L12 Atherosclerosis

Atherosclerosis is a chronic inflammatory, fibro-proliferate disease of the artery wall. Its associated with, and possible initiated by the accumulation and oxidation of circulating lipids, in particular cholesterol, in the artery wall.

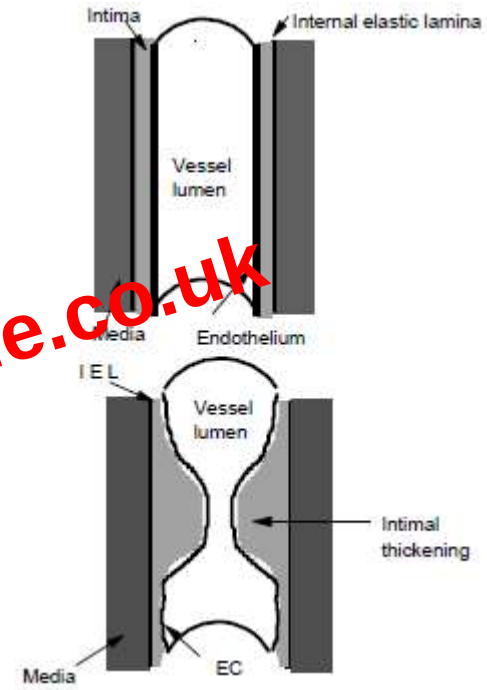
Primary atherosclerosis: as above take decades to develop symptoms
Transplant atherosclerosis: narrowing of arteries at the point of engraftment of transplant organs. Take months - years to develop symptoms
Restenosis: after cardiopulmonary bypass. Months-years to develop symptoms

Atherosclerosis distribution is not systemic. Its limited to specific areas medium-large arteries (at branching points and bifurcations). This is due to haemodynamic:

- Some flow is laminar = fine
- At bifurcations the blood hits the wall = complex patterns of flow (can get back flow and points of stasis at some points of cardiac cycle). Turbulent flow. These areas have low shear stress. Endothelial cells sense shear stress = they know where they are and what phenotype they should be. But where there is pulsating flow the cells present another phenotype

Atheroma mainly develops in the intima. As you age naturally you get a thickening of the artery wall (some of it due to initma thickening – not pathological)

If the plaque is big enough it can protrude into the media layer.



Cellular pathology of atherosclerosis

- Lots of immune cells
    - Infiltration of T cells and monocytes
    - Monocytes differentiate in to macrophages which take up cholesterol (LDL or oxidised LDL) and become foam cells (full of cholesterol ester)
    - Foam cells Drives the inflammatory response.
    - Smooth muscle cells become migratory and move into plaque and become secretory smooth muscle cells - secrete matrix proteins and pro-inflammatory cytokines.

Development of Atherosclerotic plaque

1. Fatty Streak – made up of infiltrating LDL (inflammatory stimulus) → attracts monocytes (→ foam cells) and T cells to try and remove LDL.
    a. DON'T STICK OUT LUMEN – NOT STENOTIC
2. Intermediate of Fibrofatty lesion – a connective tissue matrix (collagen fibrils, elastic, fibres, and proteoglycans)
    a. Still have inflammatory cells but also have smooth muscle cells (invaded intima) and produce matrix.
    b. STENOSIS – arteries begin to narrow
3. Advanced fibrous plaque
    a. Could cause symptomatic disease – angina
    b. Lots of foam cells and some T cells
    c. A necrotic core – accumulation of free cholesterol (foam cells die by necrosis and dump all their contents)
    d. Fibrous cap – stops it from degrading from the forces of blood flow
        i. Thick cap = stable plaque (resists blood flow, low probability of rupture) - Safer
            1. Not many active inflammatory cells, low lipid content.
        ii. Vunerable plaque – thinner cap (especially around shoulders)
            1. Very active inflammatory response, leukocytes may be make proteases that break down the plaque. High lipid and inflammatory cell content
4. Embolic mural events associated with advanced fibrous plaque