

## *Antibiotic Resistance: Playing Chicken With Essential Drugs*

### **Overview of Antibiotic Resistance**

For the past sixty years, the use of antibiotic drugs has turned bacterial infections into treatable conditions, rather than the life-threatening scourges they once were. Today, however, the effectiveness of many life-saving antibiotics is waning, the legacy of years of overuse in both human medicine and agriculture. A federal task force recently noted that antibiotic resistance is “a growing menace to all people” and cautioned that if current trends continue, treatments for common infections “will become increasingly limited and expensive – and, in some cases, nonexistent.”

Antibiotics are used to treat many illnesses caused by bacterial infections, from ear and skin infections to pneumonia, food poisoning, meningitis, and other life-threatening infections. They also make possible many modern medical procedures, such as surgery, cancer therapy and transplants. Without antibiotics, physicians could not effectively treat infections that often result from these procedures, which would then pose enormous risks. Antibiotics are essential tools for physicians: at any given time, between 25% and 40% of hospital patients are receiving antibiotics intravenously.

Today, many antibiotics are becoming ineffective against the bacterial infections they once routinely cured. Health officials in the United States are concerned that bacteria are turning into “superbugs,” resistant to more and more antibiotics. Children, the elderly, and those with weakened immune systems (including chemotherapy and transplant patients) are particularly at risk.

Public health officials attribute this alarming trend to two causes: the over-prescription and misuse of antibiotics given to human patients, and overuse of antibiotics in agriculture, particularly the routine feeding of large volumes of antibiotics to healthy livestock and poultry. The American Medical Association recently adopted a formal resolution opposing the routine feeding of medically important antibiotics to healthy livestock and poultry, and several countries (though not the United States) have restricted or banned this practice.

### **How Do Bacteria Become Resistant to Antibiotics?**

Antibiotics are designed to fight bacteria by targeting specific parts of the bacteria’s structure or cellular machinery. However, over time, bacteria can defeat antibiotics in the following ways:

- Survival of the fittest or natural selection: When bacteria are initially exposed to an antibiotic, those most susceptible to the antibiotic will die quickly, leaving any surviving bacteria to pass on their resistant features to succeeding generations.

- Biological mutation: Since bacteria are extremely numerous, random mutation of bacterial DNA generates a wide variety of genetic changes. Through mutation and selection, bacteria can develop defense mechanisms against antibiotics. For example, some bacteria have developed biochemical “pumps” that can remove an antibiotic before it reaches its target, while others have evolved to produce enzymes to inactivate the antibiotic.
- DNA exchange: Bacteria readily swap bits of DNA among both related and unrelated species. Thus, antibiotic-resistant genes from one type of bacteria may be incorporated into other bacteria. As a result, using any one antibiotic to treat a bacterial infection may result in other kinds of bacteria developing resistance to that specific antibiotic, as well as to other types of antibiotics.
- Rapid reproduction: Bacteria reproduce rapidly, sometimes in as little as 20 minutes. Therefore, it does not take long for the antibiotic-resistant bacteria to comprise a large proportion of a bacterial population.

### **Does the Development of Antibiotic-Resistant Bacteria Mean that These Drugs are Rapidly Losing their Effectiveness?**

To date, all antibiotics have over time lost effectiveness against their targeted bacteria. The earliest antibiotics were developed in the 1940s. These "miracle drugs" held at bay such devastating diseases as pneumonia and tuberculosis, which had previously been untreatable. But the steady evolution of resistant bacteria has resulted in a situation in which, for some illnesses, doctors now have only one or two drugs “of last resort” to use against infections by superbugs resistant to all other drugs. For example:

- Nearly all strains of *Staphylococcus aureus* in the United States are resistant to penicillin, and many are resistant to newer methicillin-related drugs. Since 1997, strains of *S. aureus* have been reported to have a decreased susceptibility to vancomycin, which has been the last remaining uniformly effective treatment.
- Today, one out of six cases of *Campylobacter* infections, the most common cause of food-borne illness, is resistant to fluoroquinolones (the drug of choice for treating food-borne illness). As recently as ten years ago, such resistance was negligible.

Clearly, it is important to extend the useful lifetime of any drug that is effective against human disease. And today, this is even more important because few new antibiotics are being developed, and those that are developed tend to be extremely expensive.

### **What is Causing Antibiotics to Lose their Effectiveness?**

Human Medicine: Prescribing antibiotics for patients with illnesses such as the flu or the common cold (which are viral illnesses that can't be treated or cured with antibiotics) contributes to antibiotic resistance. In 1997, the Centers for Disease Control and Prevention (CDC)

estimated that up to half of all outpatient antibiotics prescribed by doctors are unnecessary. In addition, many patients do not complete their entire course of antibiotics. Instead, they take only the initial doses, killing off the susceptible bacteria and leaving the more resistant bacteria to reproduce. Physicians and their patients need to be aware of the serious consequences of the misuse of antibiotics.

Animal Agriculture: The unnecessary feeding of antibiotics to healthy food animals, such as poultry, swine, and beef cattle is also a key cause of the proliferation of antibiotic-resistant bacteria. Although no definitive data are available, the Union of Concerned Scientists estimates that 80% of antibiotics and related drugs manufactured in the United States are given to farm animals, most often to animals that are not sick. Eliminating the overuse of antibiotics in animal farming would do much to slow the growing public health threat of antibiotic resistance.

### **How Does the Massive Use of Antibiotics in Animal Agriculture Result in Antibiotic Resistant Bacteria that Can Harm Humans?**

Antibiotics are routinely fed to healthy livestock and poultry to make them gain weight faster and to compensate for unsanitary living conditions. This “non-therapeutic” use of antibiotics – i.e., for purposes other than treating sick animals – increases profits for factory farms but puts public health at risk.

The same mechanisms that cause bacteria to develop resistance in humans are at work in animals that are fed antibiotics. When people suffer from a bacterial infection, they are given relatively high doses of antibiotics intended to kill or stop the growth of bacteria. But healthy animals raised on factory farms are regularly fed low dosage levels of antibiotics for extended periods of time, in order to promote faster growth and compensate for overcrowded and unsanitary conditions that may bring on sickness, especially in industrial-scale factory farms. Unfortunately, use of low dosages of antibiotics over an extended period is one of the best ways to promote the development of antibiotic-resistant bacteria, as it kills the susceptible bacteria while leaving the resistant strains to flourish and reproduce. Currently, several antibiotics that are used in human medical treatment (or are closely related to important human medicines) are routinely given to healthy livestock and poultry. Examples include tetracycline, penicillin and erythromycin.

In addition, antibiotics that are used to treat illness in agricultural animals can also present problems if the antibiotic plays an important role in treating human illness. In October, 2000, the U.S. Food and Drug Administration (FDA) proposed to ban a class of antibiotics known as fluoroquinolones from use in poultry, based on evidence that human resistance to this type of drug has risen dramatically since fluoroquinolones were approved for use in poultry in 1995. Fluoroquinolones are the drug-of-choice in treating severe foodborne illness in humans. Although one manufacturer of the drug (Abbott Labs) immediately phased out production, the other (Bayer Corp.) has contested the ban, and the drug remains in use on poultry farms.

## How are Resistant Bacteria Transmitted from Animals to Humans?

Direct transmission through food consumption: During the high-volume, high-speed slaughtering process, meat can become contaminated with bacteria from the skin and guts of the animals. Disease-causing bacteria can be transmitted to humans who handle or consume raw or improperly cooked contaminated meat, and other foodstuffs can be cross-contaminated by coming into contact with such meat. Food-borne illness is by no means rare; for example, *Salmonella* from poultry causes 1.4 million illnesses annually. While most people recover from food-borne illness on their own, antibiotics are needed to treat severe cases. As bacteria become increasingly resistant to antibiotics, the number of food-borne illnesses that are difficult or impossible to treat will grow.

Environmental contamination: Significant quantities of antibiotic-resistant bacteria enter the environment through the nearly two trillion pounds of animal wastes produced annually in the United States by animal agriculture operations. Because as much as 75% of an antibiotic in animal feed may pass undigested through the animal, wastes can contain antibiotics as well as antibiotic-resistant bacteria. In many cases, wastes are stored in open-air lagoons and/or spread on fields. Many of the lagoons are not lined and are prone to leaking or breaking, thereby releasing the animal wastes to surface and ground waters. The spread of manure on agricultural fields may contaminate vegetables and fruits that then can transfer resistant bacteria to humans.

In addition, factory-farm workers are routinely exposed to antibiotics as they handle animal feed, and to antibiotic resistant bacteria in animal waste. As a result, they can carry antibiotic-resistant bacteria themselves. Such workers are at elevated risk of contracting antibiotic-resistant illnesses, which may also spread to members of their family and community.

## What Should Be Done?

1. Companies that produce and market meat and poultry, including suppliers, supermarkets, restaurants and factory farms, should voluntarily stop buying or selling products that have been produced with non-therapeutic use of medically important antibiotics. A 1999 National Academy of Sciences report estimated that the elimination of all non-therapeutic antibiotics in poultry, cow and swine production would cost consumers only \$5 to \$10 per person annually. Eliminating just the medically important drugs would cost even less.
2. Congress or the U.S. Food and Drug Administration (FDA) should ban the non-therapeutic use of medically important antibiotics in animal agriculture. Such drugs should not be used for promoting growth in food animals or to compensate for overcrowded conditions at factory farms.
3. FDA should promptly finalize its proposal to ban fluoroquinolone antibiotics from use in poultry, to help combat increased resistance to fluoroquinolones in humans (fluoroquinolones are a key antibiotic for treating severe cases of foodborne illness). Bayer Corporation, the only remaining manufacturer of fluoroquinolones for poultry, should stop opposing the ban.

4. Congress or the FDA should require the collection of accurate data on the production and use of antibiotics in both human medicine and animal agriculture, and that information should be made available to the public.
5. Congress should provide adequate funding to FDA, Centers for Disease Control and Prevention, U.S. Geological Survey, and other agencies that are involved in combating antibiotic resistance and/or gathering data on the problem.

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