

EDITORIAL

Antibiotics in animals – much ado about something

John Turnidge, Professor, Microbiology and Infectious Diseases Department, Women's and Children's Hospital, Adelaide

Index words: antibiotic resistance, avoparcin, vancomycin.

(*Aust Prescr* 2001;24:26–7)

Much media attention has been focused on the use of antibiotics in animals, particularly the animals we eat, and the potential spread of resistance to bacteria which infect humans. Although the problem was recognised over 30 years ago¹, few countries acted upon it until recently. In the early 1990s a link was identified between the emergence of vancomycin-resistant *Enterococcus faecium* with the *vanA* gene (*vanA* EF) and the use of avoparcin, a vancomycin analogue, as a growth promoter in pig and poultry production.

Australian antibiotic use in farming, medicine and veterinary medicine is high. During 1992–7 an annual average of 399 tonnes or 56% of all antibiotics by weight was used in stockfeed. Humans consumed 251 tonnes or 36%, while 54 tonnes or 8% were used in veterinary therapeutics.²

A very wide range of antibiotics is used for many different reasons in animal husbandry, agriculture, and in veterinary practice. Common sense and a knowledge of bacterial genetics tell us that we need to monitor the emergence of resistance and only give antibiotics to animals when it is therapeutically rational and cost-effective to do so. Resistant bacteria can be generated in animals, transferred to humans and amplified to become a major human problem. These bacteria may either cause disease in humans or transfer their resistance genes to normal flora that may later become pathogenic. Good food

hygiene will slow the transfer rate but will not eliminate the transfer of resistance. Antibiotics should therefore be given to animals only when necessary and for the shortest effective duration.

While short courses at therapeutic doses minimise resistance selection, a significant proportion of the antibiotics used in animals are given in feed at low doses over many weeks of the production cycle. Antibiotics are used in this way by the so-called intensive animal industries, especially meat poultry and pig production, where the animals are housed in close quarters in large numbers (just like hospitals!). Cross-infection is a problem, and antibiotics play an important role in suppressing infection and controlling stock loss, as well as in promoting the animals' growth.

These patterns of use generate maximum selective pressure for antibiotic resistance. This would not be a problem if the antibiotics used were from different classes and had a different mechanism of action from those used in humans. Unfortunately, a number of drugs used in this way belong to the same classes and select for cross-resistance to human antibiotics. Examples include avoparcin (a glycopeptide), virginiamycin (a streptogramin which selects for cross-resistance to the newly released drug quinupristin/dalfopristin) and certain macrolides.

Before calling for blanket decisions to prohibit all antibiotic use in animals, we need to understand the data suggesting that resistance has been transferred from animals to humans via the food chain. The data concerning resistance transfer are limited to a small number of organisms and antibiotics such as *vanA* EF and avoparcin, thermophilic *Campylobacter* species and fluoroquinolones, multi-drug resistant *Salmonella* species and aminoglycoside resistance in *E. coli*. Apart from these examples there is little information to show just how much resistance in human bacteria can be traced back to the use of antibiotics in animals.

Data in Australia are even more limited. For instance, although avoparcin has been widely used in Australia since the mid 1980s, and vancomycin-resistant enterococci (VRE) emerged in human isolates in Australia in 1994, the predominant type of VRE contain a different gene from that attributed to avoparcin use. One small study of animal samples in the Hunter Valley revealed only two strains of VRE, and their association with avoparcin use remains unclear.³

The concern for human medicine is that avoparcin and virginiamycin select for resistance to drugs that are reserved

In this issue...

The spectre of antibiotic resistance is probably contributing to the improved use of antibiotics in the community. Jonathan Dartnell tells us that educational approaches can also improve hospital prescribing, while John Turnidge discusses how agricultural antibiotics could contribute to the resistance problem.

Mental illnesses such as depression are also increasing, but many depressed patients need not be treated with potentially toxic drugs. John Tiller explains how doctors can use cognitive behaviour therapy to help patients with mental disorders.

Coeliac disease is also being recognised more frequently than previously, and Warwick Selby tells us how to confirm the diagnosis.

for infections caused by bacteria resistant to multiple other antibiotics ('last-line' drugs). After sustained pressure about this issue the European Union decided to suspend the use of avoparcin as an in-feed antibiotic. Subsequently it was withdrawn from the international market, including Australia. The Europeans have also suspended other in-feed drugs, including virginiamycin, tylosin, spiramycin and bacitracin.

What could or should be done about antibiotic use in animals? Australia has produced a blueprint for tackling this problem.² A number of recommendations have been made in the areas of regulation, surveillance and monitoring, infection prevention, education and research. One key recommendation is that of phasing out the long-term, low dose use of antibiotics that can generate resistance to 'last-line' human antibiotics.

The most important feature of the recommendations is that rational antibiotic use is the responsibility of **all** prescribers and users, medical practitioners and veterinarians, patients

and farmers. Antibiotic use of any type and the antibiotic resistance it generates is a public health issue. The use of antibiotics in animals may be making a lesser contribution than inappropriate prescribing to resistance problems in humans. However, all users must endeavour to minimise resistance for the sake of healthy animals, food and humans.

E-mail: turnidgej@wch.sa.gov.au

REFERENCES

1. UK Joint Committee on the use of antibiotics in animal husbandry and veterinary medicine ('Swann Report'). London: Her Majesty's Stationery Office; 1969 Nov.
2. Joint Expert Technical Advisory Committee on Antimicrobial Resistance (JETACAR). The use of antibiotics in food-producing animals: antibiotic-resistant bacteria in animals and humans. Canberra: Commonwealth Department of Health and Aged Care and the Commonwealth Department of Agriculture, Fisheries and Forestry; 1999 Sept. <http://www.health.gov.au/hfs/pubs/jetacar.htm>
3. Butt H, Bell J, Ferguson J. Are vancomycin-resistant enterococci prevalent in Hunter region farm animals? *Microbiology* 1997;18:A115.

Letters

Letters, which may not necessarily be published in full, should be restricted to not more than 250 words. When relevant, comment on the letter is sought from the author. Due to production schedules, it is normally not possible to publish letters received in response to material appearing in a particular issue earlier than the second or third subsequent issue.

Topical ciprofloxacin and antibiotic resistance

Editor, – A generation or so ago, I was taught that if one wanted to render antibiotics useless, due to resistance, as quickly as possible, apply them topically. Why is ciprofloxacin being marketed in this way? Should there not be a full re-evaluation of the use and misuse of all topical antibiotics? Is there any convincing evidence that any of them are a good idea?

Peter Rout

General Practitioner

Darlington, NSW

Professor J. Turnidge, Microbiology and Infectious Diseases, Women's and Children's Hospital, Adelaide, comments:

The concern expressed by Dr Rout about the topical use of ciprofloxacin is shared by many others. The standard teaching comes from the early experience with the use of topical antibiotics to treat infected burns, where resistance emerged rapidly. It is possible that the very high counts of bacteria in infected burns made the selection of resistance easier. Whether this problem occurs with all topical antibiotic use is not clear. The concentrations of topical antibiotics are often 1000 fold higher than the minimal inhibitory concentrations of the bacteria. Thus, in theory, there should be a lower risk of resistance selection than with systemic use.

However, there is another principle that must be taken into account. The rate of resistance selection is related to the total amount of antibiotic use in the community. We should prefer topical drugs which, when resistance is selected, do not jeopardise the valuable systemic antibiotics. Indeed, in the case of fluoroquinolones, strenuous efforts have been made to ensure that availability of the systemic drug is restricted to cases of proven need. Topical application should follow the

same principle. Dr Rout will be pleased to know that the availability of topical ciprofloxacin (and other topical quinolones) has been taken up with national regulators. Although the outcome is not known, we hope that these drugs will be restricted to (rare) cases of proven need.

Treatment of panic disorder

Editor, – In writing about the 'Treatment of panic disorder' (Aust Prescr 2000;23:124–6) Professor Tiller provides the standard definition used in psychiatry. The definition ignores the most outstanding characteristic of panic disorder and panic attacks: over-breathing. Indeed, the Diagnostic and Statistical Manual (DSM) does not provide a diagnosis for hyperventilation disorder which is a common affliction in the community and certainly so among those with mental disorders.¹ Caught in this bind, Professor Tiller arrives at the task of management without any theoretical explanation of the measures he advocates.

I intend no criticism of the author. The fact that he deals with hyperventilation at all shows that he is well ahead of his academic colleagues and most working in the field. He has rediscovered the wheel earlier than they. The part that hyperventilation disorder played received full acknowledgment long ago¹ and the symptoms of cerebral hypoxia caused by cerebral vasoconstriction were explained in the 19th century. All that knowledge disappeared in the face of psychopharmacotherapy. Psychiatrists have discarded the simple clinical recognition of the deep breaths taken by the anxious patient, the revealing account of light-headedness, pins and needles in the periphery, pain in the left side of the chest, the lump in the throat, palpitations and panic. Instead of restoring normal breathing and confidence, doctors now take out the prescription pad and a reversible process becomes irreversible.