

## Antibiotic Resistant Strains

### Summary

Antibiotic-resistant pathogens, or "superbugs," are natural or man-made induced mutations created by the acquisition of new genes in disease causing bacteria resulting in the reduction or elimination of the effectiveness of antibiotics. Such resistant bacteria are presently a major public health threat and, if unresolved, threatens to evolve into a health security crisis. The Centers for Disease Control and Prevention (CDC) reported two million Americans acquire serious infections to one or more strains of antibiotic-resistant pathogens annually resulting in 23,000 deaths with many more dying from other medical conditions complicated by such infections.<sup>436</sup> In addition to their direct role in combating infectious diseases, the prophylactic use of antibiotics is essential for a wide range of basic to complex surgical and medical procedures. As antibiotic-resistance grows, so does the possibility of losing such surgical and other therapeutic interventions due to an unacceptable high risk of postoperative or procedural infections. Additionally, the public health risk of endemic bacterial contagious diseases will increase proportionately with antibiotic resistance (e.g. Group A Streptococcus (GAS) or "strep;" pneumococcal pneumonia; bacterial meningitis; multidrug-resistant tuberculosis [MDR-TB]; etc.). There is also the added risk that the public confidence in scientific evidence based medical therapies could eventually be undermined causing patients to seek unproven and hazardous alternatives cures.

Antibiotic-resistant pathogens are a direct threat to the resiliency of the nation. This would include increased morbidity and mortality rates related to trauma and contagious diseases impacting: U.S. military personnel, public safety officers and health-care workers. Moreover, services provided by critical health infrastructures such as tertiary care centers, nursing homes, dialysis centers, etc. could be dramatically impaired due to healthcare-acquired (or nosocomial) antibiotic-resistant pathogens. Antibiotic-resistant pathogens increase the strain on limited medical and public health resources at all levels of government as well as carry significant future risk to domestic and international economies.<sup>437</sup> This issue also presents an increased risk to a rapidly aging U.S. population who are more susceptible and vulnerable to infectious diseases. Current intercontinental commerce and travel provides ready opportunities for antibiotic-resistant pathogens to spread globally, severely limiting the ability of any one country to successfully tackle this issue in isolation. International cooperation will be required to avoid a post-antibiotics world.

### Discussion

In recognition of the risk posed to the nation by antibiotic-resistant pathogens, the *National Strategy for Combating Antibiotic-Resistant Bacteria* was released by the White House in

<sup>436</sup> Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States, 2013* (Washington, DC: US Department of Health and Human Services, 2013), p. 11.

<sup>437</sup> British High Commission- Chaired by Jim O'Neill (December 2014) *Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations*, United Kingdom. [http://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations\\_1.pdf](http://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1.pdf)

September 2014.<sup>438</sup> This national strategy initiative was in direct response to CDC's findings that an estimated 2 million people annually in the U.S. acquire serious bacterial infections resistant to one or more of the antibiotics, resulting in approximately 23,000 deaths.<sup>439</sup> These numbers do not include those who die from other conditions that were complicated by an antibiotic-resistant infection. Antibiotic-Resistant is defined in this National Strategy as "...resistance results from mutations or acquisition of new genes in bacteria that reduce or eliminate the effectiveness of antibiotics."

Simply stated, antibiotic-resistant pathogens are able to adapt, multiply, and cause diseases unimpeded by the use of one or more antibiotic therapies. Antibiotic-resistant pathogens result in increased severity of infection with greatly limited and more expensive treatment protocols – if treatment is available at all. Over usage of antibiotics is the primary cause for the increase in antibiotic resistance as select bacteria survive by developing mutant genes against which antibiotics have decreased effectiveness. Through reproduction and/or the exchange of genetic material between different bacteria such resistance may spread rapidly and unpredictably, potentially causing a wide scope of resistant infections. As antibiotics often belong to similar classes of medicines, specific resistance to one agent can result in resistance to an entire related class of antibiotics. In addition to circulating in human and animal populations, resistant bacteria can be also found in the human consumption food-chain.

As the risk of antibiotic-resistant pathogens grows, so will the associated morbidity and mortality rates, resulting in longer hospitalization stays, increasing the risk of compromising protection of surgical patients and others undergoing a wide-range of medical and dental procedures as well as an accompanying increase health care costs. The CDC has estimated annual excess direct health care cost of antibiotic-resistant pathogens to the U.S. economy at \$20-35 billion, including approximately 8 million additional days of hospitalization, with an annual lost productivity cost of \$35 billion.<sup>440</sup>

Inappropriate and overuse of antibiotics can exacerbate the selection resistant microorganisms to such an extent that "[t]he extensive use of antimicrobial drugs has resulted in drug resistance that threatens to reverse the medical advances of the last seventy years."<sup>441</sup> This problem is compounded in hospitals, nursing homes, etc., where the widespread use of antibiotics, along with the close proximity among the sick, provides a fertile environment for developing and transmitting antibiotic-resistant pathogens, also known as nosocomial infections. This becomes a more pressing concern given the increased risk presented by a rapidly aging U.S. population that is more susceptible and vulnerable to infectious diseases while concurrently placing greater

<sup>438</sup> The White House (September 2014) *The National Strategy for Combating Antibiotic-Resistant Bacteria*, Washington, D.C.

[https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast\\_carb\\_report\\_sept2014.pdf](https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast_carb_report_sept2014.pdf)

<sup>439</sup> Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States, 2013* (Washington, DC: US Department of Health and Human Services, 2013), p. 11

<sup>440</sup> Roberts, RR, Hota, B, Ahmad, I, et al. "Hospital and Societal Costs of Antimicrobial-resistant Infections in a Chicago Teaching Hospital: Implications for Antibiotic Stewardship," *Oxford Journal of Clinical Infectious Disease*, 49(8): 1175-1184, 2009. [www.tufts.edu/med/apua/consumers/personal\\_home\\_5\\_1451036133.pdf](http://www.tufts.edu/med/apua/consumers/personal_home_5_1451036133.pdf).

<sup>441</sup> Interagency Task Force on Antimicrobial Resistance, 2012. *A Public Health Action Plan to Combat Antimicrobial Resistance* - page 5. Washington, D.C. <http://www.cdc.gov/drugresistance/pdf/actionplan-2012.pdf>

utilization demand on such health-care facilities. The U.S. population aged 65 and over, currently at approximately 43.1 million, is projected to grow to 83.7 million in 2050.<sup>442</sup>

There is also the concern that antibiotic-resistant pathogens are being accelerated through the commercial practice of adding antibiotics to agricultural feed products to stimulate growth and/or for disease control in animals confined in crowded and unsanitary conditions, especially given that “approximately 80 percent of the antibiotics sold in the United States are used in meat and poultry production.”<sup>443</sup> To illustrate in 2011, “ground beef from the Hannaford grocery store chain in New England was linked to 19 infections and at least seven hospitalizations, all caused by a strain of *Salmonella* resistant to multiple antibiotics, including amoxicillin/clavulanic acid, ampicillin, ceftriaxone, cefoxitin, kanamycin, streptomycin, and sulfisoxazole.”<sup>444</sup> CDC has presently identified “carbapenem-resistant, *Enterobacteriaceae* (CRE), ceftriaxone-resistant *Neisseria gonorrhoeae* and *Clostridium difficile*,” within its highest or “urgent” threats.<sup>445</sup>

The following are included in the CDC’s second highest or “serious” threats category:

Multidrug-resistant *Acinetobacter*, Drug-resistant *Campylobacter*, Extended spectrum  $\beta$ -lactamase producing *Enterobacteriaceae* (ESBLs), Vancomycin-resistant *Enterococcus* (VRE), Multidrug-resistant *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), Drug-resistant *Non-typhoidal Salmonella*, Drug-resistant *Salmonella Typhi*, Drug-resistant *Shigella*, Drug-resistant *Streptococcus Pneumonia* and Drug-resistant *Tuberculosis*.<sup>446</sup>

The third level, labeled “concerning” threats include:

Vancomycin-resistant *Staphylococcus aureus* (VRSA), Erythromycin-resistant Group A *Streptococcus*, and Clindamycin-resistant Group B *Streptococcus*. CDC has also indicated that “Among all of the bacterial resistance problems, gram-negative pathogens are particularly worrisome, because they are becoming resistant to nearly all drugs that would be considered for treatment.”<sup>447</sup>

The U.S. Department of Health and Human Services (HHS) is the lead federal agency responsible for addressing and coordinating the whole of government response to this issue. The scale of antibiotic-resistant pathogens needs to be acknowledged as a global risk within the context articulated in the U.S. Department of Health and Human Services’ (HHS) *National Health Security Strategy 2015-2018*. “The health of the American people and that of the people around the world are more closely linked than ever before. Greater movement of people, animals, and goods across international borders increases the risk of exposure to health threats

<sup>442</sup> Jennifer M. Ortman, Victoria A. Velkoff, and Howard Hogan, U.S. Census Bureau, *An Aging Nation: The Older Population in the United States*, May 2014, Report Number: P25-1140. <http://www.census.gov/content/dam/Census/library/publications/2014/demo/p25-1140.pdf>

<sup>443</sup> Congresswomen Slaughter Louise M. U.S. House of Representatives. “Confirmed: 80 Percent of all antibacterial drugs used on animals, endangering human health. <http://louise.house.gov/press-releases/confirmed-80-percent-of-all-antibacterial-drugs-used-on-animals-endangering-human-health/>

<sup>444</sup> CDC. 2012. “Investigation Update: Multistate Outbreak of Human *Salmonella* Typhimurium infections Linked to Ground Beef. [www.cdc.gov/salmonella/typhimurium-groundbeef/010512/index.html](http://www.cdc.gov/salmonella/typhimurium-groundbeef/010512/index.html)

<sup>445</sup> The White House (September 2015) *The National Strategy for Combating Antibiotic-Resistant Bacteria*, Washington, D.C. [https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast\\_carb\\_report\\_sept2014.pdf](https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast_carb_report_sept2014.pdf)

<sup>446</sup> Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States, 2013* (Washington, DC: US Department of Health and Human Services, 2013), p. 7 & 22.

<sup>447</sup> Ibid

originating outside one's own country.”<sup>448</sup> To underscore how wide-spread this issue is, the European Centre for Disease Prevention and Control (ECDC) and European Medicines Agency (EMA) in 2007, estimated 25,000 deaths attributable to infections due to selected antibiotic-resistant pathogens in the European Union, Iceland and Norway.<sup>449</sup> And “In a study of resistance patterns of several common bacteria in China in 1999 and 2001, the mean prevalence of resistance among hospital-acquired infections was as high as 41%, and that among community-acquired infections was 26%.<sup>450</sup>

In an age of globalization, no country can on its own ensure the public health of its population from this risk. Every country is directly or indirectly vulnerable by forces driving international social, economic, and political interdependences such as immigration, travel, commerce, etc. Additionally, foreseen and unforeseen consequences may occur driven by natural and geopolitical crises (e.g. global climate change, conflict, mass refugee displacement, breakdown of other nation critical health infrastructure, etc.) which reduce the global resiliency to antibiotic-resistant pathogens.

In conclusion the U.S. Department of Health and Human Services (HHS) provides the leadership for ensuring that the “actions the United States takes domestically must be complemented by coordinated international action in order to ensure that resistant strains that arise in one part of the world are rapidly detected, diagnosed, and contained at the source of emergence. The United States and international partners must work to promote innovations in drug and diagnostics development, enhance stewardship of existing antibiotics in human and agricultural settings, and strengthen systems for detecting, diagnosing, and monitoring resistance so that reporting is timely, accurate, and transparent.”<sup>451</sup>

<sup>448</sup> U.S. Department of Health and Human Services (HHS). (2015, February) *The National Health Security Strategy 2015-2018 (NHSS)*. Page 29, Washington, D.C. <http://www.phe.gov/Preparedness/planning/authority/nhss/strategy/Documents/nhss-final.pdf>

<sup>449</sup> European Centre for Disease Prevention and Control ECDC/ European Medicines Agency: *EMA Joint Technical Report: The Bacterial Challenge: Time to React*. ECDC, Stockholm Sweden; 2009.

<sup>450</sup> Heddini A, Cars O, Qiang S, Tomson G., *Antibiotic Resistance in China--a Major Future Challenge*. Lancet. 2009 Jan 3;373 (9657):30. doi:10. 1016/S0140-6736(08)61956-X. [http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(08\)61956-X.pdf](http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(08)61956-X.pdf)

<sup>451</sup> The White House (September 2015) “*The National Strategy for Combating Antibiotic-Resistant Bacteria*”, page 20. Washington, D.C. [https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast\\_carb\\_report\\_sept2014.pdf](https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast_carb_report_sept2014.pdf)