

## The Emergence of Antibiotic-Resistant Bacteria

### CAUTIONING PATIENTS ABOUT THE DANGERS OF ANTIBIOTIC DRUG OVERUSE AND ABUSE

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In recent years, there has been an increased emergence of antibiotic-resistant bacteria. For instance, a recent report indicated that approximately one-third of all children and one-quarter of all adults in America show signs of drug resistance to pneumococci bacteria. This is complicated by the fact that people who demonstrate resistance to one drug often become resistant to other drugs as well. In other words, bacteria are fast learners; they will generate mutations that enable them to survive and avoid the bacteriostatic and bacteriocidal effects of antibiotics. Drug-resistant infections increase risk of death and often are associated with prolonged hospital stays, sometimes with severe complications. These infections might necessitate removing part of a ravaged lung or replacing a damaged heart valve.

Research shows that antibiotic resistance has increased over the years. According to the Centers for Disease Control and Prevention (CDC), between 1979 and 1987, only .02 percent of pneumococcus strains infecting a large number of patients were penicillin-resistant. The survey included 13 hospitals in 12 states. More recently, 6.6 percent of pneumococcus strains are resistant, according to a report in the June 15, 1994 *Journal of the American Medical Association*, by Robert F. Breiman, MD, and colleagues at the CDC. The agency also reports that in 1992, 13,300 hospital patients died of bacterial infections that were resistant to antibiotic treatment. According to a report in the April 28, 1994 issue of *The New England Journal of Medicine*, researchers identified bacteria in patient samples that resist all currently available antibiotic drugs.

#### How Antibiotic Resistance Develops

Drug resistance to antibiotics has largely occurred as a result of the overuse and abuse of these medications, which have been prescribed even when, in many instances, the patient has a viral infection for which antibiotics are not effective. Approximately 150 million prescriptions for oral antibiotics are written each year in the United States. That is about one prescription for every two people in the country. Antibiotics are the most commonly prescribed medication in primary care. The antibiotic technically does not cause the resistance, but allows it to happen by creating a situation in which an already existing variant can flourish.

As such, the use of antibiotics generates selective pressure for resistance to occur, enabling more and more organisms to develop resistance to a greater number of antibiotics. For example, penicillin kills bacteria by attaching to their cell walls and destroying a key part of the wall. The wall falls apart and the bacterium dies.

Resistant microbes, however, either alter their cell walls so penicillin can't bind, or produce enzymes that dismantle the antibiotic (penicillinase). Erythromycin attacks ribosomes, which are cellular organelles that make proteins. Resistant bacteria have slightly altered ribosomes, to which the drug cannot bind. The ribosomal route is also how bacteria become resistant to the antibiotics tetracycline, streptomycin and gentamicin. A patient can develop a drug-resistant infection, either

by contracting a resistant bug to begin with, or by having a resistant microbe emerge in the body once antibiotic treatment begins.

### Mechanisms Responsible for Development

There are four general mechanisms responsible for the development of antibiotic resistance. First, mutations occur in the gene encoding the target proteins so it no longer binds the drug. These are random events, occurring spontaneously, that confer a selective advantage to the bacteria. This can be a single or multi-step mutation, with each establishing a slight alteration in susceptibility. Examples of resistance through mutation include *Mycobacterium tuberculosis*, *Escherichia coli* and *Staphylococcus aureus*. Mutations of this nature do not require exposure to the particular drug. As a rule, antibiotics bind to specific enzyme proteins, interfering with the action of biosynthesis of key compounds the bacteria requires for its survival and/or replication. If drugs such as penicillin C bind to transpeptidases, transglycosylases, D-alanine carboxykinases, and/or there is diminished binding of the drug to protein receptors on the outer bacterial cell membrane or on the inner bacterial membrane, the antibiotic loses its efficacy. Thus, genetic mutations that lead to an alteration in the binding site of target proteins, where antibiotics must bind to in order to be effective, create drug resistance to the antibiotics that require binding to those target proteins.

The second mechanism involves transduction, whereby a virus containing DNA infects a bacterium. The virus that infects the bacterium contains plasmids, bacterial DNA that contains genes for various functions, including one providing drug resistance. Incorporation of the plasmid makes the newly infected bacterium bacterial cell-resistant and capable of passing on the trait of resistance to subsequent generations. A single plasmid can provide a slew of different resistances. In 1968, 12,500 people in Guatemala died in an epidemic of *Shigella diarrhea*. The microbe harbored a plasmid carrying resistances to four antibiotics.

One plasmid carries the code for penicillinase. Penicillinase is also known as beta-lactamase. This is a major factor in drug resistance pertaining to *Staphylococcus aureus*. Other plasmids contain codes for resistance to erythromycin, tetracycline or chloramphenicol. In the case of penicillinase, there are compounds that inhibit this enzyme; sometimes they are used in cases of drug resistance, in combination with penicillin, to help overcome the problem. Penicillinase inhibitors include clavulanic acid, sulfbactam and tazobactam.

The third mechanism involves transformation - there is a transfer of DNA that is free in the environment into the bacteria. In this case, one bacterium takes up DNA from another bacterium. Penicillin-resistant pneumococci and neisseria are examples of this.

The fourth mechanism of drug resistance is conjugation, which is the transfer of DNA from one organism to another during mating. This occurs predominantly among gram-negative bacilli such as enterobacteriaceae and *Shigella flexneri*.

### Steps to Reduce the Problem

There are a number of steps that can be taken by the medical and health care community to reduce the problem of drug resistance to antibiotics. At this critical point in time, it is imperative for this action to be taken. Health authorities are warning that they are losing the war on keeping this problem in check and that the future looks very bleak, as altered forms of bacteria are appearing at a rapid rate that have developed drug resistance mutations and adaptations.

The first step to help combat the rising incidence of antibiotic drug resistance requires physicians to only prescribe antibiotics upon confirmation of a positive test culture; or in cases in which there

is high suspicion of a bacterial infection or infection by a microbe that is susceptible to the effects of antibiotics.

The red flags for a serious bacterial infection that requires antibiotic treatment while awaiting the results of a test culture include:

- loss of appetite, usually in the presence of a high fever;
- symptoms of dehydration (dizziness when standing, unsteady walk, orthostatic changes or vital signs, urine concentration of 1.025 to 1.030, and dry mucus membranes);
- absence of fever, especially in patients with diabetes or in the extremes of life; and
- a fever higher than 102 F, with lymphadenopathy, swelling and pain; sometimes accompanied by shaking chills.

In summary, antibiotics should be restricted to patients who can truly benefit from them - that is, people with bacterial infections. Already this is being done in the hospital setting, where the routine use of antibiotics to prevent infection in certain surgical patients is being re-examined. As drug resistance is especially common in children (affecting one-third in the U.S.), it is important for practitioners not to prescribe antibiotics for children until they have confirmation of a bacterial infection or see critical, telltale signs of a bacterial infection.

This is especially important in cases of otitis media, where antibiotics have been overprescribed for years, promoting the drug resistance problems in children we see today. Physicians should no longer provide extended antibiotic prescriptions to children with recurrent ear infections, merely to prevent future infections. Also, the prescribing of long-term antibiotic therapy for adolescent acne should be discouraged. This is not a life-threatening infection, and the course of treatment often runs for a number of years, which increases the likelihood of drug-resistant staphylococcus bacteria emerging.

Another problem that arises with antibiotic use is that patients often stop taking the drug too soon, because symptoms improve. However, this merely encourages resistant microbes to proliferate. The infection returns a few weeks later, and this time a different drug must be used to treat it. Physicians should emphasize the importance of having patients complete the course of antibiotic treatment outlined by the physician and not stop the medication immediately upon improvement of symptoms.

Certain hygiene measures also should be encouraged, such as more frequent hand washing by health care workers, quick identification and isolation of patients with drug-resistant infections, and improvement of sewage systems and water purity in developing nations. Also, the CDC is encouraging local health officials to track resistance data, and the World Health Organization has initiated a global computer database for physicians to report outbreaks of drug-resistant bacterial infections.

#### Antibiotics in Animal Feed Contribute to the Problem

The overuse of antibiotics in animal feed also has emerged as a contributor to antibiotic-resistant strains of bacteria. Animals and humans constitute overlapping reservoirs of resistance; consequently, use of antibiotics in animals can impact human health. In short, antibiotics fed to food animals on a large scale to prevent infections, treat infections and as growth promoters, encourage the emergence of antibiotic-resistant bacteria, via the mechanisms outlined above. It is well-documented that these resistant bacteria from animals spread to food products during

slaughter and processing. Resistant bacteria also can spread from the farm to the environment through manure. Direct transmission of resistant enterococci between animals and farm workers

has been demonstrated in several studies. Transmission of resistant bacteria from food animals to humans results in more healthy humans in the society carrying resistant bacteria.

As such, the emerging evidence indicates that routine use of antibiotics in food animals for growth promotion constitutes a serious public health problem, especially in cases in which the same classes of antimicrobials are being used in humans. Growth promoter use creates a major food animal reservoir of resistant bacteria, with potential to spread to humans through food intake or animal contact.

Recent experience from a number of European countries has shown that the use of antimicrobials for growth promotion provides insignificant benefits to agriculture and can be terminated. Ending the use of antimicrobial growth promoters has led to reductions in the prevalence of resistant bacteria in food and food animals, as well as in humans, in the countries where this has occurred.

#### Natural Immune-Boosting Supplements Should Be Considered When Antibiotics Are Unnecessary

Another consideration is for practitioners to recommend the use of a natural supplement containing the P73 wild oregano blend (oil of oregano), developed by Dr. Cass Ingram, DO. Studies at Georgetown University research facilities have shown that its concentrations of volatile oils exert meaningful antimicrobial action against a host of pathogenic bacteria, certain viruses and *Candida albicans*. From clinical experience, I have found it to be effective in cases of chronic bronchitis; to lessen the severity and duration of the common cold by about 50 to 60 percent (effective against coronaviruses, not rhinoviruses); and in cases of *Candida* infections, nail fungus problems, acne, rosacea and some other chronic infections.

In cases in which the patient does not demonstrate a necessity for antibiotics (as reviewed above), I truly believe physicians should recommend 500 mg to 1,000 mg of P73 wild oregano blend (capsules), four times daily, until signs and symptoms are resolved. In addition, physicians should be made aware of the immune-modulating effects of certain dietary supplements and encourage their patients to take specific supplements on a daily, year-round basis to reduce the risk of virulent infections. This may be particularly important as one ages, as the immune system is less efficient, partially due to involution of the thymus gland. In my opinion, supplements of this nature include a high-potency multiple vitamin along with a supplement containing reishi mushroom extract and astragalus.

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