FACT SHEET

Antimicrobial Resistance

NATIONAL INSTITUTES OF HEALTH

Yesterday

- The success of antimicrobials against disease-causing microbes—including bacteria, viruses, and fungi—is among modern medicine's great achievements.
- The German physician Paul Ehrlich developed a narrow-spectrum antibiotic called Salvarsan in 1909 for treatment of syphilis. Discovery of penicillin by Alexander Fleming followed in 1928.
- By the mid 1940s, penicillin was the treatment of choice for *Staphylococcus aureus* (*S. aureus*), a human pathogen that can cause life-threatening infections of skin, blood, bone, heart, and other vital organs; *S. aureus* resistance to penicillin rapidly evolved in the 1950s. Over the next few decades, resistance to methicillin, which replaced penicillin as the treatment of choice for *S. aureus* infections, has also emerged. *S. aureus* strains resistant to the antibiotic are known as methicillin-resistant *S. aureus* or MRSA.
- Antibiotics and other antimicrobial drugs first became widely used in the World War II era, and have saved countless lives and blunted serious complications of many feared diseases and infections. However, some microbes have developed ways to circumvent the effects of antimicrobials. Antimicrobial resistance provides a survival benefit to microbes, making it harder to eliminate infections from the body.

Today

- The burden of health care-associated infections has increased over the past two decades due to the increase in immunocompromised and elderly patients, increasing use of invasive indwelling devices such as catheters, more complex hospital environments, and failures in infection control measures. In addition, antimicrobial resistance has emerged in virtually all health care-associated (nosocomial) pathogens. The most common nosocomial infections currently occurring in the United States are caused by coagulase-negative Staphylococci (CNS), *S. aureus*, Enterococcus, Candida and Gram-negative bacteria such as *E. coli*, Pseudomonas, Klebsiella, Acinetobacter, and Enterobacter species.
- Other diseases including tuberculosis (TB), gonorrhea, malaria, and childhood ear infections are increasingly more difficult to treat due to the emergence of resistance.
- Approximately 1.7 million patients in the United States get an infection in the hospital each year, about 99,000 of whom will die as a result. Seventy percent of the bacteria causing such infections are resistant to at least one drug commonly used to treat these infections.
- Strains of *S. aureus* resistant to methicillin are endemic in hospitals and increasing in non-hospital settings such as locker rooms, day care centers and the general community. *S. aureus* strains that evade the immune response in healthy people with no known risk factors for infection are known as community-associated MRSA (CA-MRSA). Recently, several cases overseas and in the United States were reported of *S. aureus* developing resistance to vancomycin, a very powerful antibiotic prescribed for the most intractable bacterial infections.
- In accordance with The Research Agenda of the National Institute of Allergy and Infectious Diseases for Antimicrobial Resistance (http://www.journals.uchicago.edu/doi/abs/10.1086/533451), NIH funds basic, translational, and clinical research to understand basic mechanisms of resistance, identify and characterize novel targets for new drugs, vaccines and diagnostics, and support the development of such products through preclinical and early-stage clinical trials. For example:
    - NIH-supported scientists discovered that *S. aureus* virulence genes are not expressed immediately upon infection, when low bacteria numbers would be overwhelmed by the host immune system. Instead, bacteria monitor their overall cell number and density, waiting until there is a critical mass before expressing virulence genes.

- NIH-supported researchers identified a way by which *S. aureus* resists a natural, anti-bacterial molecule—nitric oxide. This provides a potential target for the development of therapies.
- Researchers at NIH and supported institutions developed a strategy to combat CA-MRSA. By neutralizing the bacterium's toxin, the researchers were able to reduce the severity of skin and soft-tissue damage that occurs during infection in a mouse model.
- Research findings of NIH and NIH-supported scientists are yielding insights into how TB develops resistance to specific drugs and whether specific factors predispose some patients to develop multiple drug resistance.
- A successful public-private partnership between NIH and Sequella yielded a promising new TB drug that was tested in a Phase I clinical trial. Plans are underway for the next phase of clinical testing.
- NIH renewed a multi-year contract that supports over 200 domestic and international researchers, epidemiologists, and clinicians. This also supports a repository of *S. aureus* strains, including those resistant to vancomycin.
- NIH recently supported two independent partnerships to fund research—some specific for small businesses—that advance development of diagnostics that rapidly detect specific bacterial species and therapeutics to prevent antimicrobial resistance.
- Two contracts were awarded by NIH in 2007 to perform clinical trials for CA-MRSA to define out-patient skin and soft tissue treatment strategies where the disease is prevalent.
- In 2009, NIH funded contracts to improve treatment strategies to reduce the risk of antimicrobial resistance and preserve the effectiveness of existing antimicrobials. These studies will target disease areas experiencing the greatest antimicrobial selective pressure and test novel therapeutic approaches that minimize drug exposure and emergence of resistance.
- NIH, FDA, and CDC hosted a workshop on the development of Staphylococcal vaccines in 2010. An effective vaccine could reduce MRSA risk and the spread of resistant pathogens in healthcare settings.

NIH co-chairs the Federal government's *Interagency Task Force on Antimicrobial Resistance* (*http://www.cdc.gov/drugresistance/actionplan/taskforce.html*). The Task Force is revising its antimicrobial resistance action plan which will be posted in the Federal Register for public comment. It will outline specific, coordinated actions in four key areas: Surveillance, Prevention and Control, Research, and Product Development, which together comprise an effective national agenda to combat antimicrobial resistance.

Tomorrow

- NIH will continue to accelerate efforts to discover new drugs, vaccines, and diagnostics. Existing and planned NIH-industry partnerships are working to develop diagnostic technologies to allow early detection of major causes of a number of systemic infections—septicemia, bacteremia, candidemia, and community-acquired pneumonia, thereby allowing clinicians to determine the best courses of treatment.
- NIH-supported research focused on the mechanisms by which microbes develop resistance may enable health professionals to better identify which patients are most susceptible to antimicrobial-resistant pathogens and to develop new effective drugs, vaccine, and diagnostics.
- NIH-supported research on novel antimicrobial agents targeting both known and unexplored pathways will help to boost the dwindling antimicrobial pipeline.
- Data from NIAID's Targeted Clinical Trials to Reduce the Risk of Antimicrobial Resistance may inform clinicians about ways they can safely reduce the amount of antimicrobials they prescribe, thereby reducing unnecessary selective pressure on microbes and decreasing the probability of resistance.

***Additional information on antimicrobial resistance can be found at http://www.niaid.nih.gov/topics/antimicrobialresistance/Pages/default.aspx* or contact the NIAID Strategic Planning and Evaluation Branch, 301-496-6752.**

National Institute of Allergy and Infectious Diseases (NIAID):

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