National Institutes of Health

Fact Sheet — *Antimicrobial Resistance*

Yesterday

- The success of antimicrobials against disease-causing microbes 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. Development of penicillin followed in 1928 by Alexander Fleming.
- 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, bone, heart, and other vital organs; *S. aureus* resistance to penicillin rapidly evolved in the 1950s. Resistance to methicillin, a subsequent treatment for *S. aureus* infections, is known as methicillin-resistant *S. aureus* or MRSA.
- Since antibiotics and other antimicrobial drugs first became widely used in the World War II era, they have saved countless lives and blunted serious complications of many feared diseases and infections.

Today

- After more than 50 years of widespread use of antimicrobial drugs, some microbes--including bacteria, viruses, and fungi--have developed ways to circumvent their effects. Antimicrobial resistance provides a survival benefit to microbes making it harder to eliminate infections from the body.
- Diseases such as tuberculosis, gonorrhea, malaria, and childhood ear infections are more difficult to treat now compared to a few decades ago. Drug resistance is an especially difficult problem for hospitals harboring critically ill patients who are less able to fight infections without the help of antibiotics. Overuse of antibiotics in these patients can ultimately produce bacteria with greater ability to survive even in the presence of the strongest antibiotics. These even stronger drug-resistant bacteria continue to prey on vulnerable hospital patients.
- Nearly 2 million patients in the United States get an infection in the hospital each year, about 90,000 of whom will die as a result. Seventy percent of the bacteria causing such infections are resistant to at least one of the drugs most commonly used to treat these infections.
- Factors that foster the emergence of drug-resistant microbes in health care settings include indiscriminant use of broad-spectrum antibiotics; increasing numbers of immunocompromised patients; technologies such as implants, catheters, and intravenous lines that provide pathogens direct access to the body and a hospitable environment; and the breakdown in hygiene, infection control, and disease control programs. Also, when a patient does not finish taking a prescription for antibiotics, some pathogens remain, and are more likely to develop resistance.
- For extreme drug resistance, hospitals use the powerful antibiotic vancomycin for the most intractable bacterial infections. Recently, several cases of vancomycin-resistant *S. aureus* (VRSA) have been reported overseas and in the United States.
- Strains of *S. aureus* resistant to methicillin are endemic in hospitals and are increasing in non-hospital settings such as locker rooms and day care centers. Since September 2000, outbreaks of MRSA infections were reported among members of football and wrestling teams in California, Indiana, and Pennsylvania. Cases of community-associated MRSA have also been reported in patients without established risk factors.
- NIH funds research, drug development, and clinical trials to combat the problem of antimicrobial resistance, including studies on the basic biology of resistant organisms; applied research on new diagnostic techniques, therapies, and preventive measures; and studies of how bacteria develop and share resistance genes.

- NIH-funded research grants are yielding results that will help public health officials hold the line in our fight against drug-resistant microbes. 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, bacterial colonies monitor their overall cell number and density, waiting until there is a critical mass before expressing virulence genes. Experiments demonstrated that inhibiting expression of virulence genes for just a short time also interfered with abscess formation, thus limiting pathogenicity. Therapeutic value of this finding could be significant if treatment were started early.
  - Tuberculosis-control programs are threatened by the emergence of drug-resistant strains of TB. Research findings of NIH and NIH-supported scientists are yielding insights into how *Mycobacterium tuberculosis* develops resistance to specific anti-TB drugs, as well as whether specific factors predispose some patients to develop multiple drug resistance.
  - New antimicrobial drugs are desperately needed. A successful public-private partnership between NIH and Sequella yielded a promising new tuberculosis drug that was tested recently in a Phase 1a clinical trial, with plans to move into a Phase 1b trial.
  - NIH-funded researchers have identified the mechanisms whereby *S. aureus* adheres to host cellular structures, including collagen, which could eventually lead to vaccines to thwart staphylococcal infections.

- In addition to sponsoring research, NIH co-chairs the Federal government's Interagency Task Force on Antimicrobial Resistance.
  - This task force is made up of representatives from NIH, the Centers for Disease Control, the Food and Drug Administration, the Agency for Healthcare Research and Quality, the Department of Agriculture, the Department of Defense, the Department of Veterans Affairs, the Environmental Protection Agency, the Centers for Medicare and Medicaid Services, and the Health Resources and Services Administration.
  - The Task Force is working on implementing an antimicrobial resistance action plan that reflects a broad consensus of these agencies with input from a variety of constituents and collaborators. In short, antimicrobial resistance is driving up health care costs, increasing the severity of disease, and increasing the death rates from certain infections.

Tomorrow

- NIH will continue to accelerate efforts to discover new drugs, vaccines, and diagnostics and move them toward clinical trials. Improved and inexpensive diagnostics will allow clinicians to rapidly identify the pathogen causing an infection and determine the best course of treatment. Diagnostics that can be used at the point-of-care and that indicate if a pathogen is resistant to drugs and to which ones will be especially valuable.
- NIH-supported research will target the mechanisms by which microbes develop the ability to thwart antimicrobial action. Research findings will enable health professionals to better identify which patients are most susceptible to antimicrobial resistant pathogens, and lead to development of new, effective antimicrobial drugs.
- NIH-industry partnerships will speed development of diagnostic technologies to allow early detection of select major causes of a number of systemic infections—septicemia, bacteremia, candidemia, and community-acquired pneumonia. Other NIH-industry partnerships will develop drugs and diagnostics in areas that are not currently a high priority for industry but are likely to have a high impact on public health

Additional information on antimicrobial resistance can be found at http://www.niaid.nih.gov/publications/antimic.htm.