Antimicrobial Activity of Oral Anti-infectives and their Application to Common Ambulatory Infections

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Disclosures

• The speaker has served on an Advisory Board for BioCryst Pharmaceuticals, Inc. (10/2014)
Pharmacist Objectives

• Discuss the spectrum of activity for major classes of oral anti-infectives

• Identify primary pathogens associated with common outpatient ambulatory infections

• Apply consensus guideline recommendations to the treatment of patients with infections in ambulatory care settings
Technician Objectives

- Identify common sites of infections
- Discuss the major differences between antibiotic drug classes
- Recognize most treatments for most common bacterial infections seen in an ambulatory setting
Initial Assessment

Which best describes your level of comfort with the spectrum of activity and appropriate use of anti-infectives?

A. High level → I am an anti-infective expert
B. Moderate level → I can get by when needed
C. Low level → I am not comfortable with anti-infectives
D. OMG! → Pharmacy school was years ago
Which Empiric Therapy?
Answer these 3 Questions!!!

1. What is/are the likely site(s) of infection?
2. Based on #1, what are the most likely pathogens?
3. What antibiotic(s) are most likely to be active against the likely pathogens?
   - Pathogen susceptibility to antibiotics
     • Intrinsic activity (empiric) and local susceptibility (antibiogram)
   - Community vs. nosocomial pathogens
   - Achievable concentration of drug at the site of infection
   - Bactericidal vs. bacteriostatic
   - Status of patient’s immune system
# Common Gram Positive Organisms

<table>
<thead>
<tr>
<th>Organism</th>
<th>Disease/Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococci</td>
<td>Urinary tract infections, endocarditis</td>
</tr>
<tr>
<td>Streptococci A,B,C,D,G</td>
<td>A: pharyngitis, cellulitis</td>
</tr>
<tr>
<td>Viridans streptococci</td>
<td>B: neonatal sepsis</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>Endocarditis, abscess, dental caries</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Community pneumonia, septic shock, meningitis</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>Furunculosis, cellulitis, abscess, septic shock, endocarditis</td>
</tr>
<tr>
<td></td>
<td>Infection of prosthetic devices, bacteraemia</td>
</tr>
</tbody>
</table>

Common Gram Negative Organisms

- **Escherichia coli**: Urinary tract infections, septic shock, haemorrhagic colitis
- **Klebsiella spp.**: Urinary tract infections, septic shock, pneumonia
- **Enterobacter/citrobacter**: Urinary tract infections, pneumonia, septic shock
- **Pseudomonas aeruginosa**: Urinary tract infections, pneumonia, septic shock
- **Neisseria meningitidis**: Septic shock, meningitis
- **Haemophilus influenzae**: Respiratory tract infections

Sites of Infection

Overview of Bacterial infections

**Bacterial meningitis**
- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- *Haemophilus influenzae*
- *Streptococcus agalactiae*
- *Listeria monocytogenes*

**Otitis media**
- *Streptococcus pneumoniae*

**Sinusitis**
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*

**Pneumonia**
Community-acquired:
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Staphylococcus aureus*
Atypical:
- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*
- *Legionella pneumophila*
- Tuberculosis
- *Mycobacterium tuberculosis*

**Upper respiratory tract infection**
- *Streptococcus pyogenes*
- *Haemophilus influenzae*

**Gastritis**
- *Helicobacter pylori*

**Food poisoning**
- *Campylobacter jejuni*
- *Salmonella*
- *Shigella*
- *Clostridium*
- *Staphylococcus aureus*
- *Escherichia coli*

**Skin infections**
- *Staphylococcus aureus*
- *Streptococcus pyogenes*
- *Pseudomonas aeruginosa*

**Sexually transmitted diseases**
- *Chlamydia trachomatis*
- *Neisseria gonorrhoeae*
- *Treponema pallidum*
- *Ureaplasma urealyticum*
- *Haemophilus ducreyi*

**Urinary tract infections**
- *Escherichia coli*
- Other Enterobacteriaceae
- *Staphylococcus saprophyticus*
- *Pseudomonas aeruginosa*
## Oral Anti-infectives by Class

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Antivirals</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Beta-lactams</td>
<td>• Neuraminidase inhibitors</td>
</tr>
<tr>
<td>• Macrolides</td>
<td>• Nucleoside analogs</td>
</tr>
<tr>
<td>• Lincosamides</td>
<td></td>
</tr>
<tr>
<td>• Tetracyclines</td>
<td></td>
</tr>
<tr>
<td>• Fluoroquinolones</td>
<td></td>
</tr>
<tr>
<td>• Sulfonamides</td>
<td></td>
</tr>
<tr>
<td>• Oxazolidones</td>
<td></td>
</tr>
</tbody>
</table>
- **Penicillin V**

- **Penicillin V**

  - **Gram positive**
    - Drug of choice for *Streptococcus* species
    - Most *Staphylococcus* are resistant
    - Most *Enterococcus faecalis* are susceptible
    - Most *Enterococcus faecium* (VRE) are resistant

  - **Gram negative**
    - Minimal activity

  - **Anaerobes**
    - Above diaphragm bugs
    - *Clostridium* (not *difficile*)

  - **Other**
    - Drug of choice for syphilis (IM benzathine PCN)
Gram Negative Respiratory
- H. Influenzae
- M. Catarrhalis
- Neisseria Spp.

Enterics (UTI)
- E. Coli
- Klebsiella Spp.
- Proteus Spp.

Non-fermenters and other MDROs
- Pseudomonas
- Acinetobacter
- ESBLs

Other
- Respiratory Atypical
  - C. pneumoniae
  - M. pneumoniae
- Respiratory Viral
  - Influenza A
  - Influenza B
- Sexually transmitted organisms
  - Chlamydia trachomatis
  - N. Gonorrhoeae
  - Herpes simplex virus

Amino Penicillins
- Ampicillin (IV, PO)
- Amoxacillin (PO)

Spectrum of Activity
Gram positive
- Steptococcus
- Enterococcus faecalis
- Enterococcus faecium are frequently resistant
- No Staphylococcus coverage
- Listeria (ampicillin only)

Gram Negative
- Some E. coli, Proteus, Haemophilus influenzae
- **Beta-lactamase Inhibitor Combinations**
  - **Amoxacillin/clavulanate**

- **Spectrum of Activity**
  - **Gram Positive**
    - Staphylococcus (no MRSA)
    - *Streptococcus*  
    - *Enterococcus faecalis*
    - *Enterococcus faecium* are frequently resistant

  - **Gram Negative**
    - Highly active against respiratory pathogens
    - Less reliable against enterics

  - **Anaerobes**
    - Broad coverage

- **Beta-lactamase Inhibitor Combinations**
  - **Amoxacillin/clavulanate**
## Cephalosporins

<table>
<thead>
<tr>
<th>1&lt;sup&gt;st&lt;/sup&gt; Generation</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; Generation</th>
<th>3&lt;sup&gt;rd&lt;/sup&gt; Generation</th>
<th>4&lt;sup&gt;th&lt;/sup&gt; Generation &amp; Beyond</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV: Cefazolin</td>
<td>IV: Cefotetan* Cefoxitan* Cefuroxime</td>
<td>IV: Ceftriaxone Cefotaxime Ceftizoxime Ceftazidime</td>
<td>IV: Cefepime Ceftaroline Ceftolozane/tazobactam</td>
</tr>
<tr>
<td>PO: Cephalexin Cefadroxil</td>
<td>PO: Cefuroxime Cefaclor Cefprozil</td>
<td>PO: Ceftidoren Cefixime Cefdinir Ceftibuten Cefpodoxime</td>
<td></td>
</tr>
</tbody>
</table>

- No coverage of atypical organisms or *Enterococcus* spp.
- No anaerobic activity except cefamycins*
- In general, from 1<sup>st</sup> to 4<sup>th</sup> generation:
  - ↓ Gram-positive coverage (until 4<sup>th</sup>), ↑ Gram –negative coverage
Gram Positive

- **Staphylococcus**
- **Enterococcus**
- **Streptococcus**

Gram Negative

- **Respiratory**
  - *H. Influenzae*
  - *M. Catarrhalis*
  - *N. Neisseria Spp.*
- **Enterics (UTI)**
  - *E. Coli*
  - *Klebsiella Spp.*
- **Non-fermenters and other MDROs**
  - *Pseudomonas*
  - *Acinetobacter ESBLs*

Other

- **Respiratory Atypical**
  - *C. pneumoniae*
  - *M. pneumoniae*
  - *Legionella Spp.*
- **Respiratory Viral**
  - Influenza A
  - Influenza B
- **Sexually transmitted organisms**
  - *Chlamydia trachomatis*
  - *N. Gonorrhoeae*
  - *Herpes simplex virus*

**1st Generation Cephalosporins**

- **Cephalexin (PO)**
- **Cefadroxil (PO)**

**Spectrum of Activity**

- **Gram positive**
  - *Staphylococcus*
  - No MRSA
  - *Enterococcus*

- **Gram Negative**
  - *Proteus*
  - *E. Coli*
  - *Klebsiella*

- Think SSTI and UTI
Gram Negative

- Respiratory
  - H. Influenzae
  - M. Catarrhalis
  - Neisseria Spp.
- Enterics (UTI)
  - E. Coli
  - Klebsiella Spp.
  - Proteus Spp.
- Non-fermenters and other MDROs
  - Pseudomonas
  - Acinetobacter
  - ESBLs

Gram Positive

- Staphylococcus
- Enterococcus
- Streptococcus

2\textsuperscript{nd} & 3\textsuperscript{rd} Generation Cephalosporins

- Cufuroxime, cefaclor, cefprozil (2\textsuperscript{nd} Gen)
- Cefdinir, cefpodoxime, cefixime (3\textsuperscript{rd} Gen)

Spectrum of Activity

- Gram positive
  - Streptococcus
  - Staphylococcus is unreliable
  - No MRSA
  - No Enterococcus

- Gram Negative
  - Enterobacteriaceae (ALL)

Cefixime (with azithromycin) an alternative option for \textit{N. gonorrhoeae}
Fluoroquinolones

Why is ciprofloxacin excluded from the classification of respiratory fluoroquinolones?

A. It does not adequately cover a primary respiratory pathogen, *S. pneumoniae*

B. It does not achieve an adequate pulmonary concentration to treat pneumonia

C. It has failed in clinical trials studying patients with pneumonia

D. It has a boxed warning against pneumonia treatment in it’s FDA labeling
Fluoroquinolones
- Ciprofloxacin (IV, PO)
- Levofloxacin (IV, PO)
- Moxifloxacin (IV, PO)

Spectrum of Activity
- Gram Positive
  - Streptococcus
  - Staphylococcus
  - Minimal Enterococcus
- Gram Negative
  - Broad coverage including pseudomonas (except moxifloxacin)
- Atypical Respiratory
  - Mycoplasma
  - Chlamydia
  - Legionella
Gram Negative
- Respiratory
  - H. Influenzae
  - M. Catarrhalis
  - Neisseria Spp.
- Enterics (UTI)
  - E. Coli
  - Klebsiella Spp.
  - Proteus Spp.
- Non-fermenters and other MDROs
  - Pseudomonas
  - Acinetobacter
  - ESBLs
- Other
  - Respiratory Atypical
  - C. pneumoniae
  - M. pneumoniae
  - Respiratory Viral
  - Influenza A
  - Influenza B
  - Sexually transmitted organisms
    - Chlamydia trachomatis
    - N. Gonorrhoeae
    - Herpes simplex virus

Macrolides
- Azithromycin
- Clarithromycin
- Erythromycin

Spectrum of Activity
- Gram Positive
  - Streptococcus
    - Increasing resistance reported
  - No Staphylococcus or Enterococcus
- Respiratory: Gram Negative and Atypical
  - Covers all well
- STD coverage (azithromycin)
  - Chlamydia
  - Gonorrhoeae variable
Gram Negative

- **Respiratory**
  - *H. Influenzae*
  - *M. Catarrhalis*
  - *Neisseria Spp.*
- **Enterics (UTI)**
  - *E. Coli*
  - *Klebsiella Spp.*
  - *Proteus Spp.*
- **Non-fermenters and other MDROs**
  - *Pseudomonas Spp.*
  - *Acinetobacter Spp.*
  - ESBLs

Gram Positive

- **Staphylococcus**
  - MRSA
  - MSSA
- **Enterococcus**
- **Streptococcus**

**Spectrum of Activity**

- **Gram Positive**
  - Staphylococcus
  - **Includes MRSA**
  - Streptococcus
  - Resistance to *S. pneumoniae* exists
  - Most Gram positive anearboes

- **Lincosamides**
- **Clindamycin**

- **Gram Negative and Atypical Respiratory**
  - No coverage

- **STD coverage**
  - No coverage
Gram Negative

- H. Influenzae
- M. Catarrhalis
- Neisseria Spp.

Respiratory

- E. Coli
- Klebsiella Spp.
- Proteus Spp.

Enterics (UTI)

- Non-fermenters and other MDROs
- Pseudomonas
- Acinetobacter ESBLs

Other

- Respiratory Atypical
- C. pneumoniae
- M. pneumoniae

Respiratory Viral

- Influenza A
- Influenza B

Sexually transmitted organisms

- Chlamydia trachomatis
- N. Gonorrhoeae
- Herpes simplex virus

Gram Positive

- Staphylococcus
- Enterococcus
- Streptococcus

MRSA
- MSSA
- Lansfield Groups A,B,C,D,E
- S. pneumoniae

Tetracyclines

- Doxycycline
- Minocycline
- Tetracycline (?!?)

Spectrum of Activity

Gram Positive

- Streptococcus
- Staphylococcus

MRSA variable
- Minimal Enterococcus

Gram Negative

- Good URI coverage
- Not excreted in urine

Atypical Respiratory

- Mycoplasma
- Chlamydia
- Legionella
- **Sulfa Antibiotics**
  - Trimethoprim/Sulfamethoxazole

- **Spectrum of Activity**
  - **Gram Positive**
    - Staphylococcus
    - Includes MRSA
    - Best oral option for CA-MRSA?!
    - Minimal Streptococcus

- **Gram Negative**
  - Covers most UTI pathogens - resistance exists
  - Not first-line recommendation for respiratory pathogens

- **Atypical Respiratory**
  - PCP/PJP prophylaxis!
Gram Positive

- Staphylococcus
- Enterococcus
- Streptococcus
  - Neisseria Spp.
  - Enterics (UTI)
  - E. Coli
  - Klebsiella Spp.
  - Proteus Spp.
  - Non-fermenters and other MDROs
    - H. Influenzae
    - M. Catarrhalis
    - Neisseria Spp.

Gram Negative

- Respiratory
- Enterics (UTI)
- Non-fermenters and other MDROs
  - Pseudomonas
  - Acinetobacter
  - ESBLs

Other

- Respiratory Atypical
- Respiratory Viral
- Sexually transmitted organisms
  - Chlamydia trachomatis
  - N. Gonorrhoeae
  - Herpes simplex virus

Oxazolidones

- Linezolid
- Tedizolid

Spectrum of Activity

Gram Positive

- Broadly active including anearobes
- Very little resistance reported

Gram Negative

- No activity

Notable characteristics

- No generic formulations available
- Courses >2 weeks have associated toxicities
- DDIs with SSRIs/SNRIs
Other Oral Antibiotics
- Nitrofurantoin
- Fosfomycin

Spectrum of Activity
- Gram Positive
  - Activity limited to Enterococcus
  - Covers most common UTI pathogens

Notable characteristics
- Appreciable drug concentration only in bladder/urine
- Consider fosfomycin for MDR UTIs in outpatient settings
# Pregnancy Categories for Oral Antimicrobials

<table>
<thead>
<tr>
<th>Class/Agent</th>
<th>Category</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-lactams</td>
<td>B</td>
<td>Generally safe in pregnancy, and a first-line recommendation for most infection types</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>C</td>
<td>Benefit should outweigh risk if chosen for use.</td>
</tr>
<tr>
<td>Macrolides</td>
<td>B/C</td>
<td>Azithromycin (B), Clarithromycin (C). As a class, less data than Beta-lactams</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>D</td>
<td>Teratogenic</td>
</tr>
<tr>
<td>Sulfa Drugs (TMP/SMX)</td>
<td>C/D*</td>
<td>Not recommended for 3rd trimester or children &lt;2 months of age</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>B</td>
<td>Consider for purulent and non-purulent cellulitis. Association with <em>C. difficile</em> infection.</td>
</tr>
<tr>
<td>Nitrofurantoin/ Fosfomycin</td>
<td>B</td>
<td>Little data exists, risk for hemolytic anemia with nitrofurantoin. Benefit should outweigh risk for use</td>
</tr>
<tr>
<td>Oxazolidones</td>
<td>C</td>
<td>Reversible myelosuppression and partially or non-reversible neuropathies with prolonged use (&gt;2 weeks)</td>
</tr>
</tbody>
</table>

*During 3rd trimester*
Other Considerations for Antimicrobial Selection for Outpatients?

• Spectrum of activity

• Specific culture and susceptibility results?
  – Most therapy will be empiric!

• Local epidemiological data known?

• Pharmacokinetic properties of oral antimicrobials
  – Do they achieve concentrations at the site of infection?
Do We Use Antibiotics Appropriately?

- Survey of 1529 physicians for 28,787 adult office visits
- 21% of all prescriptions were for colds, URTI and bronchitis
- Patients were treated with antibiotics in:
  - 51% of colds
  - 52% of URTI
  - 66% of bronchitis

Upper Respiratory Tract Infections (URI)

- URI is a non-specific term that includes:
  - Sinusitis
  - Otitis media
  - Pharyngitis
  - Bronchitis

- Most common affliction is the common cold (viral) infection not requiring treatment
Pharyngitis

Which agent should be selected to treat a patient who reports a penicillin-allergy (unknown reaction) and has confirmed streptococcal pharyngitis (i.e. Strep throat)?

A. Azithromycin
B. Levofloxacin
C. Doxycycline
D. Trimethoprim/Sulfamethoxazole (TMP/SMX)
Pharyngitis Etiology

<table>
<thead>
<tr>
<th>Organism</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral (rhinovirus, EBV, influenza)</td>
<td>40-45%</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em> (Group A Strep)</td>
<td>20-30%</td>
</tr>
<tr>
<td>Group C, D <em>Streptococcus</em></td>
<td>5-10%</td>
</tr>
<tr>
<td>Other</td>
<td>~20%</td>
</tr>
</tbody>
</table>

- Antibiotic therapy has only been shown to make a difference in clinical outcomes for patients with Group A *Streptococcus*
- 70% of patients reporting to primary care with a sore throat are prescribed antibiotics!

## Pharyngitis Treatment

<table>
<thead>
<tr>
<th>Medication</th>
<th>Duration</th>
<th>Recommendation Strength, Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No known Drug Allergies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin V</td>
<td>10 days</td>
<td>Strong, high</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>10 days</td>
<td>Strong, high</td>
</tr>
<tr>
<td><strong>Non-Type 1 (anaphylactic) penicillin allergy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cephalexin or cefadroxil (first generation)</td>
<td>10 days</td>
<td>Strong, high</td>
</tr>
<tr>
<td><strong>Type 1 (anaphylactic) penicillin allergy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>5 days</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>10 days</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>10 days</td>
<td>Strong, moderate</td>
</tr>
</tbody>
</table>

Acute Bacterial Rhinosinusitus (ABRS)

• Frequently being referred to as “rhinosinusitis” in the literature
  – Sinusitis is often preceded by rhinitis and rarely occurs without concurrent inflammation of the nasal airways

• Viral infection is the most common predisposing condition for bacterial infection
  – Only 0.5-2% of colds result in bacterial sinusitis
  – Increased with young children, day care, siblings

• Acute Sinusitis
  – Rapid onset and purulent nasal or pharyngeal discharge for >7 days

• Subacute or Chronic Sinusitis (>3 months)
  – Long term poorly or untreated disease that results in changes in the mucosal lining or more than 3-4 episodes/year or repeated ABX failures
## Pathogens Causing Acute Rhinosinusitis

<table>
<thead>
<tr>
<th>Viral Pathogens</th>
<th>Bacterial Pathogens</th>
<th>Prevalence from 2010 Analysis (Bacterial)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinovirus</td>
<td><em>Streptococcus pneumoniae</em></td>
<td>38%</td>
</tr>
<tr>
<td>Enterovirus</td>
<td><em>Haemophilus influenzae</em></td>
<td>36%</td>
</tr>
<tr>
<td>Coronavirus</td>
<td><em>Moraxella catarrhalis</em></td>
<td>16%</td>
</tr>
<tr>
<td>Influenza A and B</td>
<td><em>Streptococcus pyogenes</em></td>
<td>4%</td>
</tr>
<tr>
<td>RSV</td>
<td><em>Staphylococcus aureus</em></td>
<td>13%</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Gram-negative bacilli</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>Anaerobes</td>
<td>---</td>
</tr>
</tbody>
</table>

## Therapy Recommendations for ABRS

### Table 10. 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><img src="https://example.com" alt="Amoxicillin-clavulanate (500 mg/125 mg PO tid, or 875 mg/125 mg PO bid)" /></td>
<td><img src="https://example.com" alt="Amoxicillin-clavulanate (2000 mg/125 mg PO bid)" /></td>
</tr>
<tr>
<td>β-lactam allergy</td>
<td><img src="https://example.com" alt="Doxycycline (100 mg PO bid or 200 mg PO qd)" /></td>
<td><img src="https://example.com" alt="Doxycycline (100 mg PO bid or 200 mg PO qd)" /></td>
</tr>
<tr>
<td>Risk for antibiotic resistance or failed initial therapy</td>
<td><img src="https://example.com" alt="Levofloxacin (500 mg PO qd)" /></td>
<td><img src="https://example.com" alt="Moxifloxacin (400 mg PO qd)" /></td>
</tr>
<tr>
<td>Severe infection requiring hospitalization</td>
<td><img src="https://example.com" alt="Ampicillin-sulbactam (1.5–3 g IV every 6 h)" /></td>
<td><img src="https://example.com" alt="Levofloxacin (500 mg PO or IV qd)" /></td>
</tr>
<tr>
<td></td>
<td><img src="https://example.com" alt="Moxifloxacin (400 mg PO or IV qd)" /></td>
<td><img src="https://example.com" alt="Ceftriaxone (1–2 g IV every 12–24 h)" /></td>
</tr>
<tr>
<td></td>
<td><img src="https://example.com" alt="Cefotaxime (2 g IV every 4–6 h)" /></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: bid, twice daily; IV, intravenously; PO, orally; qd, daily; tid, 3 times a day.

Influenza

• Neuraminidase inhibitors are active against most circulating strains of influenza A & B
  – Oseltamavir (oral option)
  – Zanamavir (inhaled option)

• Resistance is low, but can vary season to season

• adamantanes are only active against influenza A strains and are no longer recommended for use due to high rates of resistance
  – Amantadine
  – Rimantadine
Influenza Management Recommendations

• Usually self-limiting for otherwise healthy outpatients

• Data suggest there is only a benefit if treatment started within 48 hours of symptom onset

• Clinical benefit in studies was reduction of symptoms and duration of illness by 1 or 2 days

• Treatment is recommended as early as possible for any patient with confirmed or suspected influenza who:
  – Is hospitalized
  – Has severe, complicated, or progressive illness; or
  – Is at higher risk for influenza complications

CDC. Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2011;(60)1.
### Higher Risk Characteristics

<table>
<thead>
<tr>
<th>Persons at higher risk for influenza complications who are recommended for antiviral treatment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children aged younger than 2 years;</td>
</tr>
<tr>
<td>Adults aged 65 years and older</td>
</tr>
<tr>
<td>Persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematological (including sickle cell disease), and metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle, such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury)</td>
</tr>
<tr>
<td>Persons with immunosuppression, including that caused by medications or by HIV infection</td>
</tr>
<tr>
<td>Women who are pregnant or postpartum (within 2 weeks after delivery)</td>
</tr>
<tr>
<td>Persons aged younger than 19 years who are receiving long-term aspirin therapy</td>
</tr>
<tr>
<td>American Indians/Alaska Natives</td>
</tr>
<tr>
<td>Persons who are morbidly obese (i.e., body mass index is equal to or greater than 40)</td>
</tr>
<tr>
<td>Residents of nursing homes and other chronic care facilities</td>
</tr>
</tbody>
</table>

Adapted from: CDC. Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*. 2011;(60)1.
# Antiviral Agents for Influenza

<table>
<thead>
<tr>
<th>Antiviral Agent</th>
<th>Activity Against</th>
<th>Use</th>
<th>Recommended For</th>
<th>Not Recommended for Use in</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oseltamivir (Tamiflu®)</td>
<td>Influenza A and B</td>
<td>Treatment</td>
<td>Any age</td>
<td>N/A</td>
<td>Nausea, vomiting. Postmarketing reports of serious skin reactions and sporadic, transient neuropsychiatric events</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chemo-prophylaxis</td>
<td>3 months and older</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Zanamivir (Relenza®)</td>
<td>Influenza A and B</td>
<td>Treatment</td>
<td>7 yrs and older</td>
<td>People with underlying respiratory disease (e.g., asthma, COPD)²</td>
<td>Diarrhea, nausea, sinusitis, nasal signs and symptoms, bronchitis, cough, headache, dizziness, and ear, nose and throat infections.</td>
</tr>
<tr>
<td>*Contraindicated with allergy to milk protein</td>
<td></td>
<td>Chemo-prophylaxis</td>
<td>5 yrs and older</td>
<td>People with underlying respiratory disease (e.g., asthma, COPD)²</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from: CDC. Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2011;(60)1.
Empiric Uncomplicated UTI Coverage?

Which of the following would you recommend for a 35 year old female outpatient, no allergies, otherwise healthy, and diagnosed with a UTI?

A. Amoxacillin±clavulanate
B. Ciprofloxacin
C. Nitrofurantoin
D. Trimethoprim/sulfamethoxazole
E. Fosfomycin
Urinary Tract Infection (UTI)

• Uncomplicated cystitis is a leading indication for prescription of antimicrobials in otherwise healthy women

• Increasing resistance among UTI pathogens has caused wide prescribing practices
  – A threshold of >20% resistance locally be used to rule out agents for empiric use

• Narrow agents should be used where appropriate help minimize collateral damage
Microbiology of Uncomplicated UTIs

• Similar in uncomplicated upper and lower UTIs
  – *E. coli* is the most common pathogen (75-95%)
  – *S. saprophyticus*
    • Less frequent in pyelonephritis
  – *P. mirabilis, Klebsiella spp.*

• Local antimicrobial susceptibility of *E. coli* should drive empiric selection
  – Followed by patient-specific factors
  – Renally eliminated drugs usually achieve high urinary concentrations

### UTI – Recommended Regimens

<table>
<thead>
<tr>
<th>Drug (Dose)</th>
<th>Duration</th>
<th>Est. Clinical Efficacy</th>
<th>Est. Micro Efficacy</th>
<th>Adverse Effects</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin 100mg BID</td>
<td>5 days</td>
<td>93 (84-95)</td>
<td>88 (86-92)</td>
<td>Nausea, HA</td>
<td>A-I</td>
</tr>
<tr>
<td>TMP/SMX 160/800 BID</td>
<td>3 days</td>
<td>93 (90-100)</td>
<td>94 (91-100)</td>
<td>Rash, urticaria N/V, hematologic</td>
<td>A-I</td>
</tr>
<tr>
<td>Fosfomycin 3 g x 1 dose</td>
<td>Single dose sachet</td>
<td>91</td>
<td>80 (78-83)</td>
<td>Diarrhea, nausea, HA</td>
<td>A-I</td>
</tr>
<tr>
<td>Fluoroquinolones (dose varies by agent)</td>
<td>3 days</td>
<td>90 (85-98)</td>
<td>91 (81-98)</td>
<td>N/V, diarrhea, HA, drowsiness, insomnia</td>
<td>A-III</td>
</tr>
<tr>
<td>Beta-lactams (dose varies by agent)</td>
<td>5-7 days (varies by agent)</td>
<td>89 (79-98)</td>
<td>82 (74-98)</td>
<td>Diarrhea, N/V, rash, urticaria</td>
<td>B-I/B-III 3&lt;sup&gt;rd&lt;/sup&gt; gen/1&lt;sup&gt;st&lt;/sup&gt; gen Cephs</td>
</tr>
</tbody>
</table>

*Uncomplicated UTI; HA=headache, N/V=nausea/vomiting

Asymptomatic Bacteriuria

• Most common in females and elderly

• Prognosis tends to be good
  – Therapy makes little sense
  – Side effects and cost of must be considered

• Treatment not shown to be beneficial except:
  – Pregnancy!
  – Patients undergoing urologic procedures

Patient Case

• A 33 y/o with no PMH comes to the clinic complaining of redness and swelling on his lower left leg.

• In the center of the erythematous area is a small induration that is draining a small amount of pus.

• The wound is swabbed for culture and the lab calls to report Gram positive cocci on staining but has no other information.

• The physician suspects community-acquired MRSA (CA-MRSA) but cannot rule out Group A Strep and would like to discharge the patient on appropriate coverage with oral therapy after incision and drainage.
Appropriate Coverage?

Which oral option is most likely to be efficacious in treating CA-MRSA and/or Group A \textit{Strep} Skin/soft tissue infection?

A. Clindamycin  
B. Levofloxacin  
C. Doxycycline  
D. Trimethoprim/sulfamethoxazole
Summary SSTI/Cellulitis

- Most common pathogens are Group A Streptococcus (*S. pyogenes*), other B-hemolytic *Streptococcus spp.*, and *S. aureus*

- Best streptococcal coverage
  - Most any beta-lactam, clindamycin

- Best staphylococcal coverage
  - MSSA: 1st generation ceph, amoxacillin/clavulanate, trimethoprim/sulfa, clindamycin, doxycycline
  - MRSA: trimethoprim/sulfa, clindamycin, linezolid
Coverage of *S. aureus* & Beta-hemolytic *Streptococcus* spp.?

5. For empirical coverage of CA-MRSA in outpatients with SSTI, oral antibiotic options include the following: clindamycin (A-II), TMP-SMX (A-II), a tetracycline (doxycycline or minocycline) (A-II), and linezolid (A-II).

If coverage for both b-hemolytic streptococci and CA-MRSA is desired, options include the following: clindamycin alone (A-II) or TMP-SMX or a tetracycline in combination with a b-lactam (e.g. amoxicillin) (A-II) or linezolid alone (A-II).


<table>
<thead>
<tr>
<th>Indication</th>
<th>Agent</th>
<th>Likely Pathogen(s)</th>
<th>Other Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erysipelas</td>
<td>Beta-lactam, Clindamycin (BL allergy?)</td>
<td><em>S. pyogenes</em>, other B-hem Strep spp.</td>
<td>PO for outpatient, initial IV for inpatient</td>
</tr>
<tr>
<td>Cutaneous abscess (furuncle, carbuncle)</td>
<td>None following incision and drainage*</td>
<td><em>S. aureus</em></td>
<td>Decolonize with mupirocin for recurrence</td>
</tr>
<tr>
<td>Cellulitis (non-purulent)</td>
<td>B-lactam, Clindamycin, Linezolid, B-lactam + either TMP/SMX or Doxycycline/ Minocycline</td>
<td><em>S. pyogenes</em>, other B-hem Strep spp., MSSA? Role of CA-MRSA unknown</td>
<td>Rarely yields culture. Consider CA-MRSA coverage for non-response to B-lactam or systemic symptoms</td>
</tr>
<tr>
<td>Cellulitis (purulent or trauma-related)</td>
<td>Clindamycin, TMP/SMX, Doxycycline/Minocycline, Linezolid</td>
<td><em>S. aureus</em> (including MRSA)</td>
<td>Coverage of B-hem Strep spp. not guideline recommended</td>
</tr>
</tbody>
</table>

*Consider treatment for multiple sites, rapid spreading, systemic symptoms, comorbidities or immunosupression, age extremes, difficult to drain, non-response to drainage*

Sexually Transmitted Diseases

• Highest incidence
  – *Chlamydia trachomatis* urethritis/cervicitis
    • Most frequently reported infection in the United States
  – *Neisseria gonorrhoeae* urethritis
    • Second most commonly reported *communicable* disease

• Highest prevalence
  – Herpes simplex virus (HSV)
  – Approximately 50% of population is seropositive for HSV-1 or HSV-2
    • Either may manifest as oral or genital lesions

Urethritis/Cervicitis in Adolescents and Adults

• Gonorrhea and Chlamydia
  – Most common causes of urethritis, cervicitis
  – Clinical presentation includes purulent genital discharge when symptomatic
  – Frequently asymptomatic infections
    • Chlamydia/men
    • Gonorrhea/women
  – Can progress to complications including PID, ectopic pregnancy, infertility in women

• Co-infection with both is common
Gonorrhea and Chlamydia Treatment

• Recommended regimens:
  – Gonorrhea
    • Ceftriaxone 250 mg IM, AND Azithromycin 1 g PO x 1 dose each
      – OR, IF NOT AN OPTION
    • Cefixime 400 mg PO, AND Azithromycin 1 g PO x 1 dose each
  – Chlamydia
    • Azithromycin 1 g PO x 1 dose (preferred for adherence)
      – OR
    • Doxycycline 100 mg PO twice a day x 7 days

• Should strongly consider treating for both infections in all patients

Herpes Simplex Virus (HSV)

• Genital Herpes can be caused by HSV-1 or HSV-2
  – HSV-2 most common, 50 million known infected in U.S.

• Typically presents with painful, vesicular lesion(s) in genital or anal area

• All patients with first episode of genital herpes should be treated regardless of severity of symptoms!

**Recommend treatment for First Episode of HSV**

- **Acyclovir** 400 mg orally three times a day
- **Acyclovir** 200 mg orally five times a day
- **Famciclovir** 250 mg orally three times a day
- **Valacyclovir** 1 g orally twice a day

Management Strategies for Recurrent HSV Infection

• Once acquired, HSV is a chronic, life-long infection

• **Episodic therapy** for recurrent genital herpes:
  – Requires initiation of therapy within 1 day of lesion onset or during neurological prodrome
  – Requires patient-directed initiation of therapy

• **Benefits of daily suppressive therapy:**
  – Reduces frequency of recurrences by 70-80% in patients with ≥ 6 episodes/year
  – Reduces incidence of symptomatic outbreaks
  – Improved quality of life versus episodic therapy
  – Reduces frequency of outbreaks over time
  – Better psychological adjustment to HSV?
  – Reduces rate of HSV transmission (valacyclovir)
# Management Strategies for Recurrent HSV Infection

## Suppressive Therapy

<table>
<thead>
<tr>
<th>Recommended Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir 400 mg orally twice a day</td>
</tr>
<tr>
<td>Valacyclovir 500 mg orally once a day*</td>
</tr>
<tr>
<td>Valacyclovir 1 g orally once a day</td>
</tr>
<tr>
<td>Famiciclovir 250 mg orally twice a day</td>
</tr>
</tbody>
</table>

*Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in persons who have very frequent recurrences (i.e., ≥10 episodes per year).

## Episodic Treatment

<table>
<thead>
<tr>
<th>Recommended Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir 400 mg orally three times a day for 5 days</td>
</tr>
<tr>
<td>Acyclovir 800 mg orally twice a day for 5 days</td>
</tr>
<tr>
<td>Acyclovir 800 mg orally three times a day for 2 days</td>
</tr>
<tr>
<td>Valacyclovir 500 mg orally twice a day for 3 days</td>
</tr>
<tr>
<td>Valacyclovir 1 g orally once a day for 5 days</td>
</tr>
<tr>
<td>Famiciclovir 125 mg orally twice daily for 5 days</td>
</tr>
<tr>
<td>Famiciclovir 1 gram orally twice daily for 1 day</td>
</tr>
<tr>
<td>Famiciclovir 500 mg once, followed by 250 mg twice daily for 2 days</td>
</tr>
</tbody>
</table>

CDC “Get Smart” Initiative

• Centers for Disease Control (CDC) Antimicrobial use education campaign

• Includes information for healthcare professionals in most practice settings
  – Outpatient practice settings
  – Community pharmacists
  – Summarizes guideline recommendations
  – Advises on outpatient Antibiotic Stewardship

• Information and resources available to the public
Thank You for Your Attention!