Atherosclerosis

Atherosclerotic Cardiovascular Disease (ASCVD)

Pathogenesis of atherosclerosis
Normal Artery Structure

Lipoprotein particle

Apoprotein
Phospholipids
TG and CE
Cholesterol
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Figure 335-1. The density and size-distribution of the major classes of lipoprotein particles. Lipoproteins are classified by density and size, which are inversely related.
### Arteriosclerosis

**Arteriosclerosis** (Hardening of the arteries)

**Arterial wall thickening + loss of elasticity**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Characteristics</th>
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| Monckeberg medial calcific sclerosis | - Age 50  
- Radiologic calcif.  
- Lumen intact  
- Clinically insignif.               |
| Arteriolosclerosis               | - small arteries/arterioles  
- hyaline type / hyperplastic  
- hypertension / diabetes          |
| Atherosclerosis                  | - aorta & branches + coronary arteries  
- ASCVD causes 38% of all deaths in N. America |
**ATHEROSCLEROSIS:**
response-to-injury model

Atherosclerosis is a chronic inflammatory response of the arterial wall to endothelial injury.

1. Chronic endothelial injury
2. Accumulation of lipoproteins (LDL mainly)
3. Monocyte adhesion to endothelium
4. Platelet adhesion
5. Factors released $\rightarrow$ SMC recruitment
6. SMC proliferation and ECM production
7. Lipid accumulation: extracellular/mac-SMC

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**Risk Factors for Atherosclerosis**

- Hyperlipidemia
- Smoking
- Hypertension
- Turbulence
- Genetics
Endothelial injury

Early non-denuding endothelial dysfunction

Chronic—repetitive injury

-cig. smoke toxins
-homocysteine
-?? Infectious agents
-cytokines → genes for

1. Hemodynamic disturbances (turbulence)
2. Hypercholesterolemia
3. Inflammation
Endothelial injury

Chronic—repetitive injury

Early non-denuding endothelial dysfunction

- Cigarette smoke toxins
- Homocysteine
- ?? Infectious agents

IEM

Smooth muscle proliferation:
- Proliferative & synthetic phenotype in intimal SMC's (vs. SMC in media)
- Growth factors: PDGF, FGF, TGFβ

1. Hemodynamic disturbances (turbulence)
2. Hypercholesterolemia
3. Inflammation

Pathogenic sequence of atherosclerotic lesions
Normal aorta

Fatty streak

Atheromatous plaque (fibrofatty plaque)

Complicated plaque
Fatty Streaks

Atheromatous plaque (fibrofatty atheroma; plaque; atheroma)
Complicated plaque: ulcerated/thrombus

Aneurysm
Thrombus in aneurysm

Atherosclerosis: Vessel involvement: desc. order

1. abdominal aorta
2. coronary arteries
3. popliteal arteries
4. internal carotid arteries
5. circle of Willis vessels
Development of the smooth muscle cap

1. Migration of smooth muscle cells to the intima
2. Smooth muscle cell mitosis
3. Elaboration of extracellular matrix

Atherosclerostic Plaque Structure

FIBROUS CAP (smooth muscle cells, macrophages, foam cells, lymphocytes, elastin, proteoglycans, neovascularization)

NECROTIC CENTER (cell debris, cholesterol crystals, foam cells, calcium)

MEDIA
Figure 10-7

Hypertension, Hypothyroidism, Smoking, Tobacco, Hemodynamic factors, Immune reactions, Viruses

- Endothelial Injury/Dysfunction
- Monocyte adhesion and migration into intima
- Migration of smooth muscle cell precursors
- Cholesterol efflux via HDL
- Extracellular matrix synthesis
- Proliferation of smooth muscle cells
- Extracellular lipids and necrotic cells
- Migration of smooth muscle cells

Normal vessel → Progressive development of atherosclerotic plaque
Natural history of atherosclerosis

Atherosclerosis (AS): Summary

1. AS is an intima-based lesion with a fibrous cap and atheromatous (gruel-like) core
2. Constituents: SMC's, ECM, inflammm., lipid, necrotic debris
3. Endothelial injury + inflammation drive AS: risk factors influence EC dysfunction, SMC recruitment and activation
4. AS plaque complications: rupture—thrombosis—hemorrhage—embolization
5. Rx: risk factor recognition + reduction