CARDIOVASCULAR

• RHEUMATIC HEART FEVER

Immunologically mediated multisystem inflammatory disease

- group A β- hemolytic streptococcal pharyngitis / tonsilitis

2 phases → acute RF
→ Chronic RHD

m/c → children b/w 5-15yrs

Ethopathogenesis

Streptococcal infection

↓

Streptococcal antigens in body

↓

Activation of ABs & T-cell mediated rxn

↓

AB against M protein of streptococci cross react with myocardial Ag

↓

Cytotoxic mediated inflammation

↓

Cardiac & extra-cardiac lesions

JONES CRITERIA

major criteria → Pancarditis
Migratory polyarthritis
Subcutaneous nodules
Erythema marginatum
Sydenham chorea

minor criteria → Fever
Arthralgia
ECG with PR prolongation
Elevated blood levels
{
Acute phase reactants ↑

⇒ 2 maj OR 1 major + 2 minor

Acute RF

Characterised by pancarditis involving all 3 layers of heart & heart valves

- Endocarditis
  - left sided valve → inflammed & oedematous
    ↓
    fibrin deposits along lines of closure of valve leaflets
  - Small nodular or warty vegetations called verucae ∴ seen

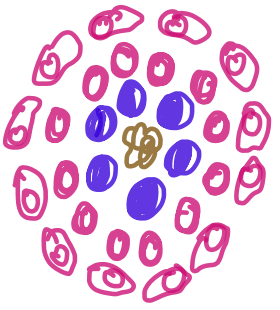
- Myocarditis
  - Microscopically multiple Aschoff bodies seen
  - Subendocardial lesion ∴ Irregular thickening called MacCallum plaques
- Pericarditis
  - ↳ Fibrinous pericarditis [Bread & butter]

ASCHOFF BODY

→ hallmark of acute RF
→ fusiform / spheroidal 1-2mm granulomatous lesion
→ Centrally - fibrinoid necrosis

→ surrounded by lymphocytes (T cells), activated macrophages (Anitschkow cells) & occasional plasma cells

→ Aschoff bodies heal by fibrosis



ANITSCHKOW CELLS

→ macrophages

→ have abundant cytoplasm

→ central round to oval nuclei

→ chromatin is disposed in central, slender, wavy ribbon - "caterpillar cells"

→ may become multinucleated - Aschoff giant cells

→ Pathognomonic for RF

Chronic RHD

Common features seen on valves (mitral & aortic)

- Affected valve shows :
  - → Deformities of cusp ✓
  - → leaflet thickening ✓
  - → commissural fusion & shortening ✓
  - → shortening & fusion of chordae tendinae ✓
  - → FISH MOUTH / BUTTONHOLE STENOSIS

→ superimposed infection causes ulcerations of cusps, perforation of valves & rupture of chordae tendinae

→ Atrial fibrillation ✓

→ Congestive changes in heart ✓

→ Right ventricular hypertrophy ✓

Microscopy → Diffuse fibrosis & neovascularization

Aschoff bodies usually not seen → only in acute

Complications

- Infective EC ✓
- Damage to valves ✓
- Cardiac murmers ✓
- Heart failure ✓
- Arrythmias ✓
- Sudden cardiac death ✓

ISCHAMIC HEART DISEASE (IHD)

Acute or chronic form of cardiac disability arising from imbalance b/w myocardial supply & demand for the oxygenated blood.

m/c cause → narrowing/obstruction of CA

- leading cause of death & ↓ incidence in developed countries

- m > f

Risk factors

* Race → white population ↑

Death in blacks occurs at earlier age

* Age ∝ IHD (55 - 64 yrs peak)

↳ happen in 30 yrs if there is high risk factors

* Sex

m/c → males (6 times more)

* use of oral contraceptives (3-4 times)
* Smoking (10-20 times ↑) even passive smoking
* Alcohol
* Personality → hard driving impatient people (type A) more prone
* Exercise reduce IHD
* Diabetes & obesity ∝ IHD
* HTN
* familial hypercholesterumia

Life style - unhealthy → ↑RF

Etiopathogenesis

1) CORONARY ATHEROSCLEROSIS

>90% → major cause

m/c site : descending ant br. of left coronary artery
Right coronary A
Circumflex br. of left coronary artery

1/3rd → single vessel disease (usually L)
3/3 — 1/3 → 2 vessel disease
1/3 → 3 vessel disease

- Almost all adult shows atherosclerotic plaques
- Atherosclerotic lesion shows more than 75% reduction in cross sectional area of CA or the branch

Complications :

- Calcification
- Thrombosis
- Embolism
- Ulceration
- Haemorrhage
- Rupture
- Aneurysm formation

iii) SUPERADDED CHANGES IN ATHEROSCLEROSIS

- Plaque haemorrhage
- Thrombosis & embolism

Due to :

- Coronary artery spasm ✓
- tachycardia ✓
- ~~Intraplaque haemorrhage~~ ✗
- Hypercholesterolemia ✓
- CA thrombosis ✓

↳ Transmural acute MI is often precipitated by partial or complete coronary thrombosis. This will occlude the lumen completely.

↳ Lipid core of plaque is highly thrombogenic

↳ Small fragments of thrombotic material are dislodged & embolised to terminal coronary branches causing microinfarcts of myocardium.

- Local platelet aggregation & coronary artery spasm : Aggregated platelets will release thromboxane A2. This causes vasospasm, leading to coronary spasm

iii) NON-ATHEROSCLEROTIC CAUSE

- Vasospasm
- Stenosis of coronary ostea
- Arteritis due to rheumatic fever, polyarthritis nodosa etc
- Embolism originating elsewhere in the body in LCA → fat, air embolism, bacterial endocarditis emboli
- Thrombotic diseases as polycythemia vera, sickle cell anaemia etc
- Trauma
- Aneurysm
- Compression of the CA by 1° or 2° tumor

Effects of IHD

- Asymptomatic to immediate mortality
  - Angina pectoris
  - MI
  - Chronic ischaemic heart disease

Classification of MI

i) Transmural & subendocardial

ii) Age of infarct
↳ Acute / fresh
old / heal

iii) According to anatomical region of left ventricle involved
↳ Inferior, Lateral, septal, circumferential

iv) Location of infarct
↳ left ventricle (m/c)
↳ right ventricle less susceptible due to thin wall which has less metabolic

Involvement

↳ left atrium → retrieval from function due to oxygenated blood in atrium

Morphological

	Gross	Microscopy
1st week		
0-6 hr	No change / pale Viability test -ve	No change / stretching & wavyness of fibers
6-12 hr	"	Coagulative necrosis + neutrophilic infiltration + edema & haemorrhage +
24 hr	Cyanotic red purple area of haemorrhage	Coagulative necrosis progresses marginal neutrophils seen
48-72 hr	Pale & hyperemic (more blood)	Coagulative necrosis complete Neutrophilic infiltrate well dev
3rd-7th day	Hyperemic border centre - yellow & soft	Neutrophils gradually disappear Macrophage appears onset of fibrovascular response
2nd week		
10th day	Red purple periphery	Most of the necrosed muscle removed Fibrovascular reaction of margin is prominent Pigmented MP, eosinophils, lymphocyte plasma cells +
14th day	-	Necrosed muscle mostly removed neutrophils disappear

3rd week	–	removed muscle fibers from larger infants removed, more ingrowth of fibrocollagenic tissue
4th – 6th weeks	thin grey-white, hard thinner fibrous scar	Increased fibrocollagenic tissue, ↓ vascularity, fewer macrophages, lymphocytes, plasma cells

Atherosclerosis

Definition: Defined as a chronic inflammatory disease in which there is a build up of fibrofatty plaques or atheromas inside arteries, particularly large & medium-sized muscular arteries, causing them thickening & hardning.

Risk factors

I major risk factors - modifiable by lifestyle / therapy

* Dyslipidaemia (↑ LDL, ↓ HDL)
* HT
* DM
* Smoking
* lifestyle risk factors (fatty diet, obesity, physical inactivity)

II Constitutional non-modifiable risk factors

* Age
* Sex
* Genetic factors
* Familial & racial factors

III Non-traditional emerging risk factors & biomarkers.

* Environmental influences
* Oestrogen hormone
* Stressfulness
* Hyperhomocystinaemia
* Homocystinuria
* Prothrombotic factors
* Infectious burden
* Excessive alcohol consumption

Pathogenesis

Endothelial dysfunction [HT, toxins in smoking, Haemodynamic stress, ↑ LDL]

↓

Inflammatory reactions (monocytes, macrophages, T-lymphocytes)

↓

Expression of cell adhesion molecules from the injured endothelial cells (selectins, ICAMs, VCAMs)

↓

Monocytes migrate through the intima (Chemoattractants - MCP 1)

↓

once, inside the intima, monocytes becomes macrophage & express scavenger receptors on their surface for LDL called macrophage-colony stimulating factor (M-CSF)

↓

M-CSF - ingestion of lipids, multiplication & differentiation of monocytes into macrophage foam cells which will leads to the formation of fatty streaks (1° lesion)

↓

Fatty streaks activates T lymphocytes

↓

↑ - cytokines & GF

↓

Proliferation of smooth muscle & FB

↓

Repeated cycles

↓

Atheroma

Morphology

- Fatty streaks & dots (1° lesions)
- Atheromatous plaques

↓

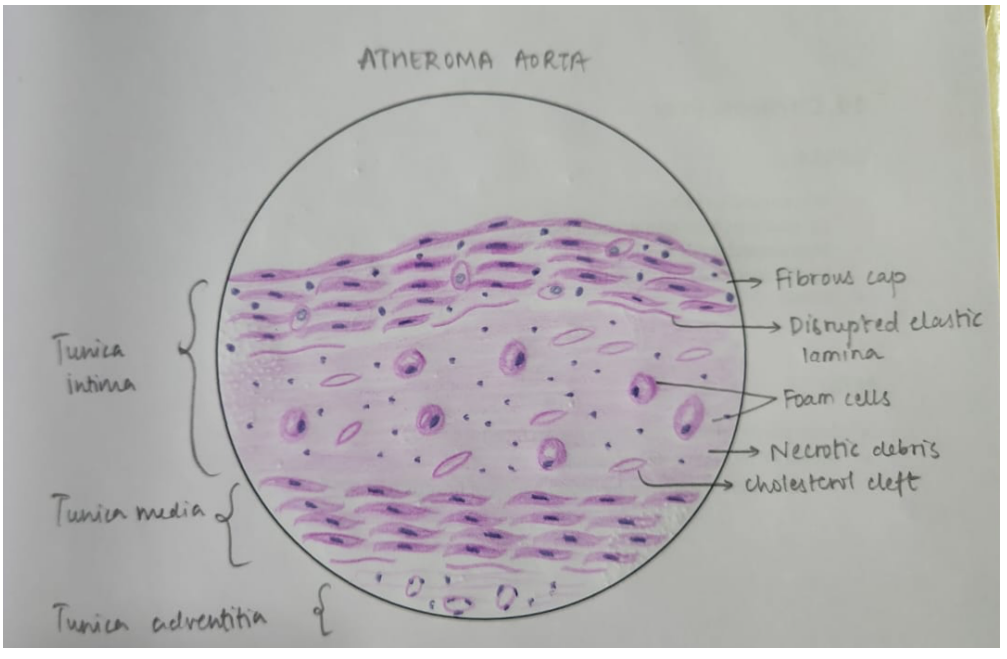
Gross → Yellowish plaques in the intima

M/S → Composed of fibrous cap (smooth muscle cells & ECM)

Beneath that cellular area composed of MP, SMC, lymphocytes

Core contains cholesterol cleft, dead cells from debris, foam cells

Periphery : Neovascularization



Cardiomyopathy

Disease of the heart muscles.

3 categories :

i) Dilated (congestive) cardiomyopathy

ii) Hypertrophic cardiomyopathy

iii) Restrictive cardiomyopathy

Dilated cardiomyopathy

- Dilation of all the 4 chambers of the heart

ETIOLOGY

* Association with viral myocarditis
* " with toxin damage
* Genetic basis
  - common mutation in
    - Cytoskeletal proteins
    - Sarcomere proteins
    - Nuclear proteins
    - Contractile proteins

PATHOLOGY

Gross → Dilation of all 4 chambers => globular appearance

M/S → hypertrophy of some myocardial fibres & atrophy of others.

Hypertrophic cardiomyopathy

ETIOLOGY

- defect in β-myosin heavy chain
- Autosomal dominant disorder.

PATHOLOGY

Gross → Cardiac enlargement (↑ in wt)

Asymmetrically enlarged

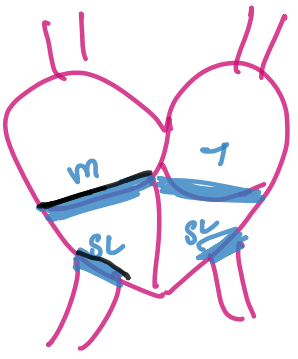
- Banana shaped heart

Restrictive cardiomyopathy

- diastolic dysfunction
- dysfunction in ventricular filling due to ↓ volume of ventricle

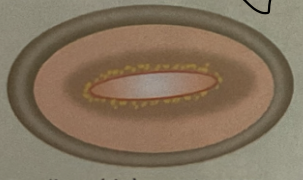
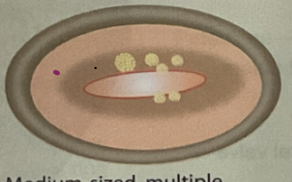
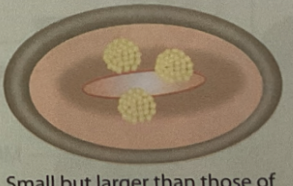
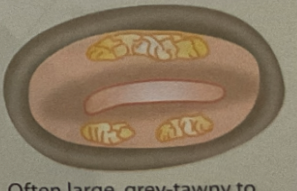
Etiology

- Amyloid
- Malignancy
- Storage disease.



Vegetations

TABLE 17.7 Distinguishing features of vegetations in major forms of endocarditis.

	FEATURE	RHEUMATIC	LIBMAN-SACKS	NON-BACTERIAL THROMBOTIC	BACTERIAL (INFECTIVE)
1.	*Valves commonly affected*	Mitral alone; mitral and aortic combined	Mitral, tricuspid	Mainly mitral; less often aortic and tricuspid	Mitral; aortic; combined mitral and aortic
2.	*Location on valve cusps or leaflets*	Occur along the line of closure, atrial surface of atrioventricular valves and ventricular surface of semilunar valves	Occur on both surfaces of valve leaflets or cusps, in the valve pockets	Occur along the line of closure	SABE more often on diseased valves; ABE on previously normal valves; location same as in RHD
3.	*Gross appearance*	 Small, multiple, warty, grey brown, translucent, firmly attached, generally produce permanent valvular deformity	 Medium-sized, multiple, generally do not produce significant valvular deformity	 Small but larger than those of rheumatic, single or multiple, brownish, firm, but more friable than those of rheumatic	 Often large, grey-tawny to greenish, irregular, single or multiple, typically friable
4.	*Microscopy*	i) Composed of fibrin with superimposed platelet thrombi and no bacteria ii) Adjacent and underlying endocardium shows oedema, proliferation of capillaries, mononuclear inflammatory infiltrate and occasional Aschoff bodies.	i) Composed of fibrinoid material with superimposed fibrin and platelet thrombi and no bacteria. ii) The underlying endocardium shows fibrinoid necrosis, proliferation of capillaries and acute and chronic inflammatory infiltrate including the haematoxylin bodies of Gross.	i) Composed of degenerated valvular tissue, fibrin platelets thrombi and no bacteria. ii) The underlying valve shows swelling of collagen, fibrinoid change, proliferation of capillaries but no significant inflammatory cell infiltrate.	i) Composed of outer eosinophilic zone of fibrin and platelets, covering colonies of bacteria and deeper zone of nonspecific acute and chronic inflammatory cells. ii) The underlying endocardium may show abscesses in ABE and inflammatory granulation tissue in the SABE.

(ABE, acute bacterial endocarditis; SABE, subacute bacterial endocarditis; RHD, rheumatic heart disease).

fibrin + platelets + mo. capillaries