ARTERIOSCLEROSIS

• Hardening of arteries due to thickening and loss of elasticity.
• The three types of arteriosclerosis are:
  1) Atherosclerosis (AS): #1 Killer, CVS disease
  2) Monckeberg’s arteriosclerosis – Medial calcification, >50 yrs of age
  3) Arteriolosclerosis: associated with hypertension.

Atherosclerosis (AS):

• slow progressive disease of large and medium sized muscular and large elastic arteries
• characterized by an elevated fibro fatty intimal plaques formed by lipid deposition, smooth muscle proliferation and synthesis of extra cellular matrix.
• It begins in childhood and manifests in middle and later life
• Risk Factors: Major – Non Modifiable: age, male gender, family history
• Potentially controllable: Hyperlipidemia, hypertension, cig.smoking & D.Mellitus (deadly quartet)
• Minor – obesity, ↓ HDL, Physical inactivity, stress, post menopause, High carbohydrate diet, alcohol, homocysteine, lipoprotein (a), chlamydial infection etc.

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**Etio-Pathogenesis**

• Hypotheses:
  • 1) Insudation hypothesis (Virchow)
  • 2) Encrustation hypothesis (Rokitansky)
  • 3) Monoclonal hypothesis (Benditt)
  • 4) Reaction to injury hypothesis (Ross).
Reaction to Injury

Chronic endothelial injury
Hyperlipid, HTN, smoking, DM, Hemodyn, Homocyst, Toxins etc

Endothelial Dysfunction
IL, TNF, GF’s, Metaloprot, Adh mol,

SMC emigration & Macrophage activation → Chronically inflammatory disease

SMC proliferation, Lipid, collagen & ECM deposition – Well formed plaque

HTN
Hemodynamic stress

Toxins cig smoke

↑ LDL

PTL adh

Damage to endo

PDGF

Diff. Plasma Prot

Oxidation LDL

Uptake

Mig Mono

Foam cells

Collagen Syn

Cytokine release

Prolif. SMC
Morphology of an Atheroma

- fibro fatty or fibro lipid plaque (Atheroma)
- abdominal aorta and at branching points of major blood vessels.
- Gross: They appear as raised / elevated pale yellow intimal lesions. Usually multifocal and range from small oval to large irregular coalesced lesions.
• Microscopic findings: 1. Fibrous cap - Located between the lumen and tunica media. It is composed of proliferating smooth muscle cells, Leukocytes & Dense connective tissue matrix
• 2. Central necrotic core: Contains dead cells, lipid, cholesterol clefts, foamy macrophages, plasma proteins and smooth muscle cells.
3. Periphery consists of proliferating capillaries.
Two common variants of plaque

- Fatty streaks
- Complicated plaques
• **Clinical significance**: Asymptomatic for decades. Progression of disease or complication of AS leads to:
  
a) Insidious, progressive narrowing of vascular lumen resulting in ischemic atrophy/gangrene of tissue/organ affected.

b) Plaque rupture & superimposed thrombosis results in sudden occlusion and ischemic necrosis/infarction as in MI & stroke.
• c) Atheroembolism: Rupture and release of core of the plaque.
• d) Aneurysm: weakening of the wall.

• Organs often affected by AS are heart, brain, kidney, lower extremities and intestines
• Is Atherosclerosis reversible?
• Vaccine for AS?

**Aneurysms**

• A true aneurysm is a localized, permanent, abnormal dilatation of a blood vessel caused by weakness of the vessel wall
• (> 50% of normal diameter)
• False (pseudo) aneurysm or pulsating hematoma is an extra vascular hematoma that communicates with the intravascular space. This usually follows an injury.
• Aneurysms can be classified by their location/ name of the vessel, configuration / morphology & etiology

• **Morphologic classification:**
  • 1. Fusiform:
  • 2. Saccular:
  • 3. Cylindrical:
  • 4. Berry:
  • 5. Dissecting hematoma
  • 6. A-V aneurysm

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**Aneurysms classified by etiology**

• **Atherosclerotic Aneurysm:** They are commonly located in abdominal aorta between renal and common iliac vessels. They may also be seen in descending thoracic aorta.
• Etiology: Atherosclerotic weakening of the wall
• Morphology – Gross: They are fusiform or saccular. Wall shows complicated plaques with mural thrombus.
• Micro: Features of a complicated plaque.
• Clinical Features: >50yrs of age, Males, Associated with Hypertension. Presents with abdominal pain, pulsatile abdominal mass. Lesions >5 cms diameter is at risk of rupture and fatal hemorrhage.
**Syphilitic (Luetic) aneurysm**

- tertiary stage of syphilis.
- Aneurysm is seen in the ascending and arch of the aorta. It can extend proximally resulting in aortic valve ring dilatation, rolling of leaflets and valvular insufficiency. This condition is associated with marked LVH (Cor bovinum).
Fundamental lesion: Syphilitic aortitis due to obliteratorative endarteritis of the vasa vasorum.

**Morphology:** Gross- Fusiform aneurysm and intima shows “Tree barking“ appearance

**Micro:** Loss of elastic fibres, smooth muscle cells due to aortic medial ischemia and weakening of the wall. Blood vessels (vasa vasorum) show perivascular lympho-plasmacytic cuffing.
Dissecting Aneurysm (Aortic dissection)

- characterized by dissection of blood along the laminar planes of the aortic media with formation of intramural blood filled channel
- men between 40 to 60yrs
- strongly associated with hypertension
- Other predisposing factors are Copper deficiency, Marfan’s Syndrome in young men, Aortopathy, pregnancy, Bicuspid valve, iatrogenic
- cystic medial degeneration of the aorta.

- **Morphology**: Gross-
  1. Intimal tear within 10cms of aortic valve ring is the portal of entry of blood. Some times it could result from bleeding vasa vasorum.
  2. Dissection occurs between middle and outer thirds in the media and it extends into major vessels of the neck, coronaries etc
  3. Outer wall is thin and can rupture into extra vascular space- pericardium, mediastinum, and pleural and abdominal cavity.
• 4. 5-10% of cases dissection ruptures back into the lumen distally and is termed as double-barreled aorta.
• 5. Aortic dissection may be classified as
  • More common ascending and descending aorta (type I), Proximal lesion involving ascending aorta (type II) or Type A
  • Distal lesion distal to origin of subclavian vessel is type III or ‘B’

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• **Micro:** Aortic dissection associated with hypertension shows non-specific degenerative changes, elastic fragmentation and collection of excess amorphous interstitial material. In Marfans syndrome cystic medial necrosis is typical of the lesion.

**C/F:** Acute onset of severe tearing chest pain mimicking MI. Loss of peripheral pulses, Aortic insufficiency, fatal hemorrhage and cardiac tamponade.
• **Berry Aneurysm**: Small aneurysms seen at the branching points in Circle of Willis. These are due to defect in muscular wall replaced by thin fibrous tissue. Rupture leads to subarachnoid hemorrhage.

• **Mycotic aneurysm (Infective)**: Seen in association with bacterial endocarditis. Bacterial/fungal infection of arterial wall with tendency to rupture and hemorrhage.