Antibiotic Resistance Threats in the United States: Stepping Back from the Brink

STEVEN L. SOLOMON, MD, and KRISTEN B. OLIVER, ME, MPH, Centers for Disease Control and Prevention, Atlanta, Georgia

In a recently issued report, the Centers for Disease Control and Prevention (CDC) estimated the national burden of illnesses and deaths caused by the most common and most worrisome antibiotic-resistant pathogens.1 The report focused on 16 antimicrobial-resistant bacterial pathogens, as well as Candida infections, which together account for more than 2 million illnesses and at least 23,000 deaths every year in the United States.1 The report also included information on Clostridium difficile infections, which, like antibiotic resistance, are driven by antibiotic use. C. difficile causes more than 250,000 clinical infections annually and is associated with more than 14,000 deaths every year in the United States.1

In this report, the CDC categorized 18 pathogens (eTable A) into three groups (urgent, serious, and concerning) based on seven criteria: clinical impact, economic impact, incidence, 10-year projection of incidence, transmissibility, availability of effective antibiotics, and barriers to prevention.1 Three types of bacteria were included in the urgent category: carbapenem-resistant Enterobacteriaceae, drug-resistant Neisseria gonorrhoeae, and C. difficile. In the past, drug-resistant strains of Enterobacteriaceae and N. gonorrhoeae have shown a propensity to spread rapidly in the United States and around the world. Some strains of carbapenem-resistant Enterobacteriaceae are currently untreatable with available antibiotics, and the cephalosporin agents to which some gonococci are now showing emerging resistance are the last available drugs to effectively treat this infection. Thus, further spread of these strains constitutes a public health crisis. C. difficile infections already cause significant morbidity and mortality, and a recently emerging epidemic strain, BI/NAP1/027, appears to be more virulent.

Prevention strategies can be effective, but the major goals of the CDC report are to (1) increase awareness of the magnitude and looming risk of untreatable infections, and (2) spur concerted action, both to prevent further spread of resistant pathogens and to preserve the effectiveness of existing antibiotics. Thinking of antibiotics as a precious and diminishing resource has engendered the concept of antimicrobial stewardship, a defined set of practices designed to improve the appropriate use of antimicrobial agents.2 Table 1 lists steps to help implement resistance prevention strategies. Family physicians have an important role in combating antibiotic resistance through carefully prescribing antibiotics, educating patients, and identifying and reporting unexpected treatment failures and suspected resistance.

There are three main elements of preventing and controlling antibiotic resistance that are most applicable to outpatient practice. First, physicians must improve their antibiotic prescribing. Antibiotic use is the principal driver of antibacterial resistance. A considerable proportion of antibiotics in inpatient and outpatient settings are prescribed in cases when they are not needed or in which the choice of antibiotic, the dose, or the duration of therapy is inappropriate.3,4 Rates of outpatient antibiotic prescribing vary widely by region and state—a much greater variation than is likely explained by differences in patient populations or rates of bacterial diseases.5 It has been documented that inappropriate antibiotic prescribing, especially for viral upper respiratory tract infections, is common in ambulatory care.6 These illnesses are the most common reason for seeking medical attention in the United States and are associated with up to 75% of total antibiotic prescriptions each year.7 The causes of the overuse of antibiotics, which is a problem throughout the world, are complex and well described.8,9
The second main element is preventing infections and the spread of resistance. Preventing an infection eliminates the possibility that the infection could be drug resistant. Immunization and rigorous infection control, including hand washing, clearly reduce the likelihood of infection. On its website, the CDC provides information for patients on how to protect themselves from many types of infections, such as by ensuring safe food handling to prevent *Salmonella* and *Campylobacter* infections and by avoiding gonorrhea and other sexually transmitted infections. Counseling patients on how to avoid spreading or becoming infected with resistant pathogens in the community is an important role for physicians. For example, if an athlete is diagnosed with a methicillin-resistant *Staphylococcus aureus* infection, he or she should keep the wound properly covered, avoid whirlpools or therapy pools, shower after participation, clean uniforms and equipment after each use, and report infection to coaches and trainers.

The third main element is public health reporting. Gathering, analyzing, and disseminating information on resistant infections and the prevalence of resistant microorganisms is a critical strategy that informs clinical and public health decision making. A key component of detecting emerging and spreading resistance is identifying the cause of unexpected treatment failures. Patients who return with persistent or recurrent symptoms shortly after treatment should be retested by culture, and isolates should be submitted for antimicrobial susceptibility testing. Any case of unexplained treatment failure or a positive culture result after appropriate empiric treatment should be reported promptly to local or state health departments. Ultimately, public health surveillance is dependent on reporting by physicians and laboratories.

---

**Table 1. Steps to Combat Antimicrobial Resistance in Outpatient Settings**

<table>
<thead>
<tr>
<th>Steps</th>
<th>Suggestions for implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Improve antibiotic prescribing</strong></td>
<td></td>
</tr>
<tr>
<td>Use current clinical guidelines to support rational and appropriate antibiotic prescribing</td>
<td>Share unremarkable findings during the examination (e.g., “no inflammation” or “normal breathing”), while acknowledging the patient is sick</td>
</tr>
<tr>
<td>Determine the likelihood of a bacterial infection, especially for upper respiratory tract infections</td>
<td>Provide a specific diagnosis (e.g., “viral bronchitis” vs. “virus”)</td>
</tr>
<tr>
<td>Weigh benefits vs. harms of antibiotics</td>
<td>Implement judicious prescribing strategies</td>
</tr>
<tr>
<td>Communicate with patients about when and why antibiotics may not be necessary</td>
<td>Explain that unnecessary antibiotic use can be harmful (e.g., adverse effects associated with antibiotic use, potential resistance development)</td>
</tr>
<tr>
<td>Explain that treating viral infections with antibiotics does not work</td>
<td>Explicitly plan treatment of symptoms by describing the expected normal course of the illness, and instruct patients to call or come back if symptoms persist or worsen; consider providing care packages with nonantibiotic therapies</td>
</tr>
<tr>
<td>Educate patients if an antibiotic is needed</td>
<td>Encourage adherence</td>
</tr>
<tr>
<td>Prevent infections and the spread of resistant bacteria</td>
<td>Discuss potential adverse effects</td>
</tr>
<tr>
<td>Ensure that all patients get recommended vaccinations</td>
<td>Start the process in the waiting room with videos, posters, and other materials</td>
</tr>
<tr>
<td>Prevent cross-transmission</td>
<td>Hang posters in examination rooms to display a commitment to not prescribe antibiotics for viral infections</td>
</tr>
<tr>
<td>Counsel patients on how to avoid spreading or becoming infected with resistant pathogens in the community (e.g., methicillin-resistant <em>S. aureus</em>)</td>
<td>Involve office personnel in the reinforcement of the physician’s messages</td>
</tr>
<tr>
<td>Monitor antibiotic-resistant infections</td>
<td></td>
</tr>
<tr>
<td>Report notifiable diseases</td>
<td>When appropriate, report to the health department any diseases caused by bacteria on the Centers for Disease Control and Prevention’s list of urgent and serious pathogens (reporting requirements differ by U.S. state and Canadian province); antibiotic-resistant strains of some bacteria (e.g., methicillin-resistant <em>S. aureus</em>) are reportable in some states</td>
</tr>
<tr>
<td>Be alert for treatment failures</td>
<td>Consider the possibility of antibiotic resistance in cases of treatment failure; obtain laboratory confirmation and notify local public health authorities in cases of unusual or unexpected treatment failure</td>
</tr>
</tbody>
</table>
The nightmare scenario of the spread of pan-resistant bacteria is a real and frightening possibility. Cases of untreatable infections are already occurring. Preventing and controlling resistance requires the engagement of many different sectors of society. However, the physician’s role in this effort is singularly important. As the threat becomes more urgent, the leadership of the medical community is the most critical factor to ensure a successful response.

The findings and conclusions of this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention. Mention of trade names or commercial products does not constitute endorsement or recommendation for use by the U.S. government.

Address correspondence to Steven L. Solomon, MD, at ssolomon@cdc.gov. Reprints are not available from the authors.

Author disclosure: No relevant financial affiliations.

REFERENCES

Be ready for ICD-10.

Help where and when you need it most.

Features of the AAFP ICD-9 to ICD-10 Referential Flash Cards: Top 823 Primary Care Diagnoses:
• Alpha listing of the codes you see most often
• Expert tips to coding accurately for proper reimbursement
• Color-coded cards for quick recognition by classes of codes

Not coding properly means lost revenue. Use this valuable coding resource from the AAFP to accurately and fully report patient conditions.

For physicians, practice managers, coders, and other office staff
<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Notable information</th>
<th>continued</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urgent</strong></td>
<td></td>
<td>-----------</td>
</tr>
</tbody>
</table>
| _Clostridium difficile_[^A1,A2] | Deaths related to _C. difficile_ increased 400% between 2000 and 2007, in part because of a stronger strain.  
Most infections are connected to receiving medical care.  
Hand sanitizer does not kill _C. difficile_, and hand washing may not be sufficient.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |-----------|
| Carbapenem-resistant Enterobacteriaceae[^A3] | Difficult to treat and, in some cases, untreatable.  
Kills up to one-half of patients who get bloodstream infections.  
Easily spreads antibiotic resistance to other bacteria.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |-----------|
| Drug-resistant *Neisseria gonorrhoeae*[^A4] | Cases in the United States are more prevalent in the West and among men who have sex with men.  
All patients treated for gonorrhea should routinely be offered condoms, referred for risk-reduction counseling, and retested for gonorrhea three months later.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |-----------|
| **Serious**                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |-----------|
| Multidrug-resistant *Acinetobacter*[^A5] | Increasingly common in U.S. health care facilities; hard to treat.  
Noted in U.S. service members wounded in Iraq and Afghanistan.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |-----------|
| Drug-resistant *Campylobacter*[^A6] | Most cases are sporadic and not part of outbreaks.  
Ciprofloxacin (Cipro) resistance to *Campylobacter* increased from 12% in 1997 to 24% in 2011.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |-----------|
| Fluconazole- (Diflucan-) resistant *Candida* (fungus)[^A7-A9] | Antifungal resistance in mucosal candidiasis varies by species.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |-----------|
| Extended spectrum β-lactamase–producing Enterobacteriaceae[^A10,A11] | Infections have become more common in recent years.  
Once confined largely to hospitals, these bacteria, especially *Escherichia coli*, are increasingly common in community-acquired infections, particularly urinary tract infections.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |-----------|
| Vancomycin-resistant *Enterococcus*[^A12,A14] | Enterococci are the fifth most common cause of health care–associated infections.  
Most likely to be found in urine and in wounds; may pose a risk for spreading in the outpatient setting.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |-----------|
| Multidrug-resistant *Pseudomonas aeruginosa*[^A15,A16] | About 8% of all health care–associated infections are caused by *P. aeruginosa*; about 13% of severe *P. aeruginosa* health care–associated infections are multidrug resistant.  
*P. aeruginosa* may be isolated from outpatients with otitis, skin rash, and urinary tract infections.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |-----------|
| Drug-resistant non-typhoidal *Salmonella*[^A17,A18] | Estimated 1.2 million cases occur each year in the United States; most go unreported.  
About 100,000 cases (8%) are caused by drug-resistant *Salmonella*.  
Outbreaks occur each year; some involve multiple states and/or national distribution.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |-----------|
| Drug-resistant *Salmonella* serotype Typhi[^A19] | Estimated 5,700 cases annually in the United States.  
Most (up to 75%) are acquired during international travel.  
Increasing resistance to antibiotics, especially fluoroquinolones.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |-----------|
| Drug-resistant *Shigella*[^A20] | High-risk groups include children in day care centers (younger than five years) and their caregivers, men who have sex with men, international travelers, and persons in custodial institutions.  
Increasing resistance to ciprofloxacin and azithromycin (Zithromax) is of particular concern.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |-----------|
| Methicillin-resistant *Staphylococcus aureus*[^A21,A23] | Although overall cases of invasive methicillin-resistant *S. aureus* are declining, the proportion of community-associated infections has increased.  
Should be considered in the differential diagnosis of skin and soft tissue infections.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |-----------|
REFERENCEs


Editorials


