3D: THE USE OF ANTIBIOTICS IN FOOD PRODUCTION ANIMALS: DOES THIS CAUSE HUMAN HEALTH PROBLEMS?

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Antibiotic use in humans and animals

Antibiotics are used extensively in both humans and in animals. In Australia the amount of antibiotics used in animals is greater than in humans.[1] The three main uses of antibiotics in livestock are for growth promotion, prophylaxis against infection and to treat sick animals.[2] Antibiotic use in animals however is also a potential problem for human medicine because antibiotic resistant bacteria can pass through the food chain to people.[1,2,3] In the past the main concerns we have had with food borne bacteria were those that produced frequent and/or severe disease in people (eg *Salmonella* and *Campylobacter* which cause gastroenteritis). However more recently there have been growing concerns about the less virulent bacteria that are transferred very frequently via the food chain to people (eg *Escherichia coli* and Enteroccci). These latter bacteria frequently carry genes encoding for antibiotic resistance (as also do *Salmonella* and *Campylobacter*).[1,2,3]

Vancomycin resistance is linked to antibiotic use in animals

In Europe there is strong evidence[3] that vancomycin resistant *Enterococci* (VRE) develop in animals that were fed an antibiotic for growth promotion purposes, called avoparcin (a glycopeptide or vancomycin-like antibiotic). These strains of VRE remained on the carcasses of animals after slaughter. VRE was then found on foods that were sold at the retail level (eg in the Netherlands in one study over 70% of chicken tested at the retail level had VRE present).[3] In different studies of the European population, between 2 - 17% of people carried these multi-antibiotic resistant bacteria present in their bowel.[3] The obvious conclusion from all this data is that VRE is widespread in Europe and that avoparcin use in animals was the major reason that VRE spread via the food chain.

Vancomycin resistance is of great concern to us in human medicine because it is a “last-line” antibiotic. Therefore if resistance develops to this antibiotic it will often mean that we have no alternative antibiotics available to treat serious infections (as occurs now for some people with VRE infections). Another even more worrying concern is whether these vancomycin resistant genes may eventually spread from VRE to much more common and aggressive bacteria such as multi-resistant strains of *Staphylococcus aureus* (MRSA). Experimentally this has been shown to occur both in the laboratory and in experimental animals. If this ever happened in our hospitals then we would have the situation where one of the most aggressive bacteria causing infections in people (*Staphylococcus aureus*) may be untreatable with antibiotics.[3]

In Australia we have much less data on the spread of VRE through the food chain because studies have not been done and published. We do however know that VRE in Australia is widespread and has been found in small community hospitals as well as large hospitals.[1,3] VRE has been isolated in food production animals in Australia.[1,3] The most logical explanation of this spread in Australia (as has been shown in Europe) is that VRE can spread through the food chain.

Wherever antibiotics are used, we know that one of the consequences of their use is that resistance can develop. The amount of resistance that eventuates is related to the total

amount of antibiotic used. The more antibiotics that are used the faster resistance develops. In 1992 over 120,000 kg of avoparcin (10% of which is the active ingredient by weight) was used in animals in Australia (predominantly as a growth promoter), while only 68 kg of vancomycin was used in people.[3] There is also now considerable doubt as to whether antibiotics used as growth promoters lead to any significant economic benefits (eg weight gains and improved feed efficiency). In some recent studies no benefits were seen.[2] In Denmark, over 200 million chickens have been produced since 1999 when the poultry industry voluntarily decided to stop using all antibiotics as growth promoters. No decrease in growth or weight gain occurred after antibiotic use stopped in chickens. It is therefore debatable whether any weight gain still occurs in animals with routine in-feed antibiotic use. If it does occur, at best this economic improvement is only a few percent in weight gain if good farming methods are in use. This translates to no more than 3 cents per chicken or a few cents per kg in pork.[1,2]

It therefore appears that the large amount of avoparcin that was used (which is in the class of antibiotics that are 'last line 'or 'critical' to humans) appears to have been a waste of a precious resource.[3] Any small economic benefits that may flow to the agricultural sector appear to be more than outweighed by the major risks to human health. The potential widespread circulation of these multi-resistant bacteria through the food chain (and associated increased hospital and medical costs to the community) is a cost that society should not have to pay.

Ciprofloxacin and third generation cephalosporin resistance is linked to antibiotic use in animals

In the USA and Europe a floroquinolone, similar to ciprofloxacin (enrofloxacin) has been associated with the spread of ciprofloxacin-resistant *Salmonella* and *Campylobacter* as well as resistant *E. coli* to humans through the food chain.[3,4,5,6] This has resulted in *Salmonella* infections in humans that are multi resistant and for which there are no available antibiotics (ciprofloxacin is also a "last-line" human antibiotic).[4,5] Third generation cephalosporins are other examples of "last line" antibiotics for people. In the USA in cattle, the use of one such antibiotic (ceftiofur) has resulted in strains of ceftriaxone resistant salmonella causing illness in people (including children where this can be the only antibiotic available to treat life threatening infections).

In Australia, fluroquinolones are not approved for use in food production animals (an application for enrofloxacin was not approved by our regulatory authorities). Australia appears to be one of the few (if not the only) country in the world where there is not a major problem with fluorquinolone-resistant *Salmonella* and *Campylobacter.*[1] Our current ban on the use of fluoroquinolones in food production animals would appear to be the main reason we do not have a problem. It also shows why it would be foolhardy to approve any other types of "last line" human antibiotics for use in food production animals.

What can we do to limit the amount of antibiotic resistance that occurs?

There will always be new antibiotics and there will always be controversy about the economic and medical costs of their use compared to their benefits (both in people and in animals). It is important that we have some antibiotics available to use in animals, as we need these to treat sick animals. However we need to limit the ways that antibiotics are used in food production animals. In particular, antibiotics should not be used for growth promotion and they should be used only sparingly for prophylaxis. It is of particular

importance that antibiotics that are 'critical' or 'last line' for human use should not be used in food production animals at all. These 'critical' antibiotics are only a small percentage of the total amount of antibiotics that are used in humans. If these "last-line" antibiotics were reserved for human use alone this is unlikely to compromise animal welfare.

The basic principles we need to follow in order to maintain or facilitate this approach not only now, but also in the future are given below.

- Antibiotics that are "critical" or "last-line" antibiotics for serious human infections should not be used in food production animals or agriculture for any purpose.
- The use of antibiotics for prophylactic purposes in animals should be kept to a minimum and eventually phased out. The overall current usage for this purpose should be rapidly and significantly reduced. The use of methods (other than antibiotics) to prevent infections should be expanded and developed.
- Antibiotics should not be used as growth promoters.

Conclusion

Antibiotics are a precious and non-renewable resource. They are of major benefit to people who have serious and life threatening bacterial infections. We are currently squandering a lot of this resource by using antibiotics much more widely than we need to and in inappropriate ways (both in people and in animals). This results in antibiotic resistance developing and then spreading not only from person to person but also via the food chain from animals to humans. It is essential that we use antibiotics wisely and prudently, otherwise these miracle drugs of the 20th century will lose their effect because of the widespread development and amplification of resistant bacteria and the genes that encode for this resistance.

Discussion notes

- Avoparcin has not been used in the USA as a growth promoter (it was not approved because it has some carcinogenic properties), and yet vancomycin-resistant enterococci (VRE) is a much bigger problem in humans in the USA than it is in Europe and Australia. The main reason for this is that much larger quantities of vancomycin were used, especially as oral therapy, in people (per capita) in the USA than in either Europe or Australia, VRE spreading from person to person. Where Europe and Australia used large quantities of the vancomycin-like antibiotic avoparcin, large numbers of VRE were found when this organism was looked for – in animals, food and carriage by the general community.
- What is important to appreciate is that antibiotic resistance is an inevitable consequence of use. Once the resistant bacteria are present, then the more antibiotics are used, the more of these resistant bacteria will result. Antibiotic use also makes it easier for them to spread from animal to animal or from person to person. If they are present in large numbers in our food then inevitably they will proliferate if a person carried them in their bowel and is then given antibiotics (e.g. in hospital with a ruptured appendix). They can then spread from person to person. In the USA their first outbreak started in New York and then spread from there. Once present in any environment, the high use of antibiotics in that environment (on humans or animals) will cause the numbers to rapidly increase and facilitate the spread of these resistant bacteria both within the same environment and to other areas. This spread to other areas can occur by many means, but one important route is via food.
- An important source of antibiotic resistance is from overuse of this valuable resource by medical practitioners, both in hospitals and general practice. Broad spectrum

antibiotics are still frequently prescribed for viral respiratory infections, which are self-limiting. It would seem preferable for medical practitioners to limit their prescribing to identifiable bacterial infections, if possible with cultures to provide information on the spectrum of antibiotic sensitivities and resistance. Establishment of this precautionary principle would require education, from medical school onwards, on the need to be more discriminating in the prescribing of antibiotics.

References

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