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PRINCIPLES FOR THE USE OF ANTIBIOTICS IN ANIMALS USED IN FOOD PRODUCTION

Summary of recommendations

1. **Antibiotics that are "critical" antibiotics for serious human infections should not be used in food production animals or agriculture.**

2. **The use of antibiotics for prophylactic purposes in animals should be kept to a minimum. The overall current usage for this purpose should be significantly reduced. The use of methods (other than antibiotics) to prevent infections should be expanded and developed.**

3. **Antibiotics should not be used as growth promoters.**

Introduction

Humans can acquire many different bacteria from animals. An important route for acquiring these bacteria is through the food chain. Bacteria that are acquired through the food chain include pathogens that can cause of serious infection in humans (eg salmonella and campylobacter). However bacteria that have a much lower potential to cause serious infection in humans (eg animal strains of E.coli and enterococcus) are also transferred through the food chain. These less pathogenic bacteria appear to be transferred more commonly than salmonella. All bacteria may carry genetic material that encodes for bacterial resistance. These resistance genes can subsequently be transferred to other bacteria (especially within the human gut). This can then lead to potential failures in antibiotic therapy if bacteria that cause serious human infection acquire these resistance genes.

How often bacteria derived from animals cause human disease is variable and has usually not been accurately quantified. We do know however that there are tens of thousands of cases of laboratory-diagnosed salmonella and campylobacter infections each year. We also know that even with these pathogenic bacteria that only a minority of human cases show significant symptoms and that only a small number of these latter cases are ever diagnosed in the laboratory. This implies that very large numbers of both pathogenic and non pathogenic bacteria (and any antibiotic resistant genetic codes they carry) are transferred through the food chain to humans each year

Antibiotic use is widespread in food producing animals. As in humans they are used both to treat and prevent infections. In contrast to humans however there is also extensive use of antibiotics in subtherapeutic doses for growth promotion (increased weight gain and improved feed utilisation). Most antibiotics are added to stockfeed and without the need for a prescription from a veterinarian (ie available "over the counter"). In Australia (as in many other countries) more antibiotics are used on a tonnage basis in animals than in humans, with most used for prophylactic and growth promotion purposes.

To minimise the potential for antibiotic resistance to develop and then subsequently be transferred to humans we recommend adherence to the following three broad principles. These principle cover the use of antibiotics in these animals for

1. therapeutic purposes (ie treatment of established infections),
2. prophylactic purposes (ie to prevent infections from occurring) and for
3. growth promotion purposes (ie to increase weight gain and to improve feed utilization efficiency)

Recommendations

1. **Antibiotics (or similar agents in the same class of antibiotics) that are "critical" or "last line" antibiotics for serious human infections should not be used in animals or agriculture.**
   There are many serious infections in humans where there are few or no alternate antibiotics that can be used if antibiotic resistance develops. Such antibiotics include

Class of antibiotic	**Examples** **(mainly human but with some animal antibiotics)**
glycopeptides	(vancomycin, teicoplanin, avoparcin)
third generation cephalosporins	(eg cefotaxime, ceftriaxone),
anti pseudomonal penicillins	(eg piperacillin, ticarcillin),
anti tuberculosis drugs	(eg rifampicin, isoniazid),
fluroquinolones	(eg ciprofloxacin, levofloxacin, enrofloxacin),
aminoglycosides	(eg amikacin, tobramycin),
carbapenems	(eg imipenem, meropenem).

   More recently because of increasing antibiotic resistance in many human pathogens and the need to develop alternate antibiotics, the streptogramins (Synercid, virginiamycin) appear to have entered this class of human antibiotics. It is also essential that if completely new classes of antibiotics are developed for human use that these be not used in animals unless it is established they are not "critical" for human use.

   It is essential that these "critical" antibiotics are not used in food producing animals and also that no other antibiotic that is in the same class as these agents is used. Examples of these would be fluroqinolones (eg ciprofloxacin or enrofloxacin). The use of enrofloxacin has resulted in the development of ciprofloxacin resistant salmonella and campylobacter. These resistant bacteria have then caused many human infections. Another example is the use of glycopeptides (avoparcin, vancomycin or teicoplanin). There is strong evidence that with the use of avoparcin in food production animals has resulted in the development and amplification of vancomycin resistant enterococcus (VRE) in Europe and subsequent colonization by a significant percentage of the human population via the food chain (between 2 to 17%).

2. **The use of antibiotics for prophylactic purposes in animals should be kept to a minimum. The current usage for this purpose should be significantly reduced. The use of methods (other than antibiotics) to prevent infections should be expanded and developed.**
   Antibiotics are extensively used for prophylactic purposes in animals in some agriculutere sectors (eg pork and chicken meat). However the use of these antibiotics can lead to the development and amplification of antibiotic resistance. Therefore their use should be kept to a minimum. This reduction in use can be achieved by the introduction of new innovations such as vaccines, probiotics, changed animal husbandry practices and research

directed to the prevention of these infections rather than relying on antibiotics. This may involve modification of diets and changing the ways animals are housed or reared. In chickens antibiotics are frequently used to prevent necrotising enterocolitis (due to Clostridia perfringens). In Sweden changes in animal husbandry practices and diet lead to the prevention of this infection without the use of prophylactic antibiotics and with an increase in the total number of chickens produced annually.

If antibiotics need to be administered then only agents that are not likely to cause problems with resistance to antibiotics used in humans (and preferably also those antibiotics used therapeutically in animals) should be used. As an example, ionophores should be used to prevent conditions such as liver abscesses and bloat in feed lot cattle rather than agents such as avoparcin, virginiamicin or macrolides. Because some sectors of the agriculture industry (eg chickens, pigs) have a perceived dependence on these antibiotics, most of this use of antibiotics will need to phased out over a period of a few years rather than immediately. During this time alternate non antibiotic methods should be implemented and developed to prevent infections. However, the use of agents that are in classes of antibiotics that have the potential to cause major problems for the therapy of human infections (particularly antibiotics similar to 'last line' human antibiotics such as the glycopeptide avoparcin) should cease immediately.

Antibiotics should not be used as growth promoters.

Antibiotics have been used for decades as growth promoters. Their main benefit appears to be altering the bacterial flora (particularly gram positive organisms) in the gut of animals. Some animals then achieve a larger weight gain over a set period of time and also may consume less feed to achieve the same weight. However the use of antibiotics for this purpose leads to the development and amplification of antibiotic resistant organisms. Humans via the food chain can then acquire these resistant bacteria.

The magnitude of these economic benefits attributed to antibiotics used as growth promoters is unclear. In some studies no benefits with antibiotics are seen. The largest benefits are seen in animals that are stressed, exposed to large doses of pathogenic bacteria or are raised under conditions of less than ideal animal husbandry. Overall if benefits are present in animals raised under conditions of good animal husbandry then the benefits are likely to be between 1 to 3% for weight gain and/or improved feed efficiency.

We believe even though there may be an economic benefit in the use of antibiotics for this purpose, that the cost of increased bacterial resistance and its potential and documented effects on infections in humans, out weights these relatively small economic benefits. Even if the postulated economic benefits (as claimed by the distributors of these growth promoters) are accepted, the value to farmers or consumers is not very large. In chickens for instance the calculated benefit in Australia is approximately 3 cents per chicken for the producer. The monetary cost to the consumer would also not be large. In the USA it has been calculated what the increased price at the retail level would be if antibiotics were not used as growth promoters. The estimates are between 3 to 6 cents per lb. for pork and 1.3 to 2.6 cents per lb for chickens.

Overall Conclusion

The use of antibiotics in food animals has resulted in increased antibiotic resistance in many bacteria and these antibiotic resistant bacteria have caused human infections. Antibiotics are however important in the care of animals. To minimize the potential harm on humans through the development, amplification and spread of bacteria and the genetic resistance codes they

carry, the three broad principles outlined in this policy paper should be implemented and followed for the use of antibiotics in animals.

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