Current Guidelines for the Management of Common Out-Patient Infections in Young Adults in an Era of Multi-drug Resistant Organisms to Avoid Treatment Failure

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REVIEW AND UPDATE:

OUTLINE

I

ORAL ANTIBIOTICS:
Overview of Commonly-Used Oral Antibiotics
Antimicrobial Resistance (AMR)

II

OUT-PATIENT MULTI-DRUG RESISTANT ORGANISMS:
Antimicrobial Resistance (AMR) Prevalence &

COMMON OUT-PATIENT INFECTIONS
Current Treatment Guidelines by CDC/IDSA

III

ORAL ANTIBIOTIC PIPELINE:
New Classes and Generations
Definitions

- **Resistance**: ability of an organism to survive exposure to antimicrobial(s)
- **Virulence**: degree of pathogenicity or ability to cause disease by an organism
- **Normal Flora**: aggregate of microorganisms that reside on the skin, in the saliva and oral mucosa, in the conjunctiva, and in the gastrointestinal tracts
- **Pathogen**: microorganism that causes disease in its host.
- **Gram staining**: rapid identification of organisms (Gram+ or Gram−; round/cocci, rods/baccilli, coccobacilli
Definitions

- **Bactericidal**: kills bacteria (Penicillins, Ampicillins, Cephalosporins, Metronidazole, Fluoroquinolones, TMP-SMX)
- **Bacteriostatic**: slows bacterial growth or reproduction (Tetracyclines, Macrolides, TMP-SMX)
- **Minimum Inhibitory Concentration (MIC)**: lowest antimicrobial concentration that will inhibit the growth of an organism
- **Tissue Concentration**: depends on ability of antimicrobials to reach the target sites (GI absorption, plasma concentration, BBB, organ/tissue affinity, metabolism, excretion)
Definitions

Infections
- URI  Upper Respiratory Infection
- ABRS Acute Bacterial Rhino-Sinusitis
- AVRS Acute Viral Rhino-Sinusitis
- LRI Lower Respiratory Infection
- CAP Community-acquired pneumonia
- GU Genito-Urinary
- UTI Urinary Tract Infection
- STI Sexually Transmitted Infection
- GI Gastro-Intestinal
- SSTI Skin and Soft-Tissue Infection

Organisms
- BHS B-Hemolytic *Streptococcus*
- DRSP Drug-Resistant *Streptococcal pneumonia*
- MRSA Methicillin-Resistance *Staph. aureus*
- MSSA Methicillin-Sensitive *Staph. aureus*
- GC *Neisseria gonorrhoea (Gonococcus)*
I
ORAL ANTIBIOTICS:
OVERVIEW OF ORAL ANTIBIOTICS
ANTIMICROBIAL RESISTANCE

Penicillins and Ampicillins
Cephalosporins
Tetracyclines
Macrolides
Clindamycin
Quinolones
TMP-SMZ
Antibiotics

- Cell Wall Synthesis
  - Penicillin
  - Cephalosporin
- DNA Gyrase
- Quinolones
- Ribosomes
- Protein Synthesis
  - Tetracycline
  - Macrolides
  - Clindamycin
- Folic Acid
- Folate Synthesis
  - TMP-SMX
Antimicrobial Resistance

- **Mechanism of AMR Acquisition**
  - **AMR genes**
    - 1) Mutation in chromosomal genes
    - 2) Acquisition of new genes
      - Mobile genetic elements
        - Plasmids
        - Bacteriophages
        - Transposons
  - **Antibiotic bacterial selection**
    - Use, Misuse or Overuse
    - Inadequate treatment
Multi-Drug Resistant Organisms Causing Common Out-Patient Infections

Empiric Antibiotic Therapy?

Current Guidelines from IDSA & CDC
## Antimicrobial Resistance & Current Empiric Therapy Guidelines

<table>
<thead>
<tr>
<th>Multi-Drug Resistant Organisms</th>
<th>Common Out-Patient Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S. aureus (MRSA)</strong></td>
<td>-----&gt; Skin and Soft Tissue (SSTI)</td>
</tr>
<tr>
<td><strong>S. pneumonia (DRSP)</strong></td>
<td>-----&gt; Pneumonia (CAP)</td>
</tr>
<tr>
<td><strong>H. influenzae (Resistant)</strong></td>
<td>----&gt; Acute Sinusitis (ABRS)</td>
</tr>
<tr>
<td><strong>E. coli (Resistant)</strong></td>
<td>----&gt; Acute Cystitis (uUTI)</td>
</tr>
<tr>
<td><strong>GI bacteria (Resistant)</strong></td>
<td>-----&gt; Acute Infectious Diarrhea</td>
</tr>
<tr>
<td><strong>N. gonorrhea (CRGC)</strong></td>
<td>-----&gt; Cervicitis/Urethritis (STI)</td>
</tr>
</tbody>
</table>
Staphylococcus aureus

- **General**
  - Gram+ cocci in clusters
  - Normal flora
    - Skin
    - Respiratory tract

- **Out-patient infections**
  - Skin and soft tissue infections

- **In-patient infections**
  - Pneumonia
  - Bacteremia and endocarditis
# Staphylococcus aureus

## Antimicrobial Resistance

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Mechanism of Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillins Ampicillins</td>
<td>Penicillin B-lactamase (Penicillinase)</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Ribosomal methylation and Macrolide efflux</td>
</tr>
<tr>
<td>Anti-Staphyloccocal Penicillins (Methicillin) Cephalosporins</td>
<td>Gene mecA coding for altered penicillin-binding protein (PBP)</td>
</tr>
<tr>
<td>Quinolones</td>
<td>GyrA gene mutations</td>
</tr>
</tbody>
</table>
Staphylococcus aureus

- MRSA Annual Visits

Figure 2. Distribution by clinical MRSA infections based on epidemiological classification, 2006-2011.
Staphylococcus aureus

- **Community-Acquired MRSA (CA-MRSA)**
  - **Infections**
    - SSTI (75%): impetigo, folliculitis, cellulitis, erysipelas, SSS syndrome, toxic shock syndrome, furuncles, carbuncles, and deep skin abscesses
    - Others (25%): UTI, Pneumonia, Sepsis
  - **Risk Factors and Trends**
    - Contact with CA-MRSA
    - Crowding (college students, military, jail, day-care)
    - Contaminated personal objects (gym)
    - Compromised skin integrity
    - Absence of cleanliness (homelessness)
    - Animal exposure (cats, livestock)
    - MSM
    - Drug use
    - Immunosuppression
Skin and Soft-Tissue Infections

- **Common Etiology**
  - **B-hemolytic Streptococcus (BHS)**
    - Non-purulent
    - Erysipelas, cellulitis
    - No anti-microbial resistance problem
  
  - **Staphylococcus aureus**
    - Folliculitis, furuncles, abscesses
    - Purulent cellulitis

- **Empiric Antibiotic Therapy**
  - **BHS** coverage? **OR**
  - **S. aureus** coverage (MRSA)? **OR**
  - Both?
<table>
<thead>
<tr>
<th>Predisposing Factor</th>
<th>Organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seawater exposure</td>
<td><em>Vibrio</em>, atypical mycobacteria</td>
</tr>
<tr>
<td></td>
<td>Atypical mycobacteria</td>
</tr>
<tr>
<td></td>
<td><em>P. aeruginosa</em></td>
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<tr>
<td>Freshwater exposure</td>
<td><em>Aeromonas hydrophila</em></td>
</tr>
<tr>
<td></td>
<td><em>Pasteurella multocida</em></td>
</tr>
<tr>
<td></td>
<td><em>Capnocytophaga canimorsus</em></td>
</tr>
<tr>
<td></td>
<td><em>Spirillum minus, Streptobacillus moniliformis</em></td>
</tr>
<tr>
<td>Animal bites</td>
<td><em>Eikenella corrodens</em></td>
</tr>
<tr>
<td>Human bites</td>
<td>Sporotrichosis</td>
</tr>
<tr>
<td>Gardening</td>
<td></td>
</tr>
<tr>
<td>Farm animal exposure</td>
<td><em>Burkholderia mallei, Bacillus anthracis,</em></td>
</tr>
<tr>
<td>Raw meat</td>
<td><em>Erysipelothrix</em></td>
</tr>
<tr>
<td>Burns</td>
<td><em>P. aeruginosa</em></td>
</tr>
<tr>
<td>Immunosuppressed patients (Neutropenia, DM)</td>
<td>Mixed, Gram-</td>
</tr>
</tbody>
</table>
Skin and Soft-Tissue Infections

**Management**
- **Minor skin infections**
  - Mupirocin 2% topical ointment (AIII)
- **Small furuncles**
  - Moist heat may be sufficient
Skin and Soft-Tissue Infections

Management

- **Cutaneous Abscess**
  - Incision and drainage is the primary treatment (AII).
    - I&D is likely adequate (85-90%)
    - Empiric antibiotic providing additional benefit controversial
      - prevent new lesions
      - improved cure rate
Skin and Soft-Tissue Infections

**Management (cont.)**

- **Cutaneous Abscess**
  - Incision and drainage
  - Empiric antibiotic therapy is recommended in the following conditions (AIII):
    - Severe, extensive, rapidly progressive
    - Associated cellulitis and phlebitis
    - Systemic illness
    - Associated co-morbidity or immunosuppression (e.g. DM, HIV, CA)
    - Extremes of age
    - Difficult to drain (face, hand, genitalia)
    - Failure to drain after I&D

- Empiric MRSA coverage
  - **TMP-SMX**
    - OR
  - **Doxycycline**
    - OR
  - **Clindamycin**
    - OR
  - **Linezolid**
• **Management (cont.)**

  o **Purulent cellulitis**
  With purulent drainage and exudate in the absence of drainable abscess (AII)
    - **Etiology**
      - MRSA 59%
      - MSSA 17%
      - BHS 2.6%
    - **Recommendation**
      - Empiric MRSA coverage
      - Empiric BHS coverage likely unnecessary
    - **Empiric MRSA coverage**
      - TMP-SMX
        - OR
      - Doxycycline
        - OR
      - Clindamycin
        - OR
      - Linezolid

  o **Non-purulent cellulitis**
  No purulent drainage or exudate or abscess (AII)
    - **Etiology**
      - BHS 73%
      - MSSA ?
      - MRSA ?
    - **Recommendation**
      - Empiric BHS (with MSSA) coverage (96%)
      - Empiric MRSA coverage role unknown
      - Empiric MRSA coverage if with risk factor, no response or with systemic toxicity
    - **Empiric BHS (with MSSA) coverage**
      - B-lactam (e.g. Cefalexin, Dicloxacillin)
    - **Empiric BHS and MRSA coverage**
      - B-lactam PLUS TMP-SMX or Doxycycline
        - OR
      - Clindamycin
        - OR
      - Linezolid
Skin and Soft-Tissue Infections

**Management (cont.)**

- **Not optimal for Empiric MRSA coverage**
  - (Resistance is common or may develop rapidly)
  - Fluoroquinolones (ciprofloxacin, levofloxacin)
  - Macrolides (erythromycin, clarithromycin, azithromycin)
  - Rifampin alone

- **Not optimal for Empiric BHS coverage**
  - (Inadequate BHS coverage)
  - TMP-SMX alone
  - Doxycycline alone
Skin and Soft-Tissue Infections

- **Diagnostic**
  - **Culture is recommended (AIII):**
    - Treated with antibiotic therapy
    - Severe local infection or signs of systemic illness
    - Not responded adequately to initial treatment
    - Concern for a cluster or outbreak

- **Duration of Antibiotic Therapy**
  - **In FDA trial studies, patients were typically treated for 7-14.**
  - **In randomized/controlled trials, uncomplicated cellulitis**
    - 5 vs. 10 days: no difference in outcome.
  - **Recommendation:**
    - Individualized on the basis of the patient’s clinical response.
    - 5-10 days
## Skin and Soft-Tissue Infections

### Empiric Oral Antibiotic Therapy

<table>
<thead>
<tr>
<th>Abscess/Purulent</th>
<th>MRSA</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TMP-SMX</td>
<td>1-2 DS BID</td>
</tr>
<tr>
<td></td>
<td>Doxycycline</td>
<td>100mg BID</td>
</tr>
<tr>
<td></td>
<td>Clindamycin</td>
<td>300-450mg TID</td>
</tr>
<tr>
<td></td>
<td>Linezolid</td>
<td>600mg BID</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abscess/Purulent</th>
<th>Non-Purulent B-hemolytic <em>Streptococcus</em></th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cephalexin</td>
<td>500mg TID-QID</td>
</tr>
<tr>
<td></td>
<td>Dicloxacillin</td>
<td>500mg QID</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Both MRSA &amp; BHS</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin (or B-lactam above)</td>
<td>500mg TID</td>
</tr>
<tr>
<td>+ TMP-SMX or</td>
<td>1-2 DS BID</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100mg BID</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300-450mg TID</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600mg BID</td>
</tr>
</tbody>
</table>
Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus Aureus* Infections in Adults and Children

Catherine Liu,1 Arnold Bayer,3,5 Sara E. Cosgrove,6 Robert S. Daum,7 Scott K. Fridkin,8 Rachel J. Gorwitz,9 Sheldon L. Kaplan,10 Adolf W. Karchmer,11 Donald P. Levine,12 Barbara E. Murray,14 Michael J. Rybak,12,13 David A. Talan,4,5 and Henry F. Chambers1,2
Streptococcus pneumoniae

- General
  - “Pneumococcal”
  - Gram+, a-hemolytic
  - Encapsulated (polysaccharide)
  - Normal upper respiratory tract flora
  - >90 serotypes

- Out-patient Infections
  - Acute sinusitis, Otitis media
  - Community-acquired Pneumonia (CAP)

- In-patient Infections
  - Meningitis
  - Bacteremia/Sepsis/Endocarditis
  - Septic arthritis
# Streptococcus pneumoniae

<table>
<thead>
<tr>
<th></th>
<th>RBC Hemolysis</th>
<th>Groups</th>
<th>Organisms</th>
<th>Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alpha-hemolytic</strong></td>
<td>Incomplete Greenish</td>
<td>-</td>
<td><em>S. pneumonia</em> <em>S. viridans</em></td>
<td>Pneumonia/URI Endocarditis</td>
</tr>
<tr>
<td><strong>Beta-hemolytic</strong></td>
<td>Complete Clear areas</td>
<td>Group A Group B-H</td>
<td><em>S. pyogenes</em> (GABHS) Others</td>
<td>SSTI Pharyngitis</td>
</tr>
<tr>
<td><strong>Gamma-hemolytic</strong></td>
<td>None</td>
<td>-</td>
<td>Enterococcus</td>
<td>Hospital/ Nosocomial</td>
</tr>
</tbody>
</table>
Streptococcus pneumoniae

- Resistance

Antibiotic resistance in S. pneumo

Year

% resistant

PCN-R
Erythro-R
CTX-R

CDC ABC Surveillance
Streptococcus pneumoniae

**Resistance Pattern**
- Cephalosporin 1\(^{st}\) 53%
- Cephalosporin 2\(^{nd}\) 31%
- Cephalosporin 3\(^{rd}\) oral 42%
- TMP-SMX 49%
- Azithromycin* 29-34%
- Amoxicillin 26%
- Doxycycline 15%
- Amoxicillin HD 11%
- Amoxicillin-clavulanate 11%
- Cephalosporin 3\(^{rd}\) iv 5%
- Quinolones 1%
**Streptococcus pneumoniae**

- **Drug-Resistant S. Pneumonia (DRSP)**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Mechanism of Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracyclines</td>
<td>tetM, tet) genes</td>
</tr>
<tr>
<td>Macrolides</td>
<td>metE, ermAM genes, efflux</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>Dihydrofolate reductase gene</td>
</tr>
<tr>
<td>Penicillin</td>
<td>PBP gene</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>PBP gene</td>
</tr>
<tr>
<td>Fluoroquinolone</td>
<td>parC, gyrA genes</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>vncS</td>
</tr>
</tbody>
</table>
Streptococcus pneumoniae

- Drug-Resistant S. Pneumoniae (DRSP)
  - Penicillin MIC
    - <0.06 Sensitive
    - 0.1-1.0 Intermediate
    - >2 Resistant
    - >4 Highly resistant
  - Cefotaxime MIC
    - <0.5 Sensitive
    - 1-2 Intermediate
    - >2 Resistant
    - >8 Highly resistant
Streptococcus pneumoniae

- Drug-Resistant S. Pneumoniae (DRSP)
- Risk factors
  - Presence of comorbidities
    - Chronic heart, lung, liver, or renal disease
  - DM
  - Alcoholism
  - Malignancies
  - Asplenia or hyposplenism
  - Immunosuppressing conditions or drugs
  - Exposure to child day care
  - Use of antimicrobials within the previous 3 months
Community-Acquired Pneumonia (CAP)

- **Common Etiology**
  - *Streptococcus pneumoniae*
  - *Mycoplasma pneumoniae*
  - *Haemophilus influenzae*
  - *Chlamydophila pneumoniae*
  - Respiratory viruses

- **Empiric Antibiotic Therapy**
  - *S. pneumoniae PLUS* Atypical pneumonia coverage
  - *S. pneumoniae* resistance (DRSP)?
Community-Acquired Pneumonia (CAP)

- **Atypical pneumonia**
  - "Atypical" bacterial organisms
    - *Mycoplasma pneumoniae*
    - *Chlamydophila pneumonia*
  - No antimicrobial resistance problem
  - Anti-microbial coverage
    - Excellent
      - Macrolides (azithromycin, clarithromycin, erythromycin)
      - Tetracyclines (doxycycline)
      - Quinolones
    - None
      - B-lactams (Penicillin, Ampicillin, Cephalosporin)
<table>
<thead>
<tr>
<th>Factors</th>
<th>Organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholism</td>
<td><em>Streptococcus pneumoniae</em>, oral anaerobes, <em>Klebsiella pneumoniae</em>, <em>Acinetobacter</em> species, MTB</td>
</tr>
<tr>
<td>COPD and/or smoking</td>
<td><em>Haemophilus influenzae</em>, <em>Pseudomonas aeruginosa</em>, <em>Legionella species</em>, <em>S. pneumoniae</em>, <em>Moraxella cararrhalis</em>, <em>Chlamydomphila pneumoniae</em></td>
</tr>
<tr>
<td>Aspiration</td>
<td>Gram-enteric pathogens, oral anaerobes</td>
</tr>
<tr>
<td>Influenza active</td>
<td><em>Influenza</em>, <em>S. pneumoniae</em>, <em>Staphylococcus aureus</em>, <em>H. influenzae</em></td>
</tr>
<tr>
<td>Cough with whoop or posttussive vomiting</td>
<td><em>Bordetella pertussis</em></td>
</tr>
<tr>
<td>Injection drug use</td>
<td><em>S. aureus</em>, anaerobes, <em>M. tuberculosis</em>, <em>S. pneumonia</em></td>
</tr>
<tr>
<td>Bat/Birds/Rabbits/Farm animals</td>
<td><em>H. capsulatum/Chlamydia psittaci/Francisella tularensis/Coxiella burnetti</em></td>
</tr>
<tr>
<td>HIV</td>
<td><em>Pneumocystis jirovecii</em>, <em>Cryptococcus</em>, <em>Histoplasma</em>, <em>Aspergillus</em>, atypical mycobacteria (<em>M. kansasii</em>), <em>P. aeruginosa</em>, <em>H. Influenza</em></td>
</tr>
<tr>
<td>Hotel or cruise ship</td>
<td><em>Legionella</em> species</td>
</tr>
<tr>
<td>Travel to Southwest USA</td>
<td><em>Coccidioides</em>, Hanta virus</td>
</tr>
</tbody>
</table>
Community-Acquired Pneumonia (CAP)

- **Initial Evaluation**
  - Clinical history and Physical examination
  - Site of Care
    - Pneumonia severity index (PSI)
    - British Thoracic Society (BTS)
    - CURB-65
Community-Acquired Pneumonia (CAP)

- **Diagnostic Evaluation**
  - **Routine diagnostic tests optional for outpatients (BII)**
    - Pretreatment blood samples for culture
    - Expectorated sputum sample for stain and culture
    - Urinary antigen tests for *Legionella* and *Streptococcus*
  - **Chest radiograph or other imaging technique is required for the diagnosis of pneumonia. (BIII)**
    - PE is less sensitive (70-90%) and specific (40-70%) than chest radiographs.
    - Differentiate CAP from other common causes of cough and fever, such as acute bronchitis.
    - Chest radiographs useful for suggesting the etiologic agent, prognosis, alternative diagnoses, and associated conditions.
Community-Acquired Pneumonia (CAP)

**Management**

- Previously healthy and no risk factors for drug-resistant *S. pneumoniae* (DRSP) infection:
  - A. Azithromycin, clarithromycin, or erythromycin* (AI)
  - OR
  - B. Doxycycline (CIII)

- *In regions with a high rate (>25%) of high-level (MIC, 16 mg/mL) macrolide-resistant *S. pneumoniae*:
  - Use non-macrolide alternative agents (BIII)
Community-Acquired Pneumonia (CAP)

- **Drug-Resistant *S. Pneumonia* (DRSP)**
  - **Risks for DRSP infection:**
    - Presence of comorbidities
      - Chronic heart, lung, liver, or renal disease
    - DM
    - Alcoholism
    - Malignancies
    - Asplenia or hyposplenism
    - Immunosuppressing conditions or drugs
    - Exposure to child day care
    - Use of antimicrobials within the previous 3 months
Management (cont)

- Risks for DRSP infection:
  - A. Respiratory fluoroquinolone (AI)
    - Moxifloxacin, gemifloxacin, or levofoxacin
    OR
  - B. B-lactam plus a Macrolide (AI)
    - High-dose Amoxicillin or Amoxicillin-clavulanate
      Plus
    - Macrolide
      - Azithromycin, clarithromycin, or erythromycin
## Empiric Antibiotic Coverage

<table>
<thead>
<tr>
<th>Drug</th>
<th><em>S. pneumoniae</em></th>
<th>Drug-resistant S. pneumoniae</th>
<th>Atypical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>√?</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>√?</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>√?</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Amoxicillin HD</td>
<td>√</td>
<td>√</td>
<td>*</td>
</tr>
<tr>
<td>Amoxicillin+Clav HD</td>
<td>√</td>
<td>√</td>
<td>*</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>√</td>
<td>√??</td>
<td>*</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>√</td>
<td>√??</td>
<td>*</td>
</tr>
</tbody>
</table>

*Add Macrolide or Doxycycline*
# Community-Acquired Pneumonia (CAP)

## Empiric Antibiotic Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>Z-pack dosing</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>1,000mg ER QD</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100mg BID</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>750mg OD</td>
</tr>
<tr>
<td><strong>Amoxicillin HD</strong></td>
<td>1gm TID</td>
</tr>
<tr>
<td><strong>Amoxicillin+Clav HD</strong></td>
<td>2gm BID</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>400mg BID</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>500mg BID</td>
</tr>
</tbody>
</table>

*Add Macrolide or Doxycycline*
Duration of Antibiotic Therapy

- **Most are treated for 7-10 days**
- **Shorter periods are as effective**
  - Minimum of 5 days
  - Afebrile (and clinically stable) for 72 hrs
Community-Acquired Pneumonia (CAP)

- **Failure to improve**
  - 24-40% with prior antibiotic therapy ends up in a hospital
  - Normal delayed response
  - Resistant microorganism
    - Uncovered pathogen
    - Inappropriate by sensitivity
  - Parapneumonic effusion/empyema
  - Noninfectious
    - Misdiagnosis: PE, CHF, vasculitis
    - Drug fever
Community-Acquired Pneumonia (CAP)

- **Pneumonia Prevention**
  - **Influenza vaccine**
  - **Pneumococcal vaccine**
    - Polysaccharide vaccine (PPSV23)
    - Conjugated vaccine (PCV13) 2010
Community-Acquired Pneumonia (CAP)

Update in Progress.
- Projected publication, Spring 2014

Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults

Lionel A. Mandell,1,2* Richard G. Wunderink,2,2* Antonio Anzueto,3,4 John G. Bartlett,5 G. Douglas Campbell,6 Nathan C. Dean,5,6 Scott F. Dowell,11 Thomas M. File, Jr.12,13 Daniel M. Musher,5,8 Michael S. Niederman,14,15 Antonio Torres,16 and Cynthia G. Whitney11
Haemophilus Influenzae

- General
  - Gram- coccobacilli
  - Encapsulated (polysaccharide)
  - Normal respiratory flora
  - Opportunistic pathogen
  - 6 types (A-F) + nontypable strains

- Out-patient infections
  - Acute sinusitis/Acute otitis media
  - Pneumonia (COPD)

- In-patient infections
  - Epiglottitis
  - Meningitis
  - Bacteremia
**Haemophilus influenzae**

- **Resistance Pattern**
  - Amoxicillin 48%
  - TMP-SMX 27%
  - Cephalosporin 1\(^{\text{st}}\) 17%
  - Azithromycin 13%

- **Sensitive**
  - Amoxicillin-Clavulanate
  - Doxycycline
  - Cephalosporin 2\(^{\text{nd}}, 3\(^{\text{rd}}\)
  - Respiratory quinolones
Acute Bacterial Rhinosinusitis
Acute Rhinosinusitis

- **Definition**
  - Inflammation of the nasal and paranasal sinus mucosal lining
  - <4 weeks

- **Etiology**
  - **Viral** 90-98%
    - Acute Viral Rhinosinusitis (AVRS)
    - Average 2-3x/year
  - **Bacterial** 2-10%
    - Acute Bacterial Rhinosinusitis (ABRS)
  - **Antibiotic prescription** 81%
Acute Rhinosinusitis

Viral (AVRS) vs. Bacterial (ABRS)

- **Gold standard**
  - Sinus aspiration (from the cavity of a paranasal sinus)
  - Bacteria in high density (>10,000 colony-forming units per ml) = ABRS

- **Radiography (X-ray or CT)**
  - Non-specific
  - Do not distinguish bacterial from viral

- **Conventional Clinical Criteria**
  - >2 Major or 1 Major + 2 Minor
  - Non-specific

<table>
<thead>
<tr>
<th>Major Symptoms</th>
<th>Minor Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purulent anterior nasal discharge</td>
<td>Headache</td>
</tr>
<tr>
<td>Purulent or discolored posterior nasal discharge</td>
<td>Ear pain, pressure, or fullness</td>
</tr>
<tr>
<td>Nasal congestion or obstruction</td>
<td>Halitosis</td>
</tr>
<tr>
<td>Facial congestion or fullness</td>
<td>Dental pain</td>
</tr>
<tr>
<td>Facial pain or pressure</td>
<td>Cough</td>
</tr>
<tr>
<td>Hyposmia or anosmia</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Fever (for acute sinusitis only)</td>
<td></td>
</tr>
</tbody>
</table>
Acute Rhinosinusitis

- Acute Viral Rhinosinusitis
Acute Rhinosinusitis

3 Clinical Presentations Best Identify ABRS (AII):

- (1) Onset with persistent symptoms:
  - >10d AND not improving

- (2) Onset with severe symptoms for 3-4 consecutive days:
  - High fever >102F AND Purulent nasal discharge or facial pain

- (3) Onset with worsening symptoms:
  - Typical viral URI symptoms that appear to improve, for 5–6 days THEN
  - Sudden onset of worsening symptoms (new onset of fever, headache, or increase in nasal discharge)
  - “Double-sickening”

None

- R/O AVRS
  - Supportive measures (analgesics, decongestants, anti-histamines, saline)
  - “Watchful waiting” and follow-up

Any of the 3

- R/O ABRS
  - Initiate empiric antimicrobial therapy (AII)
Acute Bacterial Rhinosinusitis

**ABRS Etiology**
- *Streptococcus pneumonia* 38%
- *H. influenzae* 36%
- *Moraxella catarrhalis* 16%
- *Staphylococcus aureus* 13%

**Empiric Antibiotic Therapy**
- *S. pneumoniae* PLUS *H. influenzae* coverage
- *S. pneumoniae* resistance (DRSP)?
Acute Complicated Rhinosinusitis

- **Referral Indications**
  - **Severe infection**
    - High persistent fever with temperature >102°F
    - Orbital edema, severe headache, visual disturbance, altered mental status, meningeal signs
  - **Resistant or Unusual pathogens**
    - Recalcitrant infection with failure to respond to extended course of antibiotic therapy
    - Chronic rhinosinusitis with recurrent ABRS exacerbations
    - Immunocompromised host
    - Multiple medical problems (e.g. hepatic or renal impairment)
    - Fungal sinusitis
    - Nosocomial infection
    - Granulomatous disease
  - **Hypersensitivity to antimicrobial agents**
  - **Anatomic defects causing obstruction (require surgery)**
  - **Immunotherapy for allergic rhinitis**
**Acute Bacterial Rhinosinusitis**

*IDSA*  
Infectious Diseases Society of America

- **Antimicrobial Sensitivity Patterns**

<table>
<thead>
<tr>
<th>Drug</th>
<th><em>H. influenzae</em></th>
<th><em>S. pneumonia</em></th>
<th><em>M. Catarrhalis</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>58 X</td>
<td>74 X</td>
<td>11 X</td>
</tr>
<tr>
<td>Amox-Clav</td>
<td>100</td>
<td>89</td>
<td>100</td>
</tr>
<tr>
<td>Cefaclor</td>
<td>83 X</td>
<td>47 X</td>
<td>95</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>88-99 X</td>
<td>69 X</td>
<td>98</td>
</tr>
<tr>
<td>Cefixime</td>
<td>100 X</td>
<td>58 X</td>
<td>100</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>87 X</td>
<td>63 X</td>
<td>98</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>100</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>73 X</td>
<td>51 X</td>
<td>99</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>69-85 X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>98</td>
<td>85</td>
<td>99</td>
</tr>
</tbody>
</table>
**Acute Rhinosinusitis**

**Management**
- **No Antimicrobial Resistance Risk**
- **Recommended**
  - Amoxicillin-Clavulanate (AII)
- **Alternative**
  - Doxycycline (BIII)
- **B-lactam allergy**
  - Doxycycline (AII)
  - Respiratory quinolones (AII)
    - Levofloxacin or moxifloxacin
Management (cont)

- **Antimicrobial Resistance Risk**
  - High endemic rate (>10%) of invasive Drug Resistant *S. pneumoniae* (DRNS)
  - Severe infection
    - Fever of >102F
    - Threat of suppurative complications
  - Age>65 years
  - Recent hospitalization
  - Recent antibiotic use within the past month
  - Immunocompromised
Acute Rhinosinusitis

Management (cont)

- **Antimicrobial Resistance Risk**
- **Recommended**
  - High-dose Amoxicillin-Clavulanate (BII)
  - OR
  - **Respiratory fluoroquinolones**
    - Levofloxacin or moxifloxacin
Acute Rhinosinusitis

Management (cont)

- **Not recommended for monotherapy**
  - Ampicillin/Amoxicillin (AII)
    - Very high *S. pneumonia* and *H. influenzae* resistance
  - Macrolides (AII)
    - *S. pneumoniae* resistance >30%
  - TMP-SMX (AII)
    - *S. pneumonia* and *H. influenzae* resistance >30-40%
  - Cephalosporins (BII)
    - Variable *S. pneumoniae* resistance
  - **Routine coverage for MRSA not recommended** (AII)
**Acute Rhinosinusitis**

**Antibiotic Coverage**

<table>
<thead>
<tr>
<th>Drug</th>
<th><em>S. pneumoniae</em></th>
<th>Resistant <em>S. pneumoniae</em></th>
<th><em>H. influenza</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amox-clav</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>√?</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Amox-clav (HD)</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>
</tbody>
</table>
### Acute Rhinosinusitis

![IDSA logo](https://id-sa.org)

**Empiric Antibiotic Therapy**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amox-clav</td>
<td>500/125mg TID or 875/125 mg BID</td>
</tr>
<tr>
<td>Amox-clav (HD)</td>
<td>2000mg/125 mg BID</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100mg BID or 200mg QD</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>500mg QD</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>400mg QD</td>
</tr>
</tbody>
</table>
Acute Rhinosinusitis

- **Duration of Therapy**
  - 5-7 days (BII)

- **Adjunct therapy**
  - **Recommendation**
    - Hydration
    - Analgesics
    - Intranasal saline irrigation (BIII)
    - Intranasal corticosteroids (Optional; BII)
      - Routine for patients with history of allergic rhinitis
  - **Not recommended**
    - Topical or oral decongestants (AIII)
    - Antihistamines (AIII) (except history of allergic rhinitis)
Acute Rhinosinusitis

Follow-up management

- **Non-responder**
  - Worse after 3 days
  - No improvement after 3-5 days

- **Recommendation**
  - Broaden coverage or switch
    - High-dose Amoxicillin-Clavulanate
    - Respiratory fluoroquinolones
  - Refer to specialist if no response after 3-5 days
    - CT or MRI
    - Sinus cultures
Acute Rhinosinusitis

IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

Anthony W. Chow,1 Michael S. Benninger,2 Itzhak Brook,3 Jan L. Brozek,4,5 Ellie J. C. Goldstein,6,7 Lauri A. Hicks,8 George A. Pankey,9 Mitchel Selsznick,10 Gregory Volturo,11 Ellen R. Wald,12 and Thomas M. File Jr13,14

Clinical Infectious Diseases Advance Access published March 20, 2012

Published on 03/2012 and current
**Escherichia coli**

- **General**
  - Gram-rod
  - Normal GI flora
  - Enterobacteriaceae family
  - Many serotypes and strains
    - Uro-pathogenic
    - Entero-toxigenic, -pathogenic, -invasive, -hemorrhagic

- **Out-patient Infections**
  - UTI/Cystitis/Pyelonephritis
  - Food-borne illness
Escherichia coli

- Drug-Resistant Uropathogenic *E. coli*
  - Uncomplicated Cystitis
Escherichia coli

- Drug-Resistant Uropathogenic *E. coli*
  - North American UTI Collaborative Alliance 2003-2004
  - Resistance Patterns:
    - Ampicillin 37.7%
    - TMP-SMX 21.3%
    - Ciprofloxacin 5.5%
    - Levofloxacin 5.1%
    - Nitrofurantoin 1.1%
Uncomplicated Acute Cystitis

**Definition**

- **Acute Uncomplicated UTI**
  - Premenopausal, non-pregnant women
  - No known urological abnormalities or comorbidities

- **Exclusion**
  - Male
  - Known urological abnormalities
  - Pregnant women
  - Immunosuppression
  - Recurrent UTI
  - Recent antibiotic use
  - Postmenopausal
  - DM
Uncomplicated Acute Cystitis

- **Common Etiology**
  - *E. coli* (75-95%)
  - *Proteus mirabilis*
  - *Klebsiella pneumonia*
  - *Staphylococcus saprophyticus*

- **Empiric Antibiotic Therapy**
  - *E. coli* coverage
  - *E. coli* resistance?
Uncomplicated Acute Cystitis

Management

- **Recommended**
  - Nitrofurantoin 100mg BID for 5 days (AI)
  - OR
  - TMP-SMX DS BID for 3 days (AI)
    - Note: Not recommended if local resistance prevalence >20% (BIII)
  - OR
  - Fosfomycin 3gms SD (AI)
    - Inferior efficacy
Uncomplicated Acute Cystitis

Management (cont)

- **Alternative**
  - Fluoroquinolones (AI)
    - Ciprofloxacin, levofloxacin
    - Reserved for other use
      - Complicated UTI
      - Acute pyelonephritis
  - **Alternative**
    - B-lactam (BI)
      - Only when recommended drugs cannot be used.
        - Generally inferior efficacy
        - Amoxicillin-clavulanate, cefdinir, cefaclor, cephalaxin, cefpodoxime
  - **Not recommended**
    - Amoxicillin or ampicillin
      - Relatively poor efficacy
      - High prevalence of resistance
# Uncomplicated Acute Cystitis

- **Empiric Antibiotic Therapy**

<table>
<thead>
<tr>
<th>Drug: First-line</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin</td>
<td>100mg BID for 5 days</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>DS BID for 3 days</td>
</tr>
<tr>
<td>Fosfomycin</td>
<td>3gm SD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug: Alternative</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>250mg BID or 500mg ER QD, 3 days</td>
</tr>
<tr>
<td>Levofloxacine</td>
<td>250mg QD, 3 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug: Less-effective</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-lactam</td>
<td>3-7 days</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td></td>
</tr>
<tr>
<td>Cefdinir, Cefaclor, Cefpodoxime</td>
<td></td>
</tr>
</tbody>
</table>
Acute Pyelonephritis

**Management**

- **Recommended**
  - Urine CS (AIII)
  - **Fluoroquinolones**
    - Ciprofloxacin (AI), levofloxacin (BII)

- **Note: Local resistance prevalence is >10%**
  - Fluoroquinolones *PLUS* Ceftriaxone iv 1gm initial dose (BIII)
Acute Pyelonephritis

**Management**

- **Alternative**
  - TMP-SMX
    - Uropathogen is known to be susceptible (AI)
  - TMP-SMX PLUS Ceftriaxone iv 1gm initial dose
    - Susceptibility is not known (BII)

- **Alternative but Less Effective**
  - B-lactam (BIII) PLUS Ceftriaxone 1gm iv initial dose (BII)

- **Do NOT use**
  - Nitrofurantoin
  - Fosfomycin
## Empiric Antibiotic Therapy

<table>
<thead>
<tr>
<th>Drug: First-line</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>500mg BID for 7 days</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>1000mg ER QD for 7 days</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>750 mg for 5 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug: Alternative</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP-SMX DS</td>
<td>DS BID for 14 days</td>
</tr>
<tr>
<td>+/- Ceftriaxone iv</td>
<td>1gm iv initial dose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug: Less-effective</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-lactam</td>
<td>10-14 days</td>
</tr>
<tr>
<td>+ Ceftriaxone iv</td>
<td>1gm iv initial dose</td>
</tr>
</tbody>
</table>
Uncomplicated Acute Cystitis

Published on 02/2012 and current

Diagnosis, Prevention, and Treatment of Catheter-Associated Urinary Tract Infection in Adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America

Thomas M. Hooton,1 Suzanne F. Bradley,2 Diana D. Cardenas,2 Richard Colgan,4 Suzanne E. Geerlings,7 James C. Rice,6a Sanjay Saint,5 Anthony J. Schaeffer,5 Paul A. Tambayh,9 Peter Tenke,9 and Lindsay E. Nicolle10,11
GI Bacteria

- **Bacterial Enteropathogens**
  - Non-typhoidal *Salmonella* 1.4 million
  - *Campylobacter jejuni* 1.4-2.4 million
  - *Shigella* 450,000
  - *C. difficile* 250,000
  - *E. coli*, Shiga-toxin 100,000
  - *E. coli*, Enterotoxigenic 79,000

- **Antibiotic Resistance**
  - Misuse and overuse of antibiotics by humans
  - Use of antibiotics in animal livestock for food consumption
    - Poultry, pigs, cattles
GI Bacteria

- **Antibiotic Resistance**
  - **MDR-Shigella**
    - Ampicillin and TMP-SMX resistance
  - **MDR-Campylobacter**
    - Ampicillin and TMP-SMX resistance
    - Increasing fluoroquinolone and macrolide resistance
  - **MDR-Non-typhoidal *Salmonella***
    - Ampicillin and TMP-SMX resistance
  - **MDR- *E. coli, Enterotoxigenic***
    - Ampicillin and TMP-SMX resistance
  - **C. difficile**
    - Metronidazole or vancomycin resistance still uncommon
Acute Infectious Diarrhea

Management
- Fluid and electrolyte replacement
- Anti-motility drugs
  - Avoid if without concomitant antibacterial therapy
- Antibiotic therapy

Antibiotic Therapy
- Need for antibiotic therapy?
- Bacterial resistance?
- Negative effects of antibiotics?
Acute Infectious Diarrhea

Antibiotic use:

- **General**
  - Most *mild* cases resolve quickly without antibiotics.
  - *Severe*, prolonged, recurrent infections; immunosuppressed patients, extreme of age may need antibiotics.
  - *Immunosuppressed* patients require longer duration of treatment.

- **Specific**
  - EHEC/Shiga toxin-producing *E. coli* 0157:H7
    - Antibiotic use may increase production of Shiga toxin
    - Hemolytic-Uremic Syndrome
  - Non-typhoidal *Salmonella*
    - Antibiotic use has minimal effect and may prolong carriage
    - Screen for risk for bacteremia (8%)
Acute Infectious Diarrhea

- Risk for Non-Typhoidal *Salmonella* Bacteremia
  - Infants
  - >65 (?50) years of age
  - High fever, very severe diarrhea
  - Inflammatory bowel disease
  - Hemoglobinopathies
  - Hemodialysis
  - Immunosuppression
  - Corticoid use
  - Abdominal aneurysm
  - Prosthetic heart valve
# Acute Infectious Diarrhea

## Antibiotic Therapy

<table>
<thead>
<tr>
<th>GI Bacteria</th>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-typhoidal <em>Salmonella</em></td>
<td>Ciprofloxacin 500mg BID, 3-7 days</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Azithromycin 500mg QD, 7 days</td>
</tr>
<tr>
<td><em>Campylobacter jejuni</em></td>
<td>Ciprofloxacin 500mg QD, 3-5 days</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Azithromycin 500mg QD, 3-5 days</td>
</tr>
<tr>
<td><em>Shigella</em></td>
<td>Ciprofloxacin 750mg QD, 3 days</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Azithromycin 500mg QD, 3 days</td>
</tr>
<tr>
<td><em>Enterotoxigenic E. coli</em></td>
<td>Ciprofloxacin 750mg QD, 1-3 days</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Azithromycin 1gm SD</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifaximin 200mg TID, 3 days</td>
</tr>
<tr>
<td><em>Shiga Toxin-producing E. coli (0157:H7)</em></td>
<td>NONE</td>
</tr>
<tr>
<td><em>C. difficile</em></td>
<td>Metronidazole 500mg TID, 10-14 days</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vancomycin 125mg QID, 10-14 days</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fidaxomicin 200mg BID, 10 days</td>
</tr>
</tbody>
</table>
Acute Infectious Diarrhea

- Published on 10/2009

IDSA 2001; Update in progress, Projected Publication, Spring 2014
American Gastroenterological Association 1997; Awaiting update
Neisseria gonorrhoea

- General
  - Gram- intracellular diplocci

- Out-patient infections
  - Cervicitis/Urethritis
  - PID
  - Conjunctivitis
  - Pharyngitis
  - Rectal

- In-patient infections
  - Dissemination
  - Arthritis
Neisseria gonorrhea

- Antimicrobial Resistance
  - **Penicillin and Ampicillin**
    - 1960’s
  - **Tetracycline**
    - 1970’s
  - **Quinolones (QRNG)**
    - 2002
      - Hawaii and California
    - 2004
      - MSM
    - 2007
      - General population
  - **Macrolides**
    - Rapid development of resistance in monotherapy
  - **Cephalosporin 3rd**
    - PenA gene for remodeled penicillin binding protein (PBP)
Neisseria gonorrhoea

- Cephalosporin (Ceph-RNG)
  - Increasing MICs for PO Cefixime and IM Ceftriaxone

- Ceftriaxone-resistant isolates have been identified in Japan (2009), France (2010), and Spain (2011)

* Elevated cefixime MICs defined as ≥0.25 μg/mL; elevated ceftriaxone MICs defined as ≥0.125 μg/mL.
N. Gonorrhea Infections

- **Outpatient infections**
  - Cervicitis
  - Urethritis
  - Rectal
  - Pharyngitis

- **Antibiotic Therapy**
  - *N. gonorrhea* resistance?
N. Gonorrhea Infections

- **Management**
  - Uncomplicated GC of the cervix, urethra, pharynx, and rectum
  - **Recommended regimen**
    - Ceftriaxone 250mg SD IM
    - **PLUS**
    - Azithromycin 1g SD (preferred)
    - OR
    - Doxycycline 100mg BID, 7 days
N. Gonorrhea Infections

- **Management (cont.)**
  - **Alternative regimen**
    - Cefixime 400mg SD
    - Azithromycin 1g SD (preferred) OR
    - Doxycycline 100mg BID, 7 days
  - Test-of-cure in 1 week
  - **Cephalosporin allergy**
    - Azithromycin 2g SD
    - Test-of-cure in 1 week
**N. Gonorrhea Infections**

**Management (cont.)**

- **Test of Cure: 1 week**
  - Preferred:
    - GC Culture and Sensitivity
      - Avoid “false positivity with NAAT”
      - Sensitivity to identify drug resistance and guide treatment
  - Alternative:
    - NAAT

- **Repeat Testing for Re-infection: 3 months**
  - NAAT or CS

- **Sexual partners preceding 60 days**
  - Test and empirically treat
### N. Gonorrhea Infections

#### Antibiotic Therapy

<table>
<thead>
<tr>
<th>Drug: First-line</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone (injection)</td>
<td>250mg im SD</td>
</tr>
<tr>
<td>+ Azithromycin (preferred) or Doxycycline</td>
<td>1gm SD or 100mg BID, 7 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug: Alternative</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefixime</td>
<td>400mg SD</td>
</tr>
<tr>
<td>+ Azithromycin (preferred) or Doxycycline</td>
<td>1gm SD or 100mg BID, 7 days</td>
</tr>
<tr>
<td>Test of cure, 1 week</td>
<td>C&amp;S or NAAT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug: B-lactam allergy</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>2gm SD</td>
</tr>
<tr>
<td>Test of cure, 1 week</td>
<td>C&amp;S or NAAT</td>
</tr>
</tbody>
</table>
N. Gonorrhea Infections

Published on 08/2012

Update to CDC’s Sexually Transmitted Diseases Treatment Guidelines, 2010: Oral Cephalosporins No Longer a Recommended Treatment for Gonococcal Infections

Weekly
August 10, 2012 / 61(31);590-594
N. Gonorrhea Infections

- Suspect Cephalosporin Resistance
  - Laboratory-confirmed GC infection
  - Received Cefixime or Ceftriaxone (correct dose)
  - Did not engage in sexual activity after treatment
  - Repeat GC test positive result
    - Culture positive ≥72 hours after treatment
    - NAAT positive ≥7 days after treatment
N. Gonorrhea Infections

- Suspect Cephalosporin Resistance
  - Consult
    - Local infectious diseases expert
    - State or local health department
  - Obtain Culture & Sensitivity
    - Cephalosporin antimicrobial resistance
  - Re-treat with:
    - Ceftriaxone 250mg SD IM
    - Azithromycin 2 grams SD
  - Test of cure after re-treatment
  - Test and empirically treat sex partners preceding 60 days
    - Preferably with culture
    - Same antimicrobial regimen
N. Gonorrhea Infections

- Cephalosporin Resistance
  - Sensitivity
    - Cefixime MIC $\geq 0.5 \, \mu g/ml$
    - Ceftriaxone MIC $\geq 0.25 \, \mu g/ml$
  - Notify the state or local health department within 24 hours
  - Consult with local infectious diseases expert
N. Gonorrhea Infections

Published on 08/2012

August 2012

CEPHALOSPORIN-RESISTANT NEISSERIA GONORRHOEAE PUBLIC HEALTH RESPONSE PLAN

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of STD Prevention