Antibiotic Use in the Emergency Department

Fredrick M. Abrahamian, D.O., FACEP
Associate Professor of Medicine
UCLA School of Medicine
Director of Education
Department of Emergency Medicine
Olive View-UCLA Medical Center
Sylmar, California

Decisions in Selecting Antibiotics

- Knowledge of causative organism(s)
- Spectrum of activity
- Susceptibility patterns
- Patient factors
  - Community-acquired vs healthcare
  - Age, co-morbidities, pregnancy, etc
  - Drug-drug interactions
- Side-effects
- Availability of drug & cost

Discussion Points

- Skin & soft-tissue infections
- Community-acquired pneumonia
- Intra-abdominal infections
- *Clostridium difficile* infection
- Urinary tract infections
- Acute otitis media
- Pharyngitis
Antibiotics & Abscesses

- Not for simple, 1st time, single, uncomplicated cases
- Indications for antibiotics:
  - Surrounding cellulitis
  - Signs of systemic toxicity
  - Immunocompromised host
  - High-risk locations (hands, face)
  - Recurrent abscesses or lack of response to I&D
  - Multiple or large abscess (≥ 5 cm)

Duration: 5-10 days

Prevalence of MRSA in Acute, Purulent Skin Infections, August 2008 (n=619)

The Sanford Guide. 2011, page 50.
Clin Infect Dis. 2011;52:e18-e55. [IDSA MRSA guidelines]
**In vitro CA-MRSA Antimicrobial Susceptibility Patterns**

**Resistant:**
- All penicillins
- Cephalosporins

**Variable:**
- Clindamycin: 94%
- Doxycycline: 100%
- Levofloxacin: 45%
- Erythromycin: 10%

**Susceptible:**
- TMP/SMX
- Rifampin
- Vancomycin
- Linezolid

Susceptibility patterns are dynamic, vary geographically & in patient populations.

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**TMP/SMX**
- 1-2 DS tablets PO bid
  - High rates of susceptibility
  - Resistance rates to S. pyogenes is unknown
  - Do not use near term (2 weeks before EDC)

**Clindamycin**
- 300-600 mg PO tid or qid
  - Can also be given IV (600-900 mg IV q8 hours)
  - Covers staphylococci, streptococci, anaerobes
  - Inducible resistance (D-zone disk-diffusion test)

**Doxycycline or minocycline**
- 100 mg PO bid
  - Variable rates of susceptibility
  - Excellent tissue penetration
  - Avoid during pregnancy or children ≤8 years

**Rifampin**
- 300 mg PO bid
  - Numerous drug-drug interactions
  - Risk-to-benefit ratio does not justify routine use
  - Best reserved for decolonization purposes

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**Rifampin & Drug Interactions**

- Inducer of cytochrome-P450 system
- Decreases the effect or levels of:
  - β-blockers, digoxin, ACE-inhibitors
  - Diltiazem, nifedipine
  - Corticosteroids, methadone
  - Oral anticoagulants
  - Phenytoin
  - Sulfonylureas
  - Oral contraceptives

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<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosing and Comments</th>
</tr>
</thead>
</table>
| Vancomycin         | 1 gram IV q12h  
Traditional dosing is sufficient  
Slow bactericidal activity; poor tissue penetration  
Concern for emergence of VRE, VISA |
| Linezolid (Zyvox®) | 600 mg IV/PO q12h  
Oral form 100% bioavailable  
Different pharmacokinetics compared to Vanco  
Inhibits toxin production |
| Daptomycin (Cubicin®) | 4-6 mg/kg IV q24h  
Complicated SSTIs, S. aureus bacteremia, right sided endocarditis due to MSSA & MRSA  
Binds surfactant and gets inactivated |
| Tigecycline (Tygacil™) | 1st dose 100 mg IV then 50 mg IV q12h  
Also covers Gram-negatives & anaerobes  
Does not cover Pseudomonas; ε Proteus  
Complicated SSTIs, intra-abdominal infections, CAP (not for DRSP) |

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### New FDA-Approved Antimicrobial Therapies for MRSA SSTIs

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosing and Comments</th>
</tr>
</thead>
</table>
| Telavancin (Vibativ™) | IV  
Lipoglycopeptide  
10 mg/kg qd (given over 60 min) |
| Ceftaroline (Teflaro™) | IV  
Cephalosporins with MRSA activity  
600 mg q12 hrs (given over 60 min) |

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### MRSA & Cellulitis

- Role of MRSA not clear
- Cellulitis with purulence:
  - MRSA 47%
  - MSSA 34%
  - Streptococci 13%
- Cover MRSA in severe cases
- TMP/SMX DS 1-2 tablets bid  
  **plus** Cephalexin 500 mg qid  
  Clindamycin 300 mg qid

Clin Infect Dis. 2011;52:a18-a55. [IDSA guidelines]*
Complicated Infections

- More likely mixed aerobic & anaerobic infections
- Consider in patients with:
  - Chronic infections
  - Peri-rectal infections
  - Wounds involving lower extremities (e.g., feet)
  - Vascular insufficiency (venous stasis ulcers)
  - Immunocompromising conditions (e.g., DM)
  - Bite-related wounds
  - Post-operative wounds, infected burns


<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotetan</td>
<td><em>B. fragilis</em> resistance</td>
</tr>
<tr>
<td>Ampicillin/sulbactam</td>
<td><em>E. coli</em> resistance</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>No Gram neg. coverage</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td><em>E. coli</em> resistance</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>No Gram neg. &amp; anaerobic coverage</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>Does not cover <em>Pseudomonas</em></td>
</tr>
<tr>
<td>Vancomycin, Linezolid</td>
<td>No Gram neg. &amp; anaerobic coverage</td>
</tr>
</tbody>
</table>
What Works on *Pasteurella* or *E. corrodens*

<table>
<thead>
<tr>
<th>Antibiotic(s)</th>
<th>Past/Eikenella</th>
<th>Staph/Strep</th>
<th>Anaerobes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin, amoxicillin, ampicillin</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2nd, 3rd, 4th gen. cephalosporins</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>1st gen. cephalosporins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbapenems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nafcilin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Empiric Abx for Dog, Cat, & Human Bite Infections

<table>
<thead>
<tr>
<th>Antibiotic(s)</th>
<th>Past/Eikenella</th>
<th>Staph/Strep</th>
<th>Anaerobes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amox-clav/Amp-sulb</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PCN + cephalaxin</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Cipro + Clinda</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TMP/SMX + Clinda</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Necrotizing Skin & Soft-Tissue Infections

- Hemodynamic stabilization
- Antibiotics:
  - Vancomycin plus
  - Clindamycin plus
  - Piperacillin/tazobactam
- Alternative:
  - Linezolid plus piperacillin/tazobactam

Clin Infect Dis. 2007;44:705-10. [Review article]
**CAP & CA-MRSA**
- Has emerged as a cause of severe CAP
- In addition to empiric therapy, add vancomycin if:
  - Severe illness (i.e., requiring ICU admission)
  - Necrotizing or cavitary infiltrates
  - Empyema
- Also consider in:
  - Recent Hx. or concurrent SSTI due to MRSA
  - Multilobar infiltrates; hemoptysis
  - Influenza-like prodrome
  - Nursing home residence (HCAP)

*Clin Infect Dis. 2011;52:e18-e55. [IDSA MRSA guidelines]*

**New Adult IV Vancomycin Dosing Regimen**
- Traditional dosing:
  - 1 gram or 15 mg/kg q12 hrs
- New regimen:
  - 15-20 mg/kg/dose ABW q8-12 hrs
  - Not to exceed 2 grams per dose
  - A loading dose of 25-30 mg/kg ABW in seriously ill patients
- Extend infusion period to 2 hrs if dose exceeds 1 gram


**Intra-Abdominal Infections**
- In general, direct empiric therapy towards:
  - Enterobacteriaceae & anaerobes
- Anaerobic therapy not indicated for acute cholecystitis
- Reserve anti-pseudomonal coverage for:
  - Severe infections, immunocompromised, or advanced age
- No need for routine MRSA coverage

*Clin Infect Dis. 2010;50:133-64. [2010 IDSA guidelines]*
Intra-Abdominal Infections

- Ampicillin-sulbactam not recommended
  - High rates of resistance among *E. coli*
- Cefotetan & clindamycin not recommended
  - High rates of resistance among *B. fragilis*
- Reserve aminoglycosides for patients allergic to β-lactams & quinolones

*Clin Infect Dis.* 2010;50:133-64. [2010 IDSA guidelines]

Intra-Abdominal Infections

Outpatient Antimicrobial Therapy

- Mild diverticulitis, drained peri-rectal abscess
  - TMP/SMX DS *plus* Metronidazole
  - Amoxicillin/clavulanate (2 grams bid)
  - Cipro or Levofloxacin *plus* Metronidazole
  - Moxifloxacin
- High-degree of clinda resistance to *B. fragilis*
- Treat for 7-10 days


Community-Acquired

Intra-Abdominal Infections in Adults

Mild-to-Moderate Severity

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefoxitin</td>
<td>Ertapenem</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>Tigecycline</td>
</tr>
<tr>
<td>Ticarcillin / clavulanic acid</td>
<td></td>
</tr>
<tr>
<td>Cefazolin, cefuroxime, ceftriaxone, or cefotaxime <em>plus</em> metronidazole</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin or levofloxacin <em>plus</em> metronidazole</td>
<td></td>
</tr>
</tbody>
</table>

*Clin Infect Dis.* 2010;50:133-64. [2010 IDSA guidelines]
Community-Acquired
Intra-Abdominal Infections in Adults
High Risk or Severe
- Imipenem-cilastatin
- Meropenem
- Doripenem
- Piperacillin-tazobactam
- Cefepime or ceftazidime **plus** metronidazole
- Ciprofloxacin or levofloxacin **plus** metronidazole

Clin Infect Dis. 2010;50:133-64. [2010 IDSA guidelines]

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**Clostridium difficile** Infection

- Mild-moderate disease
  - Leukocyte count < 15,000 cells/mm³ or
  - Creatinine < 1.5 times the baseline
- Severe disease
  - Leukocyte count ≥ 15,000 cells/mm³ or
  - Creatinine ≥ 1.5 times the baseline
- Severe complicated disease
  - Hypotension, shock, ileus, megacolon


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**Clostridium difficile** Infection

| Initial episode, mild-moderate | Metronidazole, 500 mg PO tid for 10-14 days |
| Initial episode, severe       | Vancomycin, 125 mg PO qid for 10-14 days |
| Initial episode, severe, complicated | Vancomycin, 500 mg PO / NG qid **plus** metronidazole, 500 mg IV tid |

**Clostridium difficile Infection**

- 6%-25% experience at least 1 episode of recurrence

<table>
<thead>
<tr>
<th></th>
<th>1st recurrence</th>
<th>2nd recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat as initial episode</td>
<td>Use vancomycin if severe disease</td>
<td>Vancomycin in a tapered and/or pulsed regimen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do not use metronidazole</td>
</tr>
</tbody>
</table>

*Infect Control Hosp Epidemiol. 2010;31:431-55. [2010 SHEA / IDSA guidelines]*

**Acute Uncomplicated Cystitis**

- More emphasis on nitrofurantoin
  - 100 mg PO bid x 5 days
  - Efficacy compared to TMP/SMX
  - Not active against *Proteus* or *Pseudomonas*
  - Category B; not recommended near term
  - Not recommended in children ≤ 12 years
  - Interaction with Mg-containing antacids

*Arch Intern Med. 2007;167:2207-12. [Short course nitrofurantoin]*

**Urinary Tract Infections**

- Acute cystitis in pregnancy: Treat for 7 days
- Outpatient pyelonephritis duration of therapy:
  - Ciprofloxacin x 7 days
  - Levofoxacin 750 mg x 5 days
  - All others x 14 days
- Pyelonephritis: Consider initial IV dose in ED
  - Ceftriaxone; ertapenem
  - Fluoroquinolone; aminoglycosides

Acute Otitis Media in Children

<table>
<thead>
<tr>
<th>Age</th>
<th>Certain Dx</th>
<th>Uncertain Dx</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 months</td>
<td>Antibiotics</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>6 mo – 2 yrs</td>
<td>Antibiotics</td>
<td>Observe if not Abxs if severe</td>
</tr>
<tr>
<td>≥ 2 yrs</td>
<td>Observe if not Abxs if severe</td>
<td>Observe</td>
</tr>
</tbody>
</table>

Severe illness is defined as temperature ≥ 39°C in the past 24 hours or moderate-severe otalgia.

Pharyngitis: Modified Centor Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature ≥ 38°C</td>
<td>1</td>
</tr>
<tr>
<td>Absence of cough</td>
<td>1</td>
</tr>
<tr>
<td>Swollen, tender anterior cervical nodes</td>
<td>1</td>
</tr>
<tr>
<td>Tonsillar swelling or exudate</td>
<td>1</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>3-14 years</td>
<td>1</td>
</tr>
<tr>
<td>15-44 years</td>
<td>0</td>
</tr>
<tr>
<td>≥ 45 years</td>
<td>-1</td>
</tr>
</tbody>
</table>

Pharyngitis: Modified Centor Criteria

<table>
<thead>
<tr>
<th>Score</th>
<th>Risk of Strep</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 0</td>
<td>1% - 2.5%</td>
<td>No further testing or antibiotic</td>
</tr>
<tr>
<td>1</td>
<td>5% - 10%</td>
<td>Culture</td>
</tr>
<tr>
<td>2</td>
<td>11% - 17%</td>
<td>Treat only + cultures</td>
</tr>
<tr>
<td>3</td>
<td>28% - 35%</td>
<td></td>
</tr>
<tr>
<td>≥ 4</td>
<td>51% - 53%</td>
<td>Treat with antibiotics</td>
</tr>
</tbody>
</table>
Take Home Points
Skin & Soft-Tissue Infections
- Traditional dosing of vancomycin is sufficient
- Avoid routine use of rifampin
- 1st gen. cephalosporins are inactive against *Pasteurella* or *Eikenella*
- Add clindamycin for necrotizing infections

Take Home Points
- CAP: Add vancomycin for severe cases
- Intra-abdominal infections: Avoid routine use of anti-pseudomonal agents
- *C. difficile* infection: Severity of disease decides between vancomycin & metronidazole
- Pyelonephritis: Fluoroquinolones for 5-7 days
- AOM: Treat at any age with temp $\geq 39^\circ C$
- Pharyngitis: Use modified Centor criteria