Rheumatic fever & acute rheumatic heart disease
# The most common cause of acquired valvular disease in developed and underdeveloped countries is rheumatic fever (R.F.)

# Now in the western world R.F. is being eradicated, but it's still the common cause (in addition to CAD and degenerative calcific diseases).

# R.F. can be presented in many ways:

   a. arthritis without cardiac involvement (as in case 1)
   b. rheumatic chorea without arthritis nor carditis (as in case 2)
   c. carditis with or without arthritis (as in case 3)
• In R.F. heart will be involved in 50% of the cases and years later because of the immunologically mediated inflammation, fibrosis & shrinkage of the valves, patients will come with valve stenosis.

• Rheumatic fever and rheumatoid arthritis are completely different diseases although both are immunologically mediated diseases.

• R.F. can cause permanent damage to the valves & myocardium.

• Rheumatoid arthritis can affect heart by causing pericarditis (as pericarditis can be caused by connective tissue disorder). But remember R.F. is more serious and more important as it can be prevented.
Case history

A 12 year old girl was brought with complaints of fever and joint pains of 5 days duration. She had pain and swelling of left knee and this subsided and she developed pain and swelling of right ankle and elbow (migratory arthritis). She had a history of sore throat 3 weeks ago (incubation period) and it subsided without treatment. On examination she had signs of inflammation in the above joints. Heart was normal on examination.
A 13 year old girl was brought with complaints of abnormal jerky movements of the limbs (chorea) of 4 days duration. She denied any history of fever or joint pains and swelling. She had a history of frequent sore throats in the past. On examination she had normal findings in cardiovascular system.
A 14 year old boy was brought with complaints of fever and breathlessness of 6 days duration. He gave a history of joint pains involving both knees one week before the onset of the illness. On questioning he gave a history of sore throat 4 weeks ago for which he had taken some medication. On examination he had no signs of inflammation in the joints (signs of inflammation has subsided). Auscultation of the heart revealed pan systolic murmur at the apex (mitral regurgitation) and early diastolic murmur along the left sternal border (aortic regurgitation) JVP was elevated (right heart failure) and he had tachypnea (left heart failure) [biventricular heart failure]
Rheumatic fever

• Rheumatic fever is an **immunologically mediated inflammatory** disorder, which occurs as a sequel to **group A streptococcal pharyngeal infection**.

  • **Multisystem** disease affecting the heart, joints, brain, cutaneous and subcutaneous tissues
  • Major **public health problem** in heavily populated underdeveloped and developing countries
  • **Preventable** disease
There is no direct invasion to the tissue by the microorganism but it's an autoimmune disease that involves Ag-Ab interaction.

It involves group A beta hemolytic streptococcus throat infection (that involves tonsils & pharynx, so tonsillectomy will not immune the patient against R.F.

It must be pharyngeal infection not skin infection.

R.F. cause permanent damage to the heart but not to the joint (only arthritis) thus it’s said “R.F. leaks the joints but bites the heart”

The incidence in Kuwait is low: before 120/1000 now 3-4/1000
Rheumatic fever-pathogenesis

• Group A streptococcal (GAS) pharyngeal infection
• Body produce antibodies against streptococci ->
• These antibodies cross react with human tissues because of the antigenic similarity between streptococcal components and human connective tissues (molecular mimicry)[there is certain amino acid sequence that is similar btw GAS and human tissue] ->
• Immunologically mediated inflammation & damage (autoimmune) to human tissues which have antigenic similarity with streptococcal components- like heart, joint, brain connective tissues
Rheumatic fever-pathogenesis
Explanation of the previous slide:

- Bcs of the similsrity btw hyaluronic acid in GAS capsule and in the connective tissue of the joints, Ab produced agaist GAS capsule will start to attack the joints and causes arthritis.

- M-protein in GAS cell wall and the myocardium are similar, thus Ab produced against GAS cell wall will attack heart and will cause carditis and so forth.
Rheumatic fever - pathogenesis
In order for R.F. to occur:

- There must be throat infection by GAS. (only when there is GAS throat infection there is R.F.)
- Antibodies must be produced by the body rapidly & in high magnitude.
- These Abs will cross react with tissue of the heart, joint, brain (especially basal ganglia), skin.
Rheumatic fever - epidemiology

- Parallels with epidemiology of streptococcal pharyngitis *(only when there is GAS throat infection, there R.F.)*
- **Incidence** –
  - 3% in epidemics of exudative streptococcal pharyngitis in closed community *(school, army)*
  - 0.3% in civilian population with sporadic streptococcal throat infection
  - 50% if there is a past history of rheumatic fever *(thus secondary prophylaxis is important)*
  - first attack between 5-15 years *(a childhood disease)*
  - poor socioeconomic conditions and overcrowding
Why not all patients that have GAS throat infection will have R.F.? (different incidence)

Bcs there are microorganisms variables and host variables:

• Microorganism variables: only certain strains that can produce the immunologically active Ag.
• Host variables: some of us will produce large amount of Abs after each infection but others don’t
Rheumatic fever-epidemiology

For rheumatic fever to occur-
- Pharyngeal infection with group A streptococci
- Certain rheumatogenic strains of GAS with M proteins
- Throat infection of sufficient duration- persistence of GAS
- Throat infection may or may not be symptomatic
- Throat infection is a must, not with pyoderma (skin infection)
- Infection of sufficient duration to produce antibody
- Brisk and sufficient antibody response to the infection
- Genetic predisposition
Rheumatic fever—diagnosis

**Jones criteria for initial attack of rheumatic fever**

- Evidence of preceding streptococcal infection *+ 2 major manifestations or one major manifestation and 2 minor manifestations indicates a high probability of acute rheumatic fever

- Jones criteria 1944 and updated in 1992
  * except rheumatoid chorea; bcs it’s a late manifestation
Rheumatic fever diagnosis

Major manifestations
• Carditis
• Polyarthritis
• Chorea
• Subcutaneous nodules
• Erythema marginatum
Rheumatic fever-diagnosis

Minor manifestations

• Clinical findings-
  • Arthralgia (*joint pain without swelling*)
  • Fever
• Laboratory findings-
  • Elevated acute phase reactants
    raised ESR
    raised CRP
  • Prolonged P-R interval
Rheumatic fever-dagnosis

Supporting evidence for antecedent Group A streptococcal infection

- Positive throat culture (in 25% of patients & 75% will be -ve)
- Rapid streptococcal antigen test
- Elevated or rising streptococcal antibody titer – ASO [anti-streptolysin]
  (others - Anti DNaseB, AH [anti-hyaluronic acid])

If these antibodies (>300 in children >200 in adults) suggest previous infection.
Rheumatic fever-diagnosis

**CARDITIS** (*pancarditis*) - all 3 layers are involved

**Clinical evidence** –
- Murmur (*mitral or aortic regurgitation-endocardium involved*)
  
  *stenotic murmur is not found in acute R.F. bcs it needs long time to develop*
- Heart failure
- Cardiac enlargement (*myocardium involvement*)
- Pericardial rub or effusion (*pericardium involvement*)

**Investigations for evidence of carditis**
- Chest x-ray – cardiomegaly, pulmonary venous congestion
- ECG - heart block, T wave changes, low voltage QRS
- Echocardiogram – cardiac dilatation, valve involvement, pericardial effusion
Rheumatic fever-diagnosis

**Arthritis**
- Polyarthritis, fleeting, migratory, large joints, no residual deformity, rapid response to aspirin (*if aspirin given, 24 to 48 hrs joint pain will disappear; thus used as diagnostic test*)

**Chorea**
- Spasmodic, unintentional, jerky choreiform movements, speech affected, fidgety, late manifestation (*thus no ESR or ASO titre elevation*)
Subcutaneous nodule
• Painless, hard nodules beneath skin, over bony prominence, tendons and joints

Erythema marginatum (rash)
• Erythematous, ring or crescent shaped, transient patches over trunk and limbs
Rheumatic fever-dx

Subcutaneous nodules
(nodules of rheumatoid arthritis are larger)
Rheumatic fever diagnosis

Erythema marginatum

Erythematous patches with central clearing
Rheumatic fever treatment

- **Bed rest** 2-6 weeks (*till inflammation subsided*)
- **Supportive therapy** - treatment of heart failure
- **Anti-streptococcal therapy** - Benzathine penicillin (*long acting*) 1.2 million units once (*IM injection*) or oral penicillin 10 days, if allergic to penicillin erythromycin 10 days  
  (*antibiotic is given even if throat culture is negative*)
- **Anti-inflammatory agents**-
  - **Aspirin** 100 mg/kg per day for arthritis and in the absence of carditis - for 4-6 weeks to be tapered off
  - **Corticosteroids** in presence of carditis – 1-2 mg/kg per day – for 4-6 weeks to be tapered off
Rheumatic fever - prevention

Secondary prevention – prevention of recurrent attacks
- Benzathine penicillin G 1.2 million units IM every 4 weeks
- Or Penicillin V 250 mg twice daily orally
- Or Sulfadiazine 1 g daily orally
- If allergic to both – Erythromycin 250 mg twice daily orally
Rheumatic fever - prevention

Duration of secondary rheumatic fever prophylaxis

• Rheumatic fever + carditis + persistent valve disease - 10 years since last episode or until 40 years of age, sometimes life long

• Rheumatic fever + carditis + no valvar disease – 10 years or well into adulthood whichever is longer

• Rheumatic fever without carditis - 5 years or until 21 years whichever is longer

(Continuous prophylaxis is important since patient may have asymptomatic GAS infection)
Rheumatic fever-prognosis

- Prognosis is good if recurrence is prevented by continuous antibiotic prophylaxis - particularly if no carditis in the initial attack.
- If carditis, half of them can develop chronic rheumatic heart disease. Recurrence following streptococcal sore throat is high in patience with previous carditis.
- For development of RHD, it takes 10-20 years in western world but earlier in underdeveloped world due to malignant nature of the disease.
- Mitral valve is most commonly affected, followed by aortic and tricuspid valves.
- So these patients need long term follow up.