Valvular Heart Disease in the Developed World and the Declining Role of Rheumatic Heart Disease

Kari Bernard, MS, PA-C
Arizona State Association of Physician Assistants Spring 2016 Conference

**Acute Rheumatic Fever**

Modified Jones Criteria to Diagnose Acute Rheumatic Fever:

Diagnostic: 1 Required Criteria and 2 Major Criteria and 0 Minor Criteria
Diagnostic: 1 Required Criteria and 1 Major Criteria and 2 Minor Criteria

**Required Criteria**
Evidence of antecedent Strep infection: ASO / Strep antibodies / Strep group A throat culture / Recent scarlet fever / anti-deoxyribonuclease B / anti-hyaluronidase

**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

**Major Criteria of ARF**
- Migratory polyarthritis (knees, ankles, elbows; spares hands, feet & hips)
- Erythema marginatum (nonpruritic annular rash trunk & limbs)
- Sydenham chorea (rare, extrems & face)
- Subcutaneous nodules extensor surfaces (elbows, knees, wrists, ankles, achilles, occiput, spinous processes)
- Carditis (valvulitis, less so pericarditis or myocarditis)
- Rheumatic Heart Disease occurs secondary to a severe 1st episode of ARF or multiple recurrent episodes of ARF; most common manifestation is valvulitis. Often presents as heart failure.

Acute Rheumatic Fever strikes in urban populations living in poor, crowded neighborhoods.
- Baltimore 1960-1964 incidence: 24 per 100,000
• Baltimore 1977-1981 incidence: 0.5 per 100,000
  o As living standards and access to healthcare improved, rates of ARF declined in developed nations.
• Salt Lake City 1987: 50 cases (18 per 100,000)
  o Next 5 years: 9 outbreaks in middle-class U.S. and on military base
• Reported RF Cases in Alaska 2000-2010

Currently, ARF & RHD rates are high in developing countries and among some indigenous populations in wealthy countries.

“Prevention of Rheumatic Fever”, Journal of the American Medical Association, May 13, 1950:
• As of 1950 in the US, ARF developed in 200,000 to 250,000 persons annually
  o 460,000 persons in the country had Rheumatic Heart Disease
  o At that time, each case of ARF among military members cost the armed services $16,000.
• JAMA’s study included 1,634 military males diagnosed with strep pharyngitis
  o 798 received PCN, 804 received no treatment
• Patients checked 3-4 weeks later for ARF, diagnosed using modified Jones Criteria
  o Of those treated with penicillin, 2 developed ARF
  o Of those not treated, 17 developed ARF
• Summary: “Evidence is presented to indicate that rheumatic fever can be prevented by the treatment of streptococcal disease with penicillin.”

Infectious Disease Society of America 2012 Guidelines
• Estimated 15 million sore throats per year
• Group A Strep is the causative agent in 5-15% of adult sore throats and 20-30% of children’s sore throats.
• The remaining etiologies are usually viral, save a few rare cases of other bacterial causes.
• Diagnosis of Group A Strep (GAS) pharyngitis should be accomplished via Rapid Antigen Detection Test (RADT) or throat culture because clinical features do not reliably discriminate GAS and viral pharyngitis unless overt viral features are present (aka rhinorrhea, cough, oral ulcers, hoarseness)
  o Negative RADT in children should have a back up culture, positive RADTs do not need to be backed up – highly specific.
  o No back up throat cultures in adults – GAS pharyngitis rare in adults, ARF rare in adults.
  o No RADT if <3 years of age because ARF is rare in this population, GAS is rare as is the classic presentation in this population.
• If GAS confirmed:
  o Treat for a duration likely to eradicate GAS from the pharynx, usually 10 days with appropriate narrow spectrum abx.
  o PCN VK 250 qid or 500 bid x 10 d, IM benzathine pcn G, 1,200,000 U x 1, Amoxicillin wt based x 10 d
  o If PCN allergic, first gen cephalosporin, clindamycin or clarithromycin x 10 days or azithromycin for 5 days.

American College of Physicians 2016 Report
• “Inappropriate antibiotic use for acute respiratory tract infections is an important contributor to antibiotic resistance”
  o Antibiotics are prescribed at 100 million office visits yearly, 41% for respiratory illnesses.
  o In US, 2 million antibiotic resistant illnesses yearly, accounting for 23,000 deaths.
  o Antibiotics are implicated in 1 of every 5 visits to the Emergency Department for adverse drug reactions, from rash or diarrhea to Stevens Johnson syndrome, anaphylaxis and sudden cardiac death.
• Most cases of pharyngitis are viral in etiology.
  o More likely viral if sore throat plus: cough, nasal congestion, conjunctivitis, hoarseness, diarrhea, oropharyngeal lesions
  o Think bacterial: persistent fever, rigors, night sweats, tender lymph nodes, tonsillopharyngeal exudates, scarlatiniform rash, palatal petechiae & swollen tonsils
• Use Centor Criteria – fever by history, tender anterior cervical lymphadenopathy, absence of cough, tonsillar exudates – to identify people with a low risk of GAS and do not treat them.
  o If patients meet fewer than 3 criteria, do not test.
  o If they have 3 or 4 Centor Criteria – test with RADT.
  o If RADT positive, treat as per IDSA “for a time likely to eradicate the bacteria.”
Don’t treat chronic carriers of GAS.

If severe pharyngitis (drooling, trouble swallowing, tender neck or swelling) evaluate for peritonsillar abscess, retropharyngeal abscess, epiglottitis or Lemierre syndrome. Fusobacterium necrophorum implicated in Lemierre syndrome – rare but deadly.

Why treat GAS pharyngitis:

- Shortens duration of pain by 1-2 days
- Limits spread to others – classmates, family members
- Prevents suppurative complications - Less acute otitis media, Less peritonsillar abscesses
- Prevents nonsuppurative complications – Acute Rheumatic Fever
  - Treatment of ARF does not prevent or modify long term disability or death, therefore treating GAS pharyngitis may not prevent Rheumatic heart disease.
- Where ARF rates are low, the risk of serious antibiotic-related complications =EQUALS= the risk of developing ARF

Valvular Heart Disease in Developed Countries:

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<tr>
<th>Occurrence of VHD in Developed Countries</th>
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<td>Aortic Stenosis</td>
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Overall, the most prevalent valve disorders and the most common causes:
- Most prevalent valve disorders – aortic stenosis and mitral regurgitation
- Most common causes – degenerative and rheumatic

Aortic stenosis
- Pathology: progressive valve stenosis produces a progressive afterload increase in the left ventricle. To reduce wall stress, the ventricle undergoes concentric hypertrophy. This left ventricular hypertrophy can be severe.
Clinical presentation: A long latency period followed by rapid progression after symptom onset.
   - Asymptomatic period: Most patients are asymptomatic until after age 60, unless a congenital bicuspid valve exists, in which case they usually become symptomatic on average 20 years earlier.
   - Symptomatic phase: After symptom onset, there is a 50% mortality within 2-3 years. Presenting signs/symptoms include left ventricular failure, syncope or angina (due to underperfusion of endocardium), all usually with exertion. 50% of patients with calcific AS also have coronary artery disease.

   - ECG will show normal or left ventricular hypertrophy
   - CXR normal or enlarged cardiac silhouette

Mitral regurgitation
   - Pathology: regurgitation causes left ventricular dilation, which in turn leads to systolic dysfunction and congestive heart failure. In chronic cases, left atrium will dilate to accommodate added volume. Causes:

   - Degenerative disease
   - Rheumatic heart disease
   - Nonrheumatic mitral regurgitation – myocardial infarction (papillary muscle dysfunction), infective endocarditis (valve perforation), dilated cardiomyopathy (leaflets unable to coapt), or mitral valve prolapse (ruptured chordae tendineae)

   - Ischemic MR may resolve as the myocardial lesion heals

   - Clinical presentation:

   - Acute mitral regurgitation can present with signs/symptoms of pulmonary edema.
   - If development is chronic, i.e. gradual over time, then left atrial enlargement develops and increased volume can be tolerated without development of pulmonary edema. Eventually patient will complain of exertional dyspnea and fatigue, with progression to left ventricular heart failure.

Evaluation when VHD suspected:
   - BNP to monitor for LV myocardial failure
   - Echocardiogram confirms VHD, monitors progression and helps determine when to operate.

   - LV Ejection fraction – identify myocardial failure
   - LV end-systolic dimensions – identify chamber dilation
   - LV wall thickness – identify chamber hypertrophy
   - Mean valve gradient – identify stenosis (square of the maximum flow velocity through the valve orifice then multiplied by 4)
   - Valve area – identify stenosis (normal aortic valve area is 3-4 cm², <1.0 cm² seen with AS, severe stenosis is <0.8 cm²)
VHD Treatment Options: surgery is indicated when symptoms develop. However, prior to surgery, significant left ventricular deterioration may already have developed and several options are being considered for intervention earlier in asymptomatic patients with severe disease noted on Echo.

- **AS** – surgery is indicated for symptoms (likely when gradient > 40 mm Hg) or when severe stenosis is present in asymptomatic patient (mean gradient > 50 mm Hg).
  - Surgical risk is low even in very elderly. Percutaneous valve replacement may be an option for high surgical risk patients.
- **MR** – surgery is indicated for symptoms or when LV EF <60%, or echo LV end-systolic dimension is > 4.0 cm.
  - In patients with mitral prolapse and severe MR, early surgery is indicated if mitral repair can be performed.
  - Percutaneous options are being studied in patients considered high risk for surgical interventions.

Prevention

- Degenerative or calcific AS has the same risk factors as atherosclerosis.
  - Hypertension, hyperlipidemia, smoking – aggressive risk factor reduction.
- Avoid infective endocarditis (IE)
  - IV drug abuse – patient education, rehabilitative efforts.
    - Beyond the scope of this presentation!
  - Appropriate prophylactic antibiotics for preexisting VHD
    - Before dental procedures that involve manipulation of gum tissue, manipulation of the periapical region of teeth and perforation of the oral mucosa – patients with prosthetic cardiac valves**, patients with previous IE, cardiac transplant recipients (especially 6 months post transplant) with valve regurgitation due to a structurally abnormal valve or patients with certain congenital heart disease conditions.
  - Good oral hygiene – bacteremia often occurs during teeth brushing or chewing.
  - No evidence to support IE prophylaxis for VHD patients undergoing gastrointestinal procedures or genitourinary procedures absent known enterococcal infection. Even with transient bacteremia in a small number of cases after colonoscopy, these GI bacteria are unlikely to cause IE. It is recommended that patients with bacteria identified before genitourinary procedure like lithotripsy should receive pre-surgical antibiotics aimed at sterilizing the urine.
- Rheumatic heart disease – still a significant cause of mitral disease.
  - Primary prevention: appropriately prescribed antibiotics for confirmed Group A strep can prevent ARF and subsequent RHD.
  - Secondary prevention: Long-term antibiotic use is indicated to prevent recurrent rheumatic fever in those with rheumatic heart
disease because even asymptomatic group A strep infections can trigger recurrent rheumatic fever.

- Patients with documented carditis and residual heart disease (confirmed valvular heart disease) should receive a regimen to prevent recurrent ARF for at least 10 years or until the age of 40, whichever is longer.
  - Penicillin G benzathine 1.2 mil units IM q 4 weeks
  - Penicillin V potassium 200 mg PO bid
  - Sulfadiazine 1 g orally QD
  - Macrolide or azalide antibiotic if penicillin allergic at appropriate dose.

- Patients with history of Rheumatic Fever but without residual heart disease or without a history of carditis should receive long term antibiotics for 10 years or until the patient is 21 years of age, which is longer.

References:


