PATHOGENESIS OF Atherosclerosis

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**DEFINITION**

*Atherosclerosis* (which is a specific type of arteriosclerosis) is a common and chronic vascular disease, it's a progressive process that may start from childhood, characterized by subintimal deposits of yellowish plaques (cholesterol) in large and medium-sized arteries, that will result in the hardening & narrowing of these arteries.
Note: veins don’t develop atheroma.
RISK FACTORS

- high levels of LDL “bad cholesterol”.
- high blood pressure (hypertension).
- Smoking.
- Diabetes.
- genetic family history of atherosclerotic diseases.
- also it has been found that men more prone than females.
The anatomic lesions of atherosclerosis usually begin in some children younger than one year old, which start first as lipid spots then lipid streaks and end up with atheroma formation. The accumulation of lipid deposits is between the intima “endothelium lining” and the media “smooth muscle layer”. Although the initial lesions of atherosclerosis have been termed “fatty streaks”, they are not actually composed of fat cells, but composed of accumulations of WBC, especially macrophages, that have taken up oxidized low-density lipoprotein (LDL) which will then be called foam cells.
LDL passes through endothelium of blood vessel and lodges in the intima (due to injury, High BP, smoking)
Oxidized LDL causes the release of MCP (monocyte chemoattractant proteins) from Endothelial and SM cells - these attract monocytes to move into the intima.
Oxidized LDL also causes monocytes to differentiate into macrophages which will release cytokines (INF-alpha, IL-1) that result in the expression of adhesion molecules (P-selectin, VCAM-1) on the endothelial cells to allow more monocytes to move into the cell.
Oxidized LDL

Also cause the release of the growth factor M-CSF (macrophage colony stimulating factor) which will causes the expression of the scavenger receptor on the macrophage - which then takes up oxidized (modified) LDL to form a foam cell.
Foam cells release cytokines that cause smooth muscle cell proliferation to form the fibrous cap of atheroma.
Unstable fibrous plaques can rupture and thrombosis occurs when the platelets try to fix the rupture.
ATHEROSCLEROSIS DEVELOPMENT

Diagram showing the normal artery wall with layers labeled:
- Intima
- Media
- Adventitia

Diagram of the human circulatory system with the heart and major blood vessels.
A fatty streak develops between the intima and the media.
ATHEROSCLEROSIS DEVELOPMENT

Stable Plaque

Thick fibrous shell
An unstable plaque develops with a fatty core and thin fibrous outer shell.
Plaque can sometimes rupture into the bloodstream.
Thrombosis is the clotting of blood which begins at the site of the plaque rupture.
As the blood clot gets larger, the amount of blood flowing by it decreases.
CLINICAL MANIFESTATIONS

- Coronary heart diseases.
- Cerebrovascular diseases.
- Peripheral vascular diseases.
- Visceral ischemia.
HDL ROLE IN ATHEROSCLEROSIS

As we know HDL (high density lipoprotein) is the good cholesterol in our body and it has a protective role against atherosclerosis as shown in the following:

1) HDL inhibits oxidation of LDL.
2) HDL promotes cholesterol efflux from foam cell.
3) HDL inhibits adhesion molecule expression.
WILD HEARTS CAN'T BE BROKEN
THANKS FOR LISTENING