The United Front Against Antibiotic Resistance (AR)

By Lisa Lucke

Two million: That's the number of people in the U.S. alone each year who become infected with antibiotic-resistant bacteria. Of that number, 23,000 people will die as a "direct result of these infections," according to the Center for Disease Control's (CDC) 2013 report, "Antibiotic resistance threats in the United States, 2013." Furthermore, "many more will die from other conditions that were complicated by an antibiotic resistant infection[1]."

The CDC is so concerned about the future of antibiotic-resistant disease control that it has launched a $264 million effort to combat the problem, called the *Antibiotic Resistance Solutions Initiative*. This comprehensive response has identified several core actions to target, which span a wide range of activities, from strengthening national surveillance efforts to combat resistance and advancing the development of innovating diagnostic tests that identify and characterize resistant bacteria, to improving collaboration and capacities for AR prevention, surveillance, control and R&D, *worldwide*. Other activities the CDC lists as critical in its report, *FY16 AR Solution Initiative,* include the following[2]:

- Stop Spread and Protect People: Action in Every State:
    - Includes establishment of networked, state AR prevention programs that improve prescription habits, track outbreaks and work to prevent infections; identify critical interventions; support development of next generation rapid susceptibility tests for drug-resistant pathogens; identify new ways to prevent human infections caused by resistant bacteria
- Track Superbugs and Measure Impact: Accelerate outbreak detection and prevention innovation:
    - Includes creation of network of AR regional labs that respond to outbreaks, more quickly determine which antibiotics work, and use cutting edge tools to stay ahead of outbreak patterns; measure impact of antibiotics on human microbiome; expand CDC's Emerging Infections Program (EIP) sites; enhance global partnerships for prevention and detection to combat AR internationally
- Track and Improve Prescribing: Improve antibiotic use and reduce antibiotic resistance:
    - Provide real-time data about antibiotic use and trends in healthcare in specific facilities and across regions using the National Healthcare Safety Network (NHSN); improve antibiotic prescribing practices in healthcare (antibiotic stewardship); provide real-time data about antibiotic use and trends for outpatient care; measure the impact of antibiotic use on human and animal health and greatly scale up rapid detection of AR infections commonly transmitted through food to humans

Additionally, new technology that provides molecular-based microbial testing offers the data needed to aggressively treat the very specific microbes that are causing the infection, resulting in saved lives, drastically faster healing, and reduced chronic infections. Dr. Randall Wolcott, M.D., a wound-care specialist and founder of biotech company PathoGenius, explains:

"The traditional culture is suited to treat acute infections caused by single cell or planktonic bacteria. Cultures are not designed to identify the collaborative communities of bacteria (biofilm) that cause

chronic infections. We now know there are over 25k species of microbes and 99% of them cannot be identified in traditional culture. Anaerobes and fungal species are especially difficult."

Acknowledgement of the Crisis—*Outside* of the Medical Establishment

The steadily increasing number of cases antibiotic resistant (AR) diseases happening in the U.S. each year is causing growing concern that reaches far beyond the medical community. On September 18, 2014, President Obama signed an Executive Order, "Combating Antibiotic Resistant Bacteria."

From that document, **Section 1, Policy**:

"The discovery of antibiotics in the early 20th century fundamentally transformed human and veterinary medicine. Antibiotics save millions of lives each year in the United States and around the world. The rise of antibiotic-resistant bacteria, however, represents a serious threat to public health and the economy. The Centers for Disease Control and Prevention (CDC) in the Department of Health and Human Services (HHS) estimates that annually at least two million illnesses and 23,000 deaths are caused by antibiotic-resistant bacteria in the United States alone."

The report also cites several lines of attack for making a difference in the future of combatting antibiotic resistance:

"Detecting, preventing, and controlling antibiotic resistance requires a strategic, coordinated, and sustained effort. It also depends on the engagement of governments, academia, industry, healthcare providers, the general public, **and the agricultural community**, as well as international partners."

From Fundamental Transformation to Current Crisis: Understanding the Cause(s)

How did we get *here*?

The current medical crisis surrounding anti-microbial resistant infection and disease is nothing new, and has been under scrutiny for many years. According to the Journal of Antimicrobial Chemotherapy, published by Oxford University Press, anti-microbial resistance was referred to as a "major" clinical and public health problem as far back as 2002. And it is a view echoed by the CDC, National Institutes of Health (NIH), and other leading medical research institutes around the world.

Also agreed upon are the origins of the issue. Since the development of antibiotics more than 70 years ago, their widespread use, over-prescription, and misuse by consumers are the most-often cited reasons for the current situation. Additionally, the advent and growing use of person hygiene products ("hand-sanitizers") and surface antimicrobials found in household cleaning agents are also contributing factors. In a paper published more than a decade ago[2], the anti-microbe agents contained in "personal use products" were already being cited as serious factors that were exacerbating the problem:

"These too enter the environment. The stage is thus set for an altered microbial ecology, not only in terms of resistant versus susceptible bacteria, but also in terms of the kinds of microorganisms surviving in the treated environment. We currently face multi-resistant infectious disease organisms that are difficult and, sometimes, impossible to treat successfully."

How Animals and Plants Contribute

The practice of pumping commercially raised livestock, including cows, chicken, and swine with antibiotics to thwart the development and spread of bacterial infections within the confines of commercial livestock facilities is well documented. In a recent paper published by leading medical journal, *The Lancet*, authors discussed the need to turn our attention to the global overuse of anti-biotics not only among humans, but the animal population as well. What's more, it isn't just meat that is a problem; plants, including commercial crops destined for the dinner table are also a factor:

"One common means by which antibiotic resistant bugs pass from animal to humans is through eating meat, explained Dr. Luke Moore, co-author of the study, from the Department of Medicine at Imperial College London: "'If you eat a chicken that contains an antibiotic resistant bacteria, such as E.coli – and the chicken is not cooked properly – the bacteria can lodge in your gut. There is then a risk of it escaping from your intestines, and perhaps travelling to your gallbladder or urinary tract, where it may potentially trigger an infection that doesn't respond to antibiotics.

"'Meat tissue may contain molecules of the antibiotic drug itself. These molecules can travel to your intestines and increase antibiotic resistance in the bacteria that naturally reside in your gut,'" he added.

It is not just meat that can carry antibiotic resistance – crops and vegetables can harbour them too, from animal manure used as fertiliser. The researchers suggest that a number of strategies are needed to tackle the issue."

Status Quo for Treatment vs. Emergence of State-of-the-Art DNA Sequencing in Fight against AR

Traditional culturing practices used to identify the presence of bacterial infections date back more than 150 years. Often taking several days or more, the practice of taking a "sample" from an infected person and then growing the culture in a lab is problematic at best, and life-threatening at worst, when compared with cutting-edge techniques now being practiced around the world. Traditionally, bacterial culturing has led doctors to often prescribe an antibiotic that combats a range of bacteria. Now, with DNA sequencing technology, doctors can obtain both immediate *and* targeted results that analyze and identify bacterial infections at the molecular level.

Promising Solutions for the Future

According to the World Health Organization (WHO), urgent and coordinated action is the key to preventing a post-antibiotic era, in which the most common infections and even minor injuries, once easily treatable, can again lead to death.

WHO is working closely with the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) to encourage best practices that are aimed at avoiding the spread of AR, including accurate and optimum use of antibiotics in both animals and humans.

An organized, networked, *global* effort to create a solution for tracking antibiotic resistance is in motion, but still has far to go before modern medicine will be able to stop, let alone reverse the steady rise in the numbers of antibiotic resistance-related infections and deaths each year. With the emergence of state-of-the-art advances in biotechnology designed specifically for this effort, along with policymakers,

medical personnel, pharmacists, and of course, increasingly better-informed patients, the numbers will hopefully change for the better in our lifetime.

References

1. www.cdc.gov

2. Journal of Antimicrobial Chemotherapy, Oxford University Press, 2002.

3. World Health Organization (WHO).