PATHOLOGY TEAM

Done by ,

Khoulod Al-Amari

Ala’a almulhem

ATHEROSCLEROSIS

INTRODUCTION

Normal Blood Vessels (anatomy)

Large (elastic) arteries • **aorta, common carotid, iliac** • **lots of elastic fibers** • **pulsatile** **Medium (muscular) arteries** • **coronary, renal arteries** • **mostly smooth muscle cells** **Small arteries/arterioles** • **all smooth muscle cells** • **blood pressure controlled here**	**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, checking for infection**

Main components of the vascular wall:

ENDOTHELIAL CELLS

single cell-thick, continuous lining of the entire cardiovascular system, collectively called the *endothelium.* Endothelial structural and functional integrity is fundamental to the maintenance of vessel wall homeostasis and normal circulatory function.

Smooth muscle cells (SMCs)

- SMCs are predominant cellular element of the vascular media.
- SMCs are responsible for vasoconstriction and dilation in response to normal or pharmacologic stimuli.
- SMCs are important elements of both normal vascular repair and pathologic processes such as atherosclerosis

In cases of vascular injury/dysfunction the SMCs are stimulated. So they:

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

Arteriosclerosis: literally means "hardening of the arteries". It is a term for thickening and loss of elasticity of arterial walls. Three patterns are recognized:

1)Atherosclerosis, the most frequent and important pattern.

2)Mönckeberg medial calcific sclerosis is characterized by calcific deposits in muscular arteries in older people.

3)Arteriolosclerosis affects small arteries and arterioles. Are of two types, hyaline and hyperplastic, both cause thickening of vessel walls with luminal narrowing and may cause ischemic injury. Is seen with hypertension and diabetes mellitus.

Atherosclerosis:

Atherosclerosis is characterized by intimal lesions called *atheromas*, or *atheromatous or fibrofatty plaques*, which protrude into and obstruct vascular lumens and weaken the underlying media. They may lead to serious complications like Coronary artery disease (MI) and Carotid atherosclerotic disease (stroke).

> **NOTE**: *Fatty streaks are harmless , they're normaly formed in our body .. and ..* lipid-filled foam cells are derived from both macrophages and smooth muscle cells which have accumulated low density lipoproteins ..

Atherosclerosis: Morphology

Fatty streaks are the earliest lesion of atherosclerosis. They are composed of lipid-filled foam cells. They are not significantly raised and thus do not cause any disturbance in blood flow. Fatty streaks begin as multiple yellow, flat spots less than 1 mm in diameter that coalesce into elongated streaks, 1 cm long or longer. They contain T lymphocytes and extracellular lipid in smaller amounts than in plaques.

The key processes in atherosclerosis are intimal thickening and lipid accumulation. An atheroma or atheromatous plaque consists of a raised focal lesion initiating within the intima, having a soft, yellow, grumous core of lipid (mainly cholesterol and cholesterol esters), covered by a firm, white fibrous cap.

The atheromatous plaques appear white to whitish yellow and impinge on the lumen of the artery. They vary in size from approximately 0.3 to 1.5 cm in diameter but sometimes coalesce to form larger masses. Atherosclerotic lesions usually involve only a partial circumference of the arterial wall ("eccentric" lesions) and are patchy and variable along the vessel length. The most heavily involved vessels are the abdominal aorta then coronary arteries, the popliteal arteries, the internal carotid arteries, and the vessels of the circle of Willis.

NOTE: the accumulation of the lipoprotein in the intima comes in one side of

Atherosclerotic plaques have three principal components:

(1) cells, including SMCs, macrophages, and other leukocytes
(2) ECM, including collagen, elastic fibers, and proteoglycans
(3) intracellular and extracellular lipid . These components occur in varying proportions.

Typically, the superficial fibrous cap is composed of SMCs and relatively dense ECM. Beneath and to the side of the cap (the "shoulder") is a cellular area consisting of macrophages, SMCs, and T lymphocytes.

Deep to the fibrous cap is a necrotic core, containing a disorganized mass of lipid (primarily cholesterol and cholesterol esters), cholesterol clefts, debris from dead cells, foam cells, fibrin, variably organized thrombus, and other plasma proteins.

Foam cells are large, lipid-laden macrophages derived from blood monocytes, but SMCs can also imbibe lipid to become foam cells. Typical atheromas contain relatively abundant lipid.

Around the periphery of the lesions, there is usually evidence of neovascularization (proliferating small blood vessels).

COMPLICATIONS: The **advanced lesion** of atherosclerosis is at risk for the following pathological changes that have clinical significance:

1) Focal **rupture, ulceration**, or **erosion** of the luminal surface of atheromatous plaques may result in exposure of highly thrombogenic substances that induce thrombus formation or discharge of debris into the bloodstream, producing microemboli composed of lesion contents **(cholesterol emboli or atheroemboli)**. **NOTE : it comes cuz of weakness of the wall**

2) **Hemorrhage** into a plaque (especially when atheroma in the coronary arteries) may be initiated by rupture of either the overlying fibrous cap or the thin-walled capillaries that vascularize the plaque. A contained hematoma may expand the plaque or induce plaque rupture **NOTE: after the rupture the blood will go out and will be interstitial hemorrhage**

3)Superimposed **thrombosis**, the most feared complication, usually occurs on disrupted lesions (those with rupture, ulceration, erosion, or hemorrhage) and may partially or completely occlude the lumen.

4) **Wall weakening with aneurysmal dilation.** Atheroma can induced atrophy of the underlying media, with loss of elastic tissue, causing weakness, aneurysm and potential rupture

5) **Calcifications:** Atheromas often undergo **calcification**. **<< very important .**

Atherosclerosis: Major Risk Factors

Non-modifiable	**Potentially modifiable**
1. **Increasing age** **Gender (Male hve high risk factor than women cause women have estrogen Harmon that protect them . But in the Menopause women the chances being the same)** 2. **Family history** 3. **Genetic abnormalities**	1. Hyperlipidemia 2. Hypertension (3. Cigarette smoking 4. Diabetes 5. C-reactive protein level

Atherosclerosis: Lesser, Uncertain, or Nonquantitated risk factors

1. Obesity
2. Physical inactivity
3. Stress ("type A" personality)
4. Postmenopausal estrogen deficiency
5. High carbohydrate intake
6. Alcohol
7. Lipoprotein Lp(a)
8. Hardened (trans)unsaturated fat intake
9. *Chlamydia pneumonia*

Types of lipoproteins

1. Low-density lipoproteins (LDLs): When too much LDL (bad) cholesterol circulates in the blood, it promotes atheroma formation in the arteries.LDLs contribute to heart disease because they carry large amounts of cholesterol.
2. Very-low-density lipoproteins (VLDLs): is also considered to be a type of bad cholesterol because it helps cholesterol build up on the walls of arteries
3. Chylomicrons also promote atherosclerosis.
4. High-density lipoproteins (HDLs): is known as "good" cholesterol, because high levels of HDL seem to protect against heart attack. Low levels of HDL also increase the risk of heart disease. HDLs help to reverse the effects of high cholesterol by collecting cholesterol from other lipoproteins and transporting it to places where it can be utilized by the cells

PATHOGENESIS of atherosclerosis: response to injury hypothesis

This is the response to injury hypothesis, and it considers atherosclerosis to be a chronic inflammatory response of the arterial wall initiated by injury to the endothelium. Central to this thesis are the following:

1. Accumulation of *lipoproteins*, mainly LDL, with its high cholesterol content, in the vessel wall
2. *Chronic endothelial injury*, usually subtle, increased permeability, leukocyte adhesion, and thrombotic potential.
3. Adhesion of *blood monocytes* (and other leukocytes) to the endothelium, followed by their migration into the intima and their transformation into *macrophages* and *foam cells*
4. Adhesion of *platelets*
5. Release of factors from activated platelets, macrophages, or vascular cells that cause *migration of SMCs* from media into the intima
6. Proliferation of smooth muscle cells in the intima, and elaboration of extracellular matrix, leading to the accumulation of collagen and proteoglycans
7. *Enhanced accumulation of lipids* both within cells (macrophages and SMCs) and extracellularly.