*"He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all."*
William Osler

# Medicine

# 430

# Rheumatic Fever and Rheumatic Heart Disease

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# Rheumatic Fever and Rheumatic Heart Disease

*Lecture outline:*

- *Acute rheumatic fever vs. rheumatic heart disease.*
- *Epidemiology*
- *Etiology*
- *Pathogenesis*
- *Clinical features of ARF*
- *Investigations*
- *Diagnosis*
- *Treatment*
- *Prevention*
- *Prognosis*
- *Chronic rheumatic heart disease*
- *Case examples*

*References:*

- *Dr. Abdullah Almobiereek's lecture slides from last year.*
- *Davidson's principles and practice of medicine.*
- *Professional guide to pathophysiology.*
- *Lecture notes.*
- *Step up to medicine.*
- *429 and 427 team handouts.*
- *Pre-test medicine cardiology + case files pathology (for case examples)*

## ▪ ACUTE RHEUMATIC FEVER VS. RHEUMATIC HEART DISEASE:

| ACUTE RHEUMATIC FEVER (ARF) | RHEUMATIC HEART DISEASE (RHD) |
|---|---|
| - Acute.<br>- Presents in childhood ***(5-15 years).***<br>- Multisystem inflammatory immune-mediated disease that occurs 2-4 weeks after an episode of ***group A beta hemolytic streptococcal*** infection.<br>- Often recurrent with cumulative damage, therefore, prevention of its recurrence is crucial.<br>- RF can progress to chronic RHD due to recurrent valvular damage.<br>***acute rheumatic heart disease: a term used to describe the cardiac manifestation of ARF.** | - Chronic.<br>- Presents in adulthood.<br>- Describes the chronic **valvular** abnormalities secondary to ARF.<br>- Recurrent ARF results in gradually increasing permanent damage to the valves by progressive fibrosis which results in chronic rheumatic heart disease. ( I.e. valve stenosis/regurgitation)<br>- CP: depends on which valve(s) are involved.<br><br>*Affects the productive age group so it has an economic impact on the country. |

## ▪ EPIDEMIOLOGY OF RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE:

- 15. 6 millions have rheumatic heart disease worldwide.
- 500,000 new cases of rheumatic fever per year worldwide nearly *half* develop carditis.
- 230,000 deaths per year due to rheumatic fever or rheumatic heart disease worldwide.
- Environmental factors affecting its incidence: overcrowding, poor sanitation, poverty. (therefore, it has become rare in industrialized countries due to improved living conditions, less overcrowding, better hygiene, and use of antibiotics)
- Rheumatic fever is common in 3rd world developing countries.
- RF/RHD remains a major cause of morbidity and mortality in poor and developing countries.
- Imposes a substantial burden on health care systems with limited budgets.
- Incidence is more during fall, winter and early spring.
- Ages 5-15 years are most susceptible to RF.
- It is rare in children < 3 years old.
- Girls > boys.

# ACUTE RHEUMATIC FEVER

## ETIOLOGY OF ARF:

- Rheumatic fever is an acute systemic inflammatory disease that occurs in children and young adults few weeks after a group A beta-hemolytic streptococcal upper respiratory tract infection (i.e. group A beta-hemolytic streptococcal pharyngitis/tonsillitis) and is often recurrent.

- It represents a delayed non-suppurative immune response in which manifestations appear following a latent period of 1-3 weeks after an URTI with GABH streptococcus.

*non-suppurative: no pus/bacteria found in the inflamed tissue, because it's an immune-mediated response.

- It is a diffuse inflammatory disease of connective tissue, primarily involving the *heart, blood vessels, joints, subcutaneous tissue, skin and central nervous system*.

## PATHOGENESIS OF ARF:

- Rheumatic fever is thought to develop because of a delayed immune-mediated response to an URTI with specific strains of GABH streptococci.

- This is triggered by molecular mimicry/antigenic mimicry in which there's a similarity between the antigens of the GABHS outer cell wall protein (M protein) and the body's own healthy tissues (i.e. cardiac myosin and laminin) which results in an autoimmune reaction where the patient's antibodies induced by the GABHS antigens *cross-reacts* and cause damage to heart valves, subcutaneous tissues, tendons, joints, and basal ganglia of the brain.

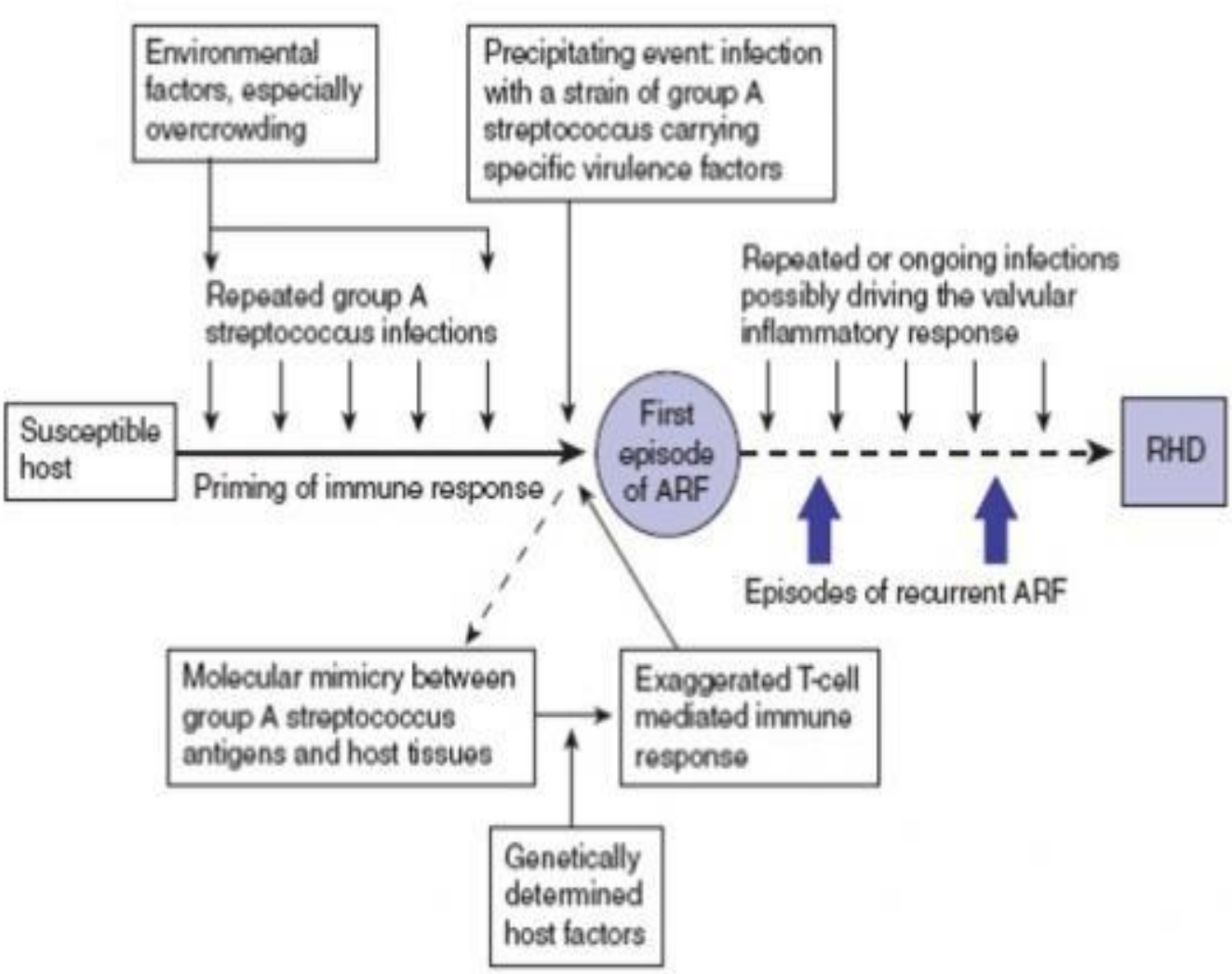
- Therefore, after a latent of period of 1-3 weeks antibody induced immunological damage occur to heart valves, joints, SC tissues and basal ganglia of the brain and manifestations of RF appear.

*The condition is not due to direct infection of the heart or the production of toxins. GABHS infection indirectly affects the heart through an autoimmune reaction which explains the typical delay in symptoms onset after original infection and the absence of streptococci in the lesions.

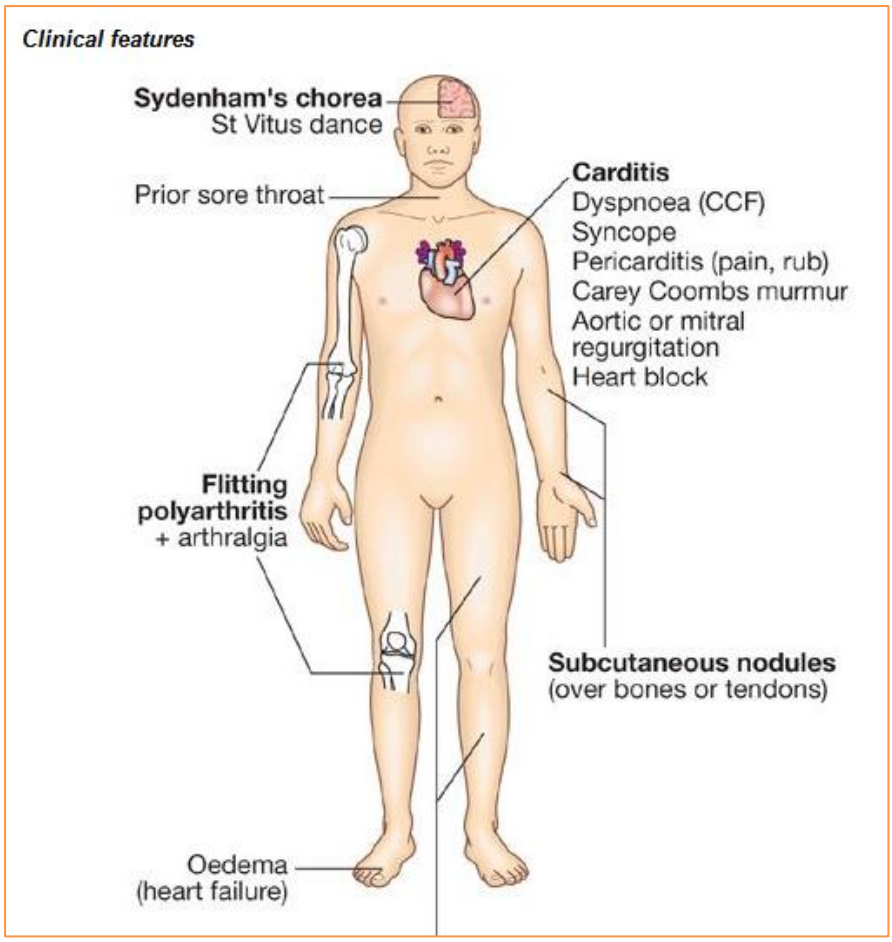
*In other words,*

*When a child complains of a sore throat caused by a special type of bacteria that attacks the pharynx/tonsils (GABHS) causing pharyngitis/tonsillitis. Normally, the immune system will respond by producing antibodies and sensitized lymphocytes which should attack the bacteria and eventually eradicate it. This ideal situation occurs in most of the patients who suffer from such types of pharyngitis/tonsillitis.*

*However, in a small group of patients (possibly genetically susceptible) the immune system fires back to both the bacteria and their own healthy tissue as well. For example, it may attack cardiac tissue, synovial joints, skin, SC tissue and CNS; therefore, they develop carditis, arthritis, erythema marginatum, SC nodules and chorea. This occurs because their immune system mistakenly cross-reacts with their own healthy tissues because of the similarity between some of the bacterial antigens that are present on their outer cell wall and our own body's cells (molecular/antigenic mimicry).*

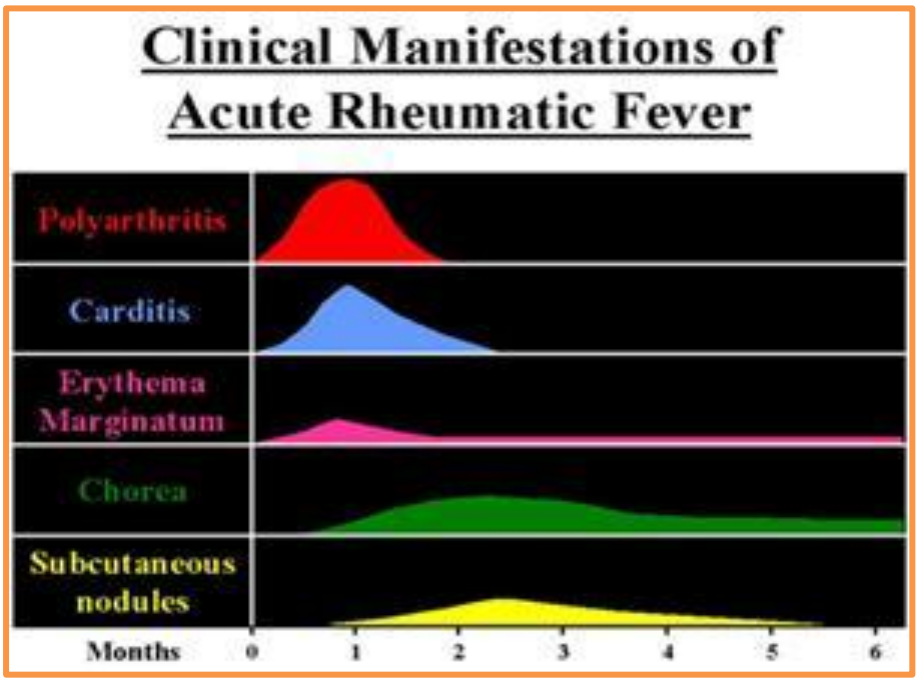


- **CLINICAL FEATURES OF ACUTE RHEUMATIC FEVER**:




## Two distinct patterns of presentation:

1. Sudden onset: fever, polyarthritis 2-4 weeks after streptococcal pharyngitis.
2. Insidious or subclinical-mild symptom joint pain.



- **MAJOR CLINICAL FEATURES:**

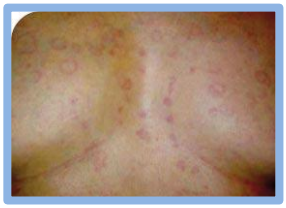
## 1. ARTHRITIS

- Most common major manifestation (80%).
- Earliest manifestation of acute rheumatic fever.
- Short duration.
- Acute painful asymmetric flitting and fleeting MIGRATORY POLYARTHRITIS, involving large joints.
  *Migratory polyarthritis? Multiple joints are inflamed and the pattern of joints involved changes with time. I.e. Two days ago, his right knee was painful and swollen, but it has improved and now his right ankle and left knee are inflamed and swollen.
- Commonly involved joints: knee, ankle, elbow and wrist
- Inflamed joints are exquisitely tender, swollen, red and painful.
- Pain rapidly responds to aspirin (salicylates)
- Arthritis DOESN'T progress to chronic disease (no residual deformity and NO permanent damage). *once the acute inflammation disappears, the rheumatic process leaves the joints normal! *"Rheumatic fever **licks** the joint, but **bites** the heart"*

## 2. SYDENHAM CHOREA (St Vitus dance)

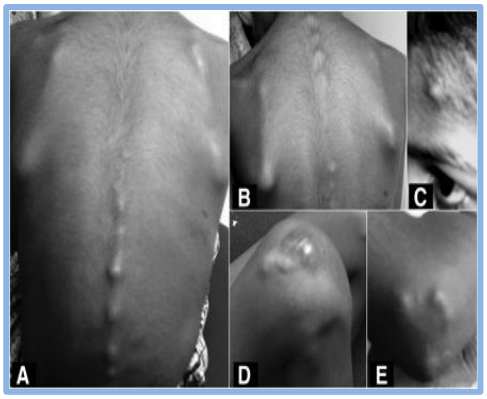
- Occurs in 5-10% of cases. (rare)
- Mainly in girls 1-15 years old.
- Late CNS manifestation that may appear even 6/12 months after the attack of rheumatic fever.
- Clinically manifest as clumsiness, deterioration of handwriting, emotional lability or grimacing of face, speech may also be affected.
- Abrupt purposeless involuntary movements of muscles of face, neck, trunk and limbs.
- A spontaneous recovery usually occurs within a few months (no permanent damage).

## 3. ERYTHEMA MARGINATUM



- Occurs in < 5%.(very rare)
- Unique, transient, serpiginous-looking lesions of 1-2 inches in size.
- Pale centered with red "erythema" irregular margins "marginatum".*lesions start as red macules that fade in the center but remain red at the edges.
- Seen more on trunks and limbs. They're non-itchy.
- Worsen with the application of heat.
- Often associated with chronic carditis.

## 4. SUBCUTANEOUS NODULES




- Occur in 10%
- Painless, hard, pea-sized, palpable nodules.
- Best felt over bony-prominences and extensor surfaces of joints, spine, scapulae, tendons and scalp.
- Associated with strong seropositivity.
- Always associated with severe carditis.
- Usually 0.5 – 2 cm in size.
- Short lived: last for few days.
- Typically appear more than 3 weeks (late) after the onset of other manifestations.

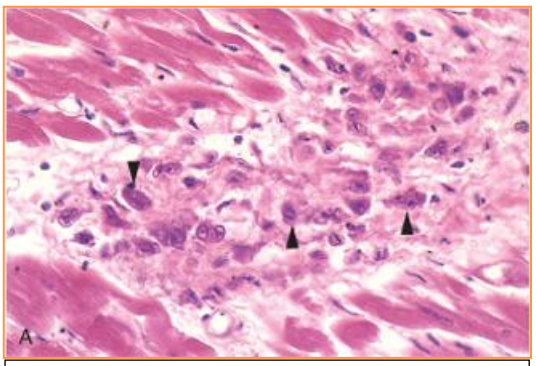
## 5. CARDITIS

- It occurs in 40-50% of the cases.
- The carditis of ARF is PANCARDITIS (involving all layers of the heart: the endocardium, myocardium and pericardium).
- Carditis is the ONLY manifestation of rheumatic fever that leaves a sequel and PERMANENT damage to the organ. (Healing of rheumatic valvulitis may cause fibrous thickening and adhesions, resulting in the most serious complication of rheumatic fever i.e. valvular stenosis and/or regurgitation)
- ACUTE phase →
  - ✓ Valvulitis; leading to tachycardia and new/changed murmurs.
    -soft mid-diastolic murmur (Carey Coombs murmur) typically occurs in mitral valvulitis.
    -soft systolic murmur due to mitral regurgitation is also common.
  - ✓ Pericarditis: pericardial chest pain, pericardial friction rub, pericardial effusion, ECG changes of pericarditis (raised ST segment)
  - ✓ Myocarditis: may result in cardiomegaly and heart failure, ECG changes of myocarditis (ST-T wave changes, T wave inverted/flattened).
  - ✓ ECG: AV block or other arrhythmias (conduction defects)
  - ✓ Dyspnea (due to pericardial effusion/heart failure).

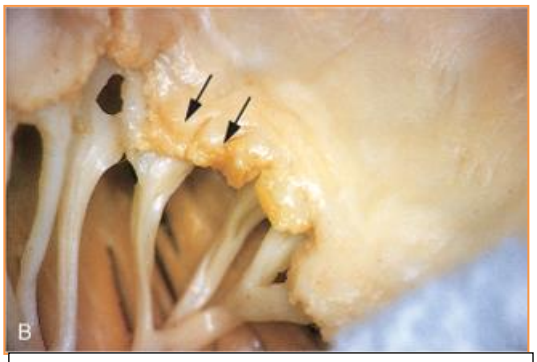
- CHRONIC phase →
  - ✓ Damage to valves leading to stenosis/regurgitation. The mitral valve is involved most frequently, followed by the aortic valve.

## Pathological lesions:

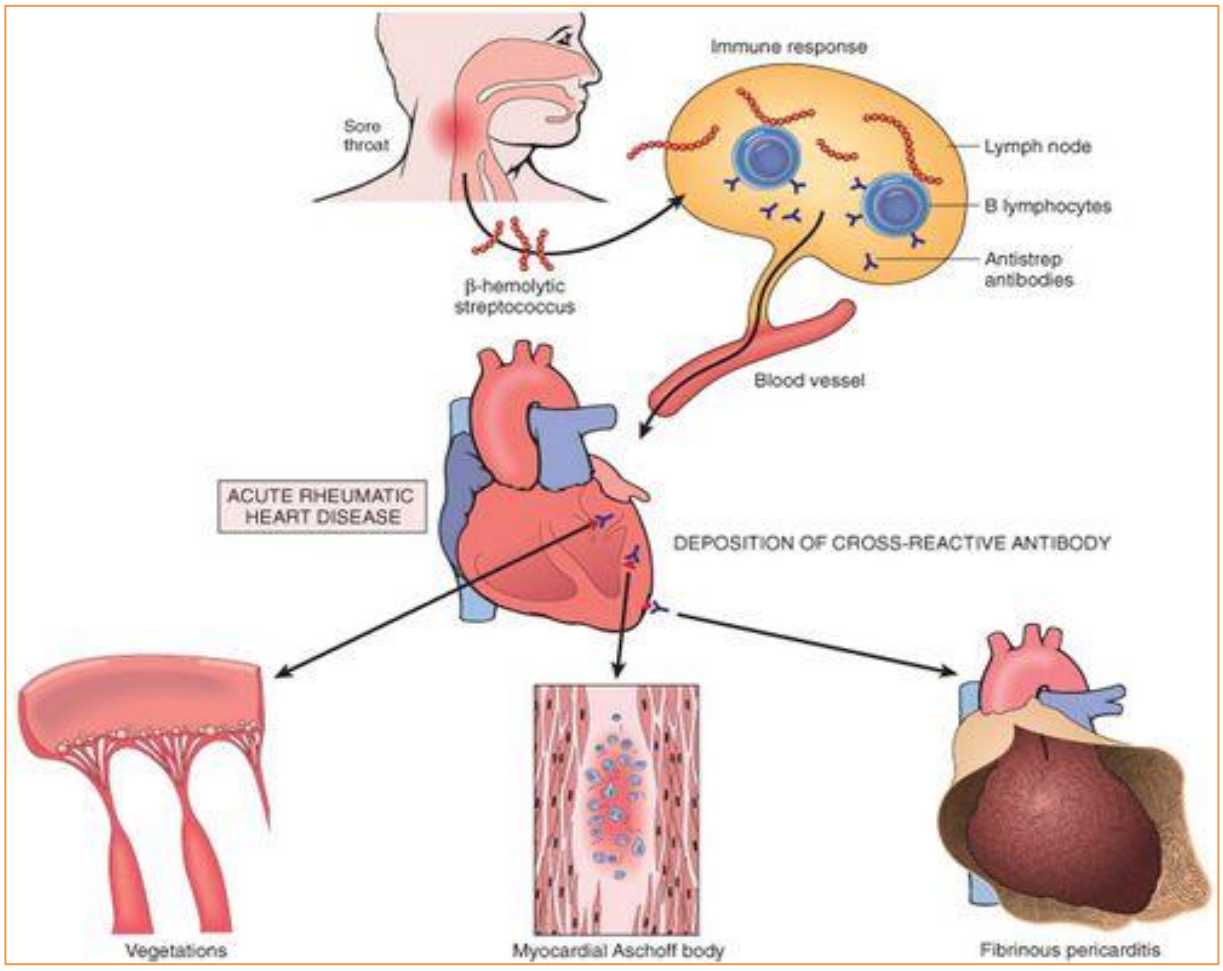
- All 3 layers of the heart can be affected by RF (PANCARDITIS).
- Myocarditis takes the form of the characteristic Aschoff bodies (granulomatous lesions with central necrotic area) which is found in acute rheumatic carditis.
- Pericarditis shows a fibrinous exudate, which generally resolves without sequel.
- In rheumatic valves, small warty verrucous vegetations are formed at the leaflet margins.
  *These warty projections probably arise from the precipitation of fibrin at sites of erosion caused by underlying inflammation. They heal by fibrosis causing permanent damage to the valves.*




*Microscopic appearance of an Aschoff body in a patient with acute rheumatic carditis; there is central necrosis with a collection of mononuclear inflammatory cells, with some activated macrophages (Anitschkow cells) with prominent nucleoli (arrowheads.)*




*Acute rheumatic mitral valvulitis superimposed on chronic rheumatic heart disease. Small vegetations (verrucae) are visible along the line of closure of the mitral valve leaflet (arrows). Previous episodes of rheumatic valvulitis have caused fibrous thickening and fusion of the chordae tendineae*



- **MINOR FEATURES:**

1. Fever
2. Arthralgia: joint pain, non-inflammatory [MINOR criterion].
   Arthritis: red, swollen, painful, tender...inflamed! [MAJOR criterion]
3. Previous rheumatic fever or rheumatic heart disease.

- **DIFFERENTIAL DIAGNOSIS:**

Juvenile rheumatoid arthritis - reactive arthritis – leukemia - infective endocarditis - SLE - myocarditis.

- **INVESTIGATIONS**

| *Evidence of systemic illness (non-specific)* | *Evidence of preceding streptococcal infection (specific)* | *Evidence of carditis* |
|---|---|---|
| 1. High ESR<br>2. CBC: Anemia, leukocytosis.<br>3. Elevated C-reactive protein | 4. Serology: Antistreptolysin O antibodies (ASO titres) >200 todd units. (Peak value attained at 3 weeks, then comes down to normal by 6 weeks).<br>5. Throat swab culture: GABH streptococci<br>*may be negative since throat infection has occurred 2-4 weeks before RF. | 6. ECG: prolonged PR interval, 2nd or 3rd degree AV blocks, ST depression, T wave inversion.<br>7. 2D Echo-cardiography: valve edema, mitral regurgitation, LA and LV dilatation, pericardial effusion, decreased contractility.<br>8. Chest x-ray: cardiomegaly; pulmonary congestion. |

- **DIAGNOSIS:**

- Rheumatic fever is mainly a clinical diagnosis.
- No single diagnostic sign or specific laboratory test available for diagnosis.
- Requires a high index of suspicion.
- Diagnosis based on **MODIFIED JONES CRITERA.**

**Table 7. Revised Jones Criteria For The Diagnosis Of Rheumatic Fever.**

**Diagnosis is made by the presence of:**

- one required criteria, two major criteria, and zero minor criteria; or
- one required criteria, one major criteria, and two minor criteria

**Required criteria:**

- Evidence of streptococcal infection (e.g., increased titer of anti-Streptococcal antibodies [ASO, others]; positive throat culture for group A *Streptococcus;* recent scarlet fever)

**Major diagnostic criteria:**

- Carditis
- Polyarthritis
- Chorea
- Erythema marginatum
- Subcutaneous nodules

**Minor diagnostic criteria:**

- Fever
- Arthralgia
- Previous rheumatic fever or rheumatic heart disease
- Acute phase reactions (ESR / CRP / leukocytosis)
- Prolonged PR interval

- MODIFIED JONES CRITERIA FOR DIAGNOSIS OF ACUTE RHEUMATIC FEVER:

A firm diagnosis requires:

1. 2 major manifestations or 1 major and 2 minor manifestations

   AND

2. Evidence of a recent streptococcal infection (required criteria)
   - However, when chorea or carditis is clearly present, evidence of an antecedent group A streptococcal infection is not necessary.

- **TREATMENT:**

- BED REST for 2-6 weeks till inflammation subsides (I.e. no fever, normal pulse rate, normal ESR, normal leukocyte count).*bed rest is important as it lessens joint pain and reduces cardiac workload.
- SUPPORTIVE THERAPY: treatment of heart failure.
- ANTI-STREPTOCOCCAL THERAPY:

1. A single dose of benzathine penicillin (long acting) 1.2 million units (IM injection).
2. OR oral penicillin for 10 days.
3. If allergic to penicillin then erythromycin for 10 days.

(Antibiotic treatment is given even if throat culture is negative!)

- ANTI-INFLAMMATORY AGENTS:

1. Aspirin (salicylates) 100 mg/kg per day for *arthritis* and in the *absence* of carditis, for 4-6 weeks to be tapered off. *rapid pain relief after using aspirin helps to confirm the diagnosis. *Keep an eye on toxicity and possible side effects.*
2. Corticosteroids are used in the *presence* of carditis, 1-2 mg/kg per day – for 4-6 weeks to be tapered off.

| Causal pathway | Preventive measure |
|---|---|
| ↓ | Primordial prevention:<br>Housing<br>Hygiene |
| **Group A streptococcal infection** | |
| ↓ | Primary prevention<br>Sore throat treatment<br>Vaccine (unavailable)<br>Control of skin infections (unproved) |
| **Acute rheumatic fever** | |
| ↓ | Secondary prevention<br>(because every recurrent attack makes it more damage)<br>Secondary prophylaxis |
| **Rheumatic heart disease** | |
| ↓ | Tertiary prevention:<br>Medication for heart failure,<br>Valve surgery, anticoagulation. |
| **Cardiac failure, stroke endocarditis, death** | |

## ▪ PREVENTION:

### - Secondary Prevention [Prevention of Recurrent Attacks]:

*Patients are susceptible to further attacks of RF if another streptococcal infection occurs, so long-term prophylaxis is very important.

1. Benzathine penicillin G 1.2 million units IM every 4 weeks (monthly)
2. Or Penicillin V 250 mg twice daily orally
3. Or Sulfadiazine 1 g daily orally
4. If allergic to both – Erythromycin 250 mg twice daily orally or Clarithromycin or Azithromycin

### - Duration of secondary rheumatic fever prophylaxis

- Rheumatic fever + carditis + persistent valvular disease →

For 10 years since last episode or until 40 years of age, sometimes lifelong.

- Rheumatic fever + carditis + no valvular 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 the patient may have asymptomatic group A streptococcal infection)*

*further attacks of RF are unusual after the age of 21.
*risk of recurrence of RF is highest during the first 5 years after the attack; 2ndry prophylaxis is always given for at least this period. After that the decision to continue or discontinue is dependent upon whether the patient has documented carditis/RHD or not.

## ▪ PROGNOSIS:

- Prognosis is good if recurrence is prevented by continuous antibiotic prophylaxis- particularly if no carditis is present in the initial attack.
- If carditis was present, half of them (50%) can develop chronic rheumatic heart disease.
- Recurrence following streptococcal sore throat is high in patients with previous carditis.
- For development of RHD, it takes 10-20 years in western world but earlier in undeveloped world due to malignant nature of the disease.
- Mitral valve is most commonly affected, followed by aortic and tricuspid valves so long term follow up is needed.

The most common valvular abnormality is mitral stenosis, but patients may have aortic or tricuspid involvement as well.

# RHEUMATIC HEART DISEASE

- Valvular deformities of chronic RHD are the most important consequence of RF; they are characterized by scarring and fibrosis of the valves resulting in permanent dysfunction.
- The functional consequence of RHD is valvular stenosis and/or regurgitation.
- It develops in at least half of those affected by rheumatic fever with carditis.
- RHD is overwhelmingly the most frequent cause of MITRAL STENOSIS.
- Two-thirds of cases occur in women.
- The mitral valve is affected in most of the cases (≈90%); the aortic valve is the next most frequently affected, followed by the tricuspid (usually 2ndry to mitral) and then the pulmonic valve.
- Chronic RHD usually doesn't cause clinical manifestations for years or even decades after the initial episode of RF. It presents in adulthood.
- Signs and symptoms of valvular disease depend on which valves are involved.
- The main pathological process in chronic rheumatic heart disease is progressive fibrosis. The heart valves are predominantly affected. Fusion of the valve's commissures and shortening of the chordae tendineae may lead to valve stenosis or regurgitation.

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*Please note that a more detailed explanation of valvular heart diseases (with their investigations and treatment) will be explained in a separate lecture.

## MITRAL STENOSIS

- RHD is the most common cause of mitral stenosis in adults.
- Pathophysiology: (pressure overload)

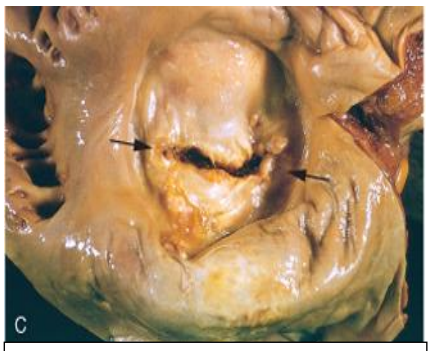
**Immune-mediated damage to the mitral valve (due to RF) leads to scarring and narrowing of the mitral orifice → MS results in elevated left atrial pressure and pulmonary venous pressure leading to pulmonary congestion → anything that increases the flow of blood across the mitral valve (exercise, tachycardia..) exacerbates the pulmonary hypertension and associated symptoms.*

- Normal mitral valve area= 4.6 $cm^2$, symptoms begin < 2 $cm^2$ , severe MS < 1 $cm^2$.
- CP of mitral stenosis:

1. Dyspnea on exertion →most common symptom & hallmark of the beginning of MS. *[Flow of blood from L atrium to L ventricle is restricted by mitral stenosis so the pressure in the L atrium increases causing pulmonary congestion which presents as dyspnea.]*
2. Fatigue [↓heart rate ↓↓left ventricle filling ↓↓cardiac output].
3. Palpitations [due to AFib]
4. Cough and hemoptysis [rupture of thin bronchial veins as a consequence of pulmonary HTN]
5. Hoarseness [pressure on left recurrent laryngeal nerve by the enlarged L atrium]
6. Dysphagia [increased pressure on esophagus by L atrium]
7. Peripheral edema and symptoms of right heart failure.

- Physical examination:
  - ✓ **Malar flush** (mitral facies).
  - ✓ **Tapping apex beat**.
  - ✓ Heart sounds: **loud S1**, loud P2 (with pulmonary hypertension)
  - ✓ Added sounds: **low-pitched mid-diastolic apical murmur/rumble**. Heard best using bell of stethoscope.
  - ✓ S2 is followed by an **opening snap**.
- Complications:

1. Atrial fibrillation
   (LA dilatation→AFib→atrial thrombus formation→systemic embolus).
2. Thromboembolic complications *e.g. a 35 year old female presents to the ER with a stroke, upon investigations she had AFib and mitral stenosis, suspect RHD.*
3. Pulmonary hypertension and congestion
4. Congestive heart failure (ascites and edema )
5. Infective endocarditis.




*Mitral stenosis with diffuse fibrous thickening and distortion of the valve leaflets, commissural fusion (arrows), and thickening and shortening of the chordae tendineae*

## MITRAL REGURGITATION:

- Pathophysiology: Chronic MR (volume overload):

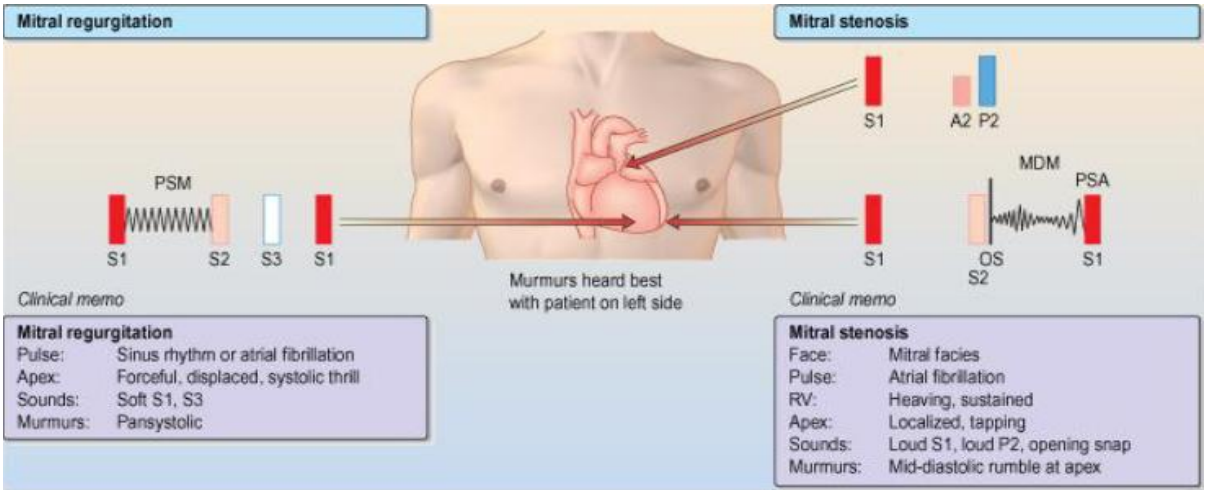
Gradual elevation of left atrial pressure in setting of dilated LA and LV→ LV dysfunction occurs due to dilatation (↓CO and ↑total stroke volume) →Pulmonary hypertension can result from chronic backflow into pulmonary vasculature.

- Clinical Presentation:

1. Dyspnea on exertion 2. Fatigue 3. Palpitations 4. Pulmonary congestion

- Physical examination:

✓ Apex beat: laterally displaced diffuse forceful apex (due to LVE)
✓ soft S1 (incomplete leaflet closure), S3 gallop .
✓ Added sounds: **pansystolic/holosystolic apical blowing murmur** (starts with S1 and continues on through S2) felt at the **apex** and radiates to the **axillae**.
✓ AFib is a common finding



## AORTIC STENOSIS:

-2ND most commonly affected valve after mitral valve.
- Pathophysiology (pressure overload): *causes obstruction to L ventricular outflow → increasing LV end-diastolic pressure →which results in left ventricular hypertrophy*.
- Clinical Presentation:
*Patients often remain asymptomatic for years.
*Symptomatic patients:
1. Angina/chest pain *(imbalance between supply and demand)*
2. Syncope *(usually upon exertion, inability to increase CO and meet reduced SVR demands)*
3. Congestive heart failure features, such as dyspnea on exertion, orthopnea, or PND.
-Physical examination:

- ✓ Aortic stenosis murmur: harsh **systolic ejection murmur**, best heard in the **aortic** area and radiates to **carotid** arteries. Systolic thrill in aortic area.
- ✓ S4 gallop *(from LVH)*
- ✓ Parvus et tardus (Carotid impulse)(parvus=low volume, tardus=late)
- ✓ Slow rising plateau
- ✓ Sustained apex beat

## AORTIC REGURGIATION:

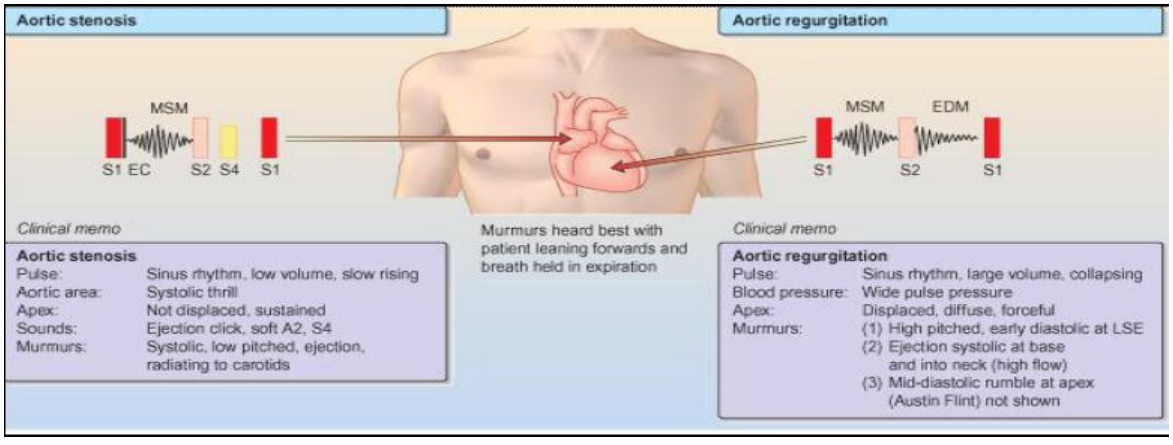
-pathophysiology: *Regurgitated blood flow increases left ventricular end diastolic volume →LV dilation occur in response in order to maintain SV and prevent diastolic pressure from increasing excessively →over time, these compensatory mechanisms fail, leading to increased left-sided and pulmonary pressures.*

- Clinical Presentation:

1. Palpitations (mild AR) 2. Dyspnea on excursion (pulmonary venous congestion) 3.Fatigue (inadequate CO)

- Physical examination:

- ✓ **Early diastolic (decrescendo) murmur** (best heard at L sternal border while the patient leaning forwards and breath held in expiration).
- ✓ Ejection systolic murmur *(increased stroke volume).*
- ✓ Austin-flint murmur (mid-diastolic murmur).
- ✓ Displaced forceful apical impulse.
- ✓ **Wide pulse pressure** *(markedly increased SBP, with decreased DBP)* Quincke: capillary pulsations in nail beds, Duroziez's sign: pistol shot sound heard over the femoral arteries, De Musset's sign: head nodding with pulse.
- ✓ Collapsing pulse/water-hammer pulse.



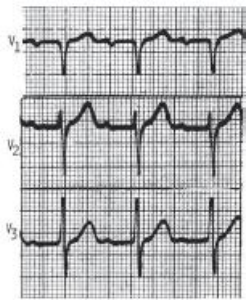
## CASE EXAMPLES

1. A 72-year-old male comes to the office with intermittent symptoms of dyspnea on exertion, palpitations, and cough occasionally productive of blood. On cardiac auscultation, a low-pitched diastolic rumbling murmur is faintly heard at the apex. What is the most likely cause of the murmur?

a. Rheumatic fever as a youth
b. Long-standing hypertension
c. A silent MI within the past year
d. A congenital anomaly
e. Anemia from chronic blood loss

*- The answer is A. The history & physical examination findings suggest mitral stenosis. Dyspnea may be present 2ndy to pulmonary congestion; palpitations are often related to atrial arrhythmias (atrial flutter or fibrillation); hemoptysis may occur as a consequence of pulmonary HTN with rupture of bronchial veins. A diastolic rumbling apical murmur is characteristic. If the patient is in sinus rhythm, a late diastolic accentuation of the murmur occurs because of increased flow across the mitral valve with atrial contraction. A loud first heart sound and early diastolic opening snap may also be present. The etiology of mitral stenosis is usually rheumatic, rarely congenital. Hypertension may cause an S4 gallop but not a diastolic murmur. MI may cause mitral regurgitation because of papillary muscle dysfunction & anemia may cause a pulmonic flow murmur; both of these are systolic murmurs.*

2. An 18-year-old male complains of fever and transient pain in both knees and elbows. The right knee was red and swollen for 1 day during the week prior to presentation. On physical examination, the patient has a low-grade fever. He has a III/VI, high pitched, apical systolic murmur with radiation to the axilla, as well as a soft, mid-diastolic murmur heard at the base. A tender nodule is palpated over an extensor tendon of the hand. There are pink erythematous lesions over the abdomen, some with central clearing. The following laboratory values are obtained:
Hct: 42
WBC: 12,000/L with 80% polymorph-nuclear leukocytes, 20% lymphocytes.
ESR: 60 mm/h
The patient's ECG is shown below.
Which of the following tests is most critical to diagnosis?




a. Blood cultures
b. Antistreptolysin O antibody
c. Echocardiogram
d. Antinuclear antibodies
e. Creatine kinase

*The answer is B. This 18-year-old presents with features of rheumatic fever. Rheumatic fever is diagnosed according to the Jones criteria. Evidence of recent streptococcal infection plus 2 major manifestations or 1 major & 2 minor manifestations satisfy the Jones criteria for diagnosis of acute rheumatic fever. Major criteria include carditis, polyarthritis, chorea, erythema marginatum, & subcutaneous nodules. Minor manifestations include fever, polyarthralgia, elevated erythrocyte sedimentation rate, & PR prolongation on ECG. This patient's clinical manifestations include arthritis, fever, & murmur (consistent with mitral regurgitation). The rash suggests erythema marginatum, & a subcutaneous nodule is noted. Rheumatic subcutaneous nodules are pea sized & usually overlie extensor tendons. The rash is usually pink with clear centers & serpiginous margins. Laboratory data include an elevated erythrocyte sedimentation rate. The ECG shows evidence of first-degree AV block. An antistreptolysin O antibody is necessary to document prior streptococcal infection. Endocarditis (for which blood cultures & an echocardiogram would be ordered) might cause fever, joint symptoms & the tender nodule but would not account for the diastolic murmur or the characteristic skin lesion. There is no evidence of lupus or myocardial infarction.*

4. A 44-year-old woman presents with worsening fatigue and dyspnea. The pertinent medical history ia that she had rheumatic fever during childhood. Physical examination reveals a loud S1, an early diastolic opening snap with a rumbling late diastolic murmur. A chest radiograph shows an enlarged left atrium. Which of the following is the most likely diagnosis?

A. Aortic regurgitation
B. Aortic stenosis
C. Mitral regurgitation
D. Mitral stenosis
E. Pulmonary stenosis

*The answer is D. The cardiac valve most often affected by chronic rheumatic fever is the mitral valve. With healing, fibrosis will result in stenosis of the valve, which grossly has an appearance described as being a "fish mouth" or "buttonhole." Clinically, mitral stenosis produces a rumbling late diastolic murmur with an opening snap (an early diastolic opening snap is characteristic of mitral stenosis).*
Underlying mechanism for these findings: Rheumatic heart disease.
Complications and prognosis for this disorder: Pulmonary edema, atrial fibrillation, and intracardiac thrombosis; prognosis is good with repair of the mitral valve.

5. Which of the following types of infection, precedes by several weeks, the development of acute rheumatic fever?

A. Group A β-hemolytic streptococcal infection of the pharynx
B. Group D α-hemolytic streptococcal infection of the heart
C. *Staphylococcus aureus* infection of the lungs
D. *Streptococcus pyogenes* infection of the skin
E. *Treponema pallidum* infection of the abdominal aorta

*Answer is A.*

6. A 6-year-old boy develops fever, joint pain, and a diffuse skin rash approximately 3 weeks after recovering from a sore throat. Physical examination finds several small skin nodules, and laboratory examination finds an elevated erythrocyte sedimentation rate along with an elevated antistreptolysin O titer. Which of the following abnormalities is most characteristic of this boy's disease?

A. Anitschkow cells within the epidermis
B. Aschoff bodies within the myocardium
C. Langhans giant cells within the dermis
D. Psammoma bodies within the endocardium
E. Virchow cells within the nasopharynx

*Answer is B.*