Unit IV – Problem 3 – Pathology: Atherosclerosis

- **Atherosclerosis is characterized by presence of intimal lesions called atheromas in: large elastic arteries + large and medium-sized muscular arteries.**
- **Because coronary artery disease is an important manifestation of atherosclerosis especially among developed countries.**
- **Risk factors for atherosclerosis:**

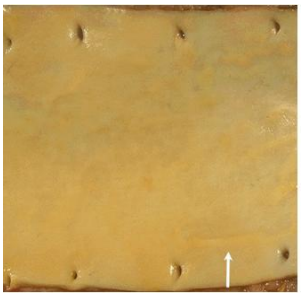
Non-modifiable	Modifiable
Genetics: family history is the most important independent risk factor for atherosclerosis (e.g., familial hypercholesterolemia)	**Hyperlipidemia**: the main cholesterol component associated with increased risk is low-density lipoproteins (LDL) cholesterol (bad cholesterol)
Age: middle age or later	**Diabetes mellitus**: it is associated with raised circulating cholesterol levels and markedly increases the risk of atherosclerosis
Gender: premenopausal women are relatively protected against atherosclerosis (and its consequences) compared with age-matched men	**Hypertension**
	Cigarette smoking.

Note: additional risk factors include the following:

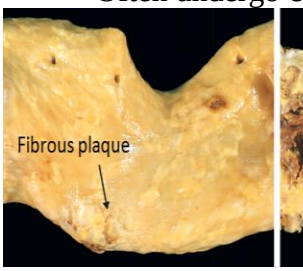
- Inflammation: inflammatory cells are present during all stages of atheromatous plaque formation and are intimately linked with plaque progression and rupture.
- CRP levels: an acute-phase reactant which is synthesized primarily by the liver in response to a variety of inflammatory cytokines. CRP levels strongly and independently predict the risk of myocardial infarction, stroke, peripheral arterial disease, and sudden cardiac death.
- Lipoprotein(a) levels: lipoprotein(a) is an LDL-like particle that contains apolipoprotein B-100 linked to apolipoprotein A. lipoprotein(a) levels are correlated with coronary and cerebrovascular disease risk.
- Metabolic syndrome.

- **Pathogenesis of atherosclerosis:**
  - **Response-to-injury hypothesis:**
    - ✓ Atherosclerosis is a chronic inflammatory response of the arterial wall to endothelial injury.
    - ✓ There will be interaction of modified lipoproteins (oxidized LDL), monocyte-derived macrophages, T lymphocytes & cellular constituents of the arterial wall.
  - **Atherosclerosis results from the following pathogenic events (see image in next page):**
    1. Endothelial injury & dysfunction.
    2. Accumulation of lipoproteins in the vessel wall (oxidized LDL)
    3. Platelet adhesion.
    4. Monocyte adhesion & differentiation into macrophages.
    5. Lipid accumulation within macrophages (foam cells).
    6. Smooth muscle cell recruitment.
    7. Smooth muscle cell proliferation and extracellular matrix production (collagen).

- **Morphology of atherosclerosis:**
  - **Common sites of atherosclerosis**: descending thoracic aorta, internal carotid artery, coronary arteries, abdominal aorta & the popliteal vein.
  - **Fatty Streaks:**
    - ✓ Begin as small yellow, flat macules that coalesce (يتكتَّل) into elongated lesions (1.5 cm).
    - ✓ Composed of lipid-filled foamy macrophages.
    - ✓ Present in all children > 10 years (normal).
    - ✓ Relationship to atherosclerotic plaques is uncertain.



  - **Atherosclerotic Plaque:**
    - ✓ White to yellow raised lesions (0.3-1.5 cm in diameter).
    - ✓ Can coalesce to form larger masses.
    - ✓ Composed of:
      - ❖ *A fibrous cap containing*: smooth muscle cells, macrophages and T cells and extracellular matrix (including collagen, elastic fibers and proteoglycans).
      - ❖ *A necrotic center containing*: cell debris, cholesterol crystals, foam cells and calcium.
    - ✓ Often undergo calcification.



- **What is the fate of an atherosclerotic plaque?**
  - Formation of an **aneurysm** which has a high risk to rupture.
  - Occlusion of the artery by a **thrombus** (in addition to the atherosclerotic plaque)
  - Progressive **plaque growth** with critical stenosis (narrowing) of the artery.