Rheumatic Fever & Rheumatic Heart Disease
• Rheumatic Fever is an acute, nonsuppurative, \textit{immunologically mediated}, multi-system inflammatory disease
• Occurs a few weeks after an episode of group A Streptococcal pharyngitis.
• Affects: heart, joints, CNS, skin and subcutaneous tissues
• RHD- chronic stage
Epidemiology

- Age: 5-15 yrs, rare <3 yrs
- Girls>boys
- Common in 3rd world countries
- Incidence:
  - related to frequency and severity of Streptococcal pharyngeal infection
  - more during winter & early spring
  - environmental factors- poor sanitation, poverty, overcrowding: greater spread of infection, following epidemics of Strep pharyngitis
Etiopathogenesis

Delayed immune response to infection with group A beta hemolytic streptococci

• H/o throat infection
• After a latent period of 1-3 weeks, antibody induced immunological damage occur to *heart valves, joints, s/c tissue & basal ganglia*
• Subsequent attacks are associated with exacerbations of RF
• Antibiotics lower incidence and severity of RF
• Elevated titres of antibodies to antigens of β hemolytic Streptococci
Etiopathogenesis - Immunological evidence

- Symptoms occur after 2-3 weeks of infection
- Organism cannot be isolated from the lesions in target tissues
- Antibodies against M-proteins of Strep cross react with glycoproteins in the heart, joints and other tissues
- Patients with RF have elevated titres of anti-streptolysin O and S, antistreptokinase, antistreptohyaluronidase and anti-DNAase B
• Antibodies against cell wall polysaccharide of group A streptococcus: cross reactive against cardiac valves and their levels are elevated in patients with cardiac valvular involvement

• Antibodies against Hyaluronate capsule: cross reactive against the human hyaluronate present in the joints

• Membrane antigens: cross react with smooth and cardiac muscle, dermal fiboblasts and neurons of caudate nucleus
Rheumatic fever - pathogenesis

**HEMOLYTIC STREPTOCOCCI**

- IMMUNOLOGIC REACTION?
- RHEUMATIC FEVER
- 10 TO 14 DAYS LATER (MUCH LONGER GAP FOR CHOREA)

**STREPTOCOCCAL THROAT INFECTION**

**JOINTS**

**HEART**

**SKIN**

**NERVOUS SYSTEM (CHOREA)**
Clinical features

Jones Criteria for Acute RF

Major manifestations
1. Migratory polyarthritis of major joints
2. Carditis
3. Sydenhams chorea
4. Subcutaneous nodules
5. Erythema marginatum of skin

Preceding evidence of streptococcal infection i.e + throat culture, elevated anti streptococcal Ab
Minor criteria
1. Nonspecific signs and symptoms: fever, arthralgia
2. Elevated blood levels of acute phase reactants: ESR, CRP
3. Previous H/O RF
**Jones Criteria (Revised) for Guidance in the Diagnosis of Rheumatic Fever***

<table>
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<th>Major Manifestation</th>
<th>Minor Manifestations</th>
<th>Supporting Evidence of Streptococal Infection</th>
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<td>Carditis</td>
<td>Clinical</td>
<td>Increased Titer of Anti-Streptococcal Antibodies ASO (anti-streptolysin O), others</td>
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<td>Polyarthritis</td>
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<td>Previous rheumatic fever or rheumatic heart disease Arthralgia Fever</td>
<td>Acute phase reactants: Erythrocyte sedimentation rate, C-reactive protein, leukocytosis</td>
</tr>
<tr>
<td>Subcutaneous Nodules</td>
<td></td>
<td>Prolonged P-R interval</td>
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*The presence of two major criteria, or of one major and two minor criteria, indicates a high probability of acute rheumatic fever, if supported by evidence of Group A streptococcal infection.*

**Recommendations of the American Heart Association**
Clinical Features

1. Arthritis

- Flitting & fleeting migratory polyarthritis, involving major joints
- Commonly - knee, ankle, elbow & wrist
- Occurs in 80%
- Involved joints are exquisitely tender, swollen
- *In children below 5 yrs arthritis usually mild but carditis more prominent*
- *Arthritis does not progress to chronic disease*
2. Carditis

- Manifests as **pancarditis** (endocarditis, myocarditis and pericarditis),
- occurs in 40-50% of cases
- **Carditis is the only manifestation of rheumatic fever that leaves a sequelae & permanent damage to the organ**
- **Valvulitis occur in acute phase**
- **Chronic phase - fibrosis, calcification & stenosis of heart valves (fish mouth valves)**
3. Sydenham Chorea

- Occurs in 5-10% of cases
- Mainly in girls of 3-15 yrs age
- Late manifestation: 6 mo after the attack of RF
- Clumsiness, deterioration of handwriting, emotional lability or grimacing of face
4. Erythema Marginatum

- Occur in <5%.
- Unique, transient, serpiginous-looking lesions of 1-2 inches in size
- Pale center with red irregular margin, non-itchy
- More on trunks & limbs
- Often associated with chronic carditis
5. Subcutaneous nodules

- Occurs in 10%
- Painless, pea-sized, palpable nodules
- Mainly over extensor surfaces of joints, spine, scapulae & scalp
- Associated with strong seropositivity
- *Always associated with severe carditis*
Rheumatic fever diagnosis

Subcutaneous nodules
(nodules of rheumatoid arthritis are larger)
Laboratory Findings

- High ESR
- Anemia, leucocytosis
- Elevated C-reactive protein
- ASO titre >200 Todd units. (Peak value attained at 3 weeks, comes down to normal by 6 weeks)
- Anti-DNAse B test
- Throat culture
- ECG- prolonged PR interval, 2nd or 3rd degree blocks, ST depression, T inversion
- 2D Echo cardiography- valve edema, mitral regurgitation, LA & LV dilatation, pericardial effusion
Morphologic changes

Cardiac Lesions
• Focal interstitial involvement of all the three layers of heart: Pan carditis
• Pathognomonic feature is Aschoff nodule/ body
• 1-2 mm tiny structures found in the vicinity of small blood vs in the endo and myocardium
Aschoff Body

• Early exudative stage:
  - edema, ↑ in acid MPS
  - fibrinoid degeneration of connective tissue
• Intermediate proliferative or granulomatous stage:
  - inflammatory cell infiltration & proliferation of plump macrophages (Anitschkow cells) resulting in formation of Ashcoff nodules
  - macrophages have abundant cytoplasm, vesicular nucleus with chromatin distributed in a slender wavy ribbon (Caterpillar cells) or owl eye appearance
  - fuse to form multinucleate Aschoff giant cells
• Late healing or fibrous stage:
  - fibrocollagenic scar after 12 weeks
Rheumatic Endocarditis: valvulitis/ mural endocarditis

- Acute RF: valves are thick, loss of transparency
- 1-3 mm small warty (verrucous) vegetations along the line of closure
- Free margins of cuff appears rough, irregular
- Attach firmly; do not embolise
- Mitral & aortic valves commonly involved- greater mechanical stress

- Mural endocarditis:
  MacCallum plaques: subendocardial thickening most frequently in post wall of Lt atrium due to regurgitant jets
• Pericarditis: serofibrinous/fibrinous pericarditis with exudates called Bread and butter pericarditis
  - chronic adhesive pericarditis in late stage
• Myocarditis: scattered Aschoff nodules in the interstitium seen as granulomas
Chronic RHD

• Organization of inflammation → heals by fibrosis
• Permanent deformity of valves:
  - leaf thickening, commisural fusion
  - shortening, thickening and fusion of chordae tendineae
• Most freq cause of Mitral stenosis (99%)- Fish mouth or button hole stenosis of Mitral valve in RHD
• MS in 65-70% cases, mitral + aortic in 25% cases
FIGURE 12-25 The pathogenetic sequence and key morphologic features of acute rheumatic heart disease.
Mitral Stenosis

- Is a thickening by fibrosis or calcification
- Valve leaflets fuse and become stiff
- This narrows the opening and prevents blood flow from the LA to the LV
- LA pressure increases, left atrium dilates
- Pulmonary artery pressure increases, RV hypertrophies
- Pulmonary congestion and RHF occurs
- LV normal
- Mild – asymptomatic, with progression – dyspnea, orthopnea, cough, hemoptysis
Cause of death

• Cardiac failure
• Bacterial endocarditis
• Embolism from thrombus in LA
• Sudden death from AS or ball thrombus in LA