# Etiology and Diagnosis of Acute Rheumatic Fever

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## Sources:

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# Introduction to Acute Rheumatic Fever (ARF)

- Autoimmune reaction to infection with Group A Strepococcus (GAS).
- Multisystem disease, affecting heart, joints, skin, movement
- Rheumatic Heart Disease (RHD), is the cardiac manifestation: valvular damage
- Most manifestations resolve spontaneously; RHD may persist

# Epidemiology

- ARF and RHD: diseases of poverty.
- Common in all counties until early 20th century.
- Reduced infection with GAS has caused ARF to virtually disappear in industrialized countries, do to: less crowding, better hygiene, introduction of antibiotics.
- 95% of ARF cases and death occur in developing countries.
- In developing countries, RHD is most common cause of heart disease in children.
- ARF mainly affects children aged 5-14 years. Initial episodes rare over age 30.
- Hot spots: sub-Saharan Africa, Pacific Nations, Australasia, Indian subcontinent

# Pathogenesis

- Basis of ARF is an autoimmune reaction to GAS caused by molecular mimicry.

- Epitopes of GAS, especially repeat reagions on M protein, resemble human myosin, keratin and other molecules

- Hypothesis of two methods for autoimmune damage:
  - T cell, sensitized to the human molecules following initial infection, are then recalled after subsequent GAS infections.

  - Cardiac valve damage caused by antibodies to GAS N-acetylglucosamine that cross react with laminin found on cardiac endothelium.

# Clinical Features

- Symptoms typically appear ~3 weeks following GAS infection. Initial GAS infection may manifest as soar throat, but often is subclinical.

- Main presentation of ARF is fever, polyarthritis and carditis.

**Heart features:**

- ~ 60% of ARF patients progress to RHD, which affects endocardium, pericardium, myocardium.

- Hallmark of RHD is valvular damage, almost always Mitral Valve, sometimes together with Aortic Valve.

Mnemonic: **M** protein -> **M**itral Valve

- Valve damage initial causes regurgitation; repeated episodes calse calification and valvular stenosis.

- Peridarditis causes friction rub, occasionally pleuritic chest pain.

- Myocardial inflammation affect electrical conduction: PR interval prolongation, softening of S1.

# Other Clinical Features

- **Joints**: Inflammatory, asymmetric polyarthritis, usually of large joints: knees, ankles, hips, elbows
- Migratory: moves to different joints over several hours. Sever disabling pain requiring anti-inflammatory meds (salicylates, NSAIDs)

- **Chorea(Sydenhms)**: Mostly in women, latency period up to 6 months. Darting of tongue, upper limbs. Usually resolves completely within 6 weeks.

- **Skin**: Classic rash is erythema marginatum: pink macules that clear centrally.
- Evanescent, appearing and disappearing before doctor's eyes.
- Subcutaneious nodules: painless, small lumps beneath skin.

- **Other features**:
- High grade fever > 39C. Signs of inflammation
- Dramatic elevation of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

# Diagnosis

- No definitive tests exists for diagnosis.
- Diagnosis based on presence of combination of clinical features together with evidence of previous GAS infection.
- Jones Criteria used to make diagnosis:  set of criteria developed by Dr. T. Jones  in 1944, revised by World Health Organization.
- **Evidence of preceding streptococcal infection:**
  - Increased antistreptolysin O or other streptococcal antibodies
  - Positive throat culture for Group A beta-hemolytic streptococci
  - Positive rapid direct Group A strep carbohydrate antigen test
  - Recent scarlet fever.

# Jones Criteria (WHO)

**Diagnosis requirements:**

1. 2 major criteria, or one major and two minor criteria
2. Evidence of recent streptococcal infection.

**Major Criteria**

- **Carditis**: All layers of cardiac tissue are affected (pericardium, epicardium, myocardium, endocardium) The patient may have a new or changing murmur, with mitral regurgitation being the most common followed by aortic insufficiency.
- **Polyarthritis**: Migrating arthritis that typically affects the knees, ankles, elbows and wrists. The joints are very painful and symptoms are very responsive to anti-inflammatory medicines.
- **Chorea**: Also known as Syndenham´s chorea, or "St. Vitus´ dance". There are abrupt, purposeless movements. This may be the only manifestation of ARF and is its presence is diagnostic. May also include emotional disturbances and inappropriate behavior.
- **Erythema marginatum**: A non-pruritic rash that commonly affects the trunk and proximal extremities, but spares the face. The rash typically migrates from central areas to periphery, and has well-defined borders.
- **Subcutaneous nodules**: Usually located over bones or tendons, these nodules are painless and firm.

**Minor Criteria:**

- Fever
- Arthralgia
- Previous rheumatic fever or rheumatic heart disease
- Acute phase reactants: Leukocytosis, elevated eritrosedimentation rate (ESR) and C-reactive protein (CRP)
- Prolonged P-R interval on electrocardiogram (ECG)