Antimicrobial Preservation and Stewardship in the Ambulatory Setting

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Learning Objectives

• Describe and analyze latest antimicrobial usage data in the ambulatory setting

• Review the management of common infectious diseases encountered in the ambulatory setting
  • Upper Respiratory Tract Infection
  • Urinary Tract Infection
  • Cellulitis
Stewardship

- Financial Stewardship
- Environmental Stewardship
- Antimicrobial Stewardship

CDC Core Elements of Hospital Antibiotic Stewardship Programs. 2018.
Antimicrobial Stewardship Goal

Improve clinical outcomes by:

• Optimizing antimicrobial utilization
• Decreasing antimicrobial resistance
Antibiotic Usage in the U.S.

• In 2014, 266.1 million courses of antibiotics were dispensed to outpatients in the U.S.
  • 5 prescriptions per year for every 6 Americans

• Estimated 30% of antibiotics prescribed in the outpatient setting are likely unnecessary

• Azithromycin and amoxicillin are the most commonly prescribed antibiotics

Source: CDC 2018
Outpatient Antibiotic Prescriptions per 1,000 Population by State in 2016

Source: CDC
Outpatient Antibiotic Prescribing by Provider Specialty - 2016

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Number of Antibiotic Prescriptions (Millions)</th>
<th>Antibiotic Prescriptions per Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Care Physicians</td>
<td>106.3</td>
<td>448</td>
</tr>
<tr>
<td>PA/NP</td>
<td>68.4</td>
<td>395</td>
</tr>
<tr>
<td>Surgical Specialties</td>
<td>19.3</td>
<td>217</td>
</tr>
<tr>
<td>Dentistry</td>
<td>25.7</td>
<td>210</td>
</tr>
<tr>
<td>Emergency Medicine</td>
<td>6.9</td>
<td>608</td>
</tr>
</tbody>
</table>
## Outpatient Antibiotic Classes Prescribed - 2016

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of Antibiotic Prescriptions (Millions)</th>
<th>Antibiotic Prescriptions per 1,000 Persons, Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillins</td>
<td>63.2</td>
<td>196</td>
</tr>
<tr>
<td>Macrolides</td>
<td>47.7</td>
<td>148</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>36.9</td>
<td>114</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>29.7</td>
<td>92</td>
</tr>
</tbody>
</table>
Massachusetts Outpatient Antibiotic Prescriptions - 2015

National: 838 antibiotic prescriptions/1,000 population

Massachusetts: 759 antibiotic prescriptions/1,000 population
Upper Respiratory Tract Infection (URTI)

Review of Guideline Recommendations
Rhinosinusitis

• Symptomatic inflammation of the nasal cavity and paranasal sinuses

• Classified further:
  • Viral
  • Bacterial
    • Uncomplicated vs. Complicated

Rhinosinusitis Epidemiology

• Incidence
  • 1 in 7 adults in the U.S. will have a rhinosinusitis episode each year
  • Incidence is higher in women than men

• Risk Factors
  • Age >45 years
  • Active smoking
  • Recent swimming
  • Asthma or allergies
  • Immunocompromised

A Clinical Challenge: Antibiotics for URTI

- A major public health issue

- A national survey of antibiotic prescriptions in the outpatient setting showed antibiotics were prescribed for ~80% of adults with acute rhinosinusitis

Acute Bacterial Rhinosinusitis (ABRS) Diagnosis

Cochrane review: Antibiotics for acute maxillary sinusitis

• Review of 63 studies in uncomplicated maxillary sinusitis

• Antibiotics vs. placebo:
  • N=1915 adult patients
  • Most patients had clinical improvement/resolution within 2 weeks
    • 9/10 patients receiving antibiotics vs. 8/10 receiving placebo

• Antibiotics vs. antibiotics:
  • No one agent found to be superior to another

• Conclusion:
  • Antibiotics will help some people somewhat, but do not provide a clear benefit to most people with acute maxillary sinusitis in outpatient setting
  • May hasten clinical cure if no spontaneous recovery by days 7-15

IDSA guidelines—antibiotic recommendations for sinusitis

**Signs & symptoms either:**
1) Persistent & not improving (>=10 days);
2) Severe (>=3-4 days); or
3) Worsening or “double-sickening” (>=3-4 days)

**Risk factors for antibiotic resistance:**
- Age <2 or >65, or in daycare
- Prior antibiotics within past 30 days
- Prior hospitalization for >5 days
- Comorbidities
- Immunocompromise

For **no increased risk for resistance**:
- Initiate amoxicillin + symptom management

For **increased risk for resistance**:
- Initiate amoxicillin/clavulanate + symptom management

Bacterial Rhinosinusitis Treatment

1. **Amoxicillin/clavulanate – Low Dose**
   - Recommended above amoxicillin alone in both children and adults
   - Dose: 875mg PO BID for adults or 45mg/kg/day in 2 doses in children

2. **Amoxicillin/clavulanate – High Dose**
   - 2000mg BID for adults or 90mg/kg/day in 2 doses in children
   - Severe infection (high fever), daycare attendant, age <2 or >65 years, recent hospitalization, antibiotic use within the past month or in immunocompromised patients

Bacterial Rhinosinusitis Treatment

3. **Doxycycline**
   - 100mg PO BID in adults
   - Recommended in *adults* as second-line therapy or in penicillin-allergic patients

4. **Levofloxacin or Moxifloxacin**
   - Recommended in children or adults as second-line therapy or in penicillin-allergic patients

<table>
<thead>
<tr>
<th></th>
<th>Adults</th>
<th>Children</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Levofloxacin</strong></td>
<td>500-750mg PO QD</td>
<td>10-20mg/kg/day</td>
<td>Renal dose-adjustments required</td>
</tr>
<tr>
<td><strong>Moxifloxacin</strong></td>
<td>400mg PO QD</td>
<td>See Notes</td>
<td>Only in children with skeletal maturity – adult dosing</td>
</tr>
</tbody>
</table>

Antibiotics that are **NOT** recommended for empiric treatment

- **Trimethoprim/sulfamethoxazole (Bactrim®)**
  - Due to high rates (30-40%) of resistance in *Strep. pneumoniae* and *Haemophilus influenzae*

- **Azithromycin or Clarithromycin**
  - Due to high rates (30%) of resistance in *Streptococcus pneumoniae*

- **Cephalosporins** – second- or third-generation
  - Due to variable resistance rates in *S. pneumoniae*

Duration of Antibiotics for ABRS

- **Adults**
  - 5-7 days

- **Children**
  - 10-14 days

Pharyngitis

• More than 70% of pharyngitis is viral
  • Options include rhinovirus, coronavirus, adenovirus, influenza virus, parainfluenza virus, Epstein-Barr virus, etc.
  • Symptoms: cough, hoarseness, rhinitis
  • Treatment should involve supportive care and symptom management

• Bacterial
  • Group A *S. pyogenes* (GAS) is the most common cause of bacterial pharyngitis
  • Symptoms: sudden sore throat, **fever**, tonsillar erythema, tender lymph nodes, and patchy tonsillar exudates

Group A Streptococcal Pharyngitis

1. **Penicillin V**
   - Children: 250mg BID or TID
   - Adolescents/Adults: 250mg QID or 500mg BID

2. **Amoxicillin**
   - 50mg/kg (max = 1000mg) QD OR
   - 25mg/kg (max= 500mg) BID

3. **Alternatives**
   - Cephalexin, cefadroxil, clindamycin, azithromycin (5 days) or clarithromycin

Duration = 10 days, unless otherwise noted

Urinary Tract Infection

Review of Guideline Recommendations for Uncomplicated Bacteriuria and Asymptomatic Bacteriuria
Urinary Tract Infection (UTI)

• The most common bacterial infection requiring medical care
  • Results in ~8.6 million ambulatory care visits in 2007
    • Primarily women
    • Stratified by age
  • Over 10.8 million patients in the U.S. visited the emergency department for treatment between 2006-09
    • Over 1.8 million were admitted to acute care facilities

• UTI ranks as the #1 infection leading to an antibiotic prescription after a healthcare visit
Trends in UTI by Gender and Age

Prevalence of UTI in primary care

Adapted from Schmiemann G et al. Dtsch Arztebl Int 2010; 107(21): 361–7
# Spectrum of Infection

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Uncomplicated UTI/cystitis</strong></td>
<td>Infection of the bladder or lower urinary tract characterized by dysuria, urinary frequency, urgency, and/or suprapubic pain</td>
</tr>
<tr>
<td><strong>Complicated UTI</strong></td>
<td>Infection of the bladder or lower urinary tract in a patient with a structural or functional abnormality of the genitourinary tract</td>
</tr>
<tr>
<td><strong>Catheter-associated UTI</strong></td>
<td>Infection occurring in a person whose urinary tract is currently catheterized or was catheterized within the past 48 hours</td>
</tr>
<tr>
<td><strong>Pyelonephritis</strong></td>
<td>Infection of the kidney or upper urinary tract characterized by flank pain &amp; tenderness, often with fever</td>
</tr>
<tr>
<td><strong>Asymptomatic bacteriuria</strong></td>
<td>Presence of quantitative bacteria in the urine without signs and symptoms of urinary infection</td>
</tr>
</tbody>
</table>

UTI Pathogenesis

- **Pyelonephritis**
  - Infection of renal parenchyma causes inflammation called pyelonephritis

- **Ascension**
  - Once sufficient colonization occurs, bacteria ascend in ureter towards the kidney

- **Uroepithelium penetration**
  - Bacterial penetration → cystitis
  - Bacteria continue to replicate and may form biofilms

- **Colonization**
  - Pathogen colonizes periurethral area & ascends up through urethra to bladder

- **Uncomplicated UTI**
  - Asymptomatic bacteriuria

Adapted from www.pathophys.org
Diagnosis/Work-Up

• Signs & symptoms of UTI
  • E.g. dysuria, frequency, urgency
  • Flank pain, fever (pyelonephritis)
  • Change in mental status, lethargy

• Urine specimen
  • Not always obtained outpatient
  • Important for analysis & culture in higher risk patients to guide antibiotic therapy

Urinalysis/culture may not be obtained in the outpatient setting → diagnosis based on symptoms only, treatment is empiric

Urine analysis

Urine specimen
• Obtained via clean catch midstream void or new catheter

Urinalysis (UA)
• Assess for WBC, leukocyte esterase, nitrites, bacteria, epithelial cells, RBC
• Consider number of WBC (i.e. >10)

Urine culture
• Identify pathogen & test antibiotic susceptibility
• Consider colony forming units (i.e. $10^5$ bacteria)

Microbiology

• Most common pathogen
  • E. coli
    • Most common pathogen in both community- and hospital-acquired UTI
    • 75-90% of the cause in uncomplicated UTIs
    • 50% of the cause in complicated UTIs

• Other pathogens
  • Other Enterobacteriaceae
    • Other Gram-negative (less common)
  • Gram-positive
    • Enterococcus
    • Coagulase-negative Staphylococcus
  • Yeast
    • Candida spp

Sobel J et al. Urinary Tract Infection. Part II Major Clinical Syndromes
Gupta K et al. Clin Infect Dis 2011;52(5):e103–e120
# IDSA Guideline—Acute Cystitis

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration</th>
<th>Comments</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin monohydrate/macrocrystals</td>
<td>5 days</td>
<td>- Minimal resistance&lt;br&gt;- Low propensity for collateral damage&lt;br&gt;- Efficacy comparable to SMX/TMP x3 days&lt;br&gt;- Avoid in CrCl &lt;40mL/min</td>
<td>A-I</td>
</tr>
<tr>
<td>100mg BID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfamethoxazole/trimethoprim (SMX/TMP)</td>
<td>3 days</td>
<td>- Efficacy demonstrated in numerous trials&lt;br&gt;- Appropriate if local resistance rates &lt;20% or pathogen is susceptible&lt;br&gt;- Monitor for side effects (SCr, potassium, CBC)&lt;br&gt;- Allergy</td>
<td>A-I</td>
</tr>
<tr>
<td>800mg/160mg (double strength tablet) BID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fosfomycin trometamol 3g</td>
<td>Single dose</td>
<td>- Minimal resistance&lt;br&gt;- Low propensity for collateral damage&lt;br&gt;- Appears to have inferior efficacy compared to standard regimens</td>
<td>A-I</td>
</tr>
</tbody>
</table>
## IDSA Guideline—Acute Cystitis

<table>
<thead>
<tr>
<th>Class/agent(s)</th>
<th>Comments</th>
<th>Grade</th>
</tr>
</thead>
</table>
| Fluoroquinolones  
ciprofloxacin 250mg BID,  
levofloxacin 250mg daily | -Highly efficacious in 3-day regimens  
-Propensity for collateral damage  
-Should be considered as alternative agents  
-*Increasing resistance* | A-III |
| Beta lactams  
amoxicillin-clavulanate, cefdinir,  
cefaclor, cefpodoxime-proxetil (BI),  
cephalexin (BIII) | -Appropriate in 3-7 day regimens when other agents cannot be used  
-Studies suggest less efficacious and more adverse effects | B-I |

Gupta K et al. Clin Infect Dis 2011;52(5):e103–e120
Collateral damage

- Term describing ecological adverse effects of antimicrobials
  - E.g. Selection of drug-resistant organisms → colonization/infection with MDROs

- Most associated with fluoroquinolones and broad-spectrum cephalosporins (e.g. ceftriaxone)

- Why do we care?

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Increased risk of...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoroquinolones</td>
<td>MRSA, FQ-resistant Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Broad-spectrum cephalosporins</td>
<td>Extended-spectrum beta-lactamases (ESBL), Clostridium difficile, vancomycin-resistant enterococcus (VRE)</td>
</tr>
</tbody>
</table>

Paterson DL. CID 2004;38(Suppl.4):S341-5
Effect of 5-Day Nitrofurantoin vs Single-Dose Fosfomycin on Clinical Resolution of Uncomplicated Lower Urinary Tract Infection in Women
A Randomized Clinical Trial

<table>
<thead>
<tr>
<th>Design</th>
<th>Patients</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multinational,</td>
<td>Inpatient and outpatient women &gt;18 years old, with symptomatic UTI,</td>
<td>1:1 Randomization</td>
<td>Clinical and microbiologic response at 28</td>
</tr>
<tr>
<td>open-label,</td>
<td>positive dipstick, no known previous infection or resistance</td>
<td>Arm 1: NF 100mg TID for 5 days</td>
<td>days defined</td>
</tr>
<tr>
<td>analyst-blinded</td>
<td></td>
<td>Arm 2: Fosfo 3g x 1</td>
<td></td>
</tr>
<tr>
<td>randomized trial</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NF=nitrofurantoin

Huttner A et al. JAMA 2018;319(17):1781-89
### Effect of 5-Day Nitrofurantoin vs Single-Dose Fosfomycin on Clinical Resolution of Uncomplicated Lower Urinary Tract Infection in Women

A Randomized Clinical Trial

<table>
<thead>
<tr>
<th>Nitrofurantoin</th>
<th>Fosfomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Cure (Per-protocol)</strong> ( (P &lt; 0.004) )</td>
<td></td>
</tr>
<tr>
<td>177/244 (70%)</td>
<td>139/241 (58%)</td>
</tr>
<tr>
<td><strong>Microbiology (Per-protocol)</strong> ( (P &lt; 0.04) )</td>
<td></td>
</tr>
<tr>
<td>129/175 (74%)</td>
<td>103/163 (63%)</td>
</tr>
</tbody>
</table>

Huttner A et al. JAMA 2018;319(17):1781-89
# Cefpodoxime vs Ciprofloxacin for Short-Course Treatment of Acute Uncomplicated Cystitis: A Randomized Trial

Thomas M. Hooton, MD, Pacita L. Roberts, MS, and Ann E. Stapleton, MD

<table>
<thead>
<tr>
<th>Design</th>
<th>Patients</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized, double-blind trial; 2 study sites; non-inferiority study (10% margin)</td>
<td>Ambulatory setting of women aged 18-55 with diagnosis of uncomplicated cystitis</td>
<td>1:1 Randomization</td>
<td>Clinical cure at 30 days; microbiological cure rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm 1: Cefpodoxime 100mg BID for 3 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm 2: Cipro 250mg BID for 3 days</td>
<td></td>
</tr>
</tbody>
</table>

Cefpodoxime vs Ciprofloxacin for Short-Course Treatment of Acute Uncomplicated Cystitis: A Randomized Trial

Thomas M. Hooton, MD, Pacita L. Roberts, MS, and Ann E. Stapleton, MD

<table>
<thead>
<tr>
<th></th>
<th>Cefpodoxime</th>
<th>Ciprofloxacin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Cure (Overall)</strong> (Difference 11%; 95%CI:3-18%)</td>
<td>123/150 (82%)</td>
<td>139/150 (93%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Microbiology (Intent-to-treat)</strong> (Difference 15%; 95%CI:8-23%)</td>
<td>104/129 (81%)</td>
<td>123/128 (96%)</td>
</tr>
</tbody>
</table>
Other Options

• Aminoglycosides
  • High urinary concentrations
  • Rapidly bactericidal
  • Minimal resistance and collateral damage
  • Potential single dose strategy leading to minimal side effects

• Goodlet K *et al*:
  • Meta-analysis of single-dose aminoglycoside therapy for UTI
    • 13 studies included representing 13,804 patients aged 2 weeks to >70
    • Inpatient and outpatient; mostly cystitis
  • Results
    • Microbiologic cure: 94.5% +/- 4.3%.
    • Clinical Cure (no recurrence): 73.4% +/- 9.6% of patients at day 30
  • Potential cephalosporin/fluoroquinolone sparring regimen

Goodlet KJ et al. AAC 2018;63:e02165–e18
NOT a UTI, but just as Important

☆ • Asymptomatic bacteriuria (ASB)
  • Defined as quantitative bacteria in the urine without associated urinary symptoms
    • Positive culture does trump symptoms
  • Not uncommon in women, prolonged catheterization
  • For most adults, we do not treat it because
    • It tends to clear without treatment
    • There is minimal risk of patient harm
    • Promotes antibiotic resistance
    • Urine analysis and culture generally represent colonization in the absence of symptoms

## Prevalence of ASB

<table>
<thead>
<tr>
<th>Population</th>
<th>Prevalence, %</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy, premenopausal women</td>
<td>1.0–5.0</td>
<td>[31]</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>1.9–9.5</td>
<td>[31]</td>
</tr>
<tr>
<td>Postmenopausal women aged 50–70 years</td>
<td>2.8–8.6</td>
<td>[31]</td>
</tr>
<tr>
<td>Diabetic patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>9.0–27</td>
<td>[32]</td>
</tr>
<tr>
<td>Men</td>
<td>0.7–11</td>
<td>[32]</td>
</tr>
<tr>
<td>Elderly persons in the community&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>10.8–16</td>
<td>[31]</td>
</tr>
<tr>
<td>Men</td>
<td>3.6–19</td>
<td>[31]</td>
</tr>
<tr>
<td>Elderly persons in a long-term care facility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>25–50</td>
<td>[27]</td>
</tr>
<tr>
<td>Men</td>
<td>15–40</td>
<td>[27]</td>
</tr>
<tr>
<td>Patients with spinal cord injuries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermittent catheter use</td>
<td>23–89</td>
<td>[33]</td>
</tr>
<tr>
<td>Sphincterotomy and condom catheter in place</td>
<td>57</td>
<td>[34]</td>
</tr>
<tr>
<td>Patients undergoing hemodialysis</td>
<td>28</td>
<td>[28]</td>
</tr>
<tr>
<td>Patients with indwelling catheter use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-term</td>
<td>9–23</td>
<td>[35]</td>
</tr>
<tr>
<td>Long-term</td>
<td>100</td>
<td>[22]</td>
</tr>
</tbody>
</table>

<sup>a</sup> Age, ≥70 years.
## ASB—to Treat or not to Treat?

<table>
<thead>
<tr>
<th>Population (reference)</th>
<th>Patients studied</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly institutionalized men (Nicolle LE et al, 1983)</td>
<td>16 T, 20 NT</td>
<td><strong>No differences</strong> in symptomatic infection or mortality</td>
</tr>
<tr>
<td>Elderly institutionalized women (Nicolle LE et al, 1987)</td>
<td>26 T, 24 NT</td>
<td><strong>No differences</strong> in symptomatic UTI, mortality; with therapy increased adverse events and reinfection with resistant organisms</td>
</tr>
<tr>
<td>Intermittent catheterization (Mohler JL et al, 1987)</td>
<td>19 T, 27 NT</td>
<td><strong>Similar rates</strong> of recurrent symptomatic UTI in treated and not treated</td>
</tr>
<tr>
<td>Chronic indwelling catheter (Warren JW et al, 1982)</td>
<td>17 T, 18 NT</td>
<td><strong>Similar infection rates</strong> (0.63/week T, 0.61/week NT)</td>
</tr>
<tr>
<td>Women, postcatheter removal (Harding GK et al, 1991)</td>
<td>70 T, 42 NT</td>
<td>Therapy significantly decreased symptomatic UTI within 14 days for women &lt;60 years old</td>
</tr>
<tr>
<td>Diabetic women (Harding GK et al, 2002)</td>
<td>55 T, 50 NT</td>
<td><strong>No difference</strong> in symptomatic UTI or complications of diabetes; increased adverse effects with therapy</td>
</tr>
</tbody>
</table>

T=Treatment (antibiotics); NT= No Treatment

The Role of Asymptomatic Bacteriuria in Young Women With Recurrent Urinary Tract Infections: To Treat or Not to Treat?

Tommaso Cai,1 Sandra Mazzoli,2 Nicola Mondaini,3 Francesca Meacci,2 Gabriella Nesi,4 Carolina D’Elia,1 Gianni Malossini,1 Vieri Boffi,5 and Riccardo Bartoletti3

• Background
  • Treatment of recurrent asymptomatic bacteriuria in young women

• Method
  • Prospective trial that studied no antibiotics treatment (group A) vs antibiotic treatment (group B) in young healthy females with recurrent asymptomatic bacteriuria

• Results
  • Followed up at 3, 6, and 12 months
    • Reoccurrence with symptomatic UTI
      • 3 months was 3.5% for group A and 8.8% for group B (p=.051)
      • 6 months was 7.6% for group A and 29.7% for group B (p<.0001)
      • 12 months was 13.1% for group A and 46.8% for group B (p=<0001)

ASB in Special Population

- **Kidney transplant:**
  - Some data suggesting treating ASB within first 2 months of transplant
  - >2 months should be based on symptoms or evaluation by transplant team

- **Elderly with altered mental status (AMS):**
  - Typically should not be treated
  - Rule out other causes of AMS
  - No other causes consider urine analysis and culture
    - Clean catch or exchange catheter and repeat testing

- **Paraplegic or quadriplegic**
  - May not be able to describe symptoms
  - Increased bladder & leg spasms, autonomic dysreflexia

Coussement J et al. *Cochrane Database Syst Rev* 2018;10(7);e3006
ASB — Treatment

• Pregnant women
  • Reduces risk of pyelonephritis (20-35% → 1-4%) and adverse consequences of pregnancy (e.g. lower birth weight infants, preterm delivery)

• Patients undergoing traumatic genitourinary procedures associated with mucosal bleeding
  • Higher risk of post-procedure bacteremia & sepsis

Summary

• UTI is the most common infection requiring medical care

• Women are more prone to UTI in comparison to men

• *E. coli* is the most common pathogen associated with both community and hospital acquired UTI

• Nitrofurantoin should be considered as first line treatment for most uncomplicated UTIs

• Asymptomatic bacteriuria should not warrant therapy in most patients with exception to pregnancies and urological procedures
Skin and Soft Tissue Infections
Skin & Soft Tissue Infections (SSTI)

• Diverse infections affecting large spectrum of host and age groups

• Incidence and causative microbiology changing over time and host factors

• Treatment is often empiric and dependent on risk factors, patient history, and presentation
Spectrum of Disease

- Erysipelas
- Impetigo
- Folliculitis

- Ecthyma
- Furunculosis
- Carbunculosis

- Cellulitis

- Necrotizing fasciitis

- Myonecrosis (clostridial and nonclostridial)

Rajan S. Cleveland Clinic Journal of Medicine. 2012;79(1):57
Main Diagnostic Classification

**Purulent**
- Furuncle, carbuncle or abscess
- *S. aureus* main culprit
- Accounts for ~75% of cases

**Non-purulent**
- Cellulitis, erysipelas or necrotizing fasciitis
- Streptococci main culprit
- β-hemolytic streptococci ~73% of cases

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P</strong></td>
<td>No systemic* signs</td>
<td>Systemic* signs of infection</td>
</tr>
<tr>
<td><strong>NP</strong></td>
<td>Typical infection without purulence</td>
<td></td>
</tr>
</tbody>
</table>

* Temperature >38°C, heart rate >90, respiratory rate >24, abnormal WBC >12,000 or <400, or immunocompromised patients

Moran et al. *NEJM* 2006; 355:666
Jeng et al. *Medicine* 2010;89:2017
Stevens et al. *Clin Infect Dis* 2014;59(2):e10
MRSA Trends (USA)

Incidence of Invasive MRSA Among Persons Not on Dialysis by Epidemiologic Class, 2009–2016

### Empiric Treatment: **Purulent SSTI**

<table>
<thead>
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<tr>
<td><strong>P</strong></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>I &amp; D + Empiric PO treatment targeting MRSA</td>
<td>I &amp; D + Empiric IV treatment targeting MRSA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>De-escalate to MSSA-targeted agents based on culture results</td>
</tr>
</tbody>
</table>

Stevens et al. *Clin Infect Dis* 2014;59(2):e10
Empiric Treatments for **Purulent SSTI**

### Empiric Oral Agents

- **MRSA:**
  - Doxycycline
  - Trimethoprim/sulfa
  - Linezolid

- **MSSA:**
  - Dicloxacillin
  - Cephalexin
  - Cefadroxil

### IV Agents

- **MRSA:**
  - Vancomycin
  - Daptomycin
  - Linezolid
  - Others

- **MSSA:**
  - Cefazolin
  - Nafcillin
  - Clindamycin
## Skin Abscesses

<table>
<thead>
<tr>
<th>Current Guidance on Antibiotics for Patients with Skin Abscesses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation</strong></td>
</tr>
<tr>
<td><strong>IDSA</strong></td>
</tr>
<tr>
<td><strong>EBM Guidelines</strong></td>
</tr>
<tr>
<td><strong>NHG</strong></td>
</tr>
<tr>
<td><strong>ESCMID</strong></td>
</tr>
<tr>
<td><strong>BMJ-Rapid Recommendations</strong></td>
</tr>
</tbody>
</table>

**Adapted from:** Vermandere et al. *BMJ* 2018;360:k243
# Trimethoprim–Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess

<table>
<thead>
<tr>
<th>Design</th>
<th>Patients</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized trial at 5 U.S. ERs</td>
<td>Outpatients &gt;12 years with uncomp. abscess treated with I&amp;D</td>
<td><strong>Arm 1</strong>: I&amp;D alone</td>
<td>clinical cure, assessed at 7-14 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Arm 2</strong>: I&amp;D + Abx</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Abx</strong>: TMP/SMX 2 DS Twice daily</td>
<td></td>
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</tbody>
</table>

**Notes:**
- **Arm 1**: I&D alone
- **Arm 2**: I&D + Abx
- **Abx**: TMP/SMX 2 DS Twice daily

**Abbreviations:**
- **I&D**: Incision and Drainage
- **Abx**: Antibiotic
- **TMP/SMX**: Trimethoprim-sulfamethoxazole
- **DS**: Double-strength

Talan et al. *NEJM* 2016;374:823
## Trimethoprim–Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess

<table>
<thead>
<tr>
<th></th>
<th>I&amp;D Alone (N=617)</th>
<th>I&amp;D + TMP/SMX (N=630)</th>
</tr>
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<tbody>
<tr>
<td><strong>Microbiology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA 47.2% + MSSA 16.5%</td>
<td>MRSA 43.5% + MSSA 15.9%</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical Cure (Per-protocol)</strong> (P &lt;0.001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>457/533 (85.7)</td>
<td>487/524 (92.9%)</td>
<td></td>
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</table>

Talan et al. *NEJM* 2016;374:823
Trimethoprim–Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess

NNT ~ 14 patients

Need to treat 14 patients with uncomplicated skin abscesses with antibiotics to achieve one additional successful treatment

Talan et al. *NEJM* 2016;374:823
## Empiric Treatment: Non-Purulent SSTI

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<td><strong>PO Abx</strong></td>
<td><strong>Empiric IV treatment targeting Strep.</strong></td>
<td><strong>Surgical emergency Broad-spectrum IV treatment</strong></td>
</tr>
</tbody>
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Stevens et al. *Clin Infect Dis* 2014;59(2):e10
Empiric Treatments for **Non-Purulent SSTI**

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<th>IV Agents</th>
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<tr>
<td>• Penicillin VK</td>
<td>• Penicillin G</td>
</tr>
<tr>
<td>• Cephalexin</td>
<td>• Ceftriaxone</td>
</tr>
<tr>
<td>• Cefadroxil</td>
<td>• Cefazolin</td>
</tr>
<tr>
<td>• Dicloxacillin</td>
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Stevens et al. *Clin Infect Dis* 2014;59(2):e10
Summary

• SSTI treatment can be stratified and treated per national guidelines

• MRSA rates continue to drop, possibly allowing MSSA-directed empiric treatment if low risk

• Antibiotics, in addition to I&D, for uncomplicated skin abscesses remains a point of discussion

• Narrow-spectrum agents should be considered first-line treatment for mild non-purulent SSTI
Final Thoughts

• Large volume of antibiotic use in the ambulatory settings pose an opportunity for improvement

• Limiting antibiotic exposure for common ambulatory infections (URI, UTI, and SSTI) greatly contributes to national antimicrobial preservation

• National treatment guidelines can direct optimal empiric and definitive treatments, including when to avoid usage

• Antimicrobial stewardship is multi-disciplinary and requires broad commitments across the healthcare continuum
Antimicrobial Preservation and Stewardship in the Ambulatory Setting

Meagan Adamsick, PharmD
Ronak Gandhi, PharmD, BCPS
Ramy Elshaboury, PharmD, BCPS-AQ ID