Antibiotic Stewardship and Overcoming Antibiotic Resistance in Upper Respiratory Tract Infections

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Antibiotic Stewardship and Overcoming Antibiotic Resistance in Upper Respiratory Tract Infections

Katherine Elsass, Austin Hilverding, Steven Blake, Brendan Rasor, Steven N. Leonard, PharmD

This knowledge-based activity is targeted for all pharmacists and is acceptable for 1.0 hour (0.1 CEU) of continuing education credit. This course requires completion of the program evaluation and at least a 70 percent grade on the program assessment questions.

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To complete the continuing education program and receive credit, please go to www.raabecollegeofpharmacy.org/PAW/.

Objectives

After completion of this program, the reader should be able to:

1. Describe changes outlined in the new CDC/ACP Acute Respiratory Tract Infection in Adults guidelines.
2. Evaluate human factors contributing to the spread of antibiotic resistance.
3. Recognize inappropriate use of antimicrobial agents.
4. Apply IDSA recommendations for ideal antimicrobial stewardship.
5. Describe the role of the pharmacist in antimicrobial stewardship.

Abstract

Antibiotic resistance has rapidly become one of the most significant challenges facing modern health care. Despite widespread public education efforts by the national government and health organizations worldwide, there remains a significant lack of public understanding of antibiotic resistance, how to prevent it and the implications if the science and health care communities fail to find a solution. The Centers for Disease Control and Prevention (CDC) in concert with the American College of Physicians (ACP) recently published updated guidelines for appropriate antibiotic use in upper respiratory tract infections. These guidelines include several key recommendations for acute bronchitis, pharyngitis and acute rhinosinusitis (including the common cold). In the United States, at least 2 million antibiotic-resistant illnesses and 23,000 deaths occur each year. These illnesses and deaths result in a large cost to patients, payers and health care institutions. Recent research has shown that numerous human factors, such as patient satisfaction and pressure on prescribers, have an impact on inappropriate antibiotic prescribing. The Infectious Diseases Society of America (IDSA) has published information on the key elements of a model antimicrobial stewardship program. Pharmacists can use this information to help reduce inappropriate use of antibiotics and reduce the spread of antimicrobial resistance.

Key Terms

Anti-infective Agents; Drug Resistance; Microbial, Pharmacists; Respiratory Tract Infections

Introduction

Antibiotic resistance has rapidly become one of the most significant challenges facing modern health care. Patients and policy makers, as well as drug manufacturers and health care providers, all stand to be adversely impacted by resistance. Despite widespread public education efforts by the national government and health organizations worldwide, there remains a significant lack of public understanding of antibiotic resistance, how to prevent it and the implications if the science and health care communities fail to find a solution. New antibiotics are being developed at record low rates, while inappropriate prescribing and excessive agricultural use continue to fuel the spread of drug-resistant species. As a follow up to the Spring 2015 article on resistance, this article further explores the topic with emphasis on recent guidelines, additional factors contributing to resistance and an expanded discussion on the pharmacist's role in minimizing the development of resistance.

Guideline Update

The Centers for Disease Control and Prevention (CDC) in concert with the American College of Physicians (ACP) recently published guidelines for appropriate antibiotic use in adults with acute respiratory tract infections. Inappropriate prescribing of antibiotics leads to thousands of adverse reactions, many deaths and billions of health care dollars spent each year. The publication updates guidelines from 2001 that stated, "Antibiotic treatment of adults with nonspecific upper respiratory tract infection does not enhance illness resolution and is not recommended." The updated guidelines specifically describe appropriate antibiotic use in four acute upper respiratory tract infections.

Acute Bronchitis

The vast majority of bronchitis cases are viral in nature, and the guidelines recommend against routine testing for nonviral causes. Treatment with antibiotics for patients with bronchitis is generally inappropriate unless pneumonia is suspected. Using antibiotics in patients with bronchitis is associated with higher incidence of adverse events and insignificant treatment results compared to control data.

Pharyngitis

The guidelines recommend against the use of antibiotics in most pharyngitis cases. Pharyngitis is typically of viral origin and self-limiting with a short presentation, so only minor benefits are noticed with antibiotic treatment.
may be useful for those patients with confirmed group A streptococcal infection. Confirmation of a group A streptococcal infection may be completed via traditional throat swab on a sheep blood agar plate, but this involves a delay. Commercial rapid antigen detection tests are more expensive but allow swift identification of the microbe. In these patients, antibiotics may reduce duration of symptoms by up to two days and complications such as acute rheumatic fever may be avoided. Penicillin is the recommended antibiotic in patients fitting this criteria and without allergy. Discretionary use of antibiotics is advised in this population.

Acute Rhinosinusitis
Viruses are normally the cause of acute rhinosinusitis, but acute bacterial rhinosinusitis may be a secondary complication. Therefore, antibiotic treatment is recommended in patients with persistent symptoms. This includes patients displaying greater than 10 days of symptoms, the onset of severe symptoms and cases of "double sickening" where patients initially improve then relapse with worsening symptoms. Amoxicillin-clavulanate is the recommended treatment for acute bacterial rhinosinusitis with doxycycline or respiratory fluoroquinolones as alternative options. Other guidelines may recommend amoxicillin as the drug of choice, but the current practice guidelines advise the need for clavulanate due to growing resistance concerns.

Common Cold
The updated guidelines caution providers against prescribing antibiotics in cases of the common cold. Only symptomatic therapy is recommended in these patients. In addition to inefficacy, antibiotics are associated with increased risks of adverse drug events in patients with the common cold.

Antibiotic Resistance
The CDC defines antibiotic resistance as "the ability of microbes to resist the effects of drugs." Resistance most often occurs due to the elimination of both harmful and beneficial bacteria, resulting in an optimal environment for the remaining drug resistant bacteria to develop and grow. In the medical community, antibiotic resistance has become an increasing concern. Not only is the quality of care affected, but the cost of sequential care escalates for the patient. In 2009, $20 billion in health care were spent on antibiotic resistance, with an additional $8,000 in hospital stays per patient and $35 billion spent in societal costs from loss of productivity due to hospitalization or death. A study conducted by Robert et al. found that a single patient with an antibiotic resistant infection could result in $29,069 in added costs. However, this dollar value was based on 2008 data, meaning there are even greater costs in present day dollar value.

In the United States, at least 2 million antibiotic-resistant illnesses and 23,000 deaths occur each year. Based on 2013 data from the CDC, invasive methicillin-resistant Staphylococcus aureus (MRSA) infections account for the largest number of antibiotic resistant deaths annually, totaling around 11,000 fatalities. Antibiotics are improperly prescribed approximately half of the time, including inappropriate duration of treatment and indication. A retrospective cohort study conducted by Gill et al. evaluated 52,135 cases of upper respiratory tract infections using electronic health records, and found that 65 percent of patients received antibiotics. Broad-spectrum antibiotics for upper respiratory infections were prescribed for over half of the cases, with 68 percent of broad-spectrum antibiotics being prescribed for acute bronchitis. This contradicts the general guideline rec-

Table 1. Summary of CDC/ACP Recommendations for Appropriate Antibiotic Use in Select Acute Respiratory Tract Infections.

<table>
<thead>
<tr>
<th>Acute Respiratory Tract Infection</th>
<th>Acute Bronchitis</th>
<th>Pharyngitis</th>
<th>Acute Rhinosinusitis</th>
<th>Common Cold</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appropriate Antibiotic Use</strong></td>
<td>Only if pneumonia is suspected.</td>
<td>Discretionary use in group A streptococcal infections.</td>
<td>Patients with persistent symptoms indicative of acute bacterial rhinosinusitis.</td>
<td>Not recommended.</td>
</tr>
</tbody>
</table>
ommendations for upper respiratory infections, which advise against the use of broad-spectrum antibiotics.²

Physicians and health care professionals often feel pressured to prescribe an antibiotic for upper respiratory infections even when antibiotic use is not indicated. In a follow-up telephone survey of 959 patients, conducted by Stearns et al., visit satisfaction scores for treatment of upper respiratory tract infections at both Veterans Administration (VA) hospital emergency departments and nonVA hospitals were studied. It was found that in the nonVA settings, an overall visit satisfaction score based on a five point Likert scale was significantly increased with an antibiotic prescription, while there was no statistical difference in scores for VA hospitals.¹³ Cordelia et al. evaluated patient satisfaction as a driving factor for health professionals when prescribing antibiotics for acute respiratory tract infections. Overall, 33.7 million antibiotic prescriptions were prescribed to a population of 53.8 million patients, with antibiotic prescriptions showing a direct correlation to higher doctor and practice satisfaction scores based on patient general practice surveys.¹⁴

In 2010, the IDSA announced the 10 X '20 Initiative, bringing together interdisciplinary leaders to stimulate new antibacterial research and development to create 10 new antibiotics by the year 2020.¹⁵ Although the 10 X '20 Initiative has been released, along with an initiative developed by the White House to bring new antibiotics to the market by 2020, the funding for new antibiotic development is often not available. On Jan. 20, 2016, more than 80 drug and medical device manufacturers requested governments along with industry leaders to declare a fight against antibiotic resistance by funding the research and development of new antibiotics. The Declaration on Combating Antimicrobial Resistance represents a monumental step in the fight against antibiotic resistance as commercial drug manufacturers, diagnostic developers and global governments unite to conserve antibiotics by focusing on three broad areas: reducing the development of drug resistance, increasing investment in research and development that meets global public health needs and improving access to high-quality antibiotics for all.¹⁶

Antimicrobial Stewardship
In order to meet the growing demands placed upon patient care by antibiotic resistance and a slowdown in introduction of new antimicrobial drug classes to market, pharmacists and other health care professionals must strive toward improved stewardship of current antimicrobials.¹⁷ Model guidelines set forth by the IDSA in 2007 detail components of an idealized stewardship program for implementation in various health

<table>
<thead>
<tr>
<th>Guideline Measure</th>
<th>Purpose</th>
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<tbody>
<tr>
<td>Prospective audits with feedback</td>
<td>Review prescribing trends, provide one-on-one pharmacist-prescriber feedback.</td>
</tr>
<tr>
<td>Formulary restriction/drug preauthorization</td>
<td>Curtail unnecessary antimicrobial agent prescribing, cut costs, improve outcomes.</td>
</tr>
<tr>
<td>Provider education/guidelines</td>
<td>Provide awareness of current antimicrobial agent prescribing recommendations.</td>
</tr>
<tr>
<td>Antimicrobial agent order forms</td>
<td>Require prescriber justification for antimicrobial agent use.</td>
</tr>
<tr>
<td>Dose-optimized therapy</td>
<td>Causative organism-specific therapy to curtail antimicrobial resistance development.</td>
</tr>
<tr>
<td>Parenteral to oral conversion</td>
<td>Decrease hospital stay length, decrease overall cost.</td>
</tr>
<tr>
<td>Computer-based clinical decision support</td>
<td>Provide real-time therapy recommendations to improve adherence to antimicrobial prescribing guidelines.</td>
</tr>
</tbody>
</table>
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In the IDSA model, prospective audits with intervention and feedback involve direct interaction between an infectious-diseases trained physician or pharmacist and the prescriber. In addition to this consult, the use of clinical guidelines and other modes of health care professional education have been met with mixed results. Potential provider education measures include educational pamphlets, outreach events and one-on-one consultations with prescribers. However, education must be coupled with active intervention or the educational interventions will have only a marginal impact on prescribing practices. Formulary restrictions and/or antimicrobial agent preauthorization can involve obtaining special approval from an advisory board before initiation of a restricted antimicrobial. Via such methods, the use of otherwise potentially unnecessary or redundant antimicrobials can be curtailed leading to significant cost reductions and improvements in overall patient health. Additionally, an appeals process and constant monitoring must be available to ensure judicious execution of a preauthorization program.

Other components of a model stewardship program include the use of antimicrobial ordering forms to improve patient outcomes and decrease antemicrobial usage. Such forms require prescribers to justify drug choice when initiating or continuing therapy. Antimicrobial ordering forms must be coordinated with appropriate, streamlined antimicrobial use. Therapy must be specific to the causative organism, as unnecessary use of broad-spectrum or combination therapy can contribute to the development of antimicrobial-resistant pathogens. Additionally, antimicrobials must be dosed appropriately to ensure adequate antimicrobial action without facilitating the development of resistance. In addition to appropriate drug selection and dosage, the route of administration also plays an important role in infection treatment, as converting antimicrobials from parenteral to oral administration when clinically appropriate can decrease hospital stay length and overall costs.

A final component of a model stewardship program includes the use of computerized monitoring and clinical decision support. In this model, real-time recommendations are displayed in the electronic medical records system when a prescriber inputs an order. These recommendations can require immediate prescriber attention before allowing completion of the order or may appear as optional advice. Such programs have demonstrated improved adherence to and physician acceptance of antimicrobial prescribing guidelines. Overall, the use of model stewardship guidelines decreases overall antimicrobial usage, health care cost, and hospital stay length and improves patient outcomes.

Update on New IDSA Guidelines
The IDSA published updated stewardship guidelines in April 2016. This update provides further guidance on how to implement a stewardship program while stressing the importance of individualizing programs according to each clinical site's characteristics, resources and needs. Table 3 provides a review of the new recommendations found in the updated guidelines.

Role of the Pharmacist
Pharmacists play a key role in the promotion of antimicrobial stewardship. In the institutional setting, pharmacists often work closely with hospital staff to monitor patient therapy and ensure the correct drug selection, dosage and route of administration. More significantly, pharmacists are frequently responsible for the daily implementation of stewardship programs in clinical settings, including management and policy development. In the community setting, pharmacists can counsel patients, educating them on the importance of antimicrobial medication adherence. Additionally, they can immunize patients and lead other public health initiatives. However, where pharmacists currently have the greatest potential to impact antimicrobial resistance is through collaborative practice with other health care professionals.

An important role for pharmacists in collaborative practice includes triage, where pharmacists assess the severity of a patient's symptoms including the appropriateness of self-treatment with over-the-counter medications or if the condition requires a physician's visit. Other collaborative practice examples include community pharmacists outside the United States (such as in Canada, the United Kingdom and New Zealand) who have entered into practice agreements with physicians where they can directly monitor and prescribe limited antimicrobials. Generally, these programs have been met with success and exemplify the potential of such agreements in the United States. In the hospital setting, pharmacists can lead antimicrobial stewardship teams, heading the fight against growing antimicrobial resistance by implementing model stewardship programs. Significantly, recent initiatives from the President's Council of Advisors on Science and Technology and the Centers for Medicare and Medicaid Services indicate a regulatory requirement for Antimicrobial Stewardship Programs (ASPs) in clinical settings, with projected implementation by 2017, and represent a potential role for pharmacists. Overall, pharmacists play an instrumental role in leading and working with other health care professionals in the fight against antimicrobial resistance.

Conclusion
While antimicrobial resistance remains an urgent challenge to modern health care, significant steps have been taken in an effort to curtail the spread of resistant organisms. New treatment guidelines help prescribers to better utilize current antimicrobials and to keep up with a rapidly changing field. The pharmaceutical industry has united to help provide new antibiotics and find new ways of treating infections. Governments and health organizations continue to educate...
### Table 3. Summary of the 28 Specific Recommendations from the 2016 IDSA Updates to Model Antimicrobial Stewardship Program (ASP)\(^{23}\)

<table>
<thead>
<tr>
<th>Guideline Measure</th>
<th>Recomm-</th>
<th>Evidence Strength</th>
<th>Guideline Measure</th>
<th>Recomm-</th>
<th>Evidence Strength</th>
<th>Guideline Measure</th>
<th>Recomm-</th>
<th>Evidence Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preauthorization/ Prospective Audit/Feedback Intervention*</td>
<td>Yes</td>
<td>Moderate</td>
<td>Develop stratified antibiograms for empiric therapy guideline development</td>
<td>Yes</td>
<td>Low</td>
<td>Aminoglycoside pharmacokinetic monitoring/adjustment</td>
<td>Yes</td>
<td>Moderate</td>
</tr>
<tr>
<td>Didactic education*</td>
<td>Do not use alone</td>
<td>Low</td>
<td>Selective reporting of antimicrobial susceptibility test results</td>
<td>Yes</td>
<td>Low</td>
<td>Vancomycin pharmacokinetic monitoring/adjustment</td>
<td>Yes</td>
<td>Low</td>
</tr>
<tr>
<td>Facility-specific practice guidelines</td>
<td>Yes</td>
<td>Low</td>
<td>Rapid viral testing use to reduce inappropriate antimicrobial use</td>
<td>Yes</td>
<td>Low</td>
<td>Alternative dosing strategies to avoid broad-spectrum β-lactam dosing for cost concerns</td>
<td>Yes</td>
<td>Low</td>
</tr>
<tr>
<td>Specific infectious disease syndrome-targeted interventions</td>
<td>Yes</td>
<td>Low</td>
<td>Rapid diagnostic testing with routine testing</td>
<td>Yes</td>
<td>Moderate</td>
<td>Appropriate IV to oral antimicrobial conversion*</td>
<td>Yes</td>
<td>Moderate</td>
</tr>
<tr>
<td>Reduce use of high risk Clostridium difficile infection-associated antimicrobials</td>
<td>Yes</td>
<td>Moderate</td>
<td>Serial Procalcitonin Testing in Intensive Care Unit patients to decrease antimicrobial use</td>
<td>Yes</td>
<td>Moderate</td>
<td>Allergy assessment and penicillin skin testing for β-lactam allergy</td>
<td>Yes</td>
<td>Low</td>
</tr>
<tr>
<td>Prescriber-led routine review of antibiotic usage*</td>
<td>Yes</td>
<td>Low</td>
<td>Use nonculture-based fungal markers in hematologic malignancy to optimize antifungal use</td>
<td>Yes</td>
<td>Low</td>
<td>Use shortest effective duration of treatment*</td>
<td>Yes</td>
<td>Moderate</td>
</tr>
<tr>
<td>Computerized clinical decision support*</td>
<td>Yes</td>
<td>Moderate</td>
<td>Monitor antimicrobial use via Days of Therapy instead of Defined Daily Dose</td>
<td>Yes</td>
<td>Low</td>
<td>Consider goals and size for syndrome-specific intervention</td>
<td>Yes</td>
<td>Good practice recommendation</td>
</tr>
<tr>
<td>Antibiotic cycling</td>
<td>No</td>
<td>Low</td>
<td>Antimicrobial cost measured by prescription/administration history instead of purchasing data</td>
<td>Yes</td>
<td>Good practice recommendation</td>
<td>Develop facility-specific guidelines for fever and neutropenia management in hematology-oncology patients</td>
<td>Yes</td>
<td>Low</td>
</tr>
<tr>
<td>ASP implementation in immunocompromised patients to improve antifungal treatment</td>
<td>Yes</td>
<td>Low</td>
<td>ASP implementation in nursing/skilled nursing homes</td>
<td>Yes</td>
<td>Good practice recommendation</td>
<td>ASP implementation in Neonatal Intensive Care Units</td>
<td>Yes</td>
<td>Good practice recommendation</td>
</tr>
<tr>
<td>ASP implementation in terminally ill patients</td>
<td>Yes</td>
<td>Good practice recommendation</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Recommendation previously found in 2007 guidelines
the public on how to do their part. Within health care practice, antimicrobial stewardship programs have become widespread and standardized. Through all of these changes, pharmacists remain at the forefront in each effort. Pharmacists are among the best prepared health care providers fighting to end the threat of widespread antimicrobial resistance.

References


15. Infectious Diseases Society of America. The 10 x '20 initiative: pursuing a global commitment to develop 10 new antimicrobial drugs by 2020.


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Assessment Questions

1. Antibiotics are never appropriate in patients with acute respiratory tract infections.
   A. True
   B. False

2. Which of the following statements about appropriate antibiotic use is correct?
   A. Recent advances show minor usefulness of antibiotic treatment of patients with a common cold.
   B. Inappropriate antibiotic use is not a concern in well-developed hospitals across the United States.
   C. Inappropriate antibiotic use is often associated with insignificant treatment outcomes as well as higher rates of adverse reactions.
   D. Inappropriate antibiotic use is not associated with antibiotic resistance although the two topics are often discussed in tandem.

3. According to recent data, how much money is spent on antibiotic resistance annually?
   A. $1 billion
   B. $2 billion
   C. $10 billion
   D. $20 billion

4. Antibiotic prescribing is not relevant to a healthcare provider's overall patient satisfaction scores.
   A. True
   B. False

5. According to the CDC, antibiotics are incorrectly prescribed what percent of the time?
   A. 30%
   B. 20%
   C. 50%
   D. 60%

6. Which of the following is NOT a part of a model stewardship program?
   A. Computer-based decision support
   B. Prospective, ongoing audits with HCP intervention and feedback
   C. Formulary restrictions
   D. Antimicrobial agent postauthorizations
   E. Use of antimicrobial agent order forms

7. Streamlined antimicrobial therapy should:
   A. Be targeted to the organism when such information is known.
   B. Be wide-spectrum when the target organism is known.
   C. Utilize the optimal dose for maximal antimicrobial action while minimizing chance of antibiotic resistance development.
   D. Both A and B.
   E. Both A and C.

8. Which of the following MOST ACCURATELY describes the role of the pharmacist in antibiotic stewardship?
   A. The pharmacist plays a role in prescribing the appropriate antibiotic at the optimal dose.
   B. The pharmacist plays a role in administering the antibiotic directly to the patient.
   C. The pharmacist plays a role in overseeing all personnel in the hospital and ensuring their compliance with institutional stewardship guidelines.
   D. The pharmacist plays a role in ensuring appropriate antibiotics are prescribed, including consulting with prescribers and patients to ensure best practices.
   E. The pharmacist does not play any significant role in antibiotic stewardship.

9. The IDSA recommends what action in order to maximize the impact of provider education regarding appropriate use of antimicrobials?
   A. Active intervention
   B. Presentations and posters
   C. Informational pamphlets
   D. Use of the most recent prescribing guidelines

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