

Acute Rheumatic Fever



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Introduction



- Acute rheumatic fever: inflammatory disease with devastating sequelae
- Link to pharyngeal infection with group A beta hemolytic streptococci
- Continues to be a problem worldwide:
 - sporadic outbreaks in developed countries
 - frequent occurrences in developing countries
- Still gaining understanding of etiology
 - link between genetic predisposition and clinical manifestations
- Best prevention still correct use of antibiotics

Acute Rheumatic Fever

A horizontal brushstroke in a vibrant yellow color, with a textured, painterly appearance, extending across the width of the slide below the title.

Epidemiology

Pathogenesis

Clinical features

Diagnosis

Treatment

Future treatments

Epidemiology



- Important cause of chronic disease and death in developing world
- Underdiagnosed and undertreated
- Estimated 30 million people suffer from ongoing heart disease from ARF, 70% dying at average age 35 years old

Epidemiology (continued)



- Usually occurs in people between 5 and 18 years old
- Males and females equally affected
- Overcrowding, poverty, lack of access to medical care contributes to transmission
- Virulence of strain important
- In tropics/subtropics: year-round incidence with peak in colder months

Pathogenesis



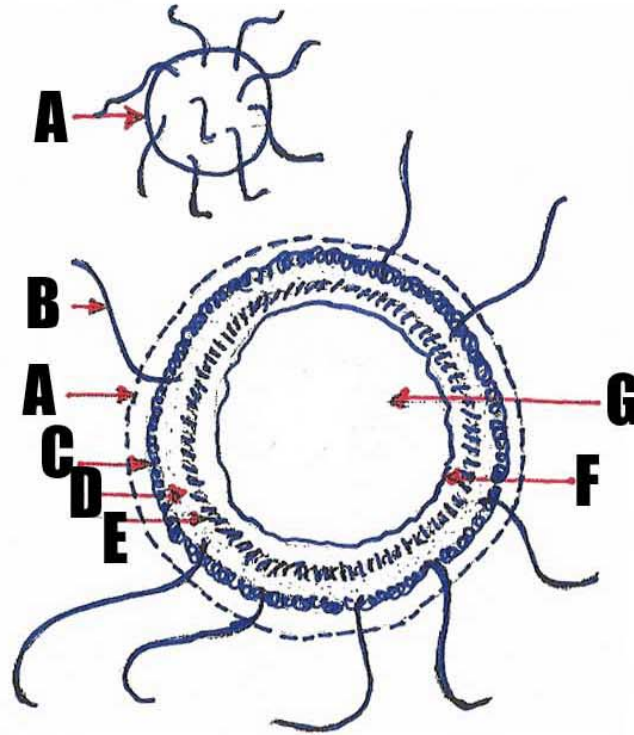
- Group A strep pharyngeal infection precedes clinical manifestations of ARF by 2 - 6 weeks
- Antibodies made against group A strep cross-react with human tissue
 - heart valve and brain share common antigenic sequences with GAS bacteria
 - theory of molecular mimicry
- Host immune responses may play a role in determining who gets ARF following infection
- Virulent strains: rheumatogenic serotypes

Pathogenesis



- Most important antigenic proteins in external layer of cell wall
 - M, T, R proteins

Streptococcal Cell Structure



**A = capsule B = fimbria C = M,T,R antigenic proteins
D = group specific carbohydrates E = peptidoglycan
F = cytoplasmic membrane G = cytoplasm
(C,D,E make up streptococcal cell wall)**

Clinical Features



Following upper airway infection with GAS

Silent period of 2 - 6 weeks

Sudden onset of fever, pallor, malaise, fatigue

Clinical Features (continued)



Characterized by:

Arthritis

Carditis

Sydenham's chorea

Erythema marginatum

Subcutaneous nodules

Called “major manifestations” of Jones criteria either because of frequency or specificity

Clinical Features (continued)



Other features:

Arthralgias

Epistaxis

Serositis

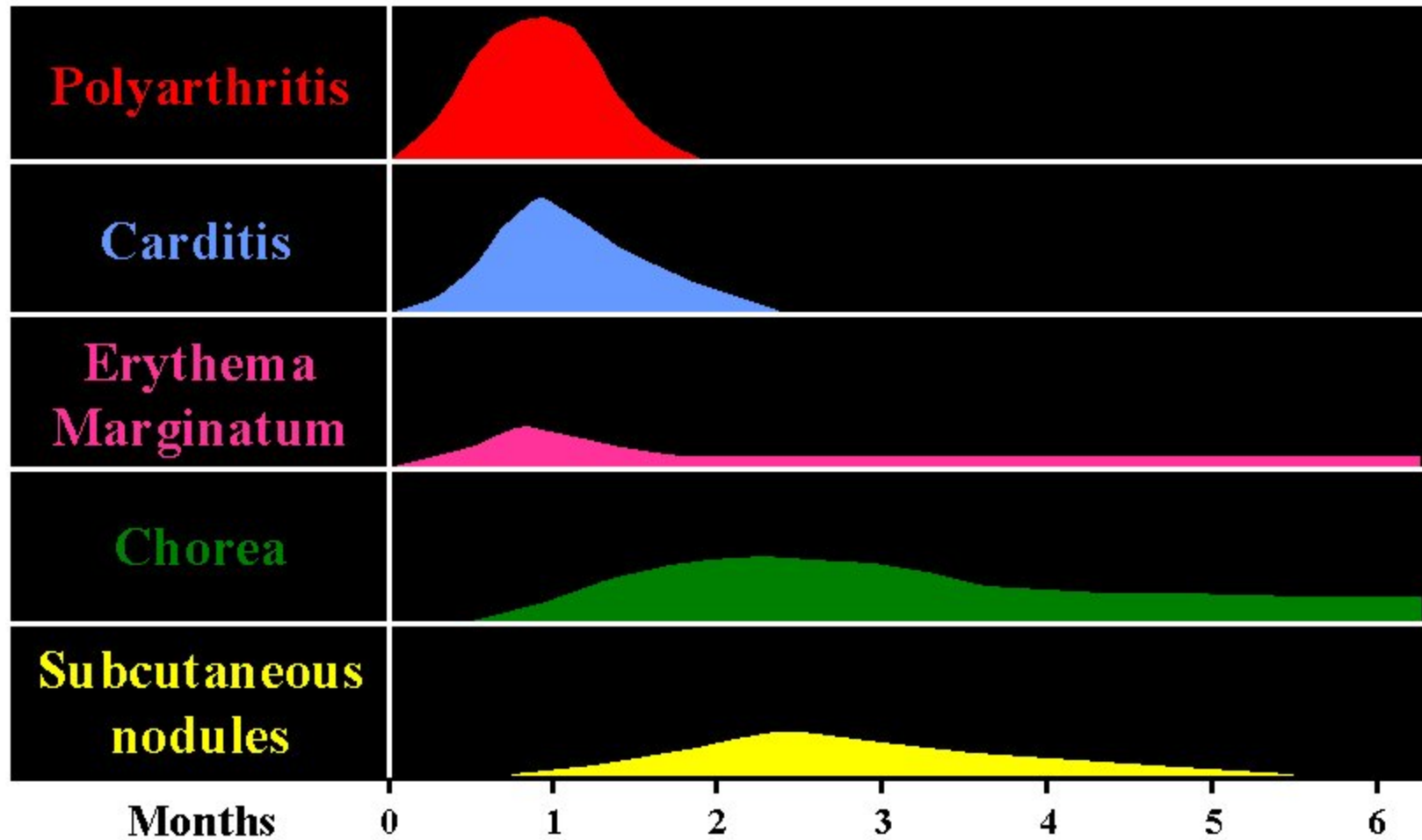
Involvement of lung, kidneys and CNS

Arthritis



- Most common feature: present in 80% of patients
- Painful, migratory, short duration, excellent response of salicylates
- Usually >5 joints affected and large joints preferred
 - Knees, ankles, wrists, elbows, shoulders
- Small joints and cervical spine less commonly involved

Clinical Manifestations of Acute Rheumatic Fever



Carditis



- Most serious manifestation
- May lead to death in acute phase or at later stage
- Any cardiac tissue may be affected
 - Valvular lesion most common: mitral and aortic
 - Seldom see isolated pericarditis or myocarditis

Carditis (continued)



- Clinical signs:
 - High pulse rate
 - Murmurs
 - Cardiomegaly
 - Rhythm disturbances (prolonged PR interval)
 - Pericardial friction rubs
 - Cardiac failure



Carditis (continued)



Mitral and aortic regurgitation most common

Apical systolic and basal diastolic murmurs

Pericarditis usually asymptomatic

Occasionally causes chest pain, friction rubs or distant heart sounds

Sydenham's Chorea



- Extrapiramidal disorder
 - Fast, clonic, involuntary movements (especially face and limbs)
 - Muscular hypotonus
 - Emotional lability
- First sign: difficulty walking, talking, writing
- Usually a late manifestation: months after infection
- Often the only manifestation of ARF

Sydenham's Chorea (continued)



- Occurs in 30% of patients with ARF
- 1/2 of these also have carditis or arthritis
- Usually benign and resolves in 2 - 3 months
- Can last for more than 2 years

Subcutaneous Nodules

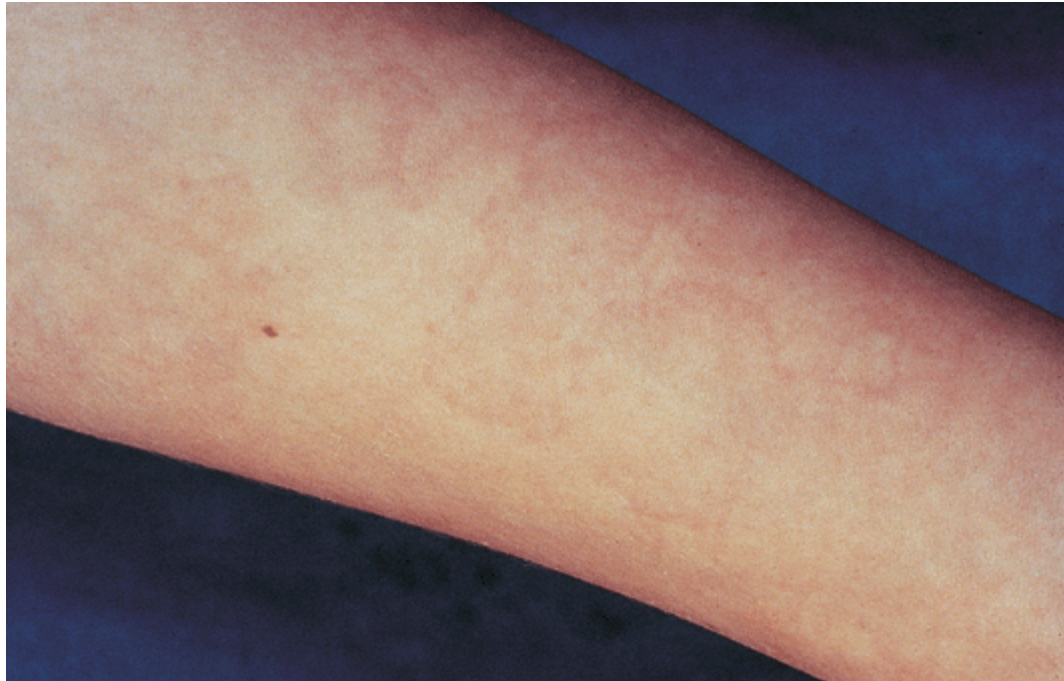


- Usually 0.5 - 2 cm long
 - Firm, non-tender, isolated or in clusters
- Most common: along extensor surfaces of joint
 - Knees, elbows, wrists
- Also: on bony prominences, tendons, dorsi of feet, occiput or cervical spine
- Last a few days only
- Occur in 9 - 20% of cases
- Often associated with carditis

Erythema Marginatum



- Present in 7% of patients
- Highly specific to ARF
- Cutaneous lesion:
 - Reddish pink border
 - Pale center
 - Round or irregular shape
- Often on trunk, abdomen, inner arms, or thighs
- Highly suggestive of carditis





Other Clinical Features



- Less frequent or less specific to ARF
 - Fever
 - Arthralgia
 - Epistaxis
 - Abdominal pain (5%) due to peritonitis
 - Hematuria (5%)/renal involvement
 - When routine biopsy done, in up to 39%
 - Pneumonitis
 - Mild pleuritis (5 - 10%)
 - Encephalitis (extremely rare)

Diagnosis



- Jones criteria
 - Criteria developed to prevent overdiagnosis
 - Some criticism regarding validity
 - Still important as guidelines
- Probability of ARF high with
 - Evidence of previous infection with streptococcal upper airway infection and
 - 2 major criteria
 - or
 - 1 major criteria and 2 minor criteria

Diagnosis: Jones Criteria



Major criteria

Arthritis

Carditis

Sydenham's chorea

Erythema marginatum

Subcutaneous nodules

Diagnosis: Jones Criteria (continued)



Minor manifestations

Fever

Arthralgia

Elevated c-reactive protein or

Erythrocyte sedimentation rate

Prolonged PR interval on EKG

Diagnosis: Evidence of Previous Infection



- Culture
- Antistreptolysin antibody
 - Often elevated in healthy children or with Rheumatoid Arthritis, Henoch-Schonlein Purpura, Takayasu's Arteritis
- Antibodies to other strep antigens
 - Anti-DNAase B, anti-hyaluronidase, anti-streptokinase, anti-nicotinamide

Diagnosis: Differential Diagnosis of ARF



Juvenile rheumatoid arthritis
Systemic lupus erythematosus
Other connective tissue diseases, including vasculitides
Bacterial endocarditis
Reactive arthritis
Seronegative spondyloarthropathies
Infections (Hansen's Disease, Lyme, Yersinia)
Familial Mediterranean Fever
Antiphospholipid Syndrome
Leukemias
Sickle cell anemia and other hemoglobin disorders
Sarcoidosis

Diagnosis: Laboratory Studies



- None capable of diagnosing ARF: clinical diagnosis
- Can help eliminate other diseases
- Aids in diagnosis
- Monitor inflammatory process
- Evaluate extent of cardiac involvement

Diagnosis: Laboratory Studies (continued)



- CBC: not very helpful
- CRP, ESR: non-specific indicators of inflammation
- Tests for anti-streptococcal antibody
- CXR
- EKG: prolonged PR interval in 1/3 patients
 - not specific to ARF
 - not associated with later cardiac sequelae

Treatment



- Eradication of the group A strep most important
 - Avoids chronic exposure of immune system to strep
- Best: single dose IM benzathine penicillin G
 - < 27 kg: 600,000 units
 - >27 kg: 1,200,000 units

Treatment (continued)



■ Alternative: oral antibiotics

- PCN VK 500 mg - 1000 mg divided bid to qid x 10 d
- Erythromycin 40 mg/kg/d divided bid to qid x 10 d
- Azithromycin x 5 d
- Cephalosporins x 5 d
 - Cefuroxime axetil
 - Cefpodoxime proxetil
 - Cefadroxil
 - Cefdinir
- NOT sulfa-derived antibiotic: do not eradicate strep

Treatment: Arthritis



- Salicylates or NSAIDs x 3 weeks
- Usually excellent response
- If poor response: diagnosis in question

Treatment: Carditis



- Potential for morbidity
- Steroid use compulsory
 - Prednisone 1 -2 mg/kg/d (max 60 mg) x 10 - 15 days
 - Taper 20 -25% each week
- Rest x 4 weeks
- If simultaneous arthritis and carditis: steroids alone sufficient

Treatment: Sydenham's Chorea



- Haloperidol 0.5 - 1 mg/kg
 - Add 0.5 mg every 3 days if not responding
 - Max 5 mg
- Alternate: Sodium valproate 15 -20 mg/kg/d
- No proven benefit of steroids

Primary Prophylaxis



- Distinguish GAS from viral causes
 - No lab test absolutely reliable
 - Good history and physical suggest
 - Virus: coryza, hoarseness, conjunctivitis, diarrhea
 - Strep: malaise, high fever, abdominal pain, soft palate petechiae

Primary Prophylaxis (continued)



■ Antibiotic use

- Systemic Benzathine PCN led to impressive fall incidence in Costa Rica

■ Social and economic factors

- Improving living conditions
- Hygiene
- Overcrowding
- Access to medical care
- Education

Secondary Prophylaxis



- Benzathine PCN given to prevent recurrences of ARF
- Prevention of chronic valve disease
 - American Heart Association
 - < 27 kg: 600,000 units
 - > 27 kg: 1,200,000 units

Secondary Prophylaxis (continued)



- Newer recommendation: every 2 wks for first 2 years then every 3 wks
- Duration: minimum 5 years after last episode or until 21 years old, whatever later
- AHA recommends: 10 years or until “well into adulthood”

Future treatments



- Immunization against GAS being developed
 - Hypersensitivity reactions a problem in early trials
- Balloon mitral valvuloplasty will reduce cost compared to surgical options and make treatment more accessible

Conclusion



- Acute Rheumatic Fever leading to Rheumatic Heart Disease is a major problem world wide.
- Appropriate treatment of group A strep pharyngitis necessary to prevent disease.
- Preventing recurrences causing chronic heart disease simple, universally available, and cost-effective.

References



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- Pichichero ME. Group A beta-hemolytic streptococcal infections, *Pediatrics in Review*. 1998; 19(9): 291-302