

# Surgeon General's Perspectives

## ANTIBIOTIC RESISTANCE: A PUBLIC HEALTH CRISIS

Infections with antibiotic-resistant bacteria, particularly respiratory infections, skin and soft tissue infections, and even urinary tract infections, are now prevalent in both the health-care and community settings. This prevalence has led to changes in the approach to empirical treatment, such as with skin infections, due to the high likelihood of methicillin-resistant *Staphylococcus aureus* causing these infections.<sup>1</sup> In addition, there are growing challenges to the definitive treatment of these infections (i.e., based on culture results); at times, antibiotic resistance leaves the clinician with few or even no approved antibiotics to which the bacteria are clearly susceptible.

Antibiotics are a type of miracle drug, but their universal effectiveness is at an end. As first- and second-line therapies become ineffective, providers end up using agents that may be more toxic and less effective. Even when effective antibiotics are available, evidence is mounting that antibiotic-resistant infections often take longer to treat, are costly, and are often associated with higher mortality than their antibiotic-susceptible cousins.<sup>2,3</sup>

A recent Centers for Disease Control and Prevention (CDC) publication estimated that about 2 million people develop infections with antibiotic-resistant pathogens each year; of those who develop infections, an estimated 23,000 people die each year as a direct result of these infections.<sup>3</sup> In addition, about 250,000 people develop diarrheal disease with *Clostridium difficile* (*C. difficile*) each year, either during hospitalization or resulting in hospitalization,<sup>3</sup> often as a direct consequence of receiving antibiotic therapy for respiratory infections or prophylaxis.<sup>4</sup>

The primary driver of antibiotic resistance is the use of antibiotics. Antibiotics are lifesaving drugs that offer tremendous benefits to patients with infections. Yet, studies have demonstrated that treatment indication, choice of agent, or duration of therapy can be incorrectly prescribed 30%–50% of the time.<sup>5,6</sup> Additionally, antibiotics often are used for longer-than-recommended durations or for treatment of colonizing or contaminating microorganisms.<sup>5</sup> When incorrect prescribing of antibiotics includes unnecessary use, it exposes individual patients to potential complications of antibiotic therapy without any therapeutic benefit.



Boris D. Lushniak, MD, MPH  
RADM, U.S. Public Health Service  
Acting Surgeon General

Patients are also placed at risk for antibiotic-resistant infections when these pathogens are transferred from one patient to another either via the hands of health-care workers or objects used in the care of patients. Although at its most fundamental level interrupting this transmission can at times fall to environmental cleaning and disinfection of patient-care equipment, all health-care providers are responsible for optimal hand hygiene—a single action that can have a tremendous impact on preventing cross-transmission of any pathogen in a health-care setting.

The impact of antibiotic-resistant infections can be minimized by reducing the prevalence of antibiotic resistance, preventing the occurrence of infections, and improving the therapeutic approach to treating infected patients. CDC recently outlined four core actions that are required to reduce antibiotic-resistant infection: (1) prevent infections and cross-transmission, (2) track resistant bacteria, (3) improve the use of existing antibiotics, and (4) promote the development of new antibiotic and diagnostic tests.<sup>3</sup> Health-care providers play a critical role in key aspects of these core actions.

First, all prescribers of antibiotics in hospitals and nursing homes should actively participate in efforts to

optimize inpatient antibiotic prescribing, often referred to as stewardship programs. Such programs serve to facilitate optimal treatment for hospitalized patients with infection and reduce unnecessary antibiotic use to minimize harm to patients and prolong the length of time antibiotics are effective. However, all prescribers are responsible for prescribing correctly—the responsibility does not just fall to the stewardship program's staff. Evidence suggests that interventions to optimize inpatient antibiotic prescribing can improve patient outcomes;<sup>7-9</sup> as such, embracing these interventions (e.g., reassessing therapy after two days) will result in better patient outcomes. Growing evidence also indicates the need to improve prescribing practices. Recent data from a post-prescription review of two common prescribing scenarios across multiple hospitals in 10 U.S. states identified opportunities to improve prescribing in 37% of these scenarios, often through the timely use of diagnostic tests or improved documentation of symptoms.<sup>6</sup> Data reported to CDC's National Healthcare Safety Network identified a threefold difference in overall antibiotic use in the most common patient-care location—hospital wards caring for both medical and surgical patients—where more similar usage rates would be expected because similar types of patients are being treated in these locations.<sup>6</sup>

Second, health-care providers need to understand the importance of eliminating the cross-transmission of antibiotic-resistant bacteria, especially those of high consequence or high potential to spread, such as *C. difficile* or carbapenem-resistant *Enterobacteriaceae*. Diligent hand hygiene before and after all patient interactions across the spectrum of health-care delivery is critical to reduce the risk of transmitting antibiotic-resistant bacteria. Compliance with infection control precautions put in place by hospital staff is also essential. Increasingly, state health departments are playing a role in improving communication among health-care facilities to raise awareness of colonization and infection status to providers to encourage compliance with established infection control precautions.

Third, identifying antibiotic-resistant infections can be challenging. However, ensuring that the appropriate diagnostic tests are ordered is a critical step toward knowing which antibiotic to use at which time. Reevaluating aspects of prescribing after diagnostic test results are available should be a routine practice for all prescribing scenarios. Diagnostic testing for specific antibiotic-resistant bacteria is in development. As these tests become available, prescribers will have additional tools to help them choose the right antibiotic at the right time. However, clarification will be needed to

identify exactly how these tests should be used in the prescribing process.

Finally, a critical step toward reducing the impact of antibiotic-resistant infections will be the development and availability of new antibiotics to treat these infections. For many antibiotic-resistant threats, there are sufficient antibiotics available that patients can still receive safely with careful clinical oversight. However, gram-negative pathogens are particularly worrisome because they are becoming resistant to nearly all drugs that would be considered for treatment. Treating gram-negative infections that are pan-resistant (i.e., resistant to all available antibiotics) or nearly pan-resistant is an increasingly common challenge, and new antibiotics will be needed to overcome this challenge. The Infectious Diseases Society of America (IDSA) recently reported that as of 2013, there were few antibacterial compounds in phase 2 or 3 development. IDSA also commented that there were unacceptably few agents in development with activity against the emerging cause of extensively resistant gram-negative bacteria in *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. However, some legislative activity that attempts to streamline the approval process for antibiotics is underway, and these attempts will hopefully make new antibiotics available for patients with difficult-to-treat antibiotic-resistant infections.<sup>10</sup> Ideally, the pharmaceutical industry and federal systems will work together to ensure that additional antibiotics are made available to reduce the impact of these infections.

Antibiotics are now a limited resource, there are currently fewer effective antibiotics available for certain health-care-associated infections than in the previous decade, and the threat of antibiotic resistance is real. In the health-care setting, clinicians can do their part to help reduce the impact of these infections on patients and the health-care system. Additionally, prescribers need to optimize their prescribing and actively participate in antibiotic stewardship programs to interrupt the transmission of antibiotic-resistant bacteria. These actions will benefit patients as newer diagnostic tests and antibiotics become available.

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