THE US GOVERNMENT'S STRATEGY AGAINST ANTIBIOTIC-RESISTANT BACTERIA

A federal initiative targets antimicrobial resistance and supports discovery efforts with $30 million in annual funding for 5 years.

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The Centers for Disease Control and Prevention (CDC) estimates that at least 2 million illnesses and 23,000 deaths are caused annually by antibiotic-resistant bacteria in the United States alone.[1] The BBC reported that, in Europe and the United States, 50,000 deaths each year are attributable to antimicrobial resistance and that, unless action is taken, deaths will rise more than 10-fold by 2050. Also by 2050, more than one in four deaths in Nigeria will be caused by drug-resistant infections, and India will lose an additional 2 million lives each year, the BBC said.[2]

On September 18, 2014, President Barak Obama issued an Executive Order affirming the US government's commitment to establishing "a strategic, coordinated, and sustained effort" for detecting, preventing, and controlling antibiotic resistance: "The Federal Government will work domestically and internationally to detect, prevent, and control illness and death related to antibiotic-resistant infections by implementing measures that reduce the emergence and spread of antibiotic-resistant bacteria and help ensure the continued availability of effective therapeutics for the treatment of bacterial infections."[3]

To support the White House's National Strategy for Combating Antibiotic-Resistant Bacteria,[4] the CDC formed the Detect and Protect Against Antibiotic Resistance Initiative (known as the AR Initiative) to focus its efforts on four areas:

- Slow the development of resistant bacteria and prevent the spread of resistant infections
- Strengthen national "one-health" surveillance efforts to combat resistance. A one-health approach "promotes the integration of public health and veterinary disease, food, and environmental surveillance. Improved detection can be achieved through appropriate data sharing, enhancement, expansion, and coordination of existing surveillance systems."[4]

NEW ANTIBIOTIC KILLS DRUG-RESISTANT BACTERIA

The National Institutes of Health reported that researchers at Northeastern University have discovered a new antibiotic called *teixobactin* in soil from a grassy field in Maine. Teixobactin is unique because of its ability to kill a wide range of infection-causing bacteria through a mechanism markedly different from those of existing antibiotics.

Teixobactin is a defensive toxin made of a few amino acids in an unusual arrangement. It is produced by the newly identified proteobacteria species *Eleftheria terrae*. Test tube experiments showed teixobactin to have excellent activity against 19 types of gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* and enterococci, which are now immune to most other antibiotics.[1] Trials on mice showed that teixobactin rapidly cleared infections of drug-resistant strains of *Mycobacterium tuberculosis* and *S aureus* bacteria, according to a study in *Nature*.[2]

The compound reportedly attacks these and other gram-positive bacteria by binding to chemicals essential to forming cell walls. Because this mechanism of action does not involve proteins, researchers think bacteria will be far less likely to develop resistance to teixobactin than to the many current antibiotics that target proteins. Teixobactin is not active against Gram-negative bacteria, however, which include the deadly and rapidly emerging threat of Klebsiella and other carbapenem-resistant Enterobacteriaceae.

Kim Lewis, PhD, MSc, the senior author of the *Nature* article, and colleagues cultivated teixobactin in the laboratory by mixing 1 g of soil with water and nutrient-rich broth and then pipetting the mixture onto a miniature device, called an iChip, capable of trapping a single microbe in each of its many wells. The iChip was then placed in a bucket of soil to incubate for 1 month. Many of the microbes replicated and formed thriving colonies, which were then removed from the iChip and cultivated on petri dishes.

In collaboration with colleagues from Germany, England, and NovoBiotic Pharmaceuticals, Dr. Lewis' team used the iChip approach to study 10,000 different species of soil bacteria. The researchers reportedly isolated more than 25 potential new drug compounds, including a number of possible antibiotics, an anticancer agent, and a compound that specifically targets the bacteria that cause tuberculosis.[1]

More safety and efficacy testing is needed in animal models before clinical trials can be conducted in humans, which could be as soon as 2 years from now.

NovoBiotic Pharmaceuticals owns the patent for the new molecule. Several of the researchers have financial stakes in the company. Financial support for the research also came from the National Institutes of Health and the German government.

1. Collins F. Digging up new antibiotics. http://directorsblog.nih.gov/2015/01/13/digging-up-new-antibiotics. National Institutes of Health website. Accessed February 19, 2015.
2. Ling LL, Schneider T, Peoples AJ, et al. A new antibiotic kills pathogens without detectable resistance. *Nature*. 2015;517:455-459.

- Advance the development and use of rapid and innovative diagnostic tests for the identification and characterization of resistant bacteria
- Improve international collaboration and capacities for antibiotic resistance prevention, surveillance, and control and antibiotic research and development

The AR Initiative is part of the CDC's strategy to target investment at antibiotic resistance. The 2015 President's Budget requests $30 million in annual funding for 5 years for the AR Initiative to achieve measurable results for detecting and tracking patterns of antibiotic resistance, responding to outbreaks, preventing infections from occurring and resistant bacteria from spreading, and supporting the National Institutes of Health (NIH) and private industry in their discovery efforts.[5]

According to the CDC,[5] a $30 million annual funding level over 5 years could achieve

- a 50% reduction in health-care-associated *Clostridium difficile*
- a 50% reduction in health-care-associated carbapenem-resistant *Enterobacteriaceae* infections
- a 30% reduction in health care-associated multidrug-resistant *Pseudomonas*, a common cause of health care-associated infections
- a 30% reduction in invasive methicillin-resistant *Staphylococcus aureus*
- a 25% reduction in multidrug-resistant *Salmonella* infections

The goal of the CDC's AR Initiative is to improve detection through the creation of a new regional laboratory network and resistant bacteria bank. It also seeks to prevent infection and improve antibiotic prescribing practices in health care facilities and in the community. ■

1. Centers for Disease Control and Prevention. National strategy to combat antibiotic-resistant bacteria. http://www.cdc.gov/drugresistance/national-strategy/index.html. Accessed February 11, 2015.
2. Walsh F. Superbugs to kill 'more than cancer' by 2050. http://www.bbc.com/news/health-30416844. Accessed January 15, 2015.
3. The White House. Executive Order: Combating Antibiotic-Resistant Bacteria. http://www.whitehouse.gov/the-press-office/2014/09/18/executive-order-combating-antibiotic-resistant-bacteria. Accessed February 11, 2015.
4. National Strategy for Combating Antibiotic Resistant Bacteria. http://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf. Accessed February 11, 2015.
5. Centers for Disease Control and Prevention. Detect and protect against antibiotic resistance. http://www.cdc.gov/drugresistance/pdf/AR_Initiative_Fact_Sheet.pdf. Accessed February 11, 2015.