Antimicrobial Update:
A focus on prescribing in the era of resistant pathogens
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The Prescribers Letter, American Nurse Today
Member, Pharmacy and Therapeutics Committee
Neighborhood Health Plan, Boston, MA

Objectives
• Having completed the learning activities, the participant will be able to:
  – Recognize the factors that influence the development of resistant pathogens.
  – Identify patient characteristics that increase the risk of infection with a resistant pathogen.

Objectives
(continued)
• Having completed the learning activities, the participant will be able to: (cont.)
  – Develop a patient care plan which takes into account the above listed data as well as the latest treatment recommendations for the treatment of select bacterial infections.

Are the bugs winning?
Is this a new problem?

Empiric Antimicrobial Therapy
• The decision-making process where the clinician chooses the agent based on patient characteristics and site of infection.

Questions to Ask Prior to Choosing an Antimicrobial
• What is/are the most likely pathogen(s) causing this infection?
• What is the spectrum of a given antimicrobial’s activity?
• What is the likelihood of resistant pathogen?
• What is the danger if there is treatment failure?
What facilitates resistance?

- Time
- Exposure
  - Unnecessary doses
  - Long tx period
- Under dosing
  - Leaves behind more resistant bugs

True or false?

- In a study of antimicrobial prescribing among primary care providers, physicians in high-volume practices and those who were in practice longer were more likely to prescribe antibiotics inappropriately.
  - Source: CMAJ • October 9, 2007; 177(8).

What determines antibiotic dose?

- The pharmacological absorption and distribution of the antibiotic will influence the dose, route and frequency of administration of the antibiotic in order to achieve an effective dose at the site of infection.
  - Source: http://pathmicro.med.sc.edu/mayer/antibiot.htm

Minimum Inhibitory Concentration (MIC) Defined

- Lowest concentration of an antimicrobial that will inhibit visible growth of a microorganism after overnight incubation under standard conditions
  - Source: http://jac.oxfordjournals.org/content/48/suppl_1/5.short

Minimum Bactericidal Concentration (MBC) Defined

- Lowest concentration of antimicrobial that will prevent growth of 99.9% of an organism after subculture on to antibiotic-free media
  - Source: http://jac.oxfordjournals.org/content/48/suppl_1/5.short

Recommended Antibiotic Doses

- Usually dosed at level to 2-4 times MIC
  - “Overkill” amount to allow for variations in absorption, distribution
Updated Treatment Guidelines for ABRS in Children and Adults

Chow, A., et al.,

Is antimicrobial needed in ABRS therapy?

• Meta-analyses of antibiotic treatment vs. placebo in ABRS
  – Number needed to treat (NNT) (95% CI)
  - In adults=13 (9–22)
  - In children=5 (4–15)
  – Source- Chow, A., et al., IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

Bacterial Pathogens Associated with ABRS

• Streptococcus pneumoniae
  - Gm pos diplococci
  - DRSP rate nationally=25%
  - Adults=38%
  - Children=21–33%
  – Source- Chow, A., et al., IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

Bacterial Pathogens Associated with ABRS (continued)

• Haemophilus influenzae
  - Gm negative rod-shaped bacterium
  - ~30% beta-lactamase production rate nationwide
  - Non-typable strains cause ABRS
  - Adults=36%
  - Children=31–32%
  – Source- Chow, A., et al., IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

Bacterial Pathogens Associated with ABRS (continued)

• Moraxella catarrhalis
  - Gram negative with =>90% beta-lactamase production rate
  - Adults=16%
  - Children=8–11%
  – Source- Chow, A., et al., IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

Treatment of ABRS

• Antimicrobial with activity against:
  - Gram positive organism S. pneumoniae with DRSP consideration
  - Gram negative organisms H. influenzae and M. catarrhalis with propensity to produce beta-lactamase
Signs and symptoms either:

1. Persistent and not improving (≥ 10 days);
2. Severe (≥ 3-4 days); or
3. Worsening or "double-sickening" (≥ 3-4 days)

Risk for Resistance

- Age <2 or >65, daycare
- Prior antibiotics within the past month
- Prior hospitalization past 5 days
- Comorbidities
- Immunocompromised

Symptomatic management

- No
- Yes

Initiate first-line antimicrobial therapy

- Amoxicillin-clavulanate 500 mg/125 mg PO TID
- Amoxicillin-clavulanate 875 mg/125 mg PO BID

Initiate second-line antimicrobial therapy

- Amoxicillin-clavulanate 2000 mg/125 mg PO BID
- Doxycycline 100 mg PO BID or 200 mg PO daily

CT or MRI to investigate noninfectious causes or suppurative complications

Sinus or meatal cultures for pathogen-specific therapy

Refer to specialist

Improvement

- Complete 5-7 days of antimicrobial therapy
- Improvement after 3-5 days
- Complete 5-7 days of antimicrobial therapy

Improvement after 3-5 days

- Complete 7-10 days of antimicrobial therapy
- Improvement
- Complete 7-10 days of antimicrobial therapy

Worsening or no improvement after 3-5 days

- Complete 7-10 days of antimicrobial therapy
- Broaden coverage or switch to different antimicrobial class
- Worsening or no improvement after 3-5 days
- Complete 7-10 days of antimicrobial therapy

If improvement after 3-5 days:

- Complete 5-7 days of antimicrobial therapy

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging

Algorithm for the Management of Acute Bacterial Rhinosinusitis

Antimicrobial Regimens for Acute Bacterial Rhinosinusitis in Adults

<table>
<thead>
<tr>
<th>Indication</th>
<th>First-line (Daily dose)</th>
<th>Second-line (Daily dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial empirical therapy</td>
<td>Amoxicillin-clavulanate 500 mg/125 mg PO TID</td>
<td>Amoxicillin-clavulanate 90 mg/kg/day PO BID</td>
</tr>
<tr>
<td></td>
<td>Or</td>
<td>Amoxicillin-clavulanate 875 mg/125 mg PO BID</td>
</tr>
<tr>
<td></td>
<td>Or</td>
<td>Doxycycline 100 mg PO BID</td>
</tr>
<tr>
<td></td>
<td>Or</td>
<td>Doxycycline 200 mg PO daily</td>
</tr>
<tr>
<td></td>
<td>Or</td>
<td>Levofoxacin 500 mg PO daily</td>
</tr>
<tr>
<td></td>
<td>Or</td>
<td>Moxifloxacin 400 mg PO daily</td>
</tr>
</tbody>
</table>

- Source: Chow, A., et al., IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

Antimicrobial Regimens for Acute Bacterial Rhinosinusitis in Children

<table>
<thead>
<tr>
<th>Indication</th>
<th>First-line (Daily dose)</th>
<th>Second-line (Daily dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial empirical therapy</td>
<td>Amoxicillin-clavulanate 45 mg/kg/day PO BID</td>
<td>Amoxicillin-clavulanate 90 mg/kg/day PO BID</td>
</tr>
</tbody>
</table>

- Source: Chow, A., et al., IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

- Resistance to clindamycin (~31%) is found frequently among *Streptococcus pneumoniae* serotype 19A isolates in different regions of the United States [94].

Antimicrobial Regimens for Acute Bacterial Rhinosinusitis in Children (continued)

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<th>Second-line (Daily dose)</th>
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<tr>
<td>Initial empirical therapy</td>
<td>Amoxicillin-clavulanate 90 mg/kg/day PO BID</td>
<td>Amoxicillin-clavulanate 90 mg/kg/day PO BID</td>
</tr>
<tr>
<td></td>
<td>Or</td>
<td>Clindamycin 30–40 mg/kg/day PO TID plus cefixime 8 mg/kg/day PO BID or cefpodoxime 10 mg/kg/day PO BID</td>
</tr>
<tr>
<td></td>
<td>Or</td>
<td>Levofoxacin 10–20 mg/kg/day PO every 12–24 h</td>
</tr>
</tbody>
</table>

- Source: Chow, A., et al., IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

Antimicrobial Regimens for Acute Bacterial Rhinosinusitis in Adults (continued)

- β-lactam allergy (Containing β-lactam ring, penicillins, cephalosporins)

- Source: Chow, A., et al., IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults
### Antimicrobial Regimens for Acute Bacterial Rhinosinusitis in Children (continued)

- **β-lactam allergy**
  - Type I hypersensitivity
  - Non-type I hypersensitivity
  - Levofloxacin 10–20 mg/kg/day PO every 12–24 h
- **Or**
  - Clindamycin (30–40 mg/kg/day PO TID) plus cefixime (8 mg/kg/day PO BID) or cefpodoxime (10 mg/kg/day PO BID)

*Resistance to clindamycin (~31%) is found frequently among Streptococcus pneumoniae serotype 19A isolates in different regions of the United States [94].*  
— Source: Chao, A., et al., IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

### How Would you Prescribe Cephalosporins to Patients with Penicillin Allergies?

*Article by Margaret A. Fitzgerald, DNP, FNP-BC, NP-C, FAANP, CSP, FAAN, DCC*

Available at http://fhea.com/main/content/Newsletter/fheanews_volume12_issue8.pdf

### Urinary Tract Infection

- Second most common infectious complaint in outpatient primary care clinics
- Most common outpatient complaint caused by bacteria

— Source: Car J. Urinary Tract Infections in Women: Diagnosis and management in primary care. BMJ. 2006;332:94-97

### Which commonly reported symptom is most sensitive for UTI?

- Frequency
- Burning
- Straining
- Urgency
- Pain with voiding


### True or false?

**Evidence-based Methods to Avoid Urinary Tract Infection in Women**

- Postcoital voiding
- Timed or frequent voiding
- Wipe front to back
- Avoid hot tub use
- Do not wear pantyhose

Acute Uncomplicated Cystitis: Risk Factors for Women

• Heterosexual intercourse
  – UTI more frequent in 15-35 year-old women
  – Intercourse often precedes UTI onset
  – Frequency of intercourse often related to UTI incidence

• Low lactobacilli colonization
  – Normal periurethral flora component
  – Produces hydrogen peroxide, lactic acid
  – Provides periurethral area, vagina w/ pH that inhibits bacterial growth, blocks potential sites of attachment toxic to uropathogens

UTI Therapies


<table>
<thead>
<tr>
<th>Type of infection</th>
<th>Usual pathogens</th>
<th>Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute, uncomplicated urinary tract infection (cystitis, urethritis) in nonpregnant women</td>
<td>E. coli (Gm neg, most common pathogen), S. saprophyticus (Gm pos), Enterococci (Gm pos)</td>
<td><strong>Primary</strong> If local E. coli resistance to TMP/SMX&lt;20% and no allergy, then TMP/SMX-DS BID x 3 days If local E. coli resistance to TMP/ SMX&gt;20% or sulfa allergy, nitrofurantoin 100 mg BID X 5 d or fosfomycin X 1 dose, all plus phenazopyridine (Pyridium®)</td>
</tr>
<tr>
<td>Acute, uncomplicated urinary tract infection (cystitis, urethritis) in nonpregnant women (cont.)</td>
<td>E. coli (Gm neg, most common pathogen), S. saprophyticus (Gm pos), Enterococci (Gm pos)</td>
<td><strong>Alternative</strong> If local E. coli resistance to TMP/ SMX&gt;20% or sulfa allergy, ciprofloxacin 250 mg BID, ciprofloxacin ER 500 mg daily, levofloxacin 250 mg daily, or moxifloxacin 400 mg daily, all for 3 days, all plus phenazopyridine (Pyridium®) Gemifloxacin not labeled for use in UTI, likely effective.</td>
</tr>
<tr>
<td>Type of infection</td>
<td>Usual pathogens</td>
<td>Regimens</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-----------------------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Acute, uncomplicated urinary tract</td>
<td>E. coli (Gm neg, most common pathogen), S. saprophyticus</td>
<td>Alternative (cont.) Amoxicillin-clavulanate 875/125 mg BID x 5-7 days or</td>
</tr>
<tr>
<td>infection (cystitis, urethritis)</td>
<td>(Gm pos), Enterococci (Gm pos)</td>
<td>an oral cephalosporin (e.g., cephalexin 500 mg QID x 5-7 days or cefpodoxime proxetil 100 mg BID x 3 days)</td>
</tr>
<tr>
<td>in nonpregnant women (cont.)</td>
<td></td>
<td>Beta-lactams generally less efficacious than fluoroquinolones or TMP-SMX and should be reserved for cases where other agents cannot be used.</td>
</tr>
</tbody>
</table>

**Fosfomycin (Monurol®)**

- **Indications**
  - Treatment of uncomplicated UTIs in women due to susceptible strains of *Escherichia coli* and *Enterococcus faecalis*
  - Not indicated for the treatment of pyelonephritis or perinephric abscess

**Fosfomycin (Monurol®) per PI**

- Do not use more than one single dose of Monurol® to treat a single episode of acute cystitis. Repeated daily doses of Monurol® did not improve the clinical success or microbiological eradication rates compared to single dose therapy, but did increase the incidence of adverse events.

**Per Sanford Guide**

- Fosfomycin
  - 3 G taken as a 1 time dose
- Spectrum of antimicrobial activity
  - Less effective vs. *E. coli* when compared to multiple doses of TMP-SMX
  - Active again *E. faecalis*, poor activity against other coliforms

**Fosfomycin (Monurol®) (continued)**

- Pregnancy risk category
  - B based largely on lab animal studies
- Cost
  - 1 packet=1 dose=\$45 on drugstore.com

**Per up to Date**

- Fosfomycin- A single-dose 3 gram sachet is an acceptable agent for women with mild to moderate infections who cannot take TMP-SMX or nitrofurantoin.

**Extended Spectrum Beta Lactamase-producing Strains**

- AKA ESBL-producing strains
  - Most often *K. pneumoniae*, *E. coli*, *Acinetobacter*
  - Usually effective antimicrobials include nitrofurantoin, fosfomycin, or amoxicillin-clavulanate plus cefdinir
  - Source: 2013 Sanford Guide

**Length of Therapy in Select Populations**

- For patients with DM, symptoms greater than 7 days, recently used antimicrobials, =>age 65 yr, or male
  - Source: Gupta, K., Stamm, W. Best Dx/Best Tx, Urinary Tract Infection, available [http://www.acpmedicine.com](http://www.acpmedicine.com)

**Length of Therapy in Select Populations (continued)**

- 7-day regimen
  - Oral TMP-SMX
  - Fluoroquinolone
  - Cefixime 400 mg daily
  - Cefpodoxime 100-200 mg daily
  - Other cephalosporin as appropriate
  - Source: Gupta, K., Stamm, W. Best Dx/Best Tx, Urinary Tract Infection, available [http://www.acpmedicine.com](http://www.acpmedicine.com)

**Skin Abscess, Boils, Furuncles**


**Purulent Skin Lesions: Boils, Furuncles, Carbuncles Abscesses**

- Incision and drainage=Mainstay of therapy
- Community-associated MRSA of concern for effective management

**Etiologies**

- *Staphylococcus aureus*
  - Gram positive cocci that appear in grape-like clusters
    - Methicillin sensitive (MSSA)
      - Implies beta-lactamase producing organism
    - Methicillin resistant (MRSA)
      - Implies altered antibiotic-binding sites within organism, could also produce beta-lactamase
Primary Regimens

• Patient is afebrile and abscess <5 cm in diameter
  – Incision and drainage only is usually effective.
  – Hot packs are helpful.
  – No need for antimicrobial therapy

Primary Regimens (continued)

• Patient afebrile abscess ≥5 cm in diameter
  – Incision and drainage
  – Likely adequate alone, as the 5 cm cut-off not rigorously established as an indication for adjunct antimicrobial therapy

Primary Regimens (continued)

• Patient is febrile and abscess is large and/or multiple abscesses
  – Outpatients
    • Empirical antibiotic therapy... (cont.)
      – Clindamycin 300-450 mg PO TID x 5-10 days
      • Or
      – Doxycycline 100 mg PO q12h
      • Or
      – Minocycline 100 mg PO q12h x 5-10 days

Primary Regimens (continued)

• Patient is febrile and abscess is large and/or multiple abscesses (cont.)
  – Outpatients (cont.)
    • Empirical antibiotic therapy...(cont.)
      – Clindamycin 300-450 mg PO TID x 7-10 days
      • Or
      – TMP-SMX 160/800 mg (i.e., 1 double strength tab) PO BID x 7-10 days
      • Or
      – Doxycycline 100 mg PO BID x 7-10 days

Primary Regimens (continued)

• Patient is febrile and abscess is large and/or multiple abscesses (cont.)
  – Outpatients (cont.)
    • Empirical antibiotic therapy...(cont.)
      – If no response after 2-3 days, look for complications and consider vancomycin 1 gm IV q12h
Alternative Regimens
(continued)

• For MRSA infections
  – Oral agents
    • Linezolid 600 mg PO q12h
  – Parenteral agents
    • Daptomycin 4 mg/kg IV q24h (give higher dose if bacteremic patient)
    • Linezolid 600 mg IV q12h

• Oral agents
  – Linezolid 600 mg PO q12h

• Parenteral agents
  – Daptomycin 4 mg/kg IV q24h (give higher dose if bacteremic patient)
  – Linezolid 600 mg IV q12h

Alternative Regimens
(continued)

• One double-strength tab of TMP-SMX twice daily as effective as two
double-strength tabs twice daily
  – Lower dosage range of TMP-SMX (1 DS instead of 2 DS) and clindamycin
    (150-300 mg instead of 450 mg) found to be associated with treatment failure
    in obese patients (BMI≥40)

Alternative Regimens
(continued)

• For documented MSSA infection
  – Oral agents
    • Dicloxacillin 500 mg PO QID
      – Or
    • Flucloxacillin 250-500 mg PO QID
      – Or
    • Cephalexin 500 mg PO QID

• For documented MSSA infection, a
  beta-lactam preferred agent (cont.)
  – Parenteral agents
    • Nafcillin or oxacillin 1 gm IV q4h
      – Or
    • Flucloxacillin 1 gm IV q6h
      – Or
    • Cefazolin 1 gm IV q8h

To pack or not to pack?

What is the evidence?
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2231432/

Recurrent Furunculosis

• There is no "gold standard" regimen.
• Optimal regimen and duration of treatment are uncertain.
Recurrent Furunculosis: Documenting Colonization (continued)

- Need to culture multiple sites
  - Nose, throat and inguinal area skin.
  - Nares only culture missed 48% of colonized individuals
    - Source: Clin Infect Dis 54:1523, 2012
- Does not apply to care of IDU

Primary Regimens: Recurrent Furunculosis

- (Doxycycline 100 mg PO BID + rifampin 300 mg PO BID x 7 days) + (mupirocin ointment in anterior nares and under fingernails 2x/day x 7 days) + (chlorhexidine 4% {Hibiclens® OTC} shower daily x 7 days)

Primary Regimens (continued)

- Resistance of S. aureus to rifampin can develop quickly. In theory, to lower the risk can give the doxycycline 100 mg PO BID for 5 days to lower the inoculum of organisms and then continue the doxycycline and add rifampin 300 mg PO BID for another 5 days. Total of 10 days of doxycycline and 5 days of rifampin.

Alternative Regimens

- TMP-SMX double strength tab PO BID + rifampin 300 mg PO BID x 7 days + mupirocin ointment (as above) + chlorhexidine shower (as above)
  - Source: Infect Control Hosp Epidemiol 32:872, 2011

Alternative Regimens (continued)

- Bleach baths (tub of warm water with 1/4 cup of 6% sodium hypochlorite (Clorox®, household bleach) for 15 minutes, is as effective as use of chlorhexidine shower body washes.
  - Source: Infect Control Hosp Epidemiol 32:872, 2011

Comments

- If patient is a known carrier of MSSA, can use dicloxacillin 500 mg PO QID instead of doxycycline or TMP-SMX.
And last but not least on antibiotic sparing behavior...

Acute bronchitis

True or false?

• In otherwise healthy patients, purulent sputum usually indicates the presence of sloughed tracheobronchial epithelium and inflammatory cells, not bacterial burden.


True or false?

• In a study involving 2781 healthy adults, the median duration of cough from acute bronchitis due to all causes was 18 days.

Table 10-8: Acute Bronchitis: Likely Causative Pathogens

<table>
<thead>
<tr>
<th>Organism</th>
<th>% of total</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory tract viruses</td>
<td>90</td>
<td>Consider using anticholinergic bronchodilator such as ipratropium bromide (Atrovent®) or inhaled beta2-agonist such as albuterol or short course of oral corticosteroid with protracted, problematic cough.</td>
</tr>
</tbody>
</table>

Table 10-8: Acute Bronchitis: Likely Causative Pathogens (continued)

<table>
<thead>
<tr>
<th>Organism</th>
<th>% of total</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial pathogens such as <em>M. pneumoniae</em>, <em>C. pneumoniae</em>, <em>B. pertussis</em></td>
<td>10</td>
<td>Consider use of macrolide or tetracycline form when antimicrobial therapy indicated.</td>
</tr>
</tbody>
</table>

Conclusion
End of Presentation!
Thank you for your time and attention.
Margaret A. Fitzgerald,
DNP, FNP-BC, NP-C, FAANP, CSP, FAAN, DCC
www.fhea.com          cs@fhea.com

All websites listed active at the time of publication.
Algorithm for the Management of Acute Bacterial Rhinosinusitis

Signs and symptoms either:
- a) Persistent and not improving (≥10 days);
- b) Severe (≥3-4 days); or
- c) Worsening or “double-sickening” (≥3-4 days)

**Risk for Resistance**

- No
  - Initiate first-line antimicrobial therapy
    - Improvement after 3-5 days
      - Complete 5-7 days of antimicrobial therapy
      - Improvement
      - Complete 5-7 days of antimicrobial therapy
    - Improvement after 3-5 days
      - Complete 5-7 days of antimicrobial therapy
  - Worsening or no improvement after 3-5 days
    - Broaden coverage or switch to different antimicrobial class
      - Worsening or no improvement after 3-5 days
        - Refer to specialist
  - Symptomatic management

- Yes
  - Initiate second-line antimicrobial therapy
    - Improvement after 3-5 days
      - Complete 5-7 days of antimicrobial therapy
  - Worsening or no improvement after 3-5 days
    - Complete 7-10 days of antimicrobial therapy

**Risk for antibiotic resistance**
- Age <2 or >65, daycare
- Prior antibiotics within the past month
- Prior hospitalization past 5 days
- Comorbidities
- Immunocompromised

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging