Current Approaches to Infectious Diseases in Primary Care

Regional Conference
Indianapolis, Indiana

October 29, 2014
Session 6: Current Approaches to Infectious Diseases in Primary Care

Learning Objectives
1. Effectively assess and diagnose patients with common community-acquired infections.
2. Apply the latest guideline recommendations for appropriate treatment of pharyngitis, urinary tract infection, and cellulitis.

Faculty

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Philadelphia, Pennsylvania

Dr Thomas Fekete graduated from Princeton University in 1974 and received his medical degree from Tufts Medical School in 1978. He trained in internal medicine at Rush-Presbyterian-St. Luke’s and in infectious diseases at the University of Chicago. He has spent his thirty year academic career at Temple University School of Medicine. His clinical work includes hospital medicine, but his practice is principally in infectious diseases with a special interest in resistant bacteria, clinical microbiology, antibiotic stewardship, and urinary tract infections. He has been section chief of infectious diseases for eight years and is executive vice chair for clinical operations in the department of medicine.

He also has a commitment to teaching; Dr Fekete has earned accolades for his teaching ranging from Golden Apples to the Lindback award to the Temple University Great Teacher award. He has been a writer and editor for MKSAP 12-16 and a contributor for UpToDate. He serves as chair of the education committee for the Infectious Disease Society of America and has been an infectious diseases liaison to the American Board of Internal Medicine.

Faculty Financial Disclosure Statement
The presenting faculty reports the following:

Thomas Fekete, MD, FACP, has no financial relationships to disclose.
SESSION 6
3:45–5:00pm
Current Approaches to Infectious Diseases in Primary Care

SPEAKER
Thomas Fekete, MD, FACP

Presenter Disclosure Information
The following relationships exist related to this presentation:

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Off-Label/Investigational Discussion

► In accordance with PMICME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Learning Objectives

- Effectively assess and diagnose patients with common community-acquired infections
- Apply the latest guideline recommendations for appropriate treatment of pharyngitis, urinary tract infection, and cellulitis

Case: Mr. Clark
A 40-year-old man presents with a 2-day history of sore throat, hoarseness, and runny nose

<table>
<thead>
<tr>
<th>Vital signs</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical exam</td>
<td>Mild conjunctivitis</td>
</tr>
<tr>
<td>Tonsils</td>
<td>Erythematous, no exudate</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>None</td>
</tr>
<tr>
<td>Rash</td>
<td>None</td>
</tr>
</tbody>
</table>

Pharyngitis: Most Cases Are Viral

Herpes simplex virus
Adenovirus
Rhinovirus
Influenza
Parainfluenza
Respiratory syncytial virus

Clinical Features: Viral Pharyngitis

- Cough
- Hoarseness
- Nasal congestion
- Runny nose
- Conjunctivitis
- Oral ulcers
Group A Streptococcus (GAS)

Responsible for only 5-15% of adult cases of pharyngitis

Reasons for identification/treatment of GAS pharyngitis:
- Prevent sequelae including acute rheumatic fever, peritonsillar abscess and acute otitis media
- Decrease duration of symptoms/culture positivity


GAS Pharyngitis

70% of patients with sore throats seen in US primary care settings receive prescriptions for antimicrobials

Less than 30% are likely to have GAS pharyngitis


Clinical Criteria for GAS Pharyngitis: The Centor Criteria

Fever Absence of cough Tonsillar exudate/swelling Tender, swollen anterior cervical lymphadenopathy


Centor Clinical Criteria

< 2 Criteria Present
- No diagnostic testing and no antibiotic treatment recommended
- Good for ruling out patients who do not have the disease

≥ 2 Criteria Present
- Different testing/empiric treatment strategies amongst experts and specialty societies including no testing or treating for patients who present with only 2 criteria


Suspected GAS Pharyngitis

Swab the throat and test for GAS pharyngitis by rapid antigen detection test (RADT) and/or culture

In one large study, slightly < 60% of patients with 4 Centor criteria tested (+) for GAS

**Bottom Line: CDC Recommendations**

<table>
<thead>
<tr>
<th>&lt; 2 Criteria Present</th>
<th>&gt; 2 Criteria Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>No diagnostic testing and no antibiotic treatment recommended</td>
<td>Test with RADT to determine whether treatment is indicated</td>
</tr>
</tbody>
</table>

**GAS Pharyngitis: Diagnostic Testing for Adults**

- **Rapid antigen detection tests (RADT) of throat swab for GAS**
  - Test
  - If (+) treat for GAS pharyngitis
  - Sensitivity 70-90%
  - Specificity 95%
  - High negative predictive value
  - If (-) do not treat

**GAS Pharyngitis: Culture of Throat Swab?**

- Routine use of back-up throat culture (if RADT is negative)
  - Not usually necessary in adults
  - Low incidence of GAS pharyngitis in adults
  - Extremely low risk of subsequent acute rheumatic fever

**GAS Pharyngitis: Treatment**

- **Amoxicillin or Penicillin (oral)**
  - 10 day course
  - Intramuscular benzathine penicillin G for patients unable to be adherent with oral course of therapy

- **For Penicillin-Allergic Patients**
  - Oral first generation cephalosporin [if allergy not IgE-mediated anaphylactic reaction] (10 days)
  - Clindamycin (10 days)
  - Azithromycin (5 days)
  - Clarithromycin (10 days)

- **NOT Recommended**
  - Tetracycline/doxycycline
  - Sulfonamides (including trimethoprim-sulfamethoxazole)
  - Fluoroquinolones
    - Ciprofloxacin not effective
    - Levofloxacin and moxifloxacin are effective but too broad-spectrum and costly
**GAS Pharyngitis**

Posttreatment RADT or throat cultures NOT routinely recommended for follow-up EXCEPT
- Recurrence of characteristic clinical features of GAS pharyngitis
- High risk of acute rheumatic fever

**Case: Ms. Adams**

A 26-year-old woman is evaluated for a 2-day history of dysuria. She has had no associated fever, nausea, vomiting, or flank pain. She has no medical problems. She takes no prescribed medications and has no known drug allergies.

<table>
<thead>
<tr>
<th>Vital signs</th>
<th>normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical exam</td>
<td>no abnormalities</td>
</tr>
<tr>
<td>Urine dipstick</td>
<td>positive for leukocyte esterase and nitrites</td>
</tr>
<tr>
<td>Urine pregnancy test</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Acute Uncomplicated Cystitis Diagnosis**

**Presentation**
- Absence of fever, flank pain, or other suspicion for pyelonephritis
- Able to take oral medication
- Premenopausal, nonpregnant women

**Microbiology**
- Primarily E. coli
- Occasionally P. mirabilis, K. pneumoniae and S. saprophyticus
- Susceptibility patterns of E. coli most important in empiric antibiotic choice

**Acute Uncomplicated Cystitis Therapy**

**Usually Empirical**

Urine culture not usually obtained if classic UTI symptoms present

**Recommended Antibiotics**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
</tr>
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<tbody>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>160/800 mg (ds) twice daily for 3 days</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>100 mg orally twice daily for 5 days</td>
</tr>
<tr>
<td>Fosfomycin</td>
<td>3 gm dose given once (appears to have inferior bacterial efficacy compared to other recommended regimens)</td>
</tr>
</tbody>
</table>

**Exceptions:**
- E. coli resistance prevalence >20%
- TMP-SMX in last 3 months

**Nitrofurantoin**

Administer with meals
Decreases adverse effects and improves absorption

**Active against**
- E. coli
- Enterobacter species
- Klebsiella species
- S saprophyticus
- S. aureus
- Enterococci

**Not active against**
- Pseudomonas

**Adverse effects**
- Common
  - Urine color change → brown
  - Nausea, headache, GI
- Rare (<1%)
  - Pulmonary toxicities, including acute hypersensitivity reaction: eosinophilia, slowly developing dry cough, SOB, fatigue, abnormal LFTs

**Fosfomycin Tromethamine**

**Phosphonic acid derivative**
- Bactericidal
- Oral formulation: powder sachet dissolved in cool water
- Convenient single dose regimen
- High urinary concentrations
- No renal/hepatic dosing restrictions

**Broad spectrum activity**
- Gram-negative organisms
  - E. coli
  - Enterobacter species
  - S. marcescens
  - P. aeruginosa
  - K. pneumoniae
  - P. mirabilis
- Gram-positive organisms
  - S. aureus
  - Enterococcus species
- High rate of E. coli susceptibility, including ESBL-producing strains

**Adverse effects**
- Mild gastrointestinal especially diarrhea

**ESBL = extended spectrum beta-lactamase**
Why Not Other Choices?

**Ciprofloxacin** X 3 days is effective

BUT...

“Collateral damage” including development of fluoroquinolone resistance and MRSA infections

...fluoroquinolones should be reserved as an alternative only when other UTI agents cannot be used

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**Why Not Other Choices?**

- **Moxifloxacin**
  - A fluoroquinolone
  - Low concentrations in urine
  - Not approved for use in treatment of urinary tract infections
  - Amoxicillin => poor efficacy
  - High prevalence of resistance

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**Final Thoughts**

**Recommended empirical treatment of acute uncomplicated cystitis:**
- Oral Nitrofurantoin
- Oral TMP-SMX
- Oral Fosfomycin

**TMP-SMX should not be used** when local resistance rates are >20% or if TMP-SMX used to treat UTI in prior 3 months.

If pyelonephritis suspected nitrofurantoin and fosfomycin should not be used due to inability to achieve therapeutic kidney tissue levels.

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**Case: Mr. Kelly**

A 31-year-old man presents with a several day history of redness on his leg that has developed around a small skin excoriation.

- No significant PMH
- No drug allergies
- Temp: 99.0°F
- Other vital signs are normal

No evidence of purulence though area is warm and minimally tender to palpation

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**Nonpurulent Cellulitis**

- **Empiric therapy for beta-hemolytic streptococci** such as:
  - Cephalexin, 500 mg orally QID
  - Dicloxacillin, 500 mg orally QID
  - Clindamycin, 300-450 mg orally TID
- Treat for 5-10 days

**Empiric therapy for methicillin-resistant Staphylococcus aureus (MRSA)** not indicated
Nonpurulent Cellulitis

Consider including Community Acquired MRSA (CA-MRSA) coverage when:

- Failure of beta-lactam therapy
- Patient appears toxic
  - High fever, malaise, etc.
- History of prior MRSA infection


CA-MRSA + Beta-hemolytic Streptococcal Coverage

**Oral Treatment Regimens**

- Beta-lactam like amoxicillin or cephalaxin PLUS TMP-SMX or a tetracycline
- Clindamycin
- Linezolid

Treat for 5-10 days


Cutaneous Abscess/Furuncle

**Incision and drainage is the primary treatment modality**


Antibiotic Therapy for CA-MRSA-Associated Abscess?

**Recommended for:**

- Extensive/severe disease (several different sites involved) or fast progression in association with cellulitis
- Very young/very old
- Presence of septic phlebitis
- Insufficient response to incision and drainage alone
- Clinical presentation consistent with systemic illness
- Co-morbidities or immunosuppression present
- Abscess located in area that is challenging/difficult to drain (hand, face, genitalia)


Furuncle/Abscess/Purulent Cellulitis

- Empiric oral therapy for CA-MRSA
  - Clindamycin, 300-450 mg TID
  - TMP-SMX, 1-2 DS tablets BID
  - Doxycycline, 100 mg BID
  - Minocycline, 200 mg × 1, then 100 mg BID
  - Linezolid, 600 mg BID
- Treat for 5-10 days

Empiric therapy for beta-hemolytic streptococci "likely unnecessary"


Case: Mr. Alvez

A 50-year-old man with a history of a mechanical mitral valve replacement is scheduled to undergo dilation of esophageal strictures.

You are contacted by the GI specialist regarding the need for infective endocarditis (IE) prophylaxis.
Infective Endocarditis Guidelines

Prevention of Infective Endocarditis:
Guidelines From the American Heart Association: A Guideline From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group

Endorsements
- American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee
- Council on Cardiovascular Disease in the Young
- Council on Clinical Cardiology; Council on Cardiovascular Surgery and Anesthesia
- Quality of Care and Outcomes Research Interdisciplinary Working Group
- American Dental Association
- Infectious Diseases Society of America
- Pediatric Infectious Diseases Society


The Evidence for Infective Endocarditis Prophylaxis

A placebo-controlled, multicenter, randomized, double-blinded study to evaluate the efficacy of IE prophylaxis in patients who undergo a dental, GI, or GU tract procedure has not been done.


Summary of Major Changes in the Updated 2007 AHA Guidelines

Antibiotic Prophylaxis Recommended for:
- Dental procedures that involve perforation of
  - Oral mucosa
  - Gingival tissue
  - Periapical region of a tooth

Only for cardiac conditions with highest risk of adverse outcome from IE (even though effectiveness unknown)


Cardiac Conditions Associated with the Highest Risk of Adverse Outcome from IE

- Prosthetic cardiac valve
- Prior episode of IE
- Heart transplant patients who develop heart valvulopathy
- Congenital Heart Disease (CHD)
  - Unrepaired cyanotic heart disease
  - Completely repaired CHD with device or prosthetic material
  - Repaired CHD with residual defects at or near site of device or patch


Summary of Major Changes in Updated 2007 AHA Guidelines

Antibiotic prophylaxis NOT recommended for other cardiac conditions

Including:
- Bicuspid aortic valve
- Acquired mitral or aortic valve disease
- Hypertrophic obstructive cardiomyopathy (HOCM)
Infective Endocarditis Prophylaxis:
Dental Procedures

<table>
<thead>
<tr>
<th>Standard</th>
<th>Penicillin-Allergic Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin, 2 grams orally 30-60 minutes before procedure (once only)</td>
<td>Clindamycin or azithromycin/clarithromycin (one dose)</td>
</tr>
</tbody>
</table>


Why No Prophylactic Antibiotics for GI/GU Procedures?

No published data demonstrate a conclusive link between GI or GU tract procedures and development of IE.

...no studies exist that demonstrate that antimicrobial prophylaxis prevents IE associated with GI or GU tract procedures.


Case: Mr. Das

A 55-year-old man presents with prolonged cough which began several weeks ago
- Sudden onset, sometimes followed by emesis and feelings of lightheadness
- Associated malaise, rhinorrhea, and conjunctival irritation

Past medical history: hypertension; remote episode of torsades de pointes
- Meds: Hydrochlorothiazide
- Allergic to macrolides
- Physical exam: normal and CXR is clear
- He states that he has received all required vaccines
- Work-up confirms a Bordetella pertussis infection

Pertussis – Signs and Symptoms

Three phase illness
1. Catarhral - malaise, rhinorrhea, mild cough, conjunctival irritation, lacrimation
   - Non-specific; lasts up to 3 weeks
2. Paroxysmal phase: 1-6 weeks
   - Vigorous cough in spasms
   - Post-tussive emesis
   - On inspiration: whooping sound
3. Convalescent phase; up to 3 weeks
   - Cough lessens in severity
   → In adolescents and adults, these symptoms may be less pronounced

Cornia et al. JAMA. 2010.304;890-6; MMWR 2012;Vol 61. No 28
Pertussis Diagnosis

• Nasopharyngeal culture is gold standard
  - Highly specific; sensitivity decreases after 2 weeks
• If cough lasting 2 - 4 weeks: do both culture and PCR
• After 4 weeks, do serology

<table>
<thead>
<tr>
<th>Cough Onset</th>
<th>Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

Pertussis Treatment

• Antibiotics decrease symptoms and reduce spread
  – Most effective before the paroxysmal phase
  – Can return to work/school after 5 days of antimicrobial therapy
• Post-exposure prophylaxis within 3 weeks of exposure for:
  • Household contacts
  • Pregnant, infant, immunocompromised
  • Contacts of high risk patients or contacts in high risk settings (NICU, pregnancy ward, etc)

Pertussis: Recommended Treatment

Macrolide
  • 5-day azithromycin
  • 7-day clarithromycin
  • 14-day erythromycin
Alternative
  • 14-day trimethoprim-sulfamethoxazole*

Treat persons aged >1 year within 3 weeks cough onset

Azithromycin and Arrhythmia Risk

FDA Drug Safety Communication: Azithromycin and the risk of potentially fatal heart rhythms

On March 12, 2013, the Food and Drug Administration issued a warning that azithromycin can cause abnormal changes in the electrical activity of the heart that may lead to a potentially fatal irregular heart rhythm in some patients.

Consider using an alternative drug in those who have known CVD:
  • Prolongation of the QT interval, a history of torsades de pointes, congenital long QT syndrome, bradyarrhythmias, or uncompensated heart failure
  • On drugs known to prolong the QT interval
  • Ongoing proarrhythmic conditions (eg, low K+, Mg+, significant bradycardia, on Class 1A or III antiarrhythmic drugs)

Other Antimicrobials for Pertussis

• Other agents such as ampicillin, tetracycline, chloramphenicol, fluoroquinolones, and cephalosporins
  – exhibit various levels of in vitro inhibitory activity against B. pertussis
  – in vitro inhibitory activity does not predict clinical effectiveness
  – clinical effectiveness of these agents has not been demonstrated

Case: Ms. Foster

A 66-year-old woman with no significant past medical history presents with
  • One day history of vesicular lesions
  • Distributed in a single unilateral thoracic dermatome
  • Minimal pain
  • Clinical diagnosis of herpes zoster ("shingles") is made
Herpes Zoster: Presentation and Diagnosis

- Reactivation of latent varicella-zoster virus
- Increased risk with immunosuppression/older age

Clinical Presentation
- Prodrome of burning or “tingling” pain often precedes the rash
- Rash typically consists of grouped vesicles on an erythematous base in a dermatomal distribution

Diagnosis
- Clinical diagnosis in most cases
- If uncertain, potential modalities include:
  - Viral culture
  - PCR
  - Antigen detection (Direct Fluorescent Antibody)
  - Serology

Herpes Zoster: Antiviral Treatment

- Ideally Initiate Therapy within 72 Hours of Onset
- Valacyclovir 1000 mg orally 3 times daily X 7 days
- Famciclovir 500 mg orally 3 times daily X 7 days
- Acyclovir* 800 mg orally 5 times daily X 7-10 days

- Benefits increased for patients >50 years vs <50 years
- Expedites healing of skin lesions
- Decreases length and intensity of associated acute neuritis
- Unclear if these agents decrease incidence of post-herpetic neuralgia

*Pharmacokinetics inferior to VAL and FAM

Herpes Zoster: Pain Management

- Opioid analgesics for severe pain
- May consider
  - Tramadol
  - Gabapentin or pregabalin
  - Tricyclic antidepressants*
  - Short tapering course corticosteroids (always with antiviral treatment) for moderate to severe pain in patients >50 years of age

*Efficacy in acute pain not established

Zoster Vaccine: Prevention

CDC-ACIP Recommendation
- Age ≥60 years regardless of previous zoster infection (wait until rash has healed)
- FDA approval for age 50+

Effective in decreasing incidence of herpes zoster and post-herpetic neuralgia

Single, 0.65-mL subcutaneous dose in deltoid
- Booster dose not currently recommended
- Common side effects: pain, tenderness, redness and swelling at injection site, headache; itching
- No antiviral medications within 24 hr prior or 14 days post-vaccination

Low Rates of Vaccination
- Partly due to cost
  - $100-$300
  - Most expensive vaccine recommended for the elderly

No need to ask or test for previous varicella infection

Adult Vaccination Rates in the United States

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Percentage of Adults Vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumococcal</td>
<td>18.5</td>
</tr>
<tr>
<td>Tetanus</td>
<td>59.7</td>
</tr>
<tr>
<td>Zoster</td>
<td>64</td>
</tr>
<tr>
<td>HPV</td>
<td>53</td>
</tr>
</tbody>
</table>

Zoster Vaccine: Contraindications

- History of:
  - Severe allergy to a component of the vaccine
  - Life-threatening hypersensitivity reaction to neomycin or gelatin
- Weakened immune system secondary to lymphoma, leukemia, or other lymphatic or bone marrow cancer
- HIV/AIDS infection with CD4 count <200/mm²
- Immunosuppressive therapy including high-dose corticosteroids
- Pregnancy