


Policy Brief and Recommendations #3
Misuse of Antibiotics in Food Animal Production

Reduce Antibiotic Use to Delay Antibiotic Resistance

APUA

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MISUSE OF ANTIBIOTICS IN FOOD ANIMAL PRODUCTION

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REDUCE ANTIBIOTIC USE TO DELAY ANTIBIOTIC RESISTANCE

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EXECUTIVE SUMMARY

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Antibiotic use drives each step in the emergence, spread and evolution of resistance genes. It selects and spreads mutants. It amplifies obscure bacteria with resistance genes and genetic events that bring those genes to infecting bacteria. It amplifies resistant bacteria in treated hosts to be the ones that then infect them or spread to the next host in the chain of spread.

The progression of antibiotic resistance seen as growing a variety of resistance genes, prevalence of resistant bacteria and prolonged sickness or death after treatment failure, seems increasingly a function of total number of bacteria killed by antibiotics, with little distinction for the species of the bacteria or their hosts. It is imperative that human beings slow the progression of resistance to increase the chances that rescuing antibiotics will arrive in time. Eliminating use of antibiotics for growth promotion and other non-therapeutic purposes (feed efficiency, poor on-farm hygiene) in food animal production would be a significant step toward preserving this precious resource.

INTRODUCTION

Oil that could be channeled into valuable specific uses has now been gushing into the Gulf of Mexico for over two months. It is quietly wreaking environmental havoc, and no one has yet been able to stop it. Antibiotics, similarly, have an extremely valuable specific use. By diffusing through sterile body tissues and killing any bacteria invading any of those tissues, they have extended human life more than anything else has. Outside of such specific use in infected tissues, however, they wreak a growing and dangerous environmental havoc, gushing into the general community for seventy years.

BACTERIAL POPULATIONS

Bacteria have been evolving and diversifying for three billion years into every niche on the planet. They are excluded mostly only from larger organisms like humans and other animals and then only temporarily, now totaling a million trillion trillion (10^{30}) bacteria of thousands of different kinds living in finely balanced ecosystems all over the world. Accordingly, the discovery 70 years ago of antibiotics able to diffuse through living tissues, kill any bacteria infecting them and save all those lives can be seen as the most valuable medical advance of all time.

The crowded lives of bacteria

Bacteria are very tiny, and one needs a 1000X magnification to see them. However, they make it up by their numbers to a mass perhaps greater than that of all the big animals combined. They have gained their huge populations not only by penetrating almost everywhere but also by packing tightly in intricately synergistic communities. A cubic millimeter of stool may contain a trillion bacteria of hundreds of kinds, and fertile soils have only a few logs less. Adjustments in such populations are made dynamic by the explosive multiplication rates that bacteria can attain, with generation times as short as twenty minutes.

The “miracle” of manufactured antibiotics

Seventy years ago, humans discovered and began to manufacture antibiotics, eventually tons and tons of many different kinds. The intent was to have small amounts of an antibiotic diffuse through the sterile tissues of infected patients, kill the bacteria that were invading, and cure the infections and save the patient’s lives. Everyone was so astonished that such a thing was possible, that for a while it was the only aspect of antibiotic use that one could think about. Where else it was going, one could care less.

Antibiotics were portable, moreover, and soon cheap and ubiquitous. Earlier control of infection had been by prevention, which meant approaching everyone, while they were healthy and not feeling any immediate need for it, with big programs of total immunization or clean water that needed advance planning and large appropriations. No one needed an antibiotic until and only when his or her child was infected. And then they were plenty motivated to get one, so distribution could be marketplace, rather than public health. Few new products had ever achieved worldwide availability so quickly.

ANTIBIOTICS --A SPECIAL CATEGORY OF DRUGS – EVERY ANTIBIOTIC USE IMPACTS RESISTANCE IN THE COMMUNITY

The extraordinary power of an antibiotic to amplify and spread resistance to itself derives from its lethality for enormous numbers of susceptible bacteria, and the speed with which a bacterial cell resistant to it can multiply to replace all the susceptible bacteria. The power of an antibiotic to amplify and spread resistance to other antibiotics is due to the accumulation in bacteria that have survived them and of the transferable mobile genetic elements in those surviving bacteria [1].

Antibiotic use drives each step in the emergence, spread and evolution of a resistance gene. It uncovers, amplifies and spreads resistant mutants, otherwise doomed to solitary obscurity. It amplifies obscure strains with prototype resistance genes, making them more available to recombinant events that may take a decade or more to bring them to infecting bacteria. It amplifies the numbers of a resistant strain colonizing any human or animal carrier that carries one, and so increases the chances that it will be the one that eventually infects that carrier or gets transferred to the next carrier in the chain of transmission.

After three billion years of bacterial evolution, the world's infecting bacteria had almost no antibiotic resistance genes, but a half century of antibiotic use then spread many into more than a quarter of them [2]. People or animals receiving antibiotics as well as countries that use more antibiotics have been found to have more antibiotic resistant bacteria [3]. From all we know, the progression of antibiotic resistance would appear to be ultimately some cumulative function of how many bacteria have encountered an antibiotic.

REDUCING ANTIBIOTIC USE TO DELAY ANTIBIOTIC RESISTANCE

If all of this had been known 70 years ago, better control of antibiotics might have been established to slow the amount gushing harmfully onto non-infecting populations of bacteria. It is difficult, however. Antibiotics that diffuse through infected tissues are also excreted into skin and gut where they encounter thousands of times more non-infecting bacteria, and in animals then also into a bacteria-rich environment. Uncertain diagnosis and excess caution combine to treat with antibiotics more people or animals who have no infecting bacteria than who do, and to treat those who do for too long. All of these increase the number of bacteria exposed to antibiotics - the basic metric for this gushing. Programs to minimize each of these types of unnecessary use have succeeded, but are hard to establish widely.

In this context, giving antibiotics to food-production animals solely to promote their growth seems their least essential use and its cessation our best opportunity to slow the gushing. Since it is a large application involving many non-infecting bacteria its ratio of non-infecting to infecting bacteria is presumably infinite. The claimed benefit is a small reduction in meat cost, which would not appear to weigh heavily against the hazard of further antibiotic resistance, particularly in a country campaigning against obesity.

Looking back over 70 years at parallel timelines for the introduction of antibiotics and for the emergence and spread of resistance to them, one has seen both in-time and not-in-time arrival of rescuing antibiotics. One needs to slow the progression of resistance to increase the chances that rescuing antibiotics, with all the uncertainties of their development, will arrive in time. The growing evidence sketched here indicates that this requires an overall reduction in the numbers of bacteria that are being exposed to antibiotics.

What can be done to slow the progression of antibiotic resistance?

Only by employing a multi-pronged approach to this serious public health problem can one hope to make an impact on preserving this precious resource to both safeguard and extend human and animal life. Part of the solution lies in reducing antibiotic use in circumstances that do not require them.

Inappropriate/over use of antibiotics in food animal production is a case in point. *It is essential that use of antibiotics in agriculture be limited to the treatment of diseased animals and should not be used for non therapeutic purposes: growth promotion, feed efficiency, or to compensate for stress of transport and on-farm conditions of crowding and poor hygiene* [4],[5]. Use of alternative infection prevention measures is encouraged, where possible. *Fluoroquinolones and third generation cephalosporins, antibiotics critical to treating human diseases, should be restricted to treating refractory infections in individual animals* [4]. *In addition, antibiotics should be administered to animals only on prescription by a veterinarian* [4].

To assess the human health risk and inform public health policy, quantitative data on antimicrobial use in agriculture should be made available by pharmaceutical manufacturers, importers and end users [4]. *Regulatory agencies should consider the ecology of antimicrobial resistance –the processes of spread and complex interactions between bacteria – both pathogens (disease causing) and non-pathogens (commensals), food animals, humans, and their environments* [4]. *Surveillance programs for antimicrobial resistance should be harmonized to permit integrated analysis of human and animal data* [4].

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