Antibiotic Use and Resistance
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Introduction
Antibiotics are essential in the fight against infectious diseases. When antibiotic resistance to antibiotics emerged, developing new antibiotics was thought to be the solution to that problem. However, after the development of numerous antibiotics, antibiotic resistance still remains a problem today and the pipeline of new antibiotics has slowed.¹

Each year in the United States, it is estimated at least 2 million people become infected by antibiotic-resistant bacteria with at least 23,000 deaths resulting from those infections.² Antibiotic resistance is quickly becoming a major public health concern because it may lead to multi-drug resistant infections that become essentially untreatable.¹,² Current data indicates most antibiotic-resistant infections occur in the community, while the majority of the deaths related to antibiotic resistance occur in hospitals and nursing home settings.² In addition to the clinical significance, these infections are also costly because they often result in extended hospitalizations, frequent doctor office visits, more expensive and/or prolonged courses of antibiotics, and can lead to greater disability and death when compared to infections caused by non-resistant bacteria.¹,² Although there are many factors involved in the development of resistance, inappropriate antibiotic use is the single most factor leading to antibiotic resistance not only in the United States but worldwide.²

Antibiotic Prescribing
Antibiotics are among the most commonly prescribed medicines, however, the Infectious Disease Society of America (IDSA) states that "up to half of antibiotic use is unnecessary or inappropriate".⁴ Data from the National Ambulatory and National Hospital Ambulatory Medical Care Surveys found that 25% of prescriptions written during outpatient ambulatory and emergency department visits between 2007-2009 were for conditions in which antibiotics are rarely indicated.⁵ In the United States, prescription rates for viral upper respiratory tract infections are estimated between 40% and 75%.⁶

In addition to promoting resistance, there are other risks associated with antibiotic use. These include: adverse effects, allergic reactions, and interactions with other medications.²,⁵ Adverse drug reactions from antibiotics account for an estimated 1 out of every 5 emergency room department visits with allergic reactions accounting for approximately 79% of those adverse reactions.² The development of C. difficile diarrhea, which is directly related to antibiotic use, is another negative consequence of antibiotic usage and is associated with high morbidity and mortality, especially in older patients.² Inappropriate overuse of antibiotics increases the chance for antibiotic resistance by allowing the bacteria that are resistant to the agent to proliferate.⁷ Antibiotic resistance is not an issue that has a simple solution. Combating it will require cooperation of healthcare providers as well as the public.

Broad-Spectrum and Narrow-Spectrum Antibiotics
Antibiotics are classified in many ways, but one common way they are differentiated is as broad-spectrum vs. narrow-spectrum agents.⁸ Narrow-spectrum antibiotics are active against a select group of bacteria (e.g., amoxicillin, sulfonamides, first generation cephalosporins),
and are typically used when the causative agent of an infection is known. Broad-spectrum antibiotics are active against a wide range of bacterial species (e.g., amoxicillin/clavulanate, fluoroquinolones, macrolides, and second and third generation cephalosporins) and are the most commonly prescribed antibiotics in the ambulatory setting. They will attack both pathogenic organisms and the body’s normal bacterial flora. Broad-spectrum antibiotics are useful when the cause of an infection is resistant to narrow-spectrum agents. They are also used as empiric therapies, prior to the identification of the causative bacteria. In the latter case, therapy should be changed to narrow-spectrum agents whenever possible to minimize the impact on the normal bacterial flora and resultant overgrowth of resistant bacteria.

**Antibiotic Resistance**

Bacterial microorganisms can have intrinsic or acquired resistance to antibiotics. Intrinsic resistance has always been present in some species due to the nature of the drug and the microorganism. Intrinsic resistance may also develop as a result of spontaneous genetic mutations. Acquired resistance develops as a result of a mutation within a genome induced by antibiotic exposure or by a genetic transfer from other microorganisms via plasmids. There are four general mechanisms of acquired antibiotic resistance as outlined in Table 1.

Acquired resistance is facilitated by widespread use of antibiotics, both in humans and in animals. Any use of antibiotics potentially results in selective pressure on a bacteria population as susceptible organisms die and resistant bacteria thrive. As resistant bacteria reproduce, a fully resistant colony may be formed. The World Health Organization, IDSA and CDC cites inappropriate use of antibiotics as one of the major causes of antibiotic resistance.

<table>
<thead>
<tr>
<th>Table 1: Mechanisms of Acquired Antimicrobial Resistance</th>
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<tbody>
<tr>
<td><strong>Mechanism of Resistance</strong></td>
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<tr>
<td>Drug Inactivation or Modification</td>
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<tr>
<td>Alteration of Target Site</td>
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<tr>
<td>Alteration of Metabolic Pathway</td>
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<td>Reduced Drug Accumulation</td>
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Recently, the CDC identified four core actions to combat the spread antibiotic resistance. These include: preventing infections from occurring and preventing resistant bacteria from spreading, tracking resistant bacteria, improving the use of antibiotics, and promoting the development of new antibiotics and new diagnostic tests for resistant bacteria.

**Inappropriate Use of Antibiotics**

Antibiotics can be inappropriately used in many ways. Inappropriate antibiotic choice, incorrect dose, incorrect duration of therapy, or inappropriate indication are all factors that increase the likelihood of antibiotic resistance. It is just as important to know when to use antibiotics and when not to use them as it is to know how to use them. For instance, antibiotics are not generally recommended in upper respiratory tract infections or acute bronchitis as they are typically of viral origin. However, respiratory disorders are among the most common condition for which antibiotics are prescribed. One study, which included data from 238,624 ambulatory visits between 2007-2009, found antibiotics were prescribed for 51% of acute respiratory tract infection visits for which antibiotics are rarely indicated. Of these prescriptions, almost 80% were written for broad-spectrum antibiotics, largely driven by prescriptions for fluoroquinolones and macrolides. Antibiotics are also usually not required in mild to moderate cases of acute rhinosinusitis, although if symptoms persist beyond seven days or are severe, they may be of benefit. Additionally, acute pharyngitis should only be treated with antibiotics if it is caused by Group A beta-hemolytic streptococcus. More information about when and when not to use antibiotics in common outpatient infections are provided in Table 2.

In some instances, prescriptions for antibiotics are written based on the patient’s perception that an antibiotic is needed. Data within a pediatric setting found physicians prescribed antibiotics for children 62% of the time if they perceived parents expected antibiotics, but only 7% of the time if they felt the parents did not expect them. Materials to help
educate patients in lieu of prescribing antibiotics when they are not indicated and other information specifically for healthcare providers regarding antibiotic resistance can be found at the CDC’s Get Smart website.\textsuperscript{12}

**Appropriate Antibiotic Use**

In addition to not using antibiotics when they are not likely to have a significant impact on course of illness, it is important to appropriately use them when they are indicated. The following are some general principles of appropriate antibiotic use.\textsuperscript{1,2,8} In many situations, samples for culture and sensitivity or diagnostic testing should be obtained before starting a course of antibiotic therapy. If therapy is started before culture results are available, such results should prompt changes in the agent selected and course of therapy when they become available, if changes are indicated. The antibiotic with the narrowest spectrum that will be effective should always be used and monotherapy promotes less resistance than combination therapy. Antibiotic pharmacokinetic and pharmacodynamic principles should be taken into account and antibiotics should be used at an effective dose for the shortest duration necessary to resolve the infection. Additionally, appropriate antibiotic selection should be guided by clinical practice guidelines, antibiograms, and local surveillance systems information about resistance patterns.\textsuperscript{1,2}

Even though appropriate antibiotic usage is an important factor in reducing antibiotic resistance, preventing infection before it even occurs limits the usage of antibiotics. Approaches to infection prevention include: proper handwashing, infection tracking, safe food handling and preparation, identification and educating patients at high risk for infections, and vaccination (e.g., pneumococcal conjugate vaccine [PCV-13] and influenza).\textsuperscript{1,2}

**Conclusion**

Antibiotic resistance is a growing problem and concern. Because spontaneous mutations are unavoidable it will remain a problem, but appropriate use of antibiotics and infection prevention measures can help to slow the development of resistant microorganisms and prevent the spread of resistant bacteria. In addition to health care providers, the public must also play a role in helping to minimize antibiotic resistance. They should be educated about when antibiotics are and are not appropriate in their care. They should also be encouraged to use their prescribed antibiotics carefully and appropriately, not missing doses and completing a prescribed course as directed rather than stopping when they start to feel better and saving the remaining supply for the next time they get sick. Appropriate antibiotic use must be a team effort involving health care providers and the public we care for. However, health care providers must take the lead in providing education rather than medication when antibiotics are not indicated and providing appropriate guidance related to appropriate use when they are.

For additional information on Antibiotic Resistance and patient education materials, please visit the following websites:

- Centers for Disease Control Get Smart Program [http://www.cdc.gov/getsmart/](http://www.cdc.gov/getsmart/)

To report medical fraud, contact the Medicaid Quality Assurance Bureau. NM Medicaid Fraud@state.nm.us or (505) 827-3100. We appreciate your continued support of our efforts to encourage quality care for our Medicaid clients.

Questions and/or comments about this newsletter may be directed to Diana Moya, R.Ph. at (505) 827-3174 or DianaJ.Moya@state.nm.us. DUR newsletters are posted on the New Mexico Human Services Department website: [http://www.hsd.state.nm.us/mad/PPharmacy.html](http://www.hsd.state.nm.us/mad/PPharmacy.html).
References


17. Braman SS. Chronic cough due to acute bronchitis. ACCP evidenced-based clinical practice guidelines. Chest 2006;129;95S-103S.

**Upper Respiratory Tract Infections (URTI)**

- Usually viral in origin with symptoms lasting 10-14 days, rarely associated with complications, and antibiotics offer no benefit.
- Antibiotics do not shorten the duration of illness or prevent complications.
- Purulent nasal/throat secretions alone do not predict bacterial infection or benefit from antibiotics.
- Consider influenza and pneumococcal vaccines in high-risk patients.

**Acute Bacterial Rhinosinusitis (ABRS)**

- Most ambulatory cases are caused by uncomplicated viral URTIs.
- Adult
  - Patients that may benefit from antibiotics include: persistent symptoms lasting > 7-10 days without improvement; severe symptoms (i.e., high fever, purulent nasal discharge or facial pain) lasting for at least 3-4 days at the beginning of an illness; OR onset of new fever, headache, or increase of worsening nasal discharge following a typical URTI that were initially improving.
  - Standard dose AMOX/clavulanate or either doxycycline or respiratory quinolone (levofloxacin, moxifloxacin), if PCN-allergic, are reasonable first-line agents in patients with uncomplicated ABRS. Macrolides and trimethoprim/sulfamethoxazole are no longer recommended for empiric therapy based on high rates of resistance.
  - High dose AMOX/clavulanate (2 g orally twice daily) is recommended in certain patients*
- Child
  - ABRS is likely when patients with a URTI present with: persistent illness (i.e., nasal discharge of any quality and/or daytime cough) > 10 days without improvement; worsening or new onset of symptoms after initial improvement; OR severe symptom onset > 3 consecutive days (i.e., fever >102.2°F and purulent nasal discharge).
  - Antibiotics should be prescribed in patients with severe onset and worsening course ABRS, while antibiotics OR a 3-day additional observation can be offered to children with persistent illness.
  - AMOX +/- clavulanate is recommended as first-line therapy. If penicillin-allergic, cefdinir, cefuroxime, cefpodoxime, a combination of clindamycin (or linezolid) and cefixime, or levofloxacin can be used.
  - High dose AMOX/clavulanate (90 mg/kg/d twice daily) is recommended in certain patients*

* Patients from regions with high endemic rates of invasive PCN non-susceptible *S. pneumoniae*, severe infection, attend daycare, aged < 2 or >65 years, have recent hospitalization or antibiotic exposure, or are immunocompromised.

**Acute Pharyngitis**

- Antibiotics should be given only to patients with Group A beta-hemolytic streptococcal (GABHS) pharyngitis; only 5-15% of adult acute pharyngitis cases and 20-30% of pediatric cases are caused by GABHS.
- Rapid antigen diagnostic testing and/or culture should be performed because often clinical features alone do not reliably discriminate between GABHS and viral pharyngitis.
- PCN or AMOX is preferred treatment. If PCN-allergic, a first-generation cephalosporin (if not anaphylactically sensitive), clindamycin, clarithromycin, or azithromycin are recommended.
- Analgesics, antipyretics, and supportive care should be offered.

**Acute Bronchitis**

- Most acute bronchitis cases (> 90%) are caused by viruses; antibiotics are not recommended regardless of the duration of the cough.
  - If cough lasts > 3 weeks or the patient has fever, tachypnea, tachycardia, or evidence of consolidation on chest exam, consider chest radiography.
  - Antibiotics are indicated for suspected or confirmed pertussis; first line agents are macrolides or trimethoprim/ sulfamethoxazole.

**Acute Otitis Media (AOM)**

- Antibiotics should be prescribed for AOM in children > 6 months with severe signs and symptoms (i.e., moderate to severe otalgia for at least 48hrs or temperature >102.2°F) and for bilateral AOM in children < 24 months without severe signs and symptoms.
- Observation with close follow-up may be appropriate for patients with non-severe signs and symptoms and are 6 to 23 months with unilateral AOM or are > 24 months with unilateral or bilateral AOM.
- High dose AMOX (80-90 mg/kg/day) is the first-line agent. High dose AMOX/clavulanate should be used if the patient received AOMO within the last 30 days, has concurrent conjunctivitis, or if coverage for a β-lactamase positive organism is needed.
- If PCN-allergic, cefdinir, cefpodoxime, cefuroxime or a macrolide may be used.
- Antibiotics are not indicated for otitis media with effusion in the absence of clinical symptoms.
- Prophylactic antibiotics should not be prescribed to reduce the risk of AOM in children with recurrent AOM.

Abbreviations: PCN: Penicillin; AMOX: Amoxicillin

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**Table 2: Recommendations for Antibiotic Use in Common Outpatient Conditions**
Antibiotic Use and Resistance
Provider Response Form

We would greatly appreciate if you would answer the following questions and return it fax to: 804-644-4241. Thank you for your professional consideration.

1. What is your area of practice?
   _____A. General Family Practice
   _____B. Pediatrician
   _____C. Psychiatrist
   _____D. Specialty Please specify: ________________________________

2. Did you find this newsletter to be informative?
   _____A. Yes
   _____B. No

3. Did the information affect the way you practice?
   _____A. Yes
   _____B. No
   Explain: ____________________________________________________________
   _________________________________________________________________

Please share any drug topic suggestions you would like to address by a newsletter.
__________________________________________________________________
__________________________________________________________________