- **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:**

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

**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.
    5. Lipid accumulation within macrophages (foam cells).
    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 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.