Atherosclerosis

Atherosclerotic Cardiovascular Disease (ASCVD)

Pathogenesis of atherosclerosis

Normal Artery Structure

Lipoprotein particle

FIGURE 335-1 The density and size-distribution of the major classes of lipoproteins in plasma. Lipoproteins are classified by density and size, which are inversely related.

EM: Negative staining

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The cholesterol in LDL accounts for approx. 70% of the plasma cholesterol.

**Arteriosclerosis**

(Hardening of the arteries)

- Arterial wall thickening + loss of elasticity
- Monckeberg medial calcific sclerosis
  - Age 50
  - > Radiologic calcific.
  - > Lumen intact
  - > Clinically insignificant.
- Arteriolosclerosis
- Atherosclerosis
  - Hyaline type
  - Hyperplastic
- 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 → SMC recruitment
6. SMC proliferation and ECM production
7. Lipid accumulation: extracellular/mac-SMC

**Risk Factors for Atherosclerosis**

- Hyperlipidemia
- Smoking
- Hypertension
- Turbulence
- Genetics

**Endothelial injury**

Early non-denuiding endothelial dysfunction

- Cig. smoke toxins
- Homocysteine
- ?? Infectious agents
- Cytokines → genes for

**Endothelial injury**

Chronic—repetitive injury

1. Hemodynamic disturbances (turbulence)
2. Hypercholesterolemia
3. Inflammation
Pathogenic sequence of atherosclerotic lesions

Normal aorta
  ↓
Fatty streak
  ↓
Atheromatous plaque (fibrofatty plaque)
  ↓
Complicated plaque
Complicated plaque: ulcerated/thrombus

Aneurysm

Thrombus in aneurysm

ATHEROSCLEROSIS: Vessel involvement: desc. order

5 circle of Willis vessels

4 internal carotid a’s

2 Cor. A’s

1 abd. aorta

3 popliteal a’s

ATHEROSCLEROSIS: 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

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Atherosclerostic Plaque Structure

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Atherosclerosis (AS): Summary

1. AS is an intima-based lesion with a fibrous cap and atheromatous (gruel-like) core
2. Constituents: SMC's, ECM, inflamm., 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