ARTERIOSCLEROSIS

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Normal blood vessels
A = artery
V = vein
Artery (A) versus vein (V)
Arteriosclerosis = "hardening of the arteries"

- arterial wall thickening and loss of elasticity.
- Three patterns are recognized, with different clinical and pathologic consequences:
1-Arteriolosclerosis

- affects small arteries and arterioles
- associated with hypertension and/or diabetes mellitus
Mönckeberg medial calcific sclerosis

- calcific deposits in muscular arteries
- typically in persons > age 50
- radiographically visible (x-rays, etc...)
- palpable vessels
- do not encroach on vessel lumen and are usually not clinically significant
2-Mönckeberg medial calcific sclerosis
• Greek word "gruel," "hardening,"

• most frequent and clinically important pattern of arteriosclerosis

• characterized by intimal lesions = *atheromas* (a.k.a. *atherosclerotic plaques*)

• atheromatous plaque = raised lesion with a core of lipid (cholesterol and cholesterol esters) covered by a firm, white fibrous cap
Atherosclerosis- Pathogenesis

• not fully understood

• ? inflammatory process in endothelial cells of vessel wall associated with retained low-density lipoprotein (LDL) particles → ? a cause, an effect, or both, of underlying inflammatory process
The major components of a well-developed intimal atheromatous plaque
Atheromatous plaque
Formation of atheromatous plaque

1. Chronic endothelial "injury":
   - Hyperlipidemia
   - Hypertension
   - Smoking
   - Homocysteine
   - Hemodynamic factors
   - Toxins
   - Viruses
   - Immune reactions

Response to injury

2. Endothelial dysfunction (e.g., increased permeability, leukocyte adhesion), monocyte adhesion and emigration

3. Macrophage activation, smooth muscle recruitment
Formation of atheromatous plaque

4. Macrophages and smooth muscle cells engulf lipid

Fatty streak

Lymphocyte

5. Smooth muscle proliferation, collagen and other ECM deposition, extracellular lipid

Fibrofatty atheroma

Lipid debris

Lymphocyte

Collagen
NOMENCLATURE AND MAIN HISTOLOGY

Initial lesion
- histologically "normal"
- macrophage infiltration
- isolated foam cells

Fatty streak
mainly intracellular lipid accumulation

Intermediate lesion
- intracellular lipid accumulation
- small extracellular lipid pools

Atheroma
- intracellular lipid accumulation
- core of extracellular lipid

Fibroatheroma
- single or multiple lipid cores
- fibrotic/calcific layers

Complicated lesion
- surface defect
- hematoma-hemorrhage
- thrombosis

SEQUENCES IN PROGRESSION OF ATHEROSCLEROSIS

EARLIEST ONSET
- from first decade
- from third decade
- from fourth decade

MAIN GROWTH MECHANISM
- growth mainly by lipid addition
- increased smooth muscle and collagen increase
- thrombosis and/or hematoma

CLINICAL COLLERATION
- clinically silent
- clinically silent or overt
Atherosclerosis: progression

Clinical Phase
Usually middle age to elderly

- Mural thrombosis
- Embolization
- Wall weakening

- Plaque rupture
- Plaque erosion
- Plaque hemorrhage
- Mural thrombosis
- Embolization

- Aneurysm and rupture

- Occlusion by thrombus

- Progressive plaque growth

- Critical stenosis
Vulnerable vs stable plaque

Vulnerable plaque
- Thick fat core
- Thin fibrous cap
- More inflammation

Stable plaque
- Thin fat core
- Thick fibrous cap
- Less inflammation
## Risk Factors for Atherosclerosis

<table>
<thead>
<tr>
<th>Major Risks</th>
<th>Lesser, Uncertain, or Non-quantitated Risks</th>
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<tbody>
<tr>
<td>Non-modifiable (non-controllable)</td>
<td>Obesity</td>
</tr>
<tr>
<td>Increasing age</td>
<td>Physical inactivity</td>
</tr>
<tr>
<td>Male gender</td>
<td>Stress (&quot;type A personality)</td>
</tr>
<tr>
<td>Family history</td>
<td>Postmenopausal estrogen deficiency</td>
</tr>
<tr>
<td>Genetic abnormalities</td>
<td>High carbohydrate intake</td>
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<tr>
<td></td>
<td>Lipoprotein(a)</td>
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<tr>
<td>Potentially modifiable (Controllable)</td>
<td>Hardened (trans)unsaturated fat intake</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Chlamydia pneumoniae infection</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Cigarette smoking</td>
<td></td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>C-reactive protein (inflammation)</td>
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</table>
1-age

- ages 40 to 60, incidence of MI in men increases 5 x
- Death rates from IHD rise with each decade

2-Gender

- Premenopausal* → protected against atherosclerosis compared with age-matched men.
- After menopause → incidence of atherosclerosis-related diseases increases

* unless they are otherwise predisposed by diabetes, hyperlipidemia, or severe hypertension.
3-Genetics

• familial predisposition is multifactorial.
• Either:
  1- **familial clustering** of other risk factors
     - e.g. HTN or DM
  or:
  2- **well-defined genetic derangements in lipoprotein metabolism**
     - e.g. **familial hypercholesterolemia**
Additional Risk Factors for atherosclerosis

- 20% of cardiovascular events occur in the absence of identifiable risk factors:
  - Hyperhomocystinemia
  - Metabolic syndrome
  - Lipoprotein a levels
  - Factors Affecting Hemostasis (Elevated levels of procoagulants; Clonal hematopoiesis)
  - Others:
    - lack of exercise
    - competitive, stressful lifestyle ("type A" personality)
    - obesity
    - High carbohydrate intake