Atherosclerosis

Def - Thickening & hardening of large & medium sized arteries - 2° due to involvement of tunica media & is characterized by fibrofatty plaque or atheromas.

m/c affected = Aorta, the coronary & the cerebral arterial system.

↓

Stroke

Others :- PVD, aneurysmal dilatation due to weakened arterial wall, chronic ischemic heart ds, ischemic encephalopathy & mesenteric arterial occlusion.

Etiology

I) MAJOR RISK FACTORS

Modifiable	Contributional
1) Dyslipidemia & AS & IHD	1.) Age
2) HTN	2.) Sex
3) DM	3) Genetic factors
4) Smoking	4.) Familial & racial factors

II. Emerging risk factors :-

1.) Environmental influences
2.) Obesity
3.) Hormones - Oestrogen def, OCP
4.) Physical inactivity
5.) Stressful life - Type A behaviour
6.) Homocystinuria
7.) Role of alcohol
8.) Prothrombotic factors - Thrombi
9.) Infections (C. pneumoniae, Herpes, CMV)
10.) High CRP

Total cholesterol < 200.
HDL > 50mg/dL LDL < 100mg/dL
VLDL < 150mg/dL

- Familial hypercholesterolemia - Autosomal codominant disorder - mutation in LDL receptor.

Pathogenesis

① Response to injury hypothesis :-

i) ENDOTHELIAL INJURY :

mech. trauma, hemodynamic forces, immunological & chemical mech, metabolic agents such as chronic dyslipidemia, homocystinemia, circulating toxins from systemic inf, hypoxia, radiation, CO & tobacco products.

2 major :- hemodynamic stress (HTN)
chronic dyslipidemia

(ii) Intimal SMOOTH muscle proliferation

Endothelial injury :- adherence, agg, & platelet release at the site of subendothelial connective tissue & infiltration of inflammatory cells.

• Proliferation of intimal smooth muscle cells & production of ECM ⊕ by IL-1 & TNF α. (by macrophages & activated platelet)

↓ ⊕

PDGF & FGF

↓

prolif & migration of SMC from media to intima.

Activated T lymphocytes ⊕→ synth of collagen

(iii) Role of blood monocytes :-

Plasma LDL on entry into intima ⇒ oxidation.

For monocytes = oxidised LDL, ~~attract, prolif.~~ immobilize & activate them + taken by scavenger receptor ⟶ lipid laden foam cell.

Endothelium :- Oxidised LDL is cytotoxic.

Death of foam cell by apoptosis release lipid to form lipid core of plaque.

(iv) Role of dyslipidemia –

LDL ⊕ foamcell

HDL ⟶ anti atherogenic

(v) Thrombosis – endothelial injury → platelet agg → thrombus becomes part of plaque.

(2) Morphological types / Morphologic features

(1) Fatty streaks & dots

↓ foam cells + lipid containing SMC + lymphoid cells

↓ lumen

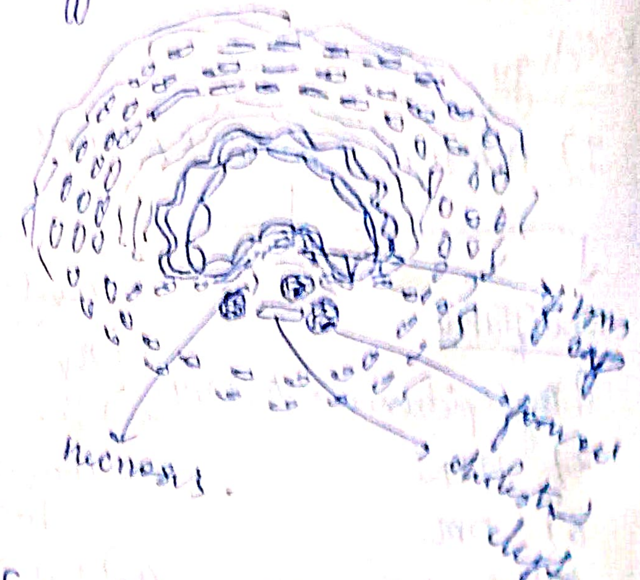
(2) Gelatinous lesion

↓

Round or oval, circumscribed grey elevations about less the diameter.

(3) Atheromatous plaques

⇒ most severely affected Abdominal aorta



FC :- SMC + CT + ECM – Proteoglycans + collagen.

cellular area – monocytes, foam cells, necrotic debris, lipid laden foam cell.

deeper central soft core – Extracellular lipid material, cholesterol clefts, fibrin, necrotic debris, lipid laden foam cell.

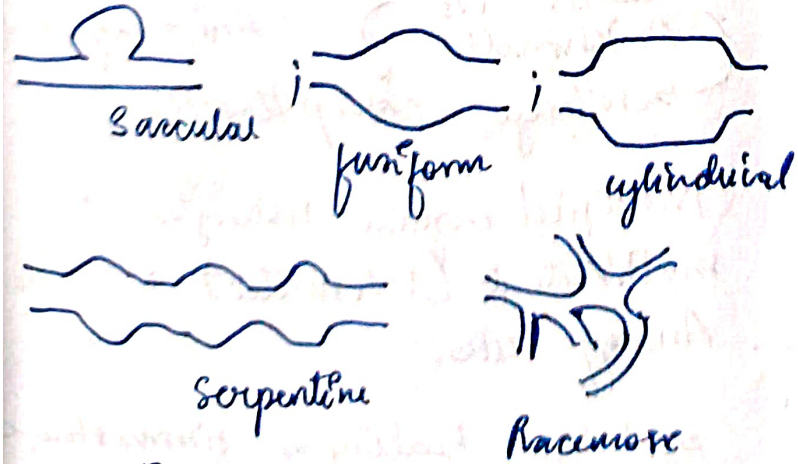
(4) Complicated Plaques :-

i) Calcification
ii) Ulceration
iii) Thrombosis
iv) Hemorrhage
v) aneurysm formation

Aneurysm - permanent abnormal dilatation of vessel wall due to congenital or acquired weakening & destruction of vessel wall.

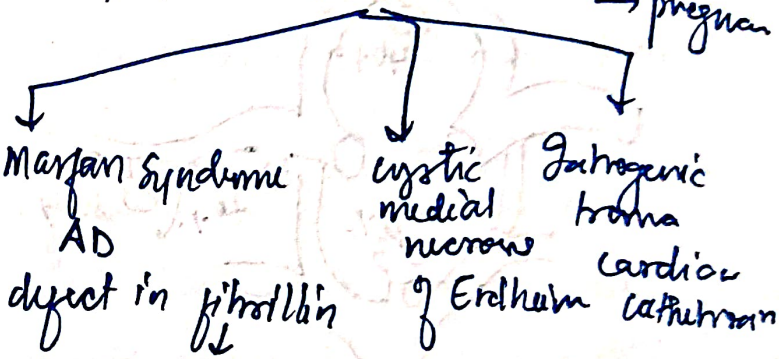
Depending upon composition :-
1. True - all the layers
2. False - having fibrous wall & occuring from trauma to the vessel.

Depending upon shape :-
1) Saccular 2.) Fusiform
3.) Cylindrical 4.) Serpentine or varicose

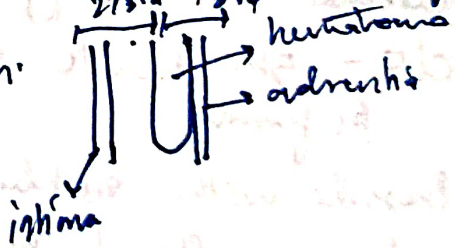


Pathogenetic mech :-
1) Atherosclerotic - mlc
2) Syphilitic - 3° syphilis
3.) Dissecting aneurysm
4.) Mycotic 5.) Berry.

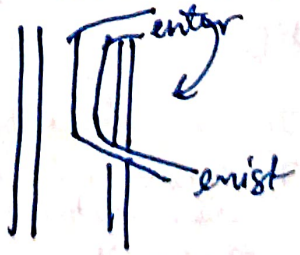
Dissecting aneurysm - blood enters separated (dissected) wall of vessel
→ mlc site :- Aorta
→ mlc in men (50-70 years)
Women - pregnancy
Patho :- weakened aortic media
↳ HTN & Non-HTN → pregnan



Morpho :- Begins in Arch of Aorta.
⇒ dissecm.



DOUBLE BARREL AORTA

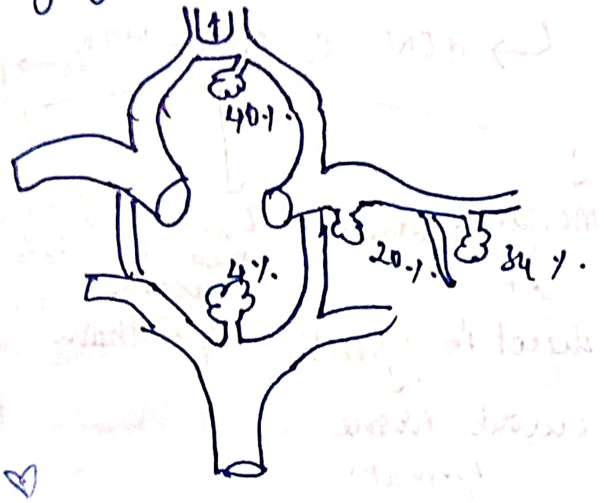


De Bakey
Type 1 : 75%. Ascending aorta } Standford type A
Type 2 : 5%. limited to AA
Type 3 : 20%. Tears begins in descend TA → SF type B.

Berry Aneurysm -

Associated with adult polycystic kidney disease (ADPKD).

There is congenital defect in the tunica media at the site of arterial bifurcation where local factors act to produce a slowly enlarging saccular aneurysm



micro - absence of int. elastic lamina in the neck of aneurysm

C/F - 5th decade & more in females.

Presents with sudden severe headache followed by loss of consciousness

RHD

Etiology
Environmental factor
Overcrowding
Poor socioeconomic
Strept A

Immuno:- Auto Rxn
Molecular mimicry & cross reactivity
Exagg. T cell response

→ 1st attack of RF → Recurrent RF ↓ RHD

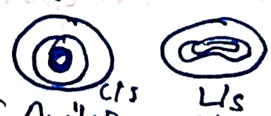
Susceptible host
family h/o occurrence genetic
in twins susceptibility

Morphological features :-

Pathognomic - Aschoff nodules or Aschoff bodies.

1) Early stage :- 4th week
oedema of connective tissue & ↑ in acid mucopolysaccharide
⇓
sep. of collagen fibres by the accumulating ground substance.
⇓
fragmented & disintegrated and affected focus takes the appearance & staining characteristics of fibrin

2) Intermediate - 4th - 13th week of illness.
Δ fibrinoid change → proliferation of cells (T cells), plasma cells, neutrophils & characteristic cardiac histiocytes → Anitschkow cells
↓



Aschoff bodies ↓ Anitschkow cells

(Anitschkow cell → owl's eye, caterpillar like)

Modified cardiac histiocytes → multinucleate (1-4 nuclei) → Aschoff cells.

3) Late - healing or fibrous stage 12-16 wks

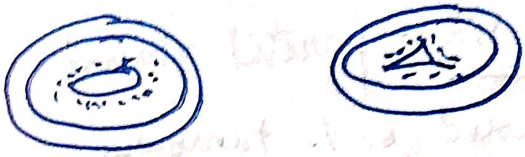
Nodule
1200μm
600μm

Anitschkow cells in AB ↓ spindle
Stain solidly.

Rheumatic Pancarditis :-

1) Endo :- R. valvulitis - warty vegetations or verrucae chiefly along the line of closure of cusps.
MS > A > T > P

Gross app of chronic healed mitral valve → fish mouth or button hole stenosis.

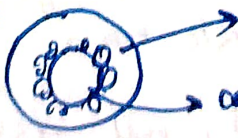


R. nodal endo :-

Gross :- Mac Callum's patch [post. wall of left atrium just above post. leaflet of mitral valve]

Micro :- ① oedema ② fibroid ↓
② cellular inf. of lymphocytes, pc,
④ macro.

Myo :- Aschoff bodies → IVS, left ventricle & left atrium.



② Rheum. Peri :- bread & butter appearance