

ANTIMICROBIAL RESISTANCE: THE CURRENT TREND

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BACKGROUND

Most antimicrobial are called antibiotics, literally meaning "against life". This is an ironic label for a group of drugs that have saved millions of lives over the last half century. They attack the microorganisms that have threatened humankind for thousands of years. While antibiotics have won many battles, they have not won the war by any means. The clever enemy keeps changing and coming back stronger than ever. Antibacterial chemotherapy is a highly valued medical science which has shaped modern humanity in a phenomenal fashion. Within the past half century, a wide variety of antibacterial substances have been discovered, designed and synthesized; literally hundreds of drugs have been successfully used in some fashion over the years. Today, the world wide anti-infective market exceeds \$20 billion dollars annually and overall antibacterial agents comprise the bulk of this trade. A number of general classes of antibacterial drugs have emerged as mainstays in modern infectious disease chemotherapy. Antimicrobial such as antibiotics is a chemical substance produced by microorganisms that can inhibit the growth of, or kill other microorganisms.¹

Today some 5,000 antibiotics are known. Only about 1,000 of these have been carefully investigated, and about 100 are currently used to treat infections.² According to Demain and Elender (1999)³, the discovery of penicillin not only led to the era of the wonder drugs but provided the most important antibiotics available to medicine. Continued efforts have resulted in the improvement of these compounds with respect to potency, breadth of spectrum, activity against resistant pathogens, stability and pharmacokinetic properties. Major advances are being made on structural and regulatory biosynthetic genes and metabolic engineering of the pathways involved on the research front.

Presently, new semi synthetic compounds especially those designed to combat resistance development are being examined in the clinic, and unusual non-antibiotic activities of these compounds are being pursued. Although seventy years of age, the beta-lactams are not yet ready for retirement. Approximately half of the world's antibiotic production is not used as human medicine but for animals. Some antibiotics for industrialized husbandry are sold freely over the counter as growth promoters. Several of these antibiotics are known for cross-resistance to those used in human medicine. It has been shown that antibiotic resistant bacteria are present in meat products and can also be found in humans who have not received these substances in the course of a medical treatment.⁴

Although so far there is no evidence for a causal relationship, this potential spread of resistance adds to the problems with antibiotics for future medical applications.⁵

THE ORIGIN OF DRUG RESISTANCE AND ITS TRANSMISSION

Ironically, resistance is promoted by both the overuse of antibiotics as well as insufficiency of dose.⁶ The gene for drugs resistant are present as both the bacteria chromosome and plasmids, small circular DNA molecules that can exist separate from the chromosome or be integrated into it. Also, spontaneous mutations will make bacteria drug resistant.⁷ Frequently, a bacteria pathogen is drug resistant because it has a plasmid bearing one or more resistant genes, such plasmids are called Rplasmids. They often code for enzymes that destroy or mortify drugs. Once a bacterial cell process an R-plasmid, the plasmid may be transferred to other cells quite rapidly through normal gene exchange processes, such as conjugation, transduction and transformation.¹

Extensive drug treatment favors the development and spread of antibiotic resistant strains because the antibiotic destroys normal, susceptible bacteria that would usually compete with drug resistant strains.⁷ The result may be the emergence of drug resistant pathogens leading to a super-injection. A possible effective alternative way of combating these resistance mechanisms is that of phage therapies, which are, viruses that live on bacteria and this offer a better advantages.⁵ The goal of antibiotics in disease such as gastroenteritis is to decrease stool water and electrolyte losses, thus limiting the morbidity resulting from dehydration. To date, several drugs have been tried in the treatment of acute diarrhea but none has met the requirements enumerated above. They are therefore of very limited value in the department of diarrhea, especially in children.¹ It is time for a new game plan.

TRENDS IN ANTIMICROBIAL RESISTANCE

According to White et al. (1999)⁸ antibioticresistant pathogens in animals pose a concern not only with respect to the health of animals but because of possible transmission to humans as food-borne pathogens. The problem is compounded by the growing number of pathogens that are resistant to multiple, structurally unrelated drugs, leading to the concern that there are likely to be few effective antimicrobials available by the end of the decade. Accordingly, more attention is now being paid to the ease with which resistance to both

single and multiple antimicrobials can develop among bacterial pathogens. If the current trends continue, we may see bacterial pathogens that are resistant to all currently available antimicrobials. The Food and Drug Administration and the United States Department of Agriculture are currently implementing strategies to address this threat.

In the past few years, strains of *E. coli* have become increasingly resistant to most first-line antibiotics, including third-generation cephalosporins, aminoglycosides, and even fluoroquinolones. Infections caused by drug-resistant organisms are a major and costly problem in animal health. These infections prolong illness and, if not treated in time with more expensive, alternative antimicrobial agents, can cause loss of stock. This potential problem will continue to be scourge and have a large impact on the animal industry and humans, across the countries of the world if not investigated and solved. For instance, in a study by White et al. (1999)⁸ on the prevalence of multiple-antibiotic resistance among *E. coli* strains showed that the most available drugs have the highest rates of bacterial resistance.

While we are being reminded daily how quickly disease can spread from jungles to urban centers, at present there is virtually no way to predict what will happen where. According to Lemonick⁹, in a recent article on emerging infection that appeared in a special edition of *Time*, the challenge for the near future undoubtedly lies in quickly identifying and isolating outbreaks and

limiting damages. Lemonick⁹ states that it is guerrilla warfare, but for the next few years at least, it may be the best we can do.¹⁰

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