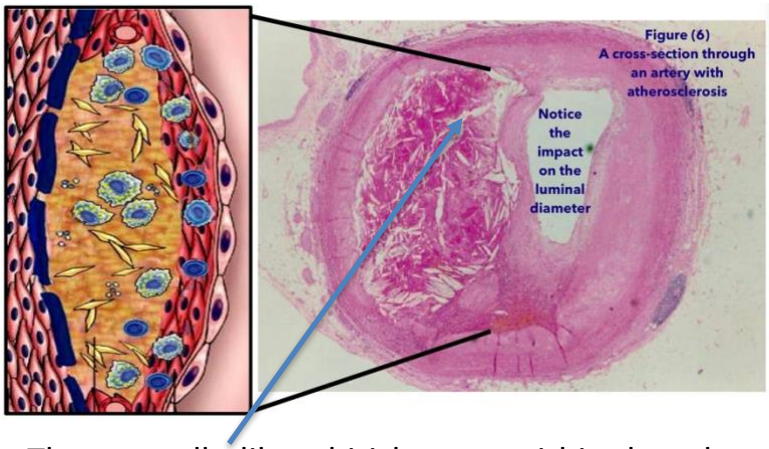
Now arises the question:

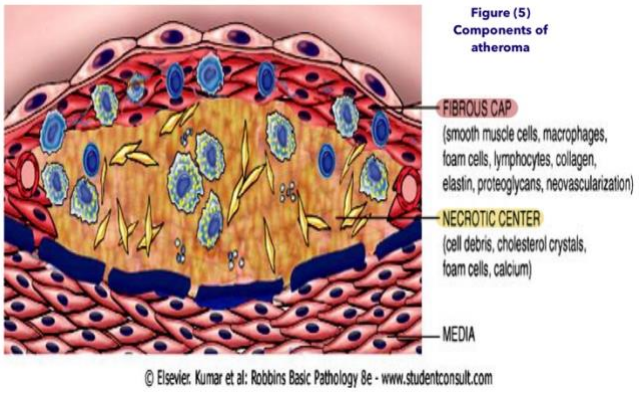
What are the major components of a well-developed intimal atheromatous plaque?

We agreed that the hallmark of atherosclerosis is atheromatous plaque (atheroma). The atheromatous plaque is of two components:

- **Fibrous cap**: composed of proteins (collagen, elastin, proteoglycans), certain types of cells (smooth muscle cells, macrophages, lymphocytes, foam cells) and neovascularisation (formation of new blood vessels for perfusion).
- **Necrotic centre**: contains cholesterol crystals (LDL) with some debris, calcium and foam cells.

Notice figures (5) and (6)



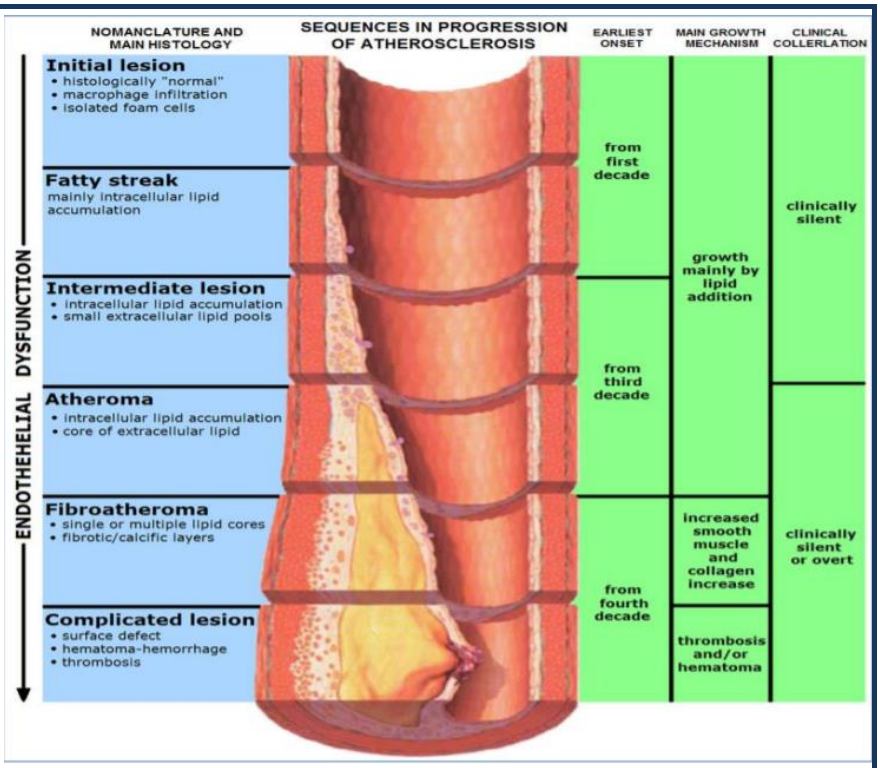


These needle-like whitish areas within the atheroma represent the **necrotic centre.**

These lesions in the intima (plaque) are endothelial injuries (activation), and these injuries are attributed to a multitude of factors like smoking, hypertension, toxins, immune reactions, *hyperlipidaemia*, homocysteine and viruses. **This event (activation) then leads to a cascade of inflammatory responses inside the wall of the artery** (smooth muscle recruitment, macrophage activation, production of ECM proteins). In addition, **the presence of deposited LDL particles within the intima maintains the inflammatory process which eventually leads to more and more macrophages and smooth muscle recruitment and engulfment of lipid leads to lipid debris formation within the atheroma.**

-Let's focus the light on something:

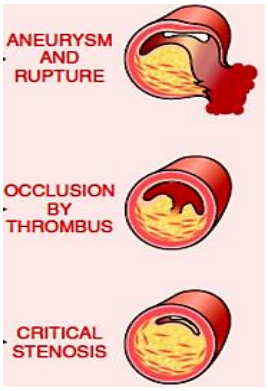
Atherosclerosis doesn't happen overnight. This condition requires many years to have the significant impact it has on the arterial luminal diameter. In fact, the pathological lesion of atherosclerosis (atheroma) develops around the 3rd decade of life. So, the clinical complications and the sequence of events that develop later in the wall of the artery will also develop later in life; in the 4th or 5th decade.



Progression ***10:00***

The clinical phase of atherosclerosis is usually seen in middle life, this is related to progression and potential complications that develop in the wall of the artery. These complications include:

- Aneurysm formation and possible rupture of the artery.
- Occlusion by a superimposed thrombus which will lead to complete obstruction of the lumen.
- Critical stenosis meaning that atherosclerosis is developing more and more and the atheromatous lesion is now increasing in size until a very small area is left of the lumen.



What determines which atheroma will have complications? What determines the rate at which complications occur?

Many factors play a role in this. The answer is: ***the concept of vulnerable vs stable plaque.*** ***Vulnerable plaque*** (i.e. vulnerable to develop complications and progression of atherosclerosis).

In this concept, the constituents of the plaque itself will determine the effect. Check figure (7)

- Plaques that have a **thin fat core, a thick fibrous cap and less inflammation** are said to be relatively **STABLE.**
- Plaques that have a **thick fat core, a thin fibrous cap and more inflammation** are said to be **VULNERABLE.**

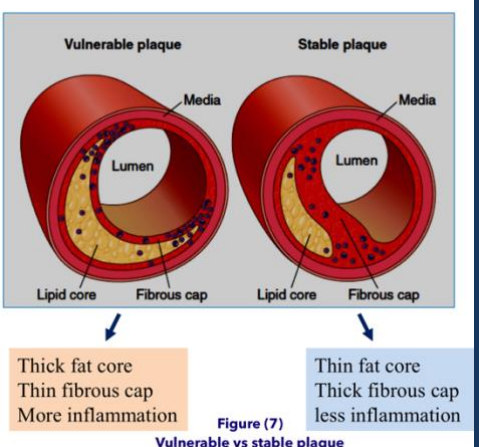


Figure (7)
Vulnerable vs stable plaque

Risk factors:

Risk factors of atherosclerosis are classified into:

- Major risk factors, which are further subdivided into:
  - Potentially modifiable (controllable) risk factors: can be controlled by medications and lifestyle modifications.
  - Non-modifiable (non-controllable) risk factors: cannot be controlled by medications and lifestyle modifications.

- Lesser, Uncertain or Non-quantitated risk factors.

  Check figure (8) for the detailed risk factors.

Figure (8) 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** (Hormonal)
Genetic abnormalities (Mainly in lipid metabolism)	**High carbohydrate intake**
	Lipoprotein abnormalities
Potentially modifiable (Controllable)	**Hardened (trans)unsaturated fat intake**
Hyperlipidemia	
Hypertension	**Chlamydia pneumoniae infection**
Cigarette smoking	
Diabetes	
C-reactive protein (inflammation)	

A closer look at the major non-modifiable risk factors:

1. **Age: ages 40-60 the incidence of *MI* as a complication of atherosclerosis increases 5x in men and the death rates from *ischaemic heart disease* -*which is the major complication of atherosclerosis- increase with each decade.***

2. **Gender:**
   a. **premenopausal women (that don't have other associated risk factors like DM, hyperlipidaemia or hypertension) are protected against atherosclerosis compared to men of the same age. (these women have high estrogen).**
   b. **postmenopausal women the incidence of atherosclerosis and platelet diseases increases. (low estrogen)**

3. **Familial predisposition to atherosclerosis is multifactorial:**
   - **Familial clustering of certain risk factors—certain families are predisposed to HTN, DM or hyperlipidaemia (all these are considered major risk factors to develop atherosclerosis).**
   - **Familial well-defined genetic derangements in lipoprotein metabolism like familial hypercholesterolaemia. (they have increased risk for atherosclerosis even without having any other risk factors).**

A closer look at the lesser, uncertain risk factors:

20% of cardiovascular events are said to happen without identifiable risk factors. These could be related somehow to the less quantitated or less certain risk factors like:

- **Metabolic problems** (hyperhomocysteinaemia, lipoprotein A metabolism, metabolic syndrome).
- **Factors affecting haemostasis** (high levels of procoagulants and clonal haematopoiesis).
- **Lack of exercise, obesity, high carbohydrate intake and competitive stressful lifestyle ("type A" personality) also contribute as risk factors to atherosclerosis.**

"Have some fire. Be unstoppable."

Good luck