Antibiotics in food production animals: cause of human health problems?

Peter Collignon • MB BS BSc(Med) FRACP FRCPA FASM
Clinical Associate/Professor, Canberra Clinical School
Infectious Diseases Physician and Microbiologist
Canberra Hospital, Australia

Abstract

Whenever antibiotics are used (in people or animals), we know that one of the consequences of their use is that resistance in bacteria can and usually does eventually develop. People become colonised and in some cases ill with bacteria that come across to them via the food chain. These bacteria can be antibiotic resistant. Some of this antibiotic resistance can be to antibiotics that are 'last line' agents in therapy of life threatening infections in people. The development and spread of these multi–resistant bacteria follows the use of last line (or similar) antibiotics in food production animals. Examples include ciprofloxacin resistant strains of Salmonella *sp and* Campylobacter *sp, as well as the vancomycin resistant enterococci (VRE). However, many of the driving factors for this antibiotic resistance could be substantially reduced or eliminated without compromising the therapy of sick animals. [AIC Aust Infect Control 2000; 5(2):21-23.]*

Introduction

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 and to treat sick animals[2].

Antibiotic use in animals, however, is also a potential problem for human medicine as 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, for example *Salmonella* sp. and *Campylobacter* sp. which cause gastroenteritis. However, more recently, there have been growing concerns about bacteria that cause disease in people less frequently, but are transferred more frequently via the food chain, i.e. *Escherichia coli* and Enterococci. These latter bacteria, as well as *Salmonella* sp. and *Campylobacter* sp. frequently carry gene encoding for antibiotic resistance[1,2,3].

Vancomycin and ciprofloxacin resistance

Vancomycin and ciprofloxacin resistance are linked to antibiotic use in animals.

Vancomycin resistance

In Europe, there is strong evidence[3] that VRE develop in animals that have been fed an antibiotic called avoparcin, a glycopeptide or vancomycin–like antibiotic. These strains of VRE may then remain on the carcasses of animals after slaughter and remain on foods that are sold at the retail level. One study in the Netherlands showed that over 70 per cent of chickens tested at the retail level had VRE present[3]. In studies of the European population, it has been found that between 2–17 per cent have these multi antibiotic resistant bacteria present in their bowel[3].

The conclusion from all of this data is that VRE is widespread in Europe and that avoparcin use in animals is the major reason why VRE has spread in the food chain. Vancomycin resistance concerns us in human medicine because it is a 'last–line' antibiotic. Therefore, if resistance develops to this antibiotic, this will mean that we usually have no alternative antibiotics available to treat serious infections. This occurs now for some people with VRE infections.

Another larger concern is whether these vancomycin resistance 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. If this ever happened in our hospitals, we would have the situation where one of the most aggressive bacteria causing infections in people may be untreatable with antibiotics[3].

In Australia, we have much less data on the spread of VRE through the food chain. We do, however, know that VRE in Australia is widespread and has been found in small community hospitals as well as larger ones[1,3]. VRE has also been isolated in food production animals in Australia[1,3]. The most logical explanation for this spread in Australia, as in Europe, is that VRE is 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 believed to be related to the total amount of antibiotic used. In 1992, over 120,000 kgs of avoparcin (10 per cent 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 a debate as to whether antibiotics used as growth promoters really lead to any significant economic benefits. i.e. weight gains and improved feed efficiency. In some recent studies, no benefits were seen[2]. At best, and with good farming methods, this weight gain is only a few per cent. Economically, this translates to no more than 3 cents per chicken or a few cents per kg in pork[1,2].

The large amount of avoparcin used, which is in the class of antibiotics that are 'last line 'or 'critical' to humans, appears to be 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 (and increased hospital costs) by the potential widespread circulation of these multi resistant bacteria through the food chain.

Ciprofloxacin resistance

In the USA and Europe, a fluoroquinolone similar to ciprofloxacin (enrofloxacin) has been associated with the spread of ciprofloxacin resistant *Salmonella* sp., *Campylobacter* sp. as well as resistant *E. coli* to humans through the food chain[3-6]. This has resulted in *Salmonella* infections in humans that are multi resistant and for which there are no available antibiotics, ciprofloxacin being a 'last–line' human antibiotic[4,5]. In Australia, fluoroquinolones 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 fluoroquinolone resistant *Salmonella* and *Campylobacter*[1]. Our current ban on the use of fluoroquinoles in food production animals would appear to be the main reason we do not have a problem.

Limiting the amount of antibiotic resistance

What can be done 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 humans and in animals. It is important that we have some antibiotics available for use in treating 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. Of particular importance is that antibiotics that are 'critical' or 'last line' for human use, should not be used in food production animals at all. These 'critical' antibiotics make up only a small percentage of the total amount of antibiotics that are used in humans. If these 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:

- Antibiotics that are 'critical' or 'last–line' for serious human infections should not be used in food production animals or agriculture.

- 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, not antibiotics, to prevent infections should be expanded and developed.

- Antibiotics should not be used as growth promoters.

Conclusion

Antibiotics are a precious but 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 loose their effect because of the wide spread development and amplification of resistant bacteria and the genes that encode for this resistance.

References

1. Joint Expert Advisory Committee on Antibiotic Resistance (Jetacar). Commonwealth Department of Health and Aged Care and the Commonwealth Department of Agriculture, Fisheries and Forestry. The Use of Antibiotics in Food–producing Animals: Antibiotic–resistant Bacteria in Animals and Humans. September 1999, Canberra.

2. Collignon P. Vancomycin–resistant enterococci and use of avoparcin in animal feed: is there a link? Med J Aust 1999; **171**: 144–146.

3. Collignon P. Antibiotics in animals: a resistance problem for man? Microbiol Aust 1999; **20**: 18–20.

4. Molbak K, Baggesen DL, Aarestrup FM, Ebbesen JM, *et al.* An outbreak of multidrug–resistant, quinolone–resistant *Salmonella enterica* serotype typhimurium DT104. N Engl J Med 1999; **341**: 1420–5.

5. Glynn MK, Bopp C, Dewitt W, Dabney P, *et al.* Emergence of multidrug–resistant *Salmonella enterica* serotype typhimurium DT104 infections in the United States. N Engl J Med 1998; **338**:1333–8.

6. Smith KE, Besser JM, Hedberg CW, Leano FT, *et al.* Quinolone–resistant *Campylobacter jejuni* infections in Minnesota, 1992–1998: Investigation Team. N Engl J Med 1999; **340**:1525–32.