



## SUPERBUGS

**Wanted Dead, Not Alive!**

BY KEVIN GLENNON, RN, BSN, CDMS, CWCP, QRP

**S**UPERBUGS—strains of bacteria that are resistant to multiple types and classes of antibiotics—are becoming a worldwide health problem. The Centers for Disease Control and Prevention (CDC) estimates that more than two million people in the U.S. contract superbug infections each year, causing 23,000 deaths. Another study projected that, if governments worldwide don't take action, superbugs could kill an extra 10 million people by 2050, making these infections deadlier than cancer.<sup>1</sup>

Not surprisingly, health leaders characterize these microbial agents as “nightmare bacteria”<sup>2</sup> that pose a catastrophic threat. Everyone should be concerned.

In this part I of a two-part series, we'll discuss how superbugs developed, and what can be done to combat the problem. We will also review several deadly and dangerous strains, and how they impact medical care and costs.

### THE RISE OF ANTIBIOTICS

In 1928, Scottish scientist Alexander Fleming discovered penicillin. The discovery of antibiotics propelled us into a new era of medicine. Physicians had a cure for deadly diseases, such as tuberculosis, scarlet fever, and bacterial meningitis. Surgery for heart disease and organ transplants could succeed because antibiotics wiped out potential infections that could arise after treatment.

In the 1940s and 1950s, new antibiotics emerged, arming physicians with novel ways to combat infections. Eventually, the distinction between broad- and narrow-spectrum antibiotics was introduced to target either a wide or narrow range of bacteria, which provided more treatment options.

## INCREASING RESISTANCE TO ANTIBIOTICS

Fewer than 100 years after antibiotics were first discovered, they're losing their lifesaving effectiveness. When bacteria are exposed to antibiotics in concentrations that are not strong enough to kill them, they develop resistance to those drugs. Ironically, it's the overuse of antibiotics that is enabling bacteria to evolve and become impervious to the current stable of antibiotics.

Scientists and public health officials have long warned that if drug-resistant bacteria continued to spread, treatment could become vastly restricted. Routine operations could become deadly. Minor infections could be life threatening. Pneumonia would become difficult to treat. And common procedures, such as treating a wound, could prove fatal—all due to a lack of effective antibiotics. If actions aren't taken to stem this tide, we'll lose many of the benefits of modern medicine.

## OVER-PRESCRIPTION: A KEY PART OF THE PROBLEM

Antibiotics are the most commonly prescribed drugs. However, 50 percent of antibiotics used in humans are estimated to be unnecessary.<sup>3</sup> Over-prescription has complex roots. In hypothetical situations, physicians follow treatment guidelines. But in actual patient encounters, they will show compassion for patients who are sick and request antibiotics to make them feel better. However, common colds and the flu are not caused by bacteria—but by viruses that are not susceptible to antibiotics. Using antibiotics won't reduce the duration of a cold or cough. In these scenarios, they could worsen a patient's condition.

## HOSPITALS: A BREEDING GROUND FOR SUPERBUGS

Every year, an estimated 648,000 people in the United States develop infections during a hospital stay and about 75,000 die from them, according to the CDC.<sup>4</sup> There are many reasons hospital patients are vulnerable. Certain superbugs are difficult to remove from medical tools that are placed into the body, such as catheters, breathing tubes and scopes. Superbugs can live on surfaces for days, and they can be passed from person to person on the hands of healthcare workers. In addition, people

in hospitals are already sick or in a weakened state, so they're more susceptible to infection. To prevent some of these exposures, hospitals must practice scrupulous hygiene.

Hospitals are also accused of overusing antibiotics—almost 50 percent of hospital patients are prescribed at least one antibiotic, but up to half the time it's inappropriate.<sup>5</sup>

## LIVESTOCK: MISUSE TO PROMOTE GROWTH

The overuse of antibiotics in hospitals and doctors' offices pales in comparison to the overuse that occurs in the meat and poultry industries. Around 1950, researchers discovered that by giving antibiotics to livestock, animals gained weight faster while consuming less feed. To boost profits, adding antibiotics to feed became a standard practice to promote growth—rather than to treat disease.

Today, the Food and Drug Administration (FDA) estimates that 80 percent of antibiotics sold in the U.S. are given to animals raised for food<sup>6</sup>—including pigs, cows, chickens, and turkeys. Due to this exposure, bacteria commonly found in food have become increasingly resistant to antibiotics. And these drug-resistant bacteria can easily spread to people. In August 2015, pork contaminated with salmonella immune to four antibiotics sickened 152 people in the state of Washington.<sup>7</sup>

## SUPERBUGS: THE MOST "UNWANTED" LIST

When dangerous bacteria become resistant to antibiotics, they represent a serious threat to public health.<sup>8</sup> The CDC ranks bacterial risks, considering a plethora of factors, including how many people are killed by these bugs each year; how quickly and easily these bugs spread and how many antibiotics are available to treat them. Using these and other considerations, the CDC developed a comprehensive list of the most "urgent" and "serious" superbug threats. Below we consider a few of the most deadly and dangerous<sup>9</sup>:

### CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE)

CRE is a family of bacteria normally found in a person's gut. As its name suggests, this bug is resistant to carbapenem, an antibiotic of last resort.

Healthy individuals are typically not susceptible to CRE infections. Most cases occur in the hospital setting. These bacteria often come to reside on medical tools, and they're difficult to remove even with cleaning. That's what happened in California after doctors unknowingly used contaminated medical scopes to view the interior of patients' bodies.

Once in the body, CRE can cause life-threatening blood infections. These bacteria kill up to 50 percent of patients who are infected.<sup>10</sup> The CDC believes CRE is among the country's most urgent threats.

### CLOSTRIDIUM DIFFICILE (C. DIFF)

C. diff also inhabits the intestines. Usually, it does so without harm. But overuse of antibiotics can knock out other beneficial bacteria in the digestive tract. Without healthy flora in the gut, C. diff can proliferate and take over. This infection can cause symptoms ranging from mild diarrhea to life-threatening colitis. In severe cases, patients may need to remove part of their infected intestine or undergo a fecal transplant. From 2000–2007, deaths spiked 400 percent when a new drug-resistant strain began to appear.<sup>11</sup>

On an annual basis, C. diff infects 290,000 Americans in hospitals and other healthcare facilities; approximately 27,000 people die from these infections,<sup>12</sup> and they cause about \$1 billion in additional medical costs.<sup>13</sup>

### METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)

Over the years, Staphylococcus aureus (S. aureus) have stayed in lock step with antibiotic development, continually developing new resistance. The latest strain is resistant to methicillin—noted as MRSA for short. By 2002, nearly 60 percent of S. aureus cases were identified as MRSA.<sup>14</sup>

Early on, S. aureus infections occurred mostly in hospitals, where bacteria find their way into patients' bodies through the lines and tubes that deliver medication and nutrition, or via surgical incisions. Once in the body, they can spread to surrounding tissue and blood. Today, approximately a quarter of infections occur outside the healthcare settings.<sup>15</sup> For example, there were several recent outbreaks among athletes.

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In 2005, an estimated 100,000 Americans suffered severe MRSA infections, and nearly 20,000 of them died—more than from HIV and tuberculosis combined.<sup>16</sup>

As dangerous as MRSA is, an infection can be cured if treated promptly with vancomycin. However, with increased use, this drug, too, has begun to lose its efficacy. A newer strain is vancomycin-resistant (VRSA). The progression of antibiotic resistance continues, as linezolid can treat VRSA, but linezolid-resistant *S. aureus* (LRSA) has developed as well.

### TRANSFERENCE: BACTERIA'S SUPERPOWER

Bacteria have a superpower with regard to developing antibiotic resistance. They're able to exchange small, circular pieces of DNA called plasmids, which carry genes of resistance. Whereas a genetic inheritance typically occurs vertically from parents to progeny, plasmid genetics can be transferred horizontally to other bacteria.<sup>17</sup>

This ability to transfer resistance amplifies the superbug threat. In July 2016, clinicians found a strain of *E. coli* in a Pennsylvania woman with a colistin-resistant gene. This gene known as MCR-1 exists on a plasmid, meaning it can be easily transferred to other bacteria. If it ends up in bacteria that already possess resistance to other antibiotics, this could result in a truly pan-resistant superbug—which would be virtually unstoppable.

### ANTIBIOTIC STEWARDSHIP: A GLOBAL FOCUS

Antibiotic stewardship is the best solution to this complex problem. It involves the prudent use of antibiotics to ensure they're used only when necessary in order to avoid overexposure. While this sounds good in principle, it is a challenge to implement.

First, stewardship must be a global effort. As people travel internationally, drug-resistant bacteria travel with them. Second, all parties must be in agreement or mandated to follow policies, including farming. Colistin, which is typically an antibiotic of last resort, has been widely used in Chinese livestock. In other countries, like India, antibiotics are sold over the counter. It's plausible that antibiotic resistance could develop in these countries and travel the globe.

### BETTER DIAGNOSTICS, BETTER STRATEGY

One of the best hopes for effectively treating bacterial infections is the development of reliable, rapid diagnostics. These tests should identify both the microbial cause of the infection and the bug's drug-resistant profile within hours, rather than the existing two-day turnaround.

Currently, as physicians wait for results, they make an educated guess as to the type of bacteria they're treating and the class of antibiotics to prescribe. If the infection is life threatening, they may start a course of aggressive broad-spectrum antibiotics, which will indiscriminately attack both pathologic and beneficial bacteria and could lead to a *C. diff* infection. With better diagnostics, doctors can prescribe with more precision using narrow-spectrum drugs.

In certain lines of insurance, such as workers' compensation, nurses serve as clinical specialists on complex cases and provide oversight that ensures safe antibiotic use. These clinical specialists work in conjunction with prescribing physicians to utilize an infusion therapy program. In this way, a three-day supply of broad-spectrum medication could be authorized. Then, when culture results are received, a narrow-spectrum antibiotic can be initiated, decreasing the risk of a superbug complication.

### AN ONGOING SEARCH FOR NEW ANTIBIOTICS

Today, most large pharmaceutical companies have abandoned antibiotic research because of unfavorable economics. Drug development is risky and expensive. Generally, it can take approximately 10 years and a billion dollars to bring a new drug to market. But complicating this is the fact that an antibiotic is a rare find. It must survive a challenging set of requirements, which include the ability to deal a lethal blow to one or more bacteria, while harmlessly being absorbed into the human body. Plus, the evolving nature of bacteria calls for a constant cycle of discovery to enable modern medicine to stay a step ahead of drug resistance.

### TAKING ACTION

Although difficult to calculate, the total economic impact of antibiotic resistance to the U.S. economy is estimated to be as high as \$20

billion in healthcare costs and an additional \$35 billion a year in lost productivity.<sup>18</sup>

Antibiotics are the foundation on which all modern medicine rests. In addition to a global approach, each individual must take steps to limit personal use of non-essential antibiotics. People should get a full understanding of the antibiotics prescribed to them. Having conversations with physicians can encourage a thoughtful approach. Also, when possible, choose meat and poultry products free of antibiotics.

Stewardship by all parties will contribute to lengthening the effectiveness of our antibiotics and preserving their use for generations to come. In the second part of this article series, we'll be discussing how public risk managers may begin to see the impact of superbugs in their workers' compensation programs, and how to mitigate those risks. ■

*Kevin Glennon, RN, BSN, CDMS, CWCP, QRP is vice president-clinical services with One Call Care Management.*

### FOOTNOTES

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