

# **THE EMERGENCE OF ANTIBIOTIC-RESISTANT BACTERIA: CAUTIONING PATIENTS ABOUT THE DANGERS OF ANTIBIOTIC DRUG OVERUSE AND ABUSE**

***James Meschino DC, MS, ROHP***

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

Antibiotic resistance spreads fast. Between 1979 and 1987, for example, only 0.02 percent of pneumococcus strains infecting a large number of patients, surveyed by the national Centers for Disease Control and Prevention, were penicillin-resistant. CDC's 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, M.D., and colleagues at 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, New England Journal of Medicine, researchers have 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 in many instances when 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 2 persons in the country. Antibiotics are the most commonly prescribed group of medication in primary care. The antibiotic does not technically cause the resistance, but allows it to happen by creating a situation where 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, then 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, 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

There are four general mechanisms that are responsible for the development of antibiotic resistance. 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 like penicillin can not 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, then 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, creates drug resistance to the antibiotics that require binding to those target proteins.

The second mechanism involves transduction, whereby a virus containing DNA, infects a bacteria. The virus that infects the bacteria contains plasmids, bacterial DNA that contains genes for various functions, including one providing drug resistance. Incorporation of the plasmid makes the newly infected bacteria 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, which are sometimes used in cases of drug resistance, in combination with penicillin, to help overcome the problem. Penicillinase inhibitors include clavulanic acid, sulbactam and tazobactam.

The third mechanism involves transformation where 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*.

There are a number of steps that can be taken by the medical and healthcare community to decrease the problem with drug resistance to antibiotics. At this critical point in time it is imperative for this action to be taken as 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 where there is a high suspicion of a bacterial infection or infection by a microbe that is susceptible to the effects of antibiotics. The red flags for serious bacterial infection that deem antibiotic treatment while awaiting the results of a test culture include:

1. Loss of appetite; usually in the presence of a high fever
2. Symptoms of dehydration (dizziness when standing, unsteady walk, orthostatic changes or vital signs, urine concentration of 1.025 to 1.030, and dry mucous membranes)
3. Absence of fever: especially in patients with diabetes or in the extremes of life
4. A fever higher than 102 degrees 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 US), it is important for practitioners not to prescribe antibiotics for children until they have confirmation of a bacterial infection or see very critical tell-tail signs of a bacterial infection. This is especially important in cases of otitis media, where antibiotics have been over prescribed over the years, promoting the drug resistance problems in children we see today. Physicians should no longer provide children with recurrent ear infections with extended antibiotic prescriptions to prevent future infections. As well, the prescribing of long-term antibiotic therapy for adolescent acne should also 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.

Some hygiene measures should also be encouraged, such as more frequent hand washing by health-care workers, quick identification and isolation of patients with drug-resistant infections, and improving sewage systems and water purity in developing nations. As well, 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 Are Also Contributing To The Problem**

The overuse of antibiotics in animal feed has also emerged as a contributor to antibiotic resistant strains of bacteria that affect human health. Animals and humans constitute overlapping reservoirs of resistance, and 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 can also 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 case where the same classes of antimicrobials are being used in humans. Growth promoter use creates a major food animal reservoir of resistant bacteria, with a potential for spread to human food intake or by 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 that it 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 Supplements Should Be Considered When Antibiotics Are Not Necessary And To Boost Immunity**

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 D.O. Studies at Georgetown University and other 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 (about 50-60% of the time, as it is effective against coronaviruses, not rhinoviruses), in cases of candida infections, nail fungus problems, acne, rosacea and some other chronic infections.

In cases where the patient does not demonstrate a necessity for antibiotics (as reviewed above) I truly believe that physicians should recommend 500-1,000 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 yearround basis to reduce risk of virulent infections from occurring. This may be particularly important as one ages, as the immune system is less efficient as we age 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.