Respiratory Illness

Pharyngitis

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Introductory remarks: 40 million office visits per year for sore throat in United States; ~25% diagnosed as pharyngitis; many potential bacterial and viral causes of pharyngitis exist, but focus in clinical practice on Streptococcus

Streptococcus: >6000 strains; classification based on hemolytic properties (α-hemolytic [partial]; β-hemolytic [complete]; γ-hemolytic [none]); β-hemolytic streptococci further classified by Lancefield serotyping (based on carbohydrates present in bacterial cell wall); Streptococcus pyogenes (group A β-hemolytic streptococci [GABHS]) strain commonly found in throat and causes pharyngitis; 130 types of S pyogenes (distinguished by amount of M protein in cell wall)

Etiology: GABHS cause of 15% to 25% of pharyngitis in children but only ~10% of pharyngitis in adults; yet 70% of adults diagnosed with pharyngitis treated with antibiotics

Reasons given for treating streptococcal pharyngitis

Prevention of acute rheumatic fever (ARF): can be prevented, but disease extremely rare in United States (last known data show only ~200 cases in 2002); in this country, treatment unlikely to prevent ARF, but not so in developing countries (i.e., ARF still highly prevalent)

Prevention of suppurrative complications: treatment unlikely to prevent development of peritonsillar abscesses (often polymicrobial and not caused by GABHS); supporting data—in study of ~30,000 patients with pharyngitis, 73 developed suppurrative complications; 40 of 73 seen in office before complication; 27 of 40 treated with antibiotics developed abscesses despite treatment; only 6 tested positive for GABHS; study in United Kingdom found 50% decrease in use of antibiotics for treating pharyngitis over 10 yr caused no increases in peritonsillar abscesses or ARF

Shorten clinical course: shortens duration by ~16 hr; however, if untreated, streptococcal pharyngitis resolves in ~6 days, compared to 5 days with treatment

Decrease contagiousness: duration possibly decreased (no good data available)

Prevention of glomerulonephritis (GN): not achieved by treatment

Advantages and disadvantages of antibiotic treatment: advantages—data show antibiotic treatment targeting GABHS prevents one death from complications of ARF for every 1,000,000 adult patients with pharyngitis; disadvantages—causes diarrhea in 20% of patients; rates of Clostridium difficile infection increasing in hospitalized children in United States; use of antibiotics increases risk for infection with community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) in children and adults; rash occurs in ~5% of patients; fatal reaction to penicillin (PCN) occurs in 1 in 10,000 patients; greater predilection for follow-up visits observed among patients who receive antibiotics (1 in 9 patients)

Indications for treatment of streptococcal pharyngitis:

Children age 4 to 15 yr at greatest risk for infection with GABHS (prevalence 15%-25%; seasonal); no consensus reached on whether patients suspected of having GABHS infection should be treated immediately or be tested first

Recommendations of Centers for Disease Control and Prevention (CDC) and American College of Physicians (ACP): use modified Centor criteria; 0 to 1 pt—indicates zero or very low risk for GABHS; no test or treatment necessary; 4 to 5 pt—indicates presence of GABHS likely; treat immediately; test patients with score of 2 to 3 (if results positive, treat; if negative, no treatment necessary); back-up throat culture unnecessary if using rapid streptococcal test (RST)

Arguments against CDC and ACP recommendations: result in missed detection of too many GABHS infections (in reality, only small number missed in patients with modified Centor score of 0-1); result in overdiagnosis of GABHS infections and increase in prescription of antibiotics (data show 80% decrease in antibiotic use with use of modified Centor criteria)

Rationale for RST without back-up throat culture: sensitivity of RSTs varies from 60% to 90%; assume RST has 70% sensitivity and 70% specificity (newer-generation RSTs significantly better); with prevalence of 10% in adult population, 30 back-up throat cultures required to find one case of GABHS

Rationale for limiting RST to patients with modified Centor score of 2 to 3: need to perform many tests on low-risk patients to find few positive results, and those with positive test likely carriers (not “true disease”); testing all patients with sore throat could “medicalize” pharyngitis

Recommendations of Infectious Disease Society of America (IDSA) and American Academy of Pediatrics (AAP): use modified Centor criteria; if score 0 to 1, do not test or treat; all patients with score 2 to 5 must have RST before treatment with antibiotics; treatment not indicated if test result negative; follow negative RST with back-up throat culture (unless sensitivity of RST known to be greater than that of culture)

Educational Objectives

The goal of this program is to improve the management of pharyngitis and nonresolving pneumonia. After hearing and assimilating this program, the clinician will be better able to:

1. Compare the advantages and disadvantages of medical therapy for streptococcal pharyngitis.
2. Prescribe effective antibiotic therapy for the patient diagnosed with streptococcal pharyngitis.
3. Consider Fusobacterium necrophorum as the possible causative pathogen in patients with sore throat.

5. Evaluate and manage a patient with nonresolving pneumonia.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio-Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, the faculty and planning committee reported nothing to disclose.
Speaker’s recommendation: physicians should choose one set of guidelines (either those from CDC and ACP, or from IDSA and AAP) and follow them (which set chosen unimportant).

**Treatment**: PCN of choice; *dose* — PCN V potassium (PCN VK) 2 or 3 times per day; benzathine PCN (given intramuscularly [IM]) alternative for young patient who refuses oral medications; erythromycin drug of choice for patients with allergy to PCN; first-generation cephalosporin and amoxicillin acceptable; *reasons to avoid amoxicillin* — can produce delayed skin rash in patients infected with Epstein-Barr virus, which may result in misdiagnosis of PCN allergy; causes more diarrhea than PCN

**Current state of antibiotic therapy for pharyngitis**: in adults, decreased by 20% between 1989 and 1999 (includes decrease in use of PCN and erythromycin, but not in broad-spectrum agents); in children, use of recommended drugs decreased between 1995 and 2003, but use of broad-spectrum agents did not change

**Shortening or simplification of therapy**: PCN — reducing dose to once per day increases rates of treatment failure and recurrence (not recommended); amoxicillin — can be reduced to daily dose, but speaker advises avoiding once-daily formulation (Moxatag; cost $13 per tablet); first-generation cephalosporins — can be given for just 5 days; small study suggests injection of ceftriaxone effective; azithromycin — can be given for 3 days, but dose must be 20 mg/kg per day; associated with increasing macrolide resistance

**Management of recurrent GABHS infection**: options include PCN plus rifampin, cephalosporin, clindamycin, and combination of amoxicillin and clavulanic acid

**Management of patients with throat cultures showing group C or G β-hemolytic streptococci**: no good data available, but Centor suggests treatment indicated (may have clinical disease)

**Treatment of sore throat pain**: acetaminophen; nonsteroidal anti-inflammatory drugs (NSAIDs); saltwater gargles; throat lozenges (especially ones with benzocaine)

**Steroids for pain relief in exudative pharyngitis**: 9 trials (6 in adults, 3 in children) all suggest benefit; oral and parenteral administration equally effective; only one dose needed

**Steroids for treatment of infectious mononucleosis**: effectiveness unclear (Cochrane review of 7 trials concluded evidence insufficient); however, commonly used in clinical practice

**Concluding comments**: Fusobacterium necrophorum — recent article by Centor et al suggests this organism should be focus of diagnosis and treatment of pharyngitis (rather than GABHS); causes Lemiere syndrome (suppurative thrombophlebitis of internal jugular vein; associated with >5% mortality and extensive morbidity); prevalence as cause of sore throat equal to that of GABHS; targets people 15 to 30 yr of age; authors recommend that patients in this age group who have high modified Centor score be treated empirically with PCN or cephalosporin, even if RST negative; use of macrolides contraindicated (organism resistant)

**Nonresolving Pneumonia**

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Case 1: 68-yr-old Hispanic man with 60 pack-yr history of smoking (quit 6 yr ago) presents with productive cough and low-grade fever; *current medications* — escitalopram (Lexapro) and albuterol as needed; chest x-ray in emergency department (ED) shows bibasilar infiltrates

**Initial assessment**: Joint Commission core measures for patient admitted to hospital for community-acquired pneumonia (CAP) — blood cultures performed within 24 hr of arrival; initial selection of antibiotic based on guidelines

**Risk stratification tools for determining site of treatment**: Pneumonia Severity Index (PSI) score — assigns points for risk factors, comorbidities, physical examination findings, and laboratory and radiographic findings; can be difficult to calculate; high score (risk class IV or V) indicates patient should be hospitalized; CURB-65 — assigns points for 5 variables (confusion; uremia; respiratory rate; low systolic or diastolic blood pressure [BP]; and age ≥65 yr); good scoring system but requires laboratory measure of serum urea nitrogen (BUN) level; CBR-65 — based on same variables as CURB-65 but excludes uremia; score of 0 indicates <1% risk for death, and patient can be safely discharged home; 3 or 4 points indicate high risk for death, and patient requires urgent hospitalization or admission to intensive care unit (ICU)

**Choice of antibiotic ([American Thoracic Society (ATS) and IDSA 2007 guidelines])**: outpatient with no comorbidities — prescribe macrolide or doxycycline; outpatient with comorbidities — treat with fluoroquinolone or β-lactam plus macrolide; inpatient (non-ICU) — treat with fluoroquinolone or β-lactam plus macrolide (some data suggest patient with bacteremia plus CAP responds better to latter option); inpatient (ICU) — prescribe vancomycin plus clindamycin or linezolid (recommended dose of vancomycin 15 mg/kg every 12 hr; target trough level 15-20 μg/mL)

**Extended-spectrum β-lactamase (ESBL)-positive organisms**: potential pathogens include Serratia, Proteus, Acinetobacter, Citrobacter, and Enterobacter; susceptible to carbapenems (eg, imipenem)

Risk factors for multidrug-resistant (MDR) pathogens: include antibiotic therapy in past 90 days; current hospitalization of >5 days; high frequency of antibiotic resistance in community; history of viral pneumonia (PNA), especially in young people

**Treatment of MDR pathogens**: combination therapy recommended for treatment of Pseudomonas aeruginosa; linezolid and vancomycin equally effective for treatment of MRSA (linezolid can cause thrombocytopenia, which usually reverses after medication discontinued)

**Time to clinical and radiologic improvement**: resolution of PNA consists of clinical improvement, radiographic resolution, and microbiologic eradication; criteria for clinical stability — afebrile; heart rate ≤100 bpm; systolic BP ≥90 mm Hg; good arterial oxygen saturation; ability to maintain oral intake; normal mental status; ≥3 days required for patients hospitalized for CAP to achieve clinical stability; time to defervescence — longest with Legionella (recommended duration of therapy 10-14 days, compared to 5-7 days generally required for CAP); time to radiographic resolution of PNA — ≤12 wk in most patients

**Reasons for nonresolving PNA**: incorrect diagnosis; complication; incorrect treatment

**Definitions**: progressive PNA — clinical deterioration occurs within 24 hr of treatment, with increase in radiographic infiltrates by 50% (needs to be treated in ICU); nonresolving PNA — patient demonstrates delayed radiographic resolution (<50% clearance at 2 wk); shows slow resolution of radiographic infiltrates and clinical improvement after 10 days of adequate treatment

**Risk factors for nonresolving PNA**: guideline-discordant therapy; pleural effusion; multilobar infiltrates; cavitation on x-ray at time of presentation (suggests presence of MRSA)

**Impact of national guidelines**: recent study in *Archives of Internal Medicine* showed causative organisms for CAP remain essentially unchanged, except for increased prevalence of MRSA in different communities and settings; study of elderly patients with CAP found guideline-concordant therapy associated with lower mortality across all risk classes of PSI; in patients with more severe PNA, guideline-discordant therapy associated with higher mortality; cephalosporins, macrolides, and fluoroquinolones associated with lower mortality compared to other antibiotics used to treat CAP

**Risk factors for slow resolution of PNA**: high comorbidity index; bacteremia (independent risk factor for death); gram-negative PNA; multilobar involvement
Risk for lung cancer after episode of PNA: recent study found incidence of lung cancer after PNA 2% to 3% (most occurs within first 6 mo); study concluded greatest potential diagnostic yield realized by restricting follow-up x-ray to patients ≥50 yr of age, particularly men or smokers

Management of nonresolving PNA: starts with clinical diagnosis of CAP; risk-stratify patient (CURB-65 or CRB-65); initiate empiric antibiotic treatment using ATS and IDSA guidelines; responders — improve within first 3 days; nonresponders — consider possibility of incorrect diagnosis, organism, or treatment; reevaluate host factors, review sensitivities, and determine whether appropriate antibiotic given; consider computed tomography (CT) or ultrasonography of chest (to rule out pleural effusion or empyema), and bronchoscopy

Resolution of Case 1: patient underwent bronchoscopy with transbronchial needle aspiration of subcarinal lymph node; diagnosis adenocarcinoma

Case 2: 44-yr-old woman referred for evaluation of persistent PNA; had progressive dyspnea on exertion and difficulty climbing flight of stairs; physical examination — tachypnic; desaturated with exertion; bilateral inspiratory crackles; CT showed alveolar interstitial infiltrates on both lung fields; connective tissue work-up performed; diagnosis polymyositis-induced interstitial lung disease; treatment lung transplantation

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1. The strain of *Streptococcus* commonly found in the throat that is a cause of pharyngitis is:
   (A) *S. anginosus*  (B) *S. sanguinis*  (C) *S. salivarius*  (D) *S. pyogenes*

2. Antibiotic treatment of streptococcal pharyngitis is essential for preventing the development of glumerulonephrosis.
   (A) True  (B) False

3. Patients at the greatest risk for developing streptococcal pharyngitis are those who are:
   (A) 6 mo to 3 yr of age  (B) 2 to 5 yr of age  (C) 4 to 15 yr of age  (D) 11 to 20 yr of age

4. The drug of choice for treatment of streptococcal pharyngitis is:
   (A) Penicillin  (B) Amoxicillin  (C) Cephalexin  (D) Cefazolin

5. Which of the following medications can be given in a 3-day regimen to treat streptococcal pharyngitis?
   (A) Amoxicillin  (B) Cephalexin  (C) Penicillin  (D) Azithromycin

6. Oral steroid therapy is _______ parenteral steroid therapy for pain relief in patients with exudative pharyngitis.
   (A) More effective than  (B) Less effective than  (C) Equally effective as

7. All the following are Joint Commission core measures for initial management of community-acquired pneumonia (CAP), except:
   (A) Assessment of oxygen saturation  (B) Blood cultures performed within 24 hr of arrival at hospital  (C) Initial selection of antibiotic based on guidelines

8. The recommended antibiotic therapy for a patient admitted to the intensive care unit for CAP is:
   (A) Macrolide or doxycycline  (B) Vancomycin plus clindamycin or linezolid  (C) Fluoroquinolone or β-lactam plus macrolide  (D) None of the above

9. It takes approximately _______ for patients hospitalized with CAP to achieve clinical stability.
   (A) 7 days  (B) 5 days  (C) 3 days  (D) 36 to 48 hr

10. Which risk factor for nonresolving pneumonia suggests the presence of methicillin-resistant *Staphylococcus aureus* (MRSA)?
    (A) Pleural effusion  (B) Multilobar infiltrates  (C) Leukopenia  (D) Cavitation on x-ray at time of presentation

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