KMA
Keegan Mason & Associates

# ANTIBIOTIC STEWARDSHIP:

## Microbial Stewardship & Antibiotic Preservation

## ANTIBIOTICS AND THE RESISTANCE DILEMMA

The discovery of antibiotics was one of the greatest advances in human health, and after their clinical introduction it was anticipated infectious disease would soon be eradicated. Use of penicillin on the battlefield during World War II marked the beginning of the "Golden Era" of antibiotics, a time during which most currently available antibiotics were discovered and marketed. Newly developed antibiotic therapies were dubbed "wonder drugs" as they effectively treated and prevented infection, which subsequently allowed for advances in surgical and chemotherapy technologies. However, almost immediately after large-scale implementation of antibiotics, the problem of drug resistance was observed. While originally thought to be of limited concern, we now know use, overuse, and misuse of antibiotics directly contributes to the rise of resistant bacteria and a subsequent decline in the arsenal of effective treatments. Antimicrobial resistance (AMR), especially in human pathogens, has spread in an unprecedented manner, and has thus been declared a global health crisis. The Centers for Disease Control and Prevention projects that by 2050, more people will die of infection than from cancer, exceeding 10 million annual deaths globally.[1]

While clinical use of antibiotics has resulted in dramatic decreases in infectious disease morbidity and mortality, their aggressive and empirical use in healthcare has been a prevailing best management practice. Although human healthcare relies on the use of antibiotics to treat infections, this paradoxically increases the emergence of the rapidly-evolving threat of antibiotic resistance [Figure 1]. Compounding the problem of ineffective antibiotics is the fact that they are vastly overprescribed and misused, resulting in limited, less effective, and more expensive treatment options [Table 1]. It is estimated that at least 30% of overall antibiotic prescriptions are unnecessary, and in acute respiratory conditions, the rate is closer to 70%.[2] Thus, AMR

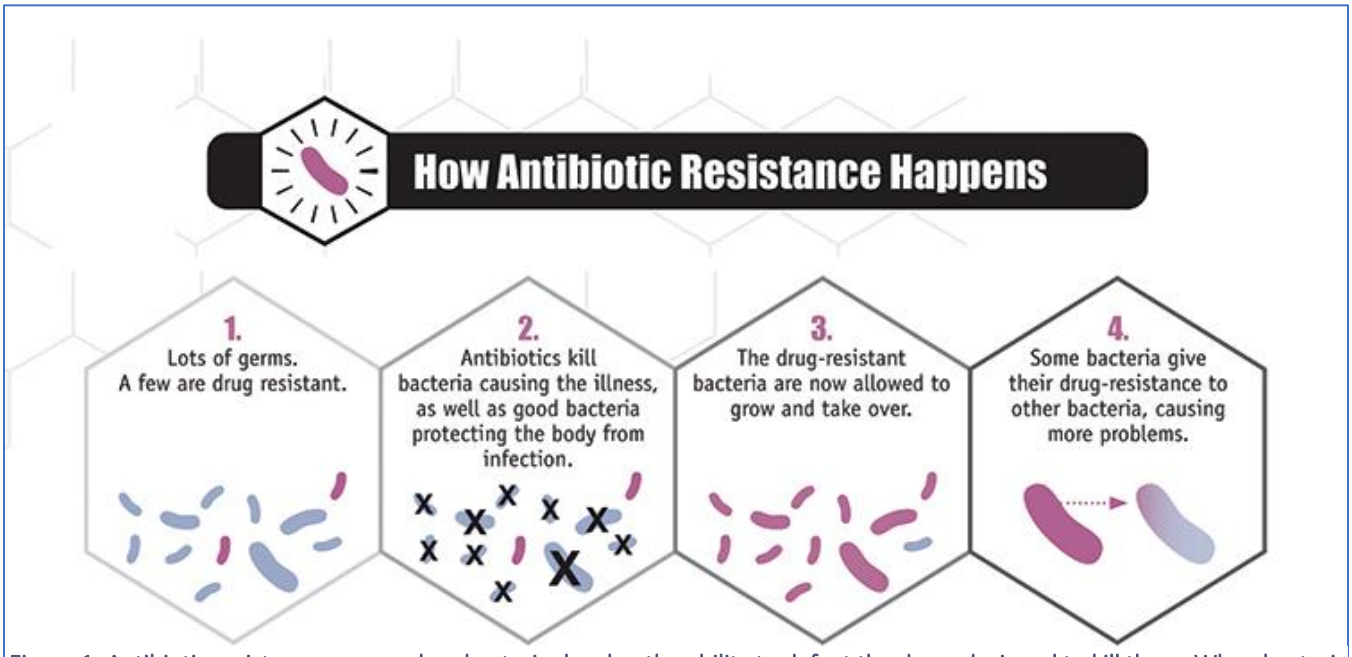


Figure 1: Antibiotic resistance occurs when bacteria develop the ability to defeat the drugs designed to kill them. When bacteria become resistant, antibiotics cannot fight them, and the bacteria multiply, worsening infection.

becomes progressively concerning, as the prevalence of bacterial infections that cannot effectively be treated with antibiotics continues to rise. Currently, in the United States, 2 million people each year are infected with resistant bacteria, directly resulting in 23,000 deaths.[1] The CDC's 2013 report on *Antibiotic Resistance Threats in the United States* provides national assessment of the most threatening antibiotic resistant organisms according to relative hazard level [Figure 2]. Many bacteria on this watchlist are multidrug resistant (MDR) organisms, or "superbugs." Highlighting the MDR threat was a recent case where a patient died from infection with a superbug that was not susceptible to ANY of the antibiotics currently on the market.

Infectious disease was a leading cause of death until the dawning of the antibiotic era. However, for every class of antibiotic that has been discovered and used clinically, resistance has appeared within a matter of years. Antibiotics are societal drugs, and the more we use them, the less effective they become. As the rate of AR increases, treatment options become exhausted and the rate of mortality correspondingly increases. As a result, most first-generation antibiotics and many of their successors are obsolete, as they have lost their efficacy due to resistance. The World Health Organization warns that we are on the verge of a pre-antibiotic era; a time when routine surgery and common infections will again become deadly. Global recognition of the need to preserve effective antibiotic therapies is necessary, and the judicial use of antibiotics is vital to preserving them for future generations.

Table 1 | Factors that Promote Antibiotic Resistance; Adapted from National Institute of Allergy and Infectious Diseases *Antibacterial Resistance Program* (2014)

- Concentrated bacterial population density in healthcare facilities; allows for transfer of resistance genes within a community and enables resistance to emerge
- Empiric use of broad-spectrum antibiotics; can exert selective pressure on commensal bacteria within the human microbiome
- Lack of emphasis on diagnostic tests to guide proper antibiotic prescribing and failure to adjust treatment upon test results
- Use of antibiotics for viral infections for which they are not effective
- Patient perception of antibiotics as a "cure-all"
- Subinhibitory concentrations of antibiotics which increase the rate of adaptive evolution of resistance
- Lack of familiarity with the community antibiogram – a measure of the degree of antimicrobial resistance

## *Clostridium difficile*: A DANGEROUS SIDE-EFFECT OF ANTIBIOTICS

Coinciding with the growing problem of antibiotic resistance is the impact that antibiotics, particularly the systemic administration of broad-spectrums, have on the diversity of, and resistome within, the microbiome of the patient, especially in the gut. The exploration of the differential effects of antibiotic use is a relatively new field of study; however, it has been demonstrated that monitoring the composition and resistance of microbiome for common patterns may be beneficial in predicting and possibly preventing some of the adverse effects of antibiotic treatments.

*Clostridium difficile* is the most common healthcare-associated pathogen, often implicated in cases of life-threatening antibiotic-induced diarrhea. Since 2000, the United States has experienced a sharp increase in both the rates and the severity of *C. difficile* infection (CDI). The major risk factors for CDI are exposure to antibiotics, particularly to fluoroquinolones, and to the healthcare system, which can be heavily - contaminated by the organism. Given the fact that CDI is the number one ranked nosocomial infection, and there are approximately half a million cases and 15,000 deaths in the U.S. annually, the CDC has ranked *C. difficile* as hazard level "urgent" in the antibiotic resistance threat assessment [Figure 2].

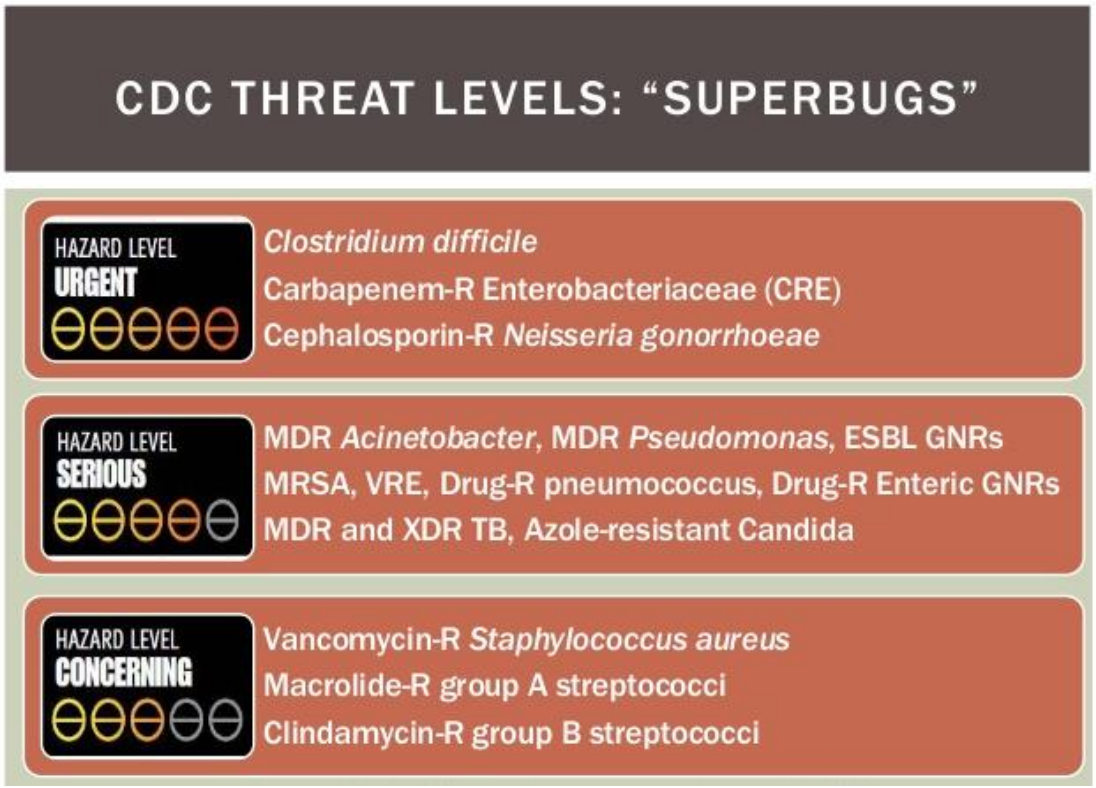


Figure 2: The assessment by the CDC of antibiotic resistance threats in the United States. Resistant organisms were assessed according to clinical impact, economic impact, incidence, 10-year projection of incidence, transmissibility, availability of effective antibiotics, and barriers to prevention.

## ANTIBIOTIC STEWARDSHIP

Antimicrobial stewardship is a coordinated effort to reduce misuse and overuse of antibiotic drugs, improve patient outcomes, and reduce clinical rates of multidrug resistant infections. The fundamental objective of an antimicrobial stewardship program (ASP) is to maintain and improve current efficacy of antibiotics and ultimately reverse the antibiotic resistance characteristics of bacteria within a community. ASP implementation has recently become a mandatory Condition of Participation by the Centers for Medicare & Medicaid Services (CMS), and is a required component to hospital accreditation by the Joint Commission.

Keegan Mason and Associates (KMA), LLC are nationally recognized leading experts in antimicrobial stewardship programs and have an extensive history of innovative practices which align with the CDC's 7 Core Elements of an effective ASP [Figure 3]. We employ a precise, deliberate, objective, and proven approach to education, guidance, monitoring, and partnership with providers to optimize successful outcomes. KMA works in tandem with Crossover Biomedical, a group of investigators who are experts in molecular biology and diagnostics, as well as full-time and adjunct faculty at two universities. Crossover Biomedical currently performs bacterial genetic and genomic research related to pathogens and antibiotic resistance.

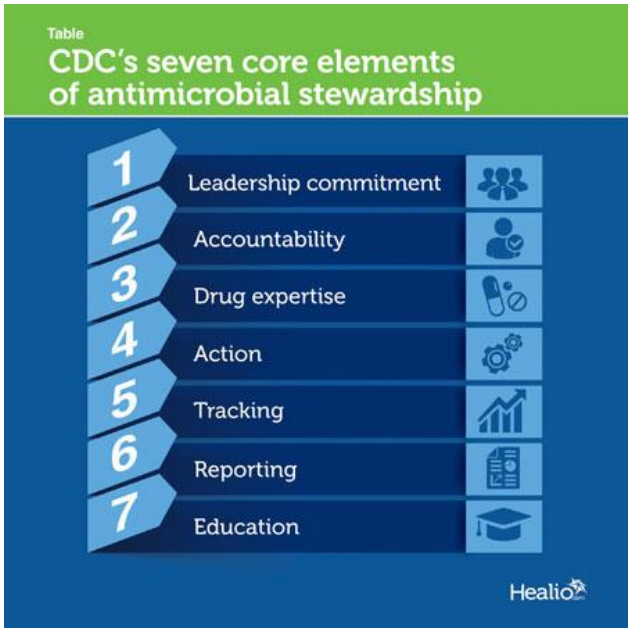


Figure 3: According to the CDC, a growing body of evidence demonstrates Antibiotic Stewardship Programs can both optimize the treatment of infections and reduce adverse events associated with antibiotic use.

The scope of our ASP involves providing education of the current science of precise antibiotic use, overseeing and analyzing data to identify areas of potential concern, and providing general recommendations for antibiotic usage. Furthermore, we work to integrate, embed, and optimize antibiotic best use practices. We recommend use of molecular diagnostic tools to guide clinical decision-making by providing timely data essential for prevention, diagnosis, and treatment under our model of "***aggressive diagnostics, conservative therapeutics.***"

Regional Health in Rapid City South Dakota is the site of a model ASP, which has been subsequently and successfully implemented in approximately 30 hospitals across the country. In 2000, we identified a rapid increase in antibiotic resistance in the Rapid City region. Through partnerships with physicians, pharmacists, laboratory managers, the Director of Infection Prevention and Control, and South Dakota Department of Health, we were able to identify and implement specific interventions, including viral diagnostic technology, to reverse the trends in resistance. Within a short time, the community antibiogram stabilized, and the protocols put in place to limit antibiotic use decreased the incidence of *Clostridium difficile* infection (CDI), methicillin-resistant *Staphylococcus aureus* (MRSA), and resistant gram-negative numbers to significantly below the national average. Further implementations of the ASP in rural South Dakota communities were successful in moving the antibiogram from below to significantly ahead of the state average, and there was a nearly 60% decrease in broad-spectrum antibiotic use.

| Primary Goals of our Antibiotic Stewardship Program |
|---|
| Establishing an antibiotic use strategy for safeguarding the protective human microbiome |
| Optimizing clinical operations based on a thorough understanding of improvement science |
| Preserving effective antibiotic therapy for future generations |
| Decreasing overall antibiotic exposure by reducing antibiotic days of therapy and length of therapy |
| Attenuating and/or reversing the rate of emergence of resistant bacteria |
| Expanding access to state-of-the-art molecular diagnostics and biomarkers to ensure patients get individualized specific therapy rather than overuse empiric therapy |
| Increasing patient safety and overall healthcare quality |
| **Secondary Outcomes of our Antibiotic Stewardship Program** |
| Better patient care and fewer readmissions |
| Impressive returns on investment in ASP, especially related to pharmacy costs |
| Ensure compliance with CMS- and Joint Commission-mandated standards on ASP |
| Avoidance of CMS Discounts for inadequate ASPs |

*Adapted from Spelberg, 2016[3]

## Key KMA Services

- 24/7 access and support from our pioneering infectious disease physician and the antibiotic stewardship team
- More than 20 years of ASP experience with proven results
- Engagement of local physician and pharmacy champions
- Quality management practices guidance
- Concurrent monitoring of prescribing activity and microbiology patterns
- Ongoing review and data analysis to ensure ASP sustainability
- Transparent reporting of outcomes
- Robust safety bundle recommendations
- Transformational change
- Process improvements through Lean methodology
- Antibiogram education
- Development of specific, individualized protocols based on local antibiograms
- Data analysis
- Molecular diagnostics expertise

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[1]Centers for Disease Control and Prevention (2017). *Antibiotic/antimicrobial resistance.*
[2]Centers for Disease Control and Prevention (2016). *CDC Newsroom: 1 in 3 antibiotics unnecessary.*
[3]Spellberg, B, Bartlett, J.G., Gilbert, D.N. Open Forum Infectious Diseases (2016). *How to pitch an antibiotic stewardship program to the hospital C-suite.*