# DEATH OF THE MAGIC BULLET

## Examining Antibiotic Resistance

The last few decades represent a time of unparalleled advancements in health and technology. While this explosion of new knowledge has reaped many life- and labor-saving benefits, it has also produced unintended consequences. Toxic substances in our food, air, and water – many of them originally introduced in the name of technological progress – prevent normal growth and functioning, and lead to acute and chronic disease. Overuse of life-saving antibiotics has reduced our ability to heal ourselves.

Grantmakers In Health recently convened a day-long meeting to examine these mounting threats to our health, and to illuminate grantmaking strategies to address these issues at local, national, and international levels. This Issue Focus is devoted to exploring the causes and potential cures for antibiotic resistance; systemic contaminants will be covered in December's Issue Focus.

### WHAT IS ANTIBIOTIC RESISTANCE?

Antibiotics are substances which kill or inhibit the growth of bacteria. When bacteria are exposed to antibiotics, those bacteria that are most sensitive to that particular antibiotic will be killed; those that are more resistant to the drug can remain and proliferate. These bacteria pass along resistance to future generations of bacteria, and, eventually, the original drug becomes ineffective. In addition, a number of natural processes enable different bacteria to exchange genetic material, passing resistance between organisms.

The issue of antibiotic resistance presents an interesting paradox. Until 1928, when Alexander Fleming discovered penicillin, there was little effective ammunition to battle many of the diseases that ravaged populations. In the years that followed, the development and use of antibiotic drugs, including streptomycin and tetracycline, flourished. These medicines were effective against a wide variety of organisms responsible for a great number of diseases, including tuberculosis, pneumonia, syphilis, and meningitis. Bacterial infections leading to mortality dropped significantly. But 80 years later, there is a rising tide of infectious diseases, due in part to the ability of bacteria to develop resistance to existing medicines. The inability – on a global level – to use antibiotics wisely has, paradoxically, put people around the world in peril from the very diseases antibiotics were developed to eliminate.

### A QUICKLY SPREADING PHENOMENON

Although antibiotic resistance is not a new phenomenon, there has been a recent surge in the resistance of bacteria to antibiotics. The following are examples:

- Between 10 percent and 40 percent of *streptococcus pneumoniae* – which cause 7 million cases of otitis media; 2,600 cases of meningitis; 63,000 bacteremia cases; and between 100,000 and 135,000 hospitalizations for pneumonia annually – are drug resistant. Twenty-five years ago, virtually all these bacteria were susceptible to penicillin (NCID 2000).
- Only five percent of *staphylococcus aureus*, which causes both minor and fatal infections, are susceptible to penicillin. New strains of staph have been found which are no longer susceptible to vancomycin, an antibiotic that is used as one of the last resorts for treating staph infections (NCID 1999).
- In some parts of Southeast Asia, 98 percent of the bacteria that cause gonorrhea are resistant to treatment (WHO 2000).
- Globally, between 1 percent and 2 percent of tuberculosis cases are known to be caused by multidrug resistant bacteria; numbers are likely much higher than that, but TB surveillance is incomplete (WHO 2000).

As international travel and commerce increase, drug-resistant strains of infectious diseases are no longer confined to national or regional borders, and pose a threat to those in nations where these diseases are not endemic. One example of this threat is typhoid fever. Typhoid fever, caused by the *salmonella typhi* bacterium, afflicts more than 12 million people annually, and causes 600,000 deaths each year. Seventy percent of the 400 cases each year in the United States are acquired by international travelers. The bacteria that causes typhoid is developing an increased resistance to the available antibiotics, including commonly prescribed fluoroquinolones (NCID 2000).

In addition to human costs, antibiotic resistance has economic implications. These costs include health care visits, the antibiotic agents themselves, and lost work days when individuals suffer recurrent bouts of disease. In addition, substantial funding is required to conduct thorough surveillance of drug-resistant disease. Treatment for standard tuberculosis, for example, averages $20 per case; treatment for multidrug resistant tuberculosis, which requires longer courses of a combination of therapies, along with expensive, directly observed therapy, averages $2,000 (WHO 2000). In 1995, the Office of Technology Assessment determined that the additional hospital costs associated with drug-resistant bacteria acquired in hospitals alone amount to $1.3 billion (Avorn and Solomon 2000).

Inappropriate use of antibiotics in health care creates the conditions that give rise to resistance. Annually, about 18 million courses of antibiotics are prescribed for the common cold, an illness for which antibiotics are usually ineffective. In one study, antibiotics were given to 60 percent of patients who presented with upper respiratory infection, while only 6 percent of cases warranted use of these drugs.

> If antimicrobial agents were used prudently for the four most common infections for which they are prescribed – otitis media, sinusitis, bronchitis, and pharyngitis – 26 million fewer prescriptions would be given annually (Abramson and Givner 1999).

Patient pressure to receive antibiotics is cited as the most common factor in antibiotic overuse. Provider-side factors include an unwillingness to resist presssure from patients, fear of poor outcomes and repeat visits, lack of understanding regarding antibiotic limitations, and pressure put on providers to limit use of diagnostic and laboratory tests, which are sometimes necessary to distinguish between viral and bacterial infections.

Agricultural overuse of antibiotics also contributes to growth of resistance. Currently, only half the antibiotics produced in this country are slated for human consumption. Those remaining are used in agriculture, to treat sick animals, and to prevent disease. In addition, subtherapeutic doses of antibiotics are provided to animals as growth enhancers. A large number of the antibiotics used in agriculture are considered "medically important" – that is, they are used to treat humans, or are closely related to antibiotics used to treat humans. Medically important antibiotics currently used in agriculture include penicillin, tetracyclines, erythromycin, and fluorquinolones (GAO 1999). Bacteria in animals can develop resistance to these antibiotics. Humans who acquire these bacteria – through direct contact or contaminated food or water – can then develop resistant infections. *Salmonella*, *Campylobacter*, and *E. coli* have all demonstrated resistance to antibiotics; when humans come in contact with these bacteria, standard treatments may be useless. Moreover, these bacteria continue to develop resistance to new antibiotics.

## OPPORTUNITIES FOR GRANTMAKERS

To date, there has been limited foundation involvement in funding antibiotic resistance projects, although in recent months interest has grown considerably. A number of non-profit groups have recently designed a nationwide campaign to limit antibiotic resistance, aimed primarily at reducing the agricultural overuse of antibiotics and the effects of agricultural use on human health. Funders, including The Nathan Cummings Foundation and The Joyce Foundation, have contributed to this effort.

Funders with diverse missions and programs can become involved in this issue. Foundations that fund public health can develop media campaigns to inform both specific audiences and the general public regarding the hazards of overuse of antibiotics. Foundations that work with health care organizations and institutions can ensure that providers have the tools and resources to ensure appropriate prescription of antibiotics. Funding can support provider training, computer and online surveillance and instruction regarding prescription habits and protocols, and patient education. In addition, foundations can use their influence as community members and stockholders of antibiotic manufacturers to encourage prudent sales and distribution of antibiotics. A final strategy, and one employed by The Nathan Cummings Foundation, is to educate other grantmakers on issues of antibiotic resistance and encourage them to begin supporting efforts to reduce this growing threat to health.

> This Issue Focus is based on the GIH Issue Dialogue, "Progress and Peril: Examining Antibiotic Resistance and Systemic Contaminants," held on October 3, 2000. A report will be available shortly. The citations from this Issue Focus will be included in the upcoming report.

## RESOURCES

Alliance for the Prudent Use of Antibiotics (APUA)
Boston, MA
617.636.0966
www.apua.org

Antimicrobial Resistance, National Center for Infectious Disease, Centers for Disease Control and Prevention
http://www.cdc.gov/drugresistance

Center for Science in the Public Interest
Antibiotic Resistance Project
www.cspinet.org
202.332.9110

World Health Organization, "Overcoming Antimicrobial Resistance: World Health Report on Infectious Diseases 2000," June 2000.
http://www.who.int/infectious-disease-report/2000/index.html

### GRANTMAKER CONTACTS

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