Diagnosis and Management of Acute Pharyngitis

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Objectives

• Identify the epidemiology and testing indications for strep throat.

• Develop treatment plans for a patient with a positive streptococcal test and in the setting of a negative rapid antigen test.

• Assess age specific causes of pharyngitis.

• Evaluate risk of disease, sequelae, and adverse drug reaction in a patient with pharyngitis.
Disclosures

• I have no relevant conflicts of interest to disclose.

• I will not be discussing off label uses of any tests or medications.

• I have been to New Orleans before. I was in college.
Strep Throat Prevalence

• Frequent reason for primary care visits
  – ~12 million pediatric visits annually for pharyngitis in US

• Most common cause of bacterial pharyngitis
  – Prevalence studies have shown that 15-37% of pharyngitis visits are caused by strep throat in children (~10% for adults)

• 53-60% of children with sore throat receive an antibiotic

• Implies that strep throat is over diagnosed and thus over treated
  – Clinical decision making is key to correct diagnosis

Clinical & Epidemiologic Features

- Sudden onset: fever, sore throat, HA, N/V, & abdominal pain
- Severe pain with swallowing
- Inflamed tonsils &/or pharynx
- Patchy discrete exudates
- Tender, enlarged anterior cervical nodes
- Scarlet fever

- Age 5-15 yrs
- Presentation in winter or early spring
- Exposure history
- Features consistent w/ viral etiology
  - Conjunctivitis, Coryza
  - Cough
  - Diarrhea

Case 1

- A 2 y/o child presents to with sore throat, coryza, and fever to 39.3°F for the last 2 days
- On exam you note: enlarged, erythematous tonsils, tender lymph nodes, mild congestion and injected sclera
Of the following, the MOST likely diagnosis for this patient is

A. Rhinovirus
B. Influenza
C. Strep throat
D. Adenovirus
E. Mononucleosis
## Viral Causes of Acute Pharyngitis

### Viral Pathogens
- Rhinovirus
- Coronavirus
- Adenovirus
- Influenza virus
- Parainfluenza virus
- Coxsackie virus
- EBV

### Features/Syndrome
- Common cold
- Common cold
- Pharyngoconjunctival fever
- Influenza
- Common cold, croup
- Herpangina, Hand-foot-mouth
- Infectious Mononucleosis
Confirming a Diagnosis

• Viruses most common cause of acute pharyngitis
• Largely a clinical diagnosis; especially as an outpatient
  – NP viral culture, RVP, shell vial culture
• Difficult to distinguish between bacterial and viral pharyngitis
• Use of stringent and validated clinical criteria are key when diagnosing pharyngitis caused by group A streptococcus

Judicious Use of Antibiotics for Acute Streptococcal Pharyngitis

Terms:
URI = Upper Respiratory Infection

Note:
Testing of children <3 years old is not generally indicated unless other risk factors.

If Penicillin allergy:
Cephalexin 50 mg/kg/day divided BID for 10 days

Serious allergy:
Clindamycin 20 mg/kg/day divided TID for 10 days
Macrolides: Not recommended unless severe allergy to penicillin and cephalosporins exist. Resistance is well known and treatment failures related to macrolide resistance have occurred.

1. Identify patient with suspected strep throat
2. Use diagnostic testing
3. Target drug of choice

1. Identify patient with suspected strep throat

- Any symptoms suggestive of URI present?
  - cough
  - hoarseness,
  - coryza, conjunctivitis
  - viral exanthem (maculopapular rash)
  - mouth ulcers
  - diarrhea
  - YES
  - Viral etiology strongly suggested; Do not test
  - NO
  - One of more of following:
    - pharyngeal erythema or exudate
    - tender cervical nodes
    - scarlatiniform rash
    - palatal petechiae
    - swollen red uvula

2. Use diagnostic testing

- Rapid Antigen Detection Test (RADT)
  - Positive
    - Preferred treatment:¹,²
      - Once daily amoxicillin 50 mg/kg/day for 10 days
      - Alternate: Oral or IM penicillin
    - Do not treat with antibiotics; Perform backup throat culture to confirm
  - Negative
    - Do not test; Streptococcal pharyngitis unlikely

3. Target drug of choice

- Do not treat with antibiotics; Perform backup throat culture to confirm
  - Positive
    - Treat patient
  - Negative
    - Provide symptomatic care

- If Penicillin allergy:
  - Cephalexin 50 mg/kg/day divided BID for 10 days
- Serious allergy:
  - Clindamycin 20 mg/kg/day divided TID for 10 days
  - Macrolides: Not recommended unless severe allergy to penicillin and cephalosporins exist. Resistance is well known and treatment failures related to macrolide resistance have occurred.
Laboratory Diagnosis

• Rapid antigen detection tests (RADTs)
  – Became available in 1980’s
  – Detects presence of cell wall carbohydrate antigen
  – Faster, but more expensive test
  – Plagued by high specificity but low sensitivity
    • Improved with newer antigen tests
  – Back up culture should be performed
  – Increases number of patients appropriately treated

Laboratory Diagnosis

• Neither RADT or culture differentiate between true infection and carrier state
  – Clinical decision making prior to ordering the test is important
• Test of cure is not generally recommended
• Exceptions:
  – Patient with history of ARF
  – Outbreak of ARF
  – In families with “ping-pong” infection

Treatment

- Amoxicillin is the first line therapy for children with a diagnosis of strep throat
- But what should we do for children who clearly have a virus?
Why do we need to treat?

- Prevent rheumatic fever
- Prevent suppurative sequelae
  - Otitis media, peritonsillar abscess, cervical adenitis, mastoiditis
- Improvement in clinical signs and symptoms
  - Rapid return to usual activities
- Decrease infectivity thereby; ↓ transmission

Worldwide Incidence of ARF

Seckeler MD, Hoke TR. Clinical Epidemiology 2011;3: 67-84.
Evolving Epidemiologic Characteristics
of Invasive Group A Streptococcal Disease
in Utah, 2002–2010

Acute Rheumatic Fever
What’s new with The Jones Criteria

- **Low Endemicity**
  - Sporadic cases
  - Rare periodic outbreaks
  - Affluent countries
  - Migratory polyarthritis of large joints
  - High spiking fever

- **High Endemicity**
  - Hyperendemicity
  - Cases occur year round
  - Absence of outbreaks
  - Developing nations
  - Monoarthritis
  - Polyarthralgia
  - Low grade fevers

1992 Jones Criteria for ARF

• **Major**
  - Carditis (50-70%)*
  - Migratory poly-arthritis (35-66%)
  - Chorea (10-30%)
  - Subcutaneous nodules (0-10%)
  - Erythema marginatum (<6%)

• **Minor**
  - Polyarthralgia
    • Unless arthritis is a major feature
  - Fever ≥38.5
  - ESR ≥ 30 mm/hr or CRP ≥ 3 mg/dL
  - Prolonged PR interval
    • Unless carditis is a major feature
# Acute Rheumatic Fever (ARF)

## Table 7. Revised Jones Criteria

| A. For all patient populations with evidence of preceding GAS infection |
|---|---|
| Diagnosis: initial ARF | 2 Major manifestations or 1 major plus 2 minor manifestations |
| Diagnosis: recurrent ARF | 2 Major or 1 major and 2 minor or 3 minor |

<table>
<thead>
<tr>
<th>B. Major criteria</th>
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<tr>
<td>Low-risk populations*</td>
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<td>Carditis†</td>
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<tr>
<td>• Clinical and/or subclinical</td>
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<tr>
<td>Arthritis</td>
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<td>• Polyarthritis only</td>
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<td>• Monoarthritis or polyarthritis</td>
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<td>• Polyarthralgia‡</td>
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* ESR ≥60 mm in the first hour and/or CRP ≥3.0 mg/dL§
| Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion) |

What does this mean for the practicing clinician?

• Echo can now be used as a major criterion for a patient in which ARF is suspected in any setting

• Use the new modified criteria for patients who come from an area with high endemicity
  – International adoption
  – Immigrants
What about the suppurative sequelae?

Peritonsillar abscess
Protective effect of antibiotics for common respiratory treat infections and number needed to treat to prevent one peritonsilar abscess

1,065,088 cases of sore throat

<table>
<thead>
<tr>
<th>Infection/adverse outcome</th>
<th>Adjusted odds ratio (95% CI)</th>
<th>Number needed to treat (95% CI)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Sore throat/quinsy</td>
<td>0.84 (0.73 to 0.97)</td>
<td>4300 (2522 to 14,586)</td>
<td>0.021</td>
</tr>
</tbody>
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100,000 children 0-15 years did not receive antibiotics & No cases of ARF were found

Hayward et al. BMJ. 2007
4,300 patients are treated for strep pharyngitis

Peritonsilar abscess prevented = 1
Risk of Adverse Drug Reaction from Antibiotics

- Cochrane review on the risk/benefits of AOM Rx
- 8 studies evaluating adverse events from antibiotic therapy vs placebo were included
  - Vomiting, diarrhea, or rash
    - RR (1.38 95% CI 1.19 to 1.59)
    - Number needed to harm 1 patient = 14
  - Severe complications were rare; no difference between groups

Venekamp RP. Cochrane Database Syst Rev. 2015.
4,300 patients are treated for strep pharyngitis

Adverse drug reaction occurred = 307
Sequelae Summary

• Acute rheumatic fever, peritonsilar abscess and mastoiditis are rare complications of strep throat infection

• Adverse drug reactions are relatively common in the setting of antibiotic use for routine infections
Case 2

• An 8 y/o boy presents to your office with a 2 day history of sore throat, headache, and temperature up to 39.1°C

• A rapid test result for Group A streptococcus is positive

• The boy has a past history of an anaphylactic reaction to amoxicillin
Of the following, the BEST choice of treatment for this patient is

A. Clindamycin for 10 days
B. Cephalexin for 10 days
C. Ciprofloxacin for 10 days
D. Doxycycline for 10 days
E. Trimethoprim-sulfamethoxazole for 10 days
Treatment of strep throat

- Effective antibiotics
  - Penicillin is the gold standard (No resistance)
    - Proven efficacy, safety, narrow spectrum, low cost
    - Amoxicillin has better taste, equal efficacy with PCN
    - Once daily for 10 days is adequate
  - Oral & parenteral options are equal
  - Cephalosporins are acceptable in mild PCN allergy (rash)
  - Clindamycin or macrolide w/ previous anaphylaxis
    - Risk of resistance

Treatment Timing

• Earlier therapy results in faster sign/symptom resolution
  – 16 hours faster

• GABHS is a self limited disease
  – Symptoms resolve spontaneously in 3-4 days
  – Objective judgment of clinical improvement difficult

• Therapy can be safely postponed for 9 days with no ↑ risk of ARF
  – The only therapy that has been evaluated & shown to prevent ARF is IM PCN

Treatment Length

• Standard of care = 10 day length

• Cochrane Review 2009
  – 20 studies included; >13,000 GABHS pharyngitis cases
    • 6 studies evaluate azithromycin treatment
  – ↓ medication non-adherence OR 0.21 (CI 0.16-0.29)
    • ↓ risk early clinical treatment failure OR 0.8 (CI 0.67-0.94)
    • No difference found for early bacteriologic failure
    • No difference found for late clinical failure
  – ↑ risk was noted for late bacteriologic failure OR 1.31 (CI 1.16-1.48)
    • Risk disappeared with removal of azithromycin studies

Treatment Length

• Self limited side effects in short treatment group
• No difference in rate of long term complications
• 3-7 days of oral therapy is safe and of comparable efficacy to standard 10 day duration of therapy
• Must be interpreted with caution in resource limited countries
  – Incidence ARF 0.5 per 100,000 (US)
  – Incidence ARF 100-200 per 100,000 (low income)

Close Contacts and Carriers

- ~25% of asymptomatic household contacts will harbor GABHS in their pharynx
  - Typically no need to test or treat if tested
  - Low rate of infection ~5%
- Would treat (+) family members in the setting of ARF
- Prophylaxis of family with TSS or fasciitis (?)
  - Attack rate 0.07% in a CDC study
  - No evidence to recommend this strategy

References:

The Recurring Sore Throat

• Patients who present a few weeks after treatment for GABHS may have:
  – Intercurrent viral infection with GABHS carriage
  – Noncompliance with initial treatment
  – New infection with different strain or different bacterial pathogen
  – Rarely repeat infection with same strain

• Difficult to differentiate; therefore use clues
  – Age, season, risk factors, local epi (influenza, *Fusobacterium* sp., enterovirus, GC)
  – Precise presenting signs and symptoms
The Recurring Sore Throat

• Typically school aged child
• Challenging clinical circumstance; likely a carrier
• Obtain a throat culture when asymptomatic to test for presence of GABHS
  – Serotyping or genotyping of isolate is possible; but not practical
• Obtain simultaneous specimens from family members & treat positives
  – If goal is to eliminate the carrier state
• No evidence that pets play a role
• Tonsillectomy may result in resolution for a short period of time

Case 3

- A 13 y/o girl presents with a 2 day history of fever, sore throat, and a rash that began on her arms and legs, which spread to her chest and back.
- Physical exam reveals a pharyngeal exudate, bilateral cervical adenopathy, and a “sandpapery” rash over her arms, legs, and trunk.
- A rapid streptococcal antigen test is negative. At 48 hours a throat culture is growing small colonies with narrow bands of hemolysis on sheep blood agar.
Of the following, the MOST appropriate antibiotic for the patient is

A. Ceftriaxone
B. Erythromycin
C. Penicillin
D. Tetracycline
E. Trimethoprim-sulfamethoxazole
Erythematous tonsils in a child with group A streptococcal pharyngitis, which is clinically indistinguishable from *Arcanobacterium haemolyticum*. 
Non-streptococcal pharyngitis

- *Arcanobacterium haemolyticum*
  - Indistinguishable from GAS pharyngitis
  - Gram positive rod w/ slow growth, improved with enriched media
  - Macrolides are treatment of choice
  - Most common in teens/young adults=3%
  - Scarlitiniform or maculopapular pruritic rash in 50%
Bacterial Causes of Acute Pharyngitis

- Group A streptococcus
- Group C & G strep
- Mixed anaerobes
- *Fusobacterium spp.*
- *A. haemolyticum*
- *N. gonorrhoeae*
- *T. pallidum*
- *F. tularensis*
- *C. diphtheriae*
- *Y. enterocolitica*
- *Y. pestis*
- *M. pneumoniae. C. pneumoniae*

- Pharyngitis, scarlet fever
- Pharyngitis
- Vincent’s angina
- Lemeirre’s syndrome
- Pharyngitis, scarletiniform rash
- Pharyngitis
- Secondary syphilis
- Pharyngeal tularemia
- Diphtheria
- Pharyngitis, enterocolitis
- Plague
- Bronchitis, pneumonia
Take Home Message

• Pharyngitis is an important childhood illness
  – Group A streptococcus is common but viruses remain more frequent
• Clinical overlap with other viruses and bacteria
• Testing and subsequent treatment should be performed on patients with clear clinical and epidemiologic features
• Therapy should be focused on using the right antibiotic for the appropriate length of time