How to Effectively Utilize Antimicrobial Stewardship to Optimize Clinical Outcomes

Shaina Doyen, PharmD
Baptist Health Louisville
Clinical Pharmacy Specialist, Infectious Diseases
Disclosure

- I have no actual or potential conflicts of interest in relation to this program or presentation
Objectives

- Review antimicrobial stewardship and how it can be applied to everyday practice.

- Discuss high risk antibiotics and alternatives that can be safely substituted for commonly encountered infections in the outpatient setting.
Antimicrobial Stewardship
Goals of Antimicrobial Stewardship

- Optimize antimicrobial therapy and patient outcomes
- Prevention of antimicrobial resistance and prescribing errors
  - Appropriate use
  - Timely, appropriate antibiotic selection
  - Dose optimization
  - De-escalation
  - Duration
- Providing education and increasing adherence to clinical practice guidelines to provide the best standard of care and minimize spread of resistance
- Regardless of the setting the primary goals are the same

Is Antimicrobial Resistance Still Theoretical?

By ASHLEY WELCH   CBS NEWS  January 13, 2017, 5:18 PM

Woman died from superbug resistant to all available antibiotics in U.S.

Carbapenem-resistant Enterobacteriaceae (CRE) bacteria is pictured in this medical illustration provided by the U.S. Centers for Disease Control and Prevention. / REUTERS/CDC

Morbidity and Mortality Weekly Report (MMWR)

Morbidity and Mortality Weekly Report (MMWR)

Notes from the Field: Part-Resistant New Delhi Metallo-Beta-Lactamase-Producing Klebsiella pneumoniae — Washoe County, Nevada, 2016


Antimicrobial Resistance and Consequences

- >2 million patients affected by antibiotic-resistant infections each year
  - At least 23,000 of those result in death
  - At least 250,000 illnesses and 14,000 deaths are due to *Clostridium difficile* infection

  Antibiotic use is the most modifiable driver of antibiotic resistance and resistant infections lead to:
  - Poor clinical outcomes, more toxic treatments, higher healthcare costs

How Does Antibiotic Resistance Develop?

1. Lots of germs. A few are drug resistant.

2. Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection.

3. The drug-resistant bacteria are now allowed to grow and take over.

4. Some bacteria give their drug-resistance to other bacteria, causing more problems.

Examples of How Antibiotic Resistance Spreads

- Animals get antibiotics and develop resistant bacteria in their guts.
- Drug-resistant bacteria can remain on meat from animals. When not handled or cooked properly, the bacteria can spread to humans.
- Fertilizer or water containing animal feces and drug-resistant bacteria is used on food crops.
- Drug-resistant bacteria in the animal feces can remain on crops and be eaten. These bacteria can remain in the human gut.
- George stays at home and in the general community. Spreads resistant bacteria.
- George gets care at a hospital, nursing home or other inpatient care facility.
- Resistant germs spread directly to other patients or indirectly on unclean hands of healthcare providers.
- Resistant bacteria spread to other patients from surfaces within the healthcare facility.

Simply using antibiotics creates resistance. These drugs should only be used to treat infections.
Four Core Actions to Fight Resistance

1. Preventing infections and spread of resistance
2. Tracking antibiotic-resistant infections
3. Improving antibiotic prescribing and stewardship
4. Developing new drugs and diagnostic tests

The commitment to always use antibiotics appropriately and safely - only when needed, the right antibiotic, and to administer correctly - IS Antimicrobial Stewardship!

Outpatient Antimicrobial Stewardship

- At least 30% of antibiotics prescribed in outpatient setting are unnecessary

  - Inappropriate use includes
    - Unnecessary antibiotic use
    - Inappropriate antibiotic selection, dosing, and duration
      - May approach 50% of all outpatient antibiotic use

- A 10% decrease in inappropriate prescribing in the community can result in 17% reduction in *C. difficile*


Outpatient Antibiotic Prescriptions by State, 2014
Antibiotic prescriptions per 1,000 people

Source: Centers for Disease Control and Prevention.
Outpatient Antibiotic Prescribing by Provider Specialty, 2014

Percent of antibiotic prescriptions

Source: Centers for Disease Control and Prevention.
Barriers to Appropriate Prescribing

1) Clinician knowledge gaps about clinical practice guidelines or best practices

2) Treating positive test results that do not correlate clinically with patient

3) Clinician perception of patient expectations for antibiotics

4) Perceived pressure to see patients quickly

5) Clinician concerns about decreased patient satisfaction when antibiotics are not prescribed
Barriers to Appropriate Prescribing

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4) Perceived pressure to see patients quickly
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I don't always go to the doctor...

But when I do I'm the guy who's going to bully the doctor into giving me antibiotics no matter what.
Commonly Encountered Infections in the Community

- Acute Uncomplicated Cystitis
- Skin and Soft Tissue Infections
- Pharyngitis
- Acute Rhinosinusitis
- Acute Uncomplicated Bronchitis
- Non-specific Upper Respiratory Tract infection
Commonly Encountered Infections in the Community

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Acute Uncomplicated Cystitis

- Most common in healthy, non-pregnant adult women
  - Most infections caused by *E. coli*

- Urinary tract infections (UTIs) are common in children affecting 8% of girls and 2% of boys by age 7
  - Approximately 85% of cases caused by *E. coli*

- Classic presenting symptoms include dysuria, frequency and urgency, hematuria, and suprapubic discomfort

Acute Uncomplicated Cystitis

- Urinalysis reflex to culture ONLY when symptoms present
  - Ensure appropriate collection method
  - Pyuria plus bacteriuria ≠ indication for treatment in asymptomatic patients
- Urinalysis and culture suggestive of infection: recommendations vary
  - At least 50,000 CFUs/mL
  - Nitrites
  - Leukocyte esterases
  - Presence of WBCs (at least ≥5)

Asymptomatic Bacteriuria

- Isolation of bacteria in appropriately collected urine specimen from patient without signs/symptoms

- Screening and treatment of asymptomatic bacteriuria is ONLY recommended in the following patients
  - Pregnant women
    - Duration of therapy (DOT): 3 to 7 days
  - Transurethral resection of prostate
    - DOT: dependent upon presence of indwelling catheter
  - Other urologic procedures for which mucosal bleeding is anticipated

Asymptomatic Bacteriuria

- Pediatrics: treatment of asymptomatic bacteriuria is NOT recommended

- Adults: screening and treatment of asymptomatic bacteriuria is NOT recommended for the following
  - Premenopausal, non-pregnant women (A-I)
  - Diabetic women (A-I)
  - Older persons living in the community (A-II)
  - Elderly, institutionalized patients (A-I)
  - Persons with spinal cord injury (A-II)
  - Catheterized patients while catheter remains in situ (A-I)


Treatment of Urinary Tract Infections

- Initial antibiotic treatment should be based on local antimicrobial susceptibility patterns

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Treatment of Urinary Tract Infections in Pediatric Patients

- Sulfamethoxazole/Trimethoprim (SMX/TMP)
- Amoxicillin/clavulanate
- Cefixime
- Cefpodoxime
- Cefprozil
- Cephalexin

Treatment of Acute Uncomplicated Cystitis

- Nitrofurantoin x 5 days
- SMX/TMP x 3 days
- Fosfomycin x 1 dose

If early pyelonephritis is suspected, AVOID nitrofurantoin and fosfomycin. If one of the above cannot be used, fluoroquinolone or beta-lactam can be considered.
Safety Concerns with Fluoroquinolone Use

- FDA Drug Safety Update
  - “These medicines are associated with disabling and potentially permanent side effects of the tendons, muscles, joints, nerves, and central nervous system that can occur together in the same patient.”

- Hypervirulent NAP1/BI/027 strain of *C. difficile* Infection
  - Dramatic increase in severity, frequency, and refractoriness of *C. difficile* has been strongly correlated to fluoroquinolone use and increased resistance

FDA Drug Safety Communication (26 July 2016).
Commonly Encountered Infections in the Community

- Acute Uncomplicated Cystitis
- **Skin and Soft Tissue Infections**
  - Pharyngitis
  - Acute Rhinosinusitis
- Acute Uncomplicated Bronchitis
- Non-specific Upper Respiratory Tract Infection
Skin and Soft Tissue Infections

- Cellulitis is most commonly observed in middle-aged and older adult patients
  - Erysipelas occurs more commonly in young children and older adults
  - Skin abscesses may occur in otherwise healthy patients with no predisposing risk factors

- Cellulitis incidence is about 200 cases per 100,000 patient years

- Gram-positive organisms, specifically beta-hemolytic streptococci and *Staphylococcus aureus*, are among the most common causes

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Skin and Soft Tissue Infections

MANAGEMENT OF SSTIs

NONPURULENT
Necrotizing Infection / Cellulitis / Erysipelas

> EMERGENT SURGICAL INSPECTION / DEBRIDEMENT
  - Rule out necrotizing process
> EMPIRIC Rx
  - Vancomycin PLUS Piperacillin/Tazobactam

Severe
  ➔ C & S

Moderate
  ➔ INTRAVENOUS Rx
  - Penicillin or
  - Ceftriaxone or
  - Cefazolin or
  - Clindamycin

Mild
  ➔ ORAL Rx
  - Penicillin VK or
  - Cephalosporin or
  - Dicloxacillin or
  - Clindamycin

Mild
  ➔ I & D C & S
  ➔ DEFINED Rx (Necrotizing Infections)
  Monomicrobial Streptococcus pyogenes
    - Penicillin PLUS Clindamycin
    - Clostridial sp.
    - Penicillin PLUS Clindamycin
  Vibrio vulnificus
    - Doxycycline PLUS Ceftazidime
    - Aeromonas hydrophila
    - Doxycycline PLUS Ciprofloxacin
  Polymicrobial
    - Vancomycin PLUS Piperacillin/Tazobactam

PURULENT
Furuncle / Carbuncle / Abscess

Severe
  ➔ EMPIRIC Rx
  - Vancomycin or
  - Daptomycin or
  - Linezolid or
  - Televancin or
  - Ceftaroline

Moderate
  ➔ DEFINED Rx
  MRSA
    - See Empiric
  MSSA
    - Nafcillin or
    - Cefazolin or
    - Clindamycin

Mild
  ➔ EMPIRIC Rx
  - TMP/SMX or
  - Doxycycline

I & D

1 Since daptomycin and televarcin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.
Commonly Encountered Infections in the Community

- Acute Uncomplicated Cystitis
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- Pharyngitis
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Pharyngitis

- Group A streptococcal (GAS) pharyngitis is primarily a disease of children age 5-15 years
  - Only 5-10% of adult sore throats are caused by GAS

- Rapid Antigen Detection Testing (RADT) criteria
  - Pediatrics: sore throat PLUS 2 or more of the following
    - Absence of cough, tonsillar exudates or swelling, fever, swollen and tender anterior cervical lymph nodes, age < 15 years
  - Adults: 2 or more Centor criteria (required for diagnosis)
    - Fever, tonsillar exudates, tender cervical lymphadenopathy, absence of cough

Treatment of Pharyngitis

Alternatives for penicillin allergic patients: cephalexin, clindamycin, clarithromycin, azithromycin
Commonly Encountered Infections in the Community

- Acute Uncomplicated Cystitis
- Skin and Soft Tissue Infections
- Pharyngitis
- **Acute Rhinosinusitis**
- Acute Uncomplicated Bronchitis
- Non-specific Upper Respiratory Tract Infection
Acute Rhinosinusitis

- Approximately 1 out of 8 adults in 2012 reported receiving a diagnosis of rhinosinusitis in previous year
  - 98% of rhinosinusitis cases are viral

- Diagnosis of acute **bacterial** rhinosinusitis
  - **Severe (>3-4 days):** fever ($\geq 102^\circ F$) and purulent nasal discharge or facial pain
  - **Persistent (>10 days) without improvement:** nasal discharge or daytime cough
  - **Worsening (3-4 days):** worsening or new onset fever, daytime cough, nasal discharge after initial improvement of viral upper respiratory infection (URI) lasting 5-6 days

Management of Acute Rhinosinusitis

- Watchful waiting is encouraged for uncomplicated cases with reliable follow-up.

- **3-4 days:** Severe or Worsening
- **>10 days:** Without Improvement

Amoxicillin OR Amoxicillin/Clavulanate

Penicillin allergic adult patients: doxycycline or respiratory fluoroquinolone are recommended.

Commonly Encountered Infections in the Community

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- Acute Rhinosinusitis
- **Acute Uncomplicated Bronchitis**
- Non-specific Upper Respiratory Tract Infection
Acute Uncomplicated Bronchitis

- The most common presenting symptom of adult patients to their primary care physician is cough
  - Acute bronchitis is typically the diagnosis in these patients
- Clinical evaluation should focus on ruling out community-acquired pneumonia
  
  - **Common misconception**: colored sputum does not indicate a bacterial infection

Management of Acute Uncomplicated Bronchitis

- Routine treatment with antibiotics is NOT recommended, regardless of cough duration.

- Recommended treatment is for symptoms management:
  - Cough suppressants: dextromethorphan, codeine
  - Antihistamines: diphenhydramine
  - Decongestants: phenylephrine, pseudoephedrine
  - Beta agonists: albuterol

Commonly Encountered Infections in the Community

- Acute Uncomplicated Cystitis
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**Non-specific Upper Respiratory Tract Infection**
Non-Specific Upper Respiratory Tract Infection (URTI)

- At least 200 identified viruses cause the common cold
  - Rhinoviruses, parainfluenza, respiratory syncytial virus, coronaviruses, enteroviruses, adenoviruses

- The common cold is the third most frequent diagnosis in office visits

- Symptoms of the common cold
  - Rhinitis, nasal congestion, postnasal drip, sore throat, malaise, cough, fever, conjunctivitis
Non-Specific Upper Respiratory Tract Infection (URTI)

- In patients with cough and acute URTI, signs, symptoms, and sinus imaging abnormalities have no specificity for bacterial infection
  - It is recommended to NOT diagnose bacterial sinusitis during first week of symptoms

Gwaltney et al

- Reviewed CT scans of sinuses in patient with recent onset colds and abnormalities were observed in 87%
- No patient received antibiotics
  - 79% of patients rescanned at days 13-20 had resolution or marked improvement in abnormalities

Management of Non-Specific Upper Respiratory Tract Infection (URTI)

- Symptom management
  - Adults:
    - Decongestants PLUS a first-generation antihistamine
    - Non-steroidal anti-inflammatory drugs
  - Pediatrics:
    - For children < 6 years, there is potential of harm and no proven benefit of over-the-counter cough and cold medications
    - Oral prednisolone and inhaled corticosteroids do NOT improve outcomes in children without asthma

- Patients and providers must weigh the benefits and harms of symptomatic therapy

Short vs Long-Course in Outpatient Settings

- Meta-analysis of randomized controlled trials for commonly treated bacterial infections in outpatient setting

- No difference in clinical cure for adults with the following:
  - Acute bacterial sinusitis: 3-7 vs 6-10 days
    - (RR 0.95, 95% CI:0.81, 1.21)
  - Uncomplicated cystitis in non-pregnant women: 3 vs ≥ 5 days
    - (RR 1.10, 95% CI:0.96,1.25)
  - Acute pyelonephritis: 7-14 vs 14-42 days
    - (RR 1.03, 95% CI:0.80,1.32)
  - Community acquired pneumonia: ≤ 7 vs > 7 days
    - (RR:0.96, 95% CI:0.74,1.26)
  - Uncomplicated cystitis in elderly women: 3-6 vs 7-14 days
    - (RR 0.98, 95% CI:0.62,1.54)

The New Antibiotic Mantra—“Shorter is Better”

- Multiple trials have been performed comparing short versus longer-course antibiotic therapy in commonly treated infections
  - Short-course therapy has been proven just as effective with reduced selective pressure driving resistance

<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatment, Days</th>
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<tbody>
<tr>
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<td>3-5 7-10</td>
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<tr>
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<td>≤8 10-15</td>
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<tr>
<td>Pyelonephritis&lt;sup&gt;10&lt;/sup&gt;</td>
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<td>Intraabdominal infection&lt;sup&gt;11&lt;/sup&gt;</td>
<td>4 10</td>
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<td>Chronic osteomyelitis&lt;sup&gt;15&lt;/sup&gt;</td>
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Abbreviation: COPD, chronic obstructive pulmonary disease.

What is the Conclusion?

- The goal is to customize duration of therapy **based upon the patient’s clinical response** rather than a set number.

- “New, evidence-based dogma—shorter is better”
Opportunities for the Future

- **Outpatient Antimicrobial Stewardship Programs**
  - Implement effective strategies to modify prescribing behaviors to align with evidence-based recommendations

# Outpatient Antimicrobial Stewardship Programs

<table>
<thead>
<tr>
<th>Authors</th>
<th>Studies (#)</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
</table>
| Arnold SR, et al.         | 39          | • Small changes using printed educational materials; active education most effective  
• Delayed prescriptions reduced antibiotic use without negatively affecting patient outcomes | • Multifaceted interventions are most effective.  
• No single intervention recommended for all settings |
| Drekonja DM, et al.       | 50          | • Communication skills training and laboratory testing can lower antibiotic use  
• Several types of stewardship interventions were effective in improving antibiotic prescribing | • Outpatient antibiotic stewardship programs can improve prescribing without negatively affecting outcomes  
• Sustainability and scalability of specific interventions less clear |
| McDonagh M, et al.        | 133         | Interventions that showed improvement in antibiotic prescribing without worsening outcomes  
• Clinic-based parent education (21% reduction)  
• Public patient campaigns + clinician education (7% reduction without increasing follow-up visits)  
• Procalcitonin for adults (12-72% reduction)  
• Electronic decision support (5-9% reduction) | • Several interventions safely reduced antibiotic prescribing or improved appropriate antibiotic selection without affecting outcomes |
| Van der Velden AW, et al. | 58          | • Interventions targeting decrease in overall use was more effective than targeting selection  
• Prescriptions on average were reduced by 11.6%; first-line antibiotics decreased 9.6%  
• Interventions targeting clinician education was among one of the largest effect sizes | • Clinician education, especially communication skills training is important to optimize antibiotic use |

Opportunities for the Future

- **Outpatient Antimicrobial Stewardship Programs**
  - Implement effective strategies to modify prescribing behaviors to align with evidence-based recommendations
  - For proven infections:
    - Consult your local antibiogram
    - Utilize narrow therapy for the shortest recommended duration
  - Educate patients and parents on appropriate antibiotic use and unintended consequences of misuse
    - *C. difficile* Infection
    - Adverse Events
    - Antimicrobial Resistance

How to Effectively Utilize Antimicrobial Stewardship to Optimize Clinical Outcomes

Shaina Doyen, PharmD
Baptist Health Louisville
Clinical Pharmacy Specialist, Infectious Diseases
Post-Test Question #1

Antimicrobial Stewardship is a coordinated program that promotes which of the following:

a. Appropriate use of antimicrobials
b. Improvement in patient outcomes
c. An increase in antimicrobial resistance
d. a and b
e. All of the above
The IDSA asymptomatic bacteriuria guidelines recommend treatment of asymptomatic bacteriuria in which of the following patients:

a. 65 year old female with diabetes mellitus
b. 28 year old pregnant female
c. 62 year old male with hypertension presenting for check-up
d. 82 year old male presenting for replacement of long-term indwelling foley catheter
e. All of the above
A 72 year old healthy female presents during the month of December with complaints of shortness of breath, cough, fever, myalgia, and weakness for 1 day. Patient denies dysuria, urgency, or suprapubic pain. Lab results include rapid influenza antigen test positive for Influenza A and urine culture positive for ESBL-producing *E. coli*. What treatment would you select for this patient?

a. Oseltamivir plus levofloxacin  
b. **Oseltamivir alone**  
c. Oseltamivir plus meropenem  
d. Meropenem alone  
e. Any of the above
Post-Test Question #4

According to the IDSA SSTI Guidelines, what is the recommended clinical management for a cutaneous abscess in an otherwise healthy adult patient without systemic symptoms?

a. Sulfamethoxazole/trimethoprim daily for 10 days
b. Incision and drainage plus cephalexin daily for 5 days
c. Incision and drainage
d. Vancomycin IV, patient specific dosing, for 7 days
e. Any of the above