Antimicrobial Stewardship in Primary Care

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Resources

• Get Smart: Know When Antibiotics Work
  http://www.cdc.gov/getsmart/community/about/index.html

• IDSA Practice Guidelines
  http://www.idsociety.org/Templates/Landing.aspx?id=23622320151

• Free CME: To Prescribe or Not To Prescribe? Antibiotics and Outpatient Infections
  https://med.stanford.edu/cme/courses/online/improving-antibiotics-pcs.html
Antibacterial drugs have been the most effective of all medicines. Their success is reflected by their continued use and the decrease in morbidity and mortality from bacterial infections over the past 80 years.
The time to the emergence of antibiotic resistance in select bacteria has accelerated. Data below is from the CDC report titled: “Antibiotic Resistance Threats in the United States, 2013”

- From the 1940s through the 1980s, average time to resistance exceeded 10 years (excluding penicillin). The average time to resistance is now approximately 1 year.
• Antibiotic use is the most important modifiable driver of antibiotic resistance, and antibiotic-resistant infections lead to higher healthcare costs, poor health outcomes, and more toxic treatments.

• Over half of antibiotic prescribing in outpatient settings may be inappropriate, and most of this inappropriate use is for acute respiratory infections, such as pharyngitis, sinusitis, or bronchitis.

• Antibiotics are the most common cause of adverse drug events (ADEs) in children, accounting for 7 of the top 15 drugs leading to pediatric ADE-related emergency room (ER) visits. In adults, ADEs account for 1 out of 5 ADE-related visits to the ER.

• Harm can be reduced by improving antibiotic prescribing. A 10% decrease in inappropriate prescribing in the community can result in a 17% reduction in Clostridium difficile infection, a severe form of diarrhea usually caused by antibiotic exposure.

• Clinical practice guidelines for common infections help establish standards of care, focus quality improvement efforts, and improve patient outcomes.
The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.
NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

MARCH 2015
<table>
<thead>
<tr>
<th>TABLE 1: National Targets to Combat Antibiotic-Resistant Bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>By 2020, the United States will:</td>
</tr>
<tr>
<td><strong>For CDC Recognized Urgent Threats:</strong></td>
</tr>
<tr>
<td>Reduce by 50% the incidence of overall <em>Clostridium difficile</em> infection compared to estimates from 2011.</td>
</tr>
<tr>
<td>Reduce by 60% carbapenem-resistant Enterobacteriaceae infections acquired during hospitalization compared to estimates.</td>
</tr>
<tr>
<td>Maintain the prevalence of ceftriaxone-resistant <em>Neisseria gonorrhoeae</em> below 2% compared to estimates from 2013.</td>
</tr>
<tr>
<td><strong>For CDC Recognized Serious Threats:</strong></td>
</tr>
<tr>
<td>Reduce by 35% multidrug-resistant <em>Pseudomonas spp.</em> infections acquired during hospitalization compared to estimates from 2011.</td>
</tr>
<tr>
<td>Reduce by at least 50% overall methicillin-resistant <em>Staphylococcus aureus</em> (MRSA) bloodstream infections by 2020 as compared to 2011.*</td>
</tr>
<tr>
<td>Reduce by 25% multidrug-resistant non-typhoidal <em>Salmonella</em> infections compared to estimates from 2010-2012.</td>
</tr>
<tr>
<td>Reduce by 15% the number of multidrug-resistant TB infections.¹</td>
</tr>
<tr>
<td>Reduce by at least 25% the rate of antibiotic-resistant invasive pneumococcal disease among &lt;5 year-olds compared to estimates from 2008.</td>
</tr>
<tr>
<td>Reduce by at least 25% the rate of antibiotic-resistant invasive pneumococcal disease among &gt;65 year-olds compared to estimates from 2008.</td>
</tr>
</tbody>
</table>
Preventing *C. difficile* Is Now a National Priority!

National Action Plan for Combating Antibiotic Resistance Issued By the White House in March 2015

2015 — 2020

- Goal is to reduce the incidence of overall *C. difficile* infection by 50% compared to rates in 2011
- Implementation of plan and tracking of outcomes will accomplished by several government agencies

Source: https://www.whitehouse.gov/sites/default/files/dags/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf
Incidence of Nosocomial Clostridium difficile Infection.
C. difficile infection
England 2015/16

Overall rate
26 people out of every 100,000 will acquire a C. difficile infection (CDI)

Trends in rates of C. difficile infection
Rate, per 100,000 population

Financial Year
• The National Action Plan for Combating Antibiotic Resistant Bacteria
• Goal:
  Reduction of inappropriate outpatient antibiotic use by 50% by 2020
What is antimicrobial stewardship?

Coordinated approach to improve the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen:

• right choice of antibiotic
• right route of administration
• right dose
• right time
• right duration
• minimise harm to the patient and future patients.
Key U.S. Statistics

Below are a number of statistics that help describe how antibiotics are currently being prescribed in outpatient settings in the United States and how these practices are contributing to the larger issue of antibiotic resistance.

- In 2014, 266.1 million courses of antibiotics are dispensed to outpatients in U.S. community pharmacies. This equates to more than 5 prescriptions written each year for every 6 people in the United States.¹
- At least 30% of antibiotics prescribed in the outpatient setting are unnecessary, meaning that no antibiotic was needed at all.²
- Total inappropriate antibiotic use, inclusive of unnecessary use and inappropriate selection, dosing and duration, may approach 50% of all outpatient antibiotic use.³⁴⁵
- Antibiotic prescribing in the outpatient setting varies by state.¹
- Performance on quality measures for appropriate outpatient antibiotic prescribing varies both by region and health plan.⁶
- Local outpatient prescribing practices contribute to local resistance patterns.⁷
- Outpatient antibiotic prescribing is greatest in the winter months.⁸
- The majority (>60%) of antibiotic expenditures are associated with the outpatient setting.⁹
- An estimated 80-90% of the volume of human antibiotic use occurs in the outpatient setting.¹⁰¹¹
- Azithromycin and amoxicillin are among the most commonly prescribed antibiotics.¹
Community Antibiotic Prescriptions per 1,000 Population by State — 2014

At least 30% of antibiotics prescribed in doctors’ offices, emergency departments and hospital clinics are unnecessary.*

Data source: IMS Health Xponent 2014.

“If you cannot measure it, you cannot improve it”
Lord Kelvin
Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011


- The National Action Plan for Combating Antibiotic Resistant Bacteria Goal: Reduction of inappropriate outpatient antibiotic use by 50% by 2020
- What is the extent of inappropriate OP antibiotic use? What is the fraction of antibiotic use that is inappropriate and amenable to reduction?

- NAMCS/NHAMCS
  - National Ambulatory Medical Care Survey (office based physicians)/National Hospital Ambulatory Medical Care Survey (hospital outpatient and ED)
  - 184,032 visits/2 years (2010-2011)
Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011


- 12.6% visits resulted in antibiotic prescriptions
- Evaluated diagnoses for which ATB are indicated (PNA/UTI)/ may be indicated (sinusitis, pharyngitis)/ not indicated (acute bronchitis)
- Collectively, acute respiratory conditions per 1000 population led to 221 antibiotic prescriptions (95%CI, 198-245) annually, but only 111 antibiotic prescriptions were estimated to be appropriate for these conditions.
- Estimated annual antibiotic prescription rate per 1000 population of 506, but only an estimated 353 antibiotic prescriptions were likely appropriate, supporting the need for establishing a goal for outpatient antibiotic stewardship.
More than 12% of all outpatient visits in the United States in 2010–2011 resulted in an antibiotic prescription, of which approximately 30% were inappropriate, according to this population-based analysis.
Frequency of First-line Antibiotic Selection Among US Ambulatory Care Visits for Otitis Media, Sinusitis, and Pharyngitis

JAMA Internal Medicine Published online October 24, 2016
Figure. Percentage of Visits in Which Antibiotics Were Prescribed That Are First-line and Non-First-line for Otitis Media, 2010-2011


Estimates were based on 1705 sampled visits for otitis media, 463 for pediatric sinusitis, 1223 for adult sinusitis, 1006 for pediatric pharyngitis and 830 for adult pharyngitis. Broad cephalosporin includes second- and third-generation agents. Pediatric patients were defined as those 19 years or younger.
Figure 1
Outpatient Antibiotic Prescriptions, 2010-11

Note: The recommended first-line antibiotic for middle ear infections is amoxicillin. An alternative first-line therapy in select circumstances is amoxicillin with clavulanate, which is recommended as initial therapy only in select circumstances (for example, concurrent ear and eye infections). Recommended first-line antibiotics for sinus infections include amoxicillin or amoxicillin with clavulanate. Recommended first-line antibiotics for pharyngitis include amoxicillin or penicillin.

Sources: Analysis of NAMCS and NHAMCS data on U.S. antibiotic prescribing, 2010-2011.
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Frequency of First-line Antibiotic Selection Among US Ambulatory Care Visits for Otitis Media, Sinusitis, and Pharyngitis

- National Ambulatory Medical Care Survey (office based physicians)/National Hospital Ambulatory Medical Care Survey (hospital outpatient and ED)
- Otitis media, sinusitis, pharyngitis – one-third of OP antibiotics
- Percentage of visits that received first line antibiotics
  - Ranged 37% (adult sinusitis, pharyngitis) to 67% (peds OM)
  - All 3 conditions – 52% received first line agents
  - First line therapy more commonly to peds than adults (P<.001)
  - Macrolides most common non first line
  - 80% should be treated with first line therapy (10% PCN allergy, 10% fail first line)
Frequency of First-line Antibiotic Selection Among US Ambulatory Care Visits for Otitis Media, Sinusitis, and Pharyngitis

• Substantial overuse of non first line Rx for 3 most common conditions in ambulatory care collectively account for 40 million prescriptions annually

• Supports that stewardship interventions should address inappropriate antibiotic selection
Healthcare Effectiveness Data and Information Set

HEDIS is a performance measurement tool used by over 90% of the nation’s health plans. HEDIS makes it possible to compare the performance of health plans. CDC and the National Committee on Quality Assurance have written three HEDIS measures related to antibiotic use in outpatient settings.

• The pediatric measures, which were incorporated into HEDIS in 2004, are

• **Appropriate testing for children with pharyngitis**: percentage of children 2 to 18 years of age who were diagnosed with pharyngitis, prescribed an antibiotic and received a group A *Streptococcus* (strep) test for the episode.
  • Nationally, in 2012, mean performance across all health plans was 80% (range 2–97%), compared to a goal of 100%.

• **Appropriate treatment for children with upper respiratory infection (URI)**: percent of children 3 months to 18 years of age with a diagnosis of URI who were not prescribed antibiotics on or three days after the episode date.
  • Nationally, in 2012, mean performance across all health plans was 83% (range 45–99%), compared to a goal of 100%.

• The adult measures, which were incorporated into HEDIS in 2006, are

• **Avoidance of antibiotic treatment in adults with acute bronchitis** (inverted the measure rate and renamed measure for 2008): percent of adults diagnosed with acute bronchitis who were not dispensed an antibiotic prescription.
  • Nationally, in 2012, mean performance across all health plans was 23% (range 7-72), compared to a goal of 100%.
Improving Prescribing

• http://www.cdc.gov/getsmart/community/improving-prescribing/index.html
Interventions that work

• Audit and Feedback
• Academic Detailing
• Clinical Decision Support
• Delayed Prescribing Practices
• Poster-Based Interventions
Audit and Feedback

• Audit and feedback is a system of quality improvement that promotes individualized adherence to evidence-based practices. The most effective methods involving audit and feedback are programs that compare individual clinician prescribing rates to co-workers’ or expected prescribing rates based on clinical practice guidelines. In combination with clinician education, audit and feedback has been shown to be an effective method to improve antibiotic prescribing for common infections among outpatients.
Academic Detailing

Academic detailing is a systematic provision of clinical education for healthcare professionals to reinforce or change prescribing behavior. Though academic detailing has been widely used by pharmaceutical manufacturers to influence prescribing behaviors, it has also been used to improve clinical decision-making to maximize quality of care and cost-effective medicine.

The core tenants of academic detailing involve:

• assessing baseline knowledge;
• focusing efforts on specific clinicians or clinician leaders;
• using active education strategies;
• highlighting and repeating essential messages; and
• using positive reinforcement to reward desired behaviors.

Academic detailing has been shown to limit unnecessary medical costs and reduce inappropriate prescribing
Clinical Decision Support

• Clinical decision support (CDS) provides clinicians with information at specific times during the patient encounter to facilitate accurate diagnoses and treatment. Clinical information, such as signs and symptoms, can be entered electronically or on paper to determine if an antibiotic is needed. CDS has been shown to be effective at reducing inappropriate antibiotic prescribing for common outpatient infections. It is important that messages are clear and concise, and appear during times that do not interrupt workflow or add time pressure to the clinician.
Delayed Prescribing Practices

- Delayed antibiotic prescribing is a strategy in which a patient is asked to wait (usually 24-48 hours) after a clinical visit to determine if an antibiotic is needed for an illness that may not appear to immediately warrant an antibiotic.

- There are several ways to give a delayed antibiotic prescription, including:
  - writing a post-dated prescription;
  - re-contacting a patient after a clinical visit; or
  - providing a prescription and giving a verbal order to fill the prescription after a predetermined length of time if symptoms do not improve.
Poster-Based Interventions

• Appropriate antibiotic use posters on display within a clinical setting can serve several purposes, including educating patients and clinicians, reducing patient expectations for an antibiotic, and advertising clinician commitment to judicious antibiotic prescribing to patients and office staff.
A Commitment to Our Patients about Antibiotics

Antibiotics only fight infections caused by bacteria. Like all drugs, they can be harmful and should only be used when necessary. Taking antibiotics when you have a virus can do more harm than good: you will still feel sick and the antibiotic could give you a skin rash, diarrhea, a yeast infection, or worse.

Antibiotics also give bacteria a chance to become more resistant to them. This can make future infections harder to treat. It means that antibiotics might not work when you really do need them. Because of this, it is important that you only use an antibiotic when it is necessary to treat your illness.

How can you help? When you have a cough, sore throat, or other illness, tell your doctor you only want an antibiotic if it is really necessary. If you are not prescribed an antibiotic, ask what you can do to feel better and get relief from your symptoms.

Your health is important to us. As your healthcare providers, we promise to provide the best possible treatment for your condition. If an antibiotic is not needed, we will explain this to you and offer a treatment plan that will help. We are dedicated to prescribing antibiotics only when they are needed, and we will avoid giving you antibiotics when they might do more harm than good.

If you have any questions, please feel free to ask us.

Sincerely,
Safe Antibiotic Use:
An Important Message From Your Providers

Dear Patient,

We want to give you some important information about antibiotics.

- Antibiotics only fight infections caused by bacteria.
- Antibiotics will NOT help you feel better if you have a viral infection like:
  - Cold or runny nose
  - Bronchitis or chest cold
  - Flu
- If you take antibiotics when you don’t really need them, they can cause more harm than good:
  - You might feel worse
  - You can get diarrhea, rashes, or yeast infections
  - Antibiotics may NOT work when you really need them because antibiotics make bacteria more resistant to them. This can make future infections harder to treat.

What can you do as a patient? Talk with me about the treatment that is best for you. Follow the treatment plan that we discuss.

As your healthcare provider, I will give you the best care possible. I am dedicated to avoid prescribing antibiotics when they are likely to do more harm than good. If you have any questions, please ask me, your nurse, or your pharmacist.

Sincerely,

Provider Name  Provider Name  Provider Name  Provider Name

The best care is the right care. Only use antibiotics when needed.
Example of ideal location

Poster is in clear view.
Example of less desirable location

Cords obstructing view of the poster.
Viruses or Bacteria
What's got you sick?

Antibiotics only treat bacterial infections. Viral illnesses cannot be treated with antibiotics. When an antibiotic is not prescribed, ask your healthcare professional for tips on how to relieve symptoms and feel better.

<table>
<thead>
<tr>
<th>Illness</th>
<th>Usual Cause</th>
<th>Antibiotic Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold/Ruuny Nose</td>
<td>✅ Viruses</td>
<td>NO</td>
</tr>
<tr>
<td>Bronchitis/Chest Cold (in otherwise healthy children and adults)</td>
<td>✅ Viruses</td>
<td>NO</td>
</tr>
<tr>
<td>Whooping Cough</td>
<td>✅ Viruses</td>
<td>Yes</td>
</tr>
<tr>
<td>Flu</td>
<td>✅ Viruses</td>
<td>NO</td>
</tr>
<tr>
<td>Strep Throat</td>
<td>✅ Viruses</td>
<td>Yes</td>
</tr>
<tr>
<td>Sore Throat (except strep)</td>
<td>✅ Viruses</td>
<td>NO</td>
</tr>
<tr>
<td>Fluid in the Middle Ear (otitis media with effusion)</td>
<td>✅ Viruses</td>
<td>NO</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>✅ Viruses</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Antibiotics Aren’t Always the Answer

www.cdc.gov/getsmart
Symptom Relief for Viral Illnesses

Name: ________________________________
Date: ________________________________

Diagnosis:
☐ Cold or Flu
☐ Middle ear fluid (Otitis Media with Effusion, OME)
☐ Cough
☐ Viral Sore Throat
☐ Bronchitis
☐ Other: ________________________________

You have been diagnosed with an illness caused by a virus. Antibiotics do not cure viral infections. If given when not needed, antibiotics can be harmful. The treatments prescribed below will help you feel better while your body’s own defenses are fighting the virus.

General instructions:
☐ Drink extra water and fluids.
☐ Use cool mist vaporizer or saline nasal spray to relieve congestion.
☐ For sore throats in older children and adults, use ice chips, sore throat spray, or lozenges.
☐ Use honey to relieve cough. Do not give honey to an infant less than 1 year of age.

Specific medicines:
☐ Fever or aches: ________________________________
☐ Ear pain: ________________________________
☐ Sore throat and Congestion: ________________________________

Use medicines according to the package instructions or as directed by your healthcare professional. Stop the medication when the symptoms get better.

Follow up:
☐ If not improved in ____ days/hours, if new symptoms occur, or if you have other concerns, please call or return to the office for a recheck.
☐ Phone: ________________________________
☐ Other: ________________________________

Signed: ________________________________

For more information visit www.cdc.gov/getsmart
What is Delayed Prescribing?

WAIT. Do not fill your prescription just yet. Your healthcare professional believes your illness may resolve on its own.

First, follow your healthcare professional’s recommendations to help you feel better without antibiotics and continue to monitor your own symptoms over the next few days.

- Rest
- Drink extra water and fluids
- Use cool mist vaporizer or saline nasal spray to relieve congestion
- For sore throats in older adults and children, try ice chips, sore throat spray, or lozenges

If you do not feel better in ___ days/hours, or get worse, go ahead and fill your prescription.

If you feel better, you do not need the antibiotic, and do not have to risk the side effects.

Waiting to see if you really need an antibiotic can help you take antibiotics only when it is actually necessary. Antibiotics can cause side effects like a skin rash, diarrhea, a yeast infection, or worse.

Antibiotics can also make future bacterial infections stronger and harder to treat. You can protect yourself and others by learning when antibiotics are and aren’t needed.

For more information visit www.cdc.gov/getsma
Core Elements of Outpatient Antibiotic Stewardship

Sanchez GV, Fleming-Dutra KE, Roberts RM, Hicks LA. Core Elements of Outpatient Antibiotic Stewardship. MMWR Recomm Rep 2016;65(No. RR-6):1–12. DOI: http://dx.doi.org/10.15585/mmwr.rr6506a1
Four Core Elements of Outpatient Antibiotic Stewardship

• **Commitment**
  • Commit to improving antibiotic prescribing

• **Action for policy and practice**
  • Implement at least one policy/practice aimed at improving prescribing practices

• **Tracking and reporting**
  • Clinics/Healthcare systems track prescribing practices and regularly report these data back to clinicians

• **Education and expertise**
  • Clinicians provide education/resources to pts & families on appropriate ATB use
  • Clinics/Healthcare systems provide clinicians with education to improve prescribing and access to persons with expertise in antibiotic stewardship
## FIGURE 1. Clinician checklist for core elements of outpatient antibiotic stewardship

CDC recommends that outpatient clinicians take steps to implement antibiotic stewardship activities. Use this checklist as a baseline assessment of policies and practices that are in place. Then use the checklist to review progress in expanding stewardship activities on a regular basis (e.g., annually).

### Commitment

1. Can you demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety related to antibiotics?  
   - Yes  
   - No
   If yes, indicate which of the following are in place.  
     - Write and display public commitments in support of antibiotic stewardship.

### Action

2. Have you implemented at least one practice to improve antibiotic prescribing?  
   - Yes  
   - No
   If yes, indicate which practices which you use. (Select all that apply.)  
     - Use evidence-based diagnostic criteria and treatment recommendations.
     - Use delayed prescribing practices or watchful waiting, when appropriate.

### Tracking and Reporting

3. Do you monitor at least one aspect of antibiotic prescribing?  
   - Yes  
   - No
   If yes, indicate which of the following are being tracked. (Select all that apply.)  
     - Self-evaluate antibiotic prescribing practices.
     - Participate in continuing medical education and quality improvement activities to track and improve antibiotic prescribing.

### Education and Expertise

4. Do you provide education to patients and seek out continuing education on antibiotic prescribing?  
   - Yes  
   - No
   If yes, indicate how you provide antibiotic stewardship education. (Select all that apply.)  
     - Use effective communications strategies to educate patients about when antibiotics are and are not needed.
     - Educate about the potential harms of antibiotic treatment.
     - Provide patient education materials.
FIGURE 2. Facility checklist for core elements of outpatient antibiotic stewardship

CDC recommends that outpatient care facilities take steps to implement antibiotic stewardship activities. Use this checklist as a baseline assessment of policies and practices that are in place. Then use the checklist to review progress in expanding stewardship activities on a regular basis (e.g., annually).

Commitment

1. Can your facility demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety related to antibiotics? [ ] Yes [ ] No

   If yes, indicate which of the following are in place. (Select all that apply.)
   - Identify a single leader to direct antibiotic stewardship activities within a facility.
   - Include antibiotic stewardship-related duties in position descriptions or job evaluation criteria.
   - Communicate with all clinic staff members to set patient expectations.

Action

2. Has your facility implemented at least one policy or practice to improve antibiotic prescribing? [ ] Yes [ ] No

   If yes, indicate which interventions are in place. (Select all that apply.)
   - Provide communications skills training for clinicians.
   - Require explicit written justification in the medical record for nonrecommended antibiotic prescribing.
   - Provide support for clinical decisions.
   - Use call centers, nurse hotlines, or pharmacist consultations as triage systems to prevent unnecessary visits.

Tracking and Reporting

3. Does your facility monitor at least one aspect of antibiotic prescribing? [ ] Yes [ ] No

   If yes, indicate which of the following are being tracked. (Select all that apply.)
   - Track and report antibiotic prescribing for one or more high-priority conditions.
   - Track and report the percentage of all visits leading to antibiotic prescriptions.
   - (If already tracking and reporting one of the above) Track and report, at the level of a health care system, complications of antibiotic use and antibiotic resistance trends among common outpatient bacterial pathogens.
   - Assess and share performance on quality measures and established reduction goals addressing appropriate antibiotic prescribing from health care plans and payers.

Education and Expertise

4. Does your facility provide resources to clinicians and patients on evidence-based antibiotic prescribing? [ ] Yes [ ] No

   If yes, indicate how your facility provides antibiotic stewardship education. (Select all that apply.)
   - Provide face-to-face educational training (academic detailing).
   - Provide continuing education activities for clinicians.
   - Ensure timely access to persons with expertise.
"Half of everything we teach you is wrong... unfortunately, we don't know which half."

Earliest citation of similar content:
James Boswell’s *Life of (Samuel) Johnson* published 1791
Myth Busting
Five Myths Debunked


- **Humans invented antibiotics in the 20th century**
  - After 2 billion years of microbial evolutionary warfare, microbes have already invented antibiotics to poison every possible biochemical pathway, and resistance mechanisms to protect every one of those pathways

- **Inappropriate antibiotic use causes the development of resistance**
  - Appropriate use applies the same selective pressure as does inappropriate use. The difference is that we can and should stop inappropriate use because it offers no benefit. In contrast, appropriate antibiotic use is necessary to reduce mortality and morbidity from bacterial infections

- **To prevent resistance, patients must complete every dose of antibiotics prescribed, even after they feel better**
  - Patients should be told that if they feel substantially better, with resolution of symptoms of infection, they should call the clinician to determine whether antibiotics can be stopped early. Clinicians should be receptive to this concept, and not fear customizing the duration of therapy.

- **When antibiotic resistance emerges, it is usually a consequence of new mutations at the site of infection**
  - After exposure to antibiotics, somewhere in the patient's body, strains of normal flora that are resistant to the antibiotics used have been enriched. Those strains can cause future infections, or spread to others in communities or hospitals.

- **Cidal antibiotics result in superior clinical outcomes and less risk for emergence of resistance than do static antibiotics**
  - Whether an antibiotic is static or cidal should not be a factor in determining antibiotic therapy for patients.
**Table. Infections for Which Short-Course Therapy Has Been Shown to Be Equivalent in Efficacy to Longer Therapy**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatment, Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired pneumonia, nosocomial pneumonia, pyelonephritis</td>
<td>3-5 7-10</td>
</tr>
<tr>
<td>Intraabdominal infection</td>
<td>4 10</td>
</tr>
<tr>
<td>Acute exacerbation of chronic bronchitis and COPD</td>
<td>≤5  ≥7</td>
</tr>
<tr>
<td>Acute bacterial sinusitis</td>
<td>5  10</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>5-6 10</td>
</tr>
<tr>
<td>Chronic osteomyelitis</td>
<td>42  84</td>
</tr>
</tbody>
</table>

Abbreviation: COPD, chronic obstructive pulmonary disease.
Top 10 Tips for Wise Antimicrobial Prescribing

1. In general, beta-lactams (esp. penicillins and cephalosporins) are preferred agents when multiple options exist (with respect to efficacy, cost, and safety).

2. Antibiotics with excellent oral bioavailability can be used for most infections (if patients can swallow them) - e.g., cephalexin, amoxicillin-clavulanate, metronidazole, azithromycin, TMP-SMX and quinolones.

3. Non-purulent cellulitis, even in patients with diabetes, is almost always caused by beta-hemolytic streptococci or S.aureus and should be treated with cephalexin or cefazolin.

4. *Staphylococcus aureus* bacteremia must **ALWAYS** be treated with at least 2 weeks of IV antibiotics. It is **NEVER** a contaminant in blood.

5. The likelihood of infection with MRSA in a patient who has recently screened negative is low... thus, vancomycin is generally unnecessary as empiric therapy for non-life-threatening S. aureus infections.

6. Ciprofloxacin resistance is ~30% in urinary isolates of E.coli in patients presenting to emergency departments making this drug a poor choice for empiric treatment of urinary tract infections.

7. Except in rare circumstances (e.g., fever during chemotherapy-induced neutropenia), patients presenting with community-acquired infections **DO NOT** require empiric Pseudomonas coverage (e.g., piperacillin-tazobactam).

8. Any antimicrobial can be associated with the development of C.difficile infection, although clindamycin and fluoroquinolones are **MAJOR** culprits. Avoid unnecessary antimicrobials and, when needed, consider alternative agents.

9. Most patients who report a penicillin allergy **DO NOT** have a true allergy. A thorough allergy history should be taken in all patients and those with non-life threatening reactions (e.g., rash or GI upset) can safely be given a trial of cephalosporins.

10. With the exception of pregnant women and patients undergoing urologic procedures, asymptomatic bacteriuria does not need treatment.
Alternatives to Fluoroquinolones:
U.S Food and Drug Administration medication safety alert

The FDA, as of July 2016, has approved changes to the labeling of systemic fluoroquinolones to include a Boxed Warning initially announced in May 2016 that the **risks of serious side effects associated with the antibiotics generally outweigh the benefits** due to potentially permanent, disabling serious side effects. This warning is especially true in patients with other treatment options for acute bronchitis, acute sinusitis and uncomplicated urinary tract infections.

This is not the first warning released by the FDA safety review for fluoroquinolones.

- **July 2008**: Boxed warning release for increased tendinitis and tendon rupture
- **February 2011**: Boxed warning release on the risk of worsening symptoms for those with myasthenia gravis
- **August 2013**: Updates to the label for risk of irreversible peripheral neuropathy
- **November 2015**: FDA advisory committee initially announced that the serious risks associated with use of fluoroquinolones outweighed the benefit for uncomplicated infections with other treatment options.

The FDA safety review has associated fluoroquinolones with disabling and potentially permanent serious side effects involving the tendons, muscles, joints, nerves and central nervous system. These side effects can occur hours to weeks after exposure to fluoroquinolones and may potentially be permanent.

**For this reason the FDA is urging health care professionals to stop systemic fluoroquinolone treatment immediately, especially when alternative agents are available for use.**
Fluoroquinolones Not First Line

- Late 1980s – “wonder drugs”
- Widely embraced
- Little diminishment in use in ambulatory settings for uncomplicated UTI and respiratory tract infection
- No longer useful for gonorrhea, uncomplicated cystitis
- Adverse effects: *C difficile* infection, tendinopathy, arthropathy, QT prolongation, retinal issues, central and peripheral nervous system toxicities.
- FDA warnings accumulating. Latest May 2016. Recommendation to avoid use in ambulatory settings for respiratory and urinary tract infections
- “It does not make sense to prescribe these drugs, which have quite broad-spectrum activity, to treat conditions that could be treated with a narrower-spectrum and more targeted drug”
Effective Communication Strategies

• **Gain trust**
• **Empathize**
• **Take time to elicit expectations**
• **Share findings (reassuring components of exam, results)**
• **Make your diagnosis specific (avoid dismissive statements)**
• **Articulate the next step (expectations, contingency plan)**
• **Resist antibiotics (educate, reassure)**
• **Treat (give specific instructions for symptomatic relief, ATB duration)**
| Common cold or non-specific upper respiratory tract infection (URI)⁶,⁷ | The common cold is the third most frequent diagnosis in office visits, and most adults experience two to four colds annually. At least 200 viruses can cause the common cold. | Prominent cold symptoms include fever, cough, rhinorrhea, nasal congestion, postnasal drip, sore throat, headache, and myalgias. | Decongestants (pseudoephedrine and phenylephrine) combined with a first-generation antihistamine may provide short-term symptom relief of nasal symptoms and cough. Non-steroidal anti-inflammatory drugs can be given to relieve symptoms. Evidence is lacking to support antihistamines (as monotherapy), opioids, intranasal corticosteroids, and nasal saline irrigation as effective treatments for cold symptom relief. Providers and patients must weigh the benefits and harms of symptomatic therapy. |
The course of most uncomplicated viral URIs is 5 to 10 days. Most patients with viral URI are afebrile. If fever is present, it tends to occur on the first two days of illness, in concert with constitutional symptoms (e.g., headache, myalgia). As fever and/or constitutional symptoms resolve, respiratory symptoms become more prominent, peaking in severity on days three to six of illness. Respiratory symptoms may continue to be present on day 10 of illness, but are less severe than earlier in the course.
Common Cold, Non-specific URI – Tips and Pearls

• Third most frequent diagnosis in office visits
• Prominent symptoms: Fever, cough, rhinorrhea, nasal congestion, postnasal drip, sore throat, headache and myalgias
• Secretions will appear purulent and thick. Not an indication for antibiotics
• Symptomatic therapy: decongestants +/- 1st gen antihistamines, NSAIDS
• Evidence lacking: antihistamine alone, opioids, intranasal steroids, nasal saline irrigation
• Potential harm: cough/cold meds in children < 6 yo (top 20 substances leading to death in children < 5 yo)
<table>
<thead>
<tr>
<th>Condition</th>
<th>Epidemiology</th>
<th>Diagnosis</th>
<th>Management</th>
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| Acute rhinosinusitis | About 1 out of 8 adults (12%) in 2012 reported receiving a diagnosis of rhinosinusitis in the previous 12 months, resulting in more than 30 million diagnoses. Ninety-98% of rhinosinusitis cases are viral, and antibiotics are not guaranteed to help even if the causative agent is bacterial. | Diagnose acute bacterial rhinosinusitis based on symptoms that are:  
  o Severe (>3-4 days), such as a fever ≥39°C (102°F) and purulent nasal discharge or facial pain;  
  o Persistent (>10 days) without improvement, such as nasal discharge or daytime cough; or  
  o Worsening (3-4 days) such as worsening or new onset fever, daytime cough, or nasal discharge after initial improvement of a viral upper respiratory infections (URI) lasting 5-6 days.  
   Sinus radiographs are not routinely recommended. | If a bacterial infection is established:  
   - Watchful waiting is encouraged for uncomplicated cases for which reliable follow-up is available.  
   - Amoxicillin or amoxicillin/clavulanate is the recommended first-line therapy.  
   - Macrolides such as azithromycin are not recommended due to high levels of Streptococcus pneumoniae antibiotic resistance (~40%).  
   - For penicillin-allergic patients, doxycycline or a respiratory fluoroquinolone (levofloxacin or moxifloxacin) are recommended as alternative agents. |
<table>
<thead>
<tr>
<th>Table 1. Clinical Criteria for the Diagnosis of Acute Bacterial Sinusitis.</th>
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<tbody>
<tr>
<td>Persistent symptoms</td>
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<tr>
<td>- Nasal congestion, rhinorrhea, or cough</td>
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<td>- $\geq 10$ Days’ duration without improvement</td>
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<tr>
<td>Severe symptoms</td>
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<td>- Temperature $\geq 38.5^\circ C$ for 3–4 days</td>
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<tr>
<td>- Purulent rhinorrhea for 3–4 days</td>
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<tr>
<td>Worsening symptoms</td>
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<tr>
<td>- Return of symptoms after initial resolution</td>
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<tr>
<td>- New or recurrent fever, increase in rhinorrhea, or increase in cough</td>
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</table>
Time to eradication of pathogens from the maxillary sinus

- S. pneumoniae (23)
- H. influenzae (26)
- M. catarrhalis (8)
Acute Rhinosinusitis - Tips and Pearls

• 90-98% viral

• Diagnose bacterial rhinosinusitis based on symptoms that are severe, persistent or worsening

• If bacterial
  • Watchful waiting
  • Amoxicillin/clavulanate
  • Avoid macrolides
  • PCN allergic: Doxycycline or, as a last resort, fluoroquinolone, avoid monotherapy with 2nd/3rd gen cephalosporin
  • Treat 5 days
<table>
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<tr>
<th>Pharyngitis</th>
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</table>
| • Group A beta-hemolytic streptococcal (GAS) infection is the only common indication for antibiotic therapy for sore throat cases.  
• Only 5–10% of adult sore throat cases are caused by GAS. | • Clinical features alone do not distinguish between GAS and viral pharyngitis; a rapid antigen detection test (RADT) is necessary to establish a GAS pharyngitis diagnosis  
• Those who meet two or more Centor criteria (e.g., fever, tonsillar exudates, tender cervical lymphadenopathy, absence of cough) should receive a RADT. Throat cultures are not routinely recommended for adults. | • Antibiotic treatment is NOT recommended for patients with negative RADT results.  
• Amoxicillin and penicillin V remain first-line therapy due to their reliable antibiotic activity against GAS.  
• For penicillin-allergic patients, cephalexin, cefadroxil, clindamycin, or macrolides are recommended.  
• GAS antibiotic resistance to azithromycin and clindamycin are increasingly common.  
• Recommended treatment course for all oral beta lactams is 10 days. |
Adult Pharyngitis – Tips and Pearls

• Group A Strep (GAS) is the only common indication for ATB in sore throat
• Only 5-10% adult sore throats caused by GAS
• Clinical features do not distinguish between GAS and viral
• Rapid antigen detection test (RADT) if two or more of:
  • (Centor criteria) Fever, tonsillar exudates, tender cervical LAN, absence of cough
• Throat cultures not recommended for adults
• Negative RADT => No antibiotic
• Positive RADT =>
  • First line: amoxicillin, PCN VK (10 days)
  • PCN allergic: cephalexin, (clindamycin & macrolides have increasing GAS resistance)
Additional tips and pearls for pediatric pharyngitis

- Winter/spring up to 20% asymptomatic children colonized with GAS => false positive RADT
- Streptococcal pharyngitis – primarily 5 – 15 yo, rare in preschool age
- Don’t test children < 3 yo in whom GAS rarely causes pharyngitis and rheumatic fever is uncommon.
- If 2 or more Centor criteria are met => RADT
- RADT +, treat without culture
- RADT negative, send back up culture
| Acute uncomplicated bronchitis\textsuperscript{3-5} | • Cough is the most common symptom for which adult patients visit their primary care provider, and acute bronchitis is the most common diagnosis in these patients. | • Evaluation should focus on ruling out pneumonia, which is rare among otherwise healthy adults in the absence of abnormal vital signs (heart rate $\geq$ 100 beats/min, respiratory rate $\geq$ 24 breaths/min, or oral temperature $\geq$ 38 °C) and abnormal lung examination findings (focal consolidation, egophony, fremitus). Colored sputum does not indicate bacterial infection. For most cases, chest radiography is not indicated. | Routine treatment of uncomplicated acute bronchitis with antibiotics is not recommended, regardless of cough duration. Options for symptomatic therapy include:  
• Cough suppressants (codeine, dextromethorphan);  
• First-generation antihistamines (diphenhydramine);  
• Decongestants (phenylephrine); and  
• Beta agonists (albuterol). |
Acute Uncomplicated Bronchitis – Tips and Pearls

• Most common diagnosis in patients who present with cough
• Evaluation focus: R/O pneumonia which is rare in the absence of abnormal vital signs/exam
• Colored sputum does not indicate bacterial infection
• Antibiotics are not recommended regardless of cough duration
• Symptomatic therapy
| Acute uncomplicated cystitis | Cystitis is among the most common infections in women and is usually caused by *E. coli*. | Classic symptoms include dysuria, frequent voiding of small volumes, and urinary urgency. Hematuria and suprapubic discomfort are less common. Nitrites and leukocyte esterase are the most accurate indicators of acute uncomplicated cystitis. | For acute uncomplicated cystitis in healthy adult non-pregnant, premenopausal women:
- Nitrofurantoin, trimethoprim/sulfamethoxazole (TMP-SMX, where local resistance is <20%), and fosfomycin are appropriate first-line agents.
- Fluoroquinolones (e.g. ciprofloxacin) should be reserved for situations in which other agents are not appropriate. |
Acute Uncomplicated Cystitis – Tips and Pearls

• 75-95% E coli

• Nitrofurantoin 100mg po BID X 5 days
  • Advantages: higher sensitivity of E coli, less disruption of microbiome, updated Beers criteria 2015: use in CrCl >30
  • Disadvantage: Not effective in the renal parenchyma (if pyelo is considered)

• TMP/SMX DS po BID X 3 days

• Fosfomycin 3g po X1, sensitivity testing not routinely available

• Avoid fluoroquinolones
Asymptomatic Bacteriuria – Tips and Pearls

• Avoid treatment
• Neither pyuria nor growth in culture are criteria to treat
• Two exceptions: pregnant women and prior to GU procedure
Unintended consequences of antimicrobial misuses can include the following:

a) Adverse events
b) Clostridium difficile infections
c) Emergence of drug resistance
d) Allergic reactions
e) All of the above
The bacterial species most commonly associated with cutaneous abscesses is:

a) Staphylococcus aureus
b) Streptococcus pyogenes
c) Coagulase-negative Staphylococcus species
d) Escherichia coli
e) All of the above
The recommended clinical management of a healthy adult with a cutaneous abscess located in an accessible region, depending on such factors as the size of the lesion and the presence or absence of systemic symptoms, is:

a) Incision and drainage alone
b) Antibiotics alone
c) Incision and drainage plus antibiotics
d) A or C
Pyuria can be used to differentiate urinary tract infection (UTI) from asymptomatic bacteriuria.

a) True
b) False
The 2005 Infectious Diseases Society of America (IDSA) guidelines support the screening and treatment of asymptomatic bacteriuria in the following types of patients:

a) Pregnant women
b) Non-pregnant women of child-bearing age
c) Patients about to undergo an invasive genitourinary procedure
d) A and C
The bacterial species most commonly associated with uncomplicated urinary tract infections in women is:

a) Staphylococcus saprophyticus
b) Pseudomonas aeruginosa
c) Klebsiella pneumonia
d) Escherichia coli
e) All of the above
According to the 2010 Infectious Diseases Society Guidelines, the recommended first line agents for treating uncomplicated urinary tract infections in women include all of the following EXCEPT:

a) Nitrofurantoin
b) Fosfomycin
c) Trimethoprim-sulfamethoxazole if the prevalence of E coli resistance to it is smaller than 20%
d) Fluoroquinolones
The bacterial species most commonly associated with non-purulent cellulitis is:

a) Staphylococcus aureus  
b) Beta-hemolytic streptococci, including Streptococcus pyogenes  
c) Coagulase-negative Staphylococcus species  
d) Escherichia coli  
e) All of the above
Which of the following would be an appropriate orally administered option for a non-allergic, non-toxic otherwise healthy patient with non-purulent cellulitis?

a) Cephalexin
b) Amoxicillin/clavulanate
c) Moxifloxacin
d) Azithromycin
What is the prevalence of group A streptococcus pharyngitis in adults with sore throats in the U.S.?

a) 0-5%
b) 5-15%
c) 15-25%
d) 25-35%
What is the recommended duration of antibiotic therapy for acute bacterial rhinosinusitis?

a) 5-10 days
b) 11-14 days
c) 15-21 days
d) >21 days
All of the following are examples of effective communication strategies that could be used to discuss antibiotic decisions with patients EXCEPT:

a) Show empathy
b) Share reassuring physical exam findings
c) Communicate that they just have a viral infection
d) Provide a contingency plan