Antibiotic Resistance

ACVM information paper

Background

Within New Zealand and internationally, concerns have been raised about an association between antibiotics used routinely to protect the health of animals farmed for food and the problem of growing resistance to antibiotics by some micro-organisms.

Antibiotics, a type of antimicrobial medicine, are chemical substances capable of destroying or preventing the growth of bacteria. Penicillin, discovered by Sir Alexander Fleming in the 1920s, revolutionised the treatment of what were then life-threatening bacterial infections, including human tuberculosis (Tb), pneumonia and infections from wounds. Animals have also benefited from the use of antibiotics.

Certain strains of bacteria have now evolved with the ability to survive exposure to some antibiotics. Human Tb is on the rise again worldwide, and other new strains of bacteria such as MRSA (methicillin-resistant staphylococcus aureus) have been found in some hospitals.

Evidence indicates that in some specific instances the use of antibiotics in animals may contribute, at least in part, to the level of antibiotic resistance in humans. Since 1972, the Ministry of Health has monitored the prevalence of antibiotic resistance among important human bacterial pathogens (disease causing micro-organisms).

Though antibiotic use in animals may not be a significant contributor to antibiotic resistance in people, evidence of such trends is continually monitored and regulatory control is adjusted as necessary. At the same time, the prudent use of antibiotics in animals must be encouraged for the health and welfare of the animals concerned.

What is antibiotic resistance?

Antibiotic resistance in bacteria is either an inherent (naturally occurring) or acquired ability to withstand treatment to one or more antibiotic. If bacteria are resistant to certain antibiotics, then the disease under treatment cannot be cured or controlled by treatment with those antibiotics.

What causes it?

Antibiotic resistance can be caused by any of the following:

- a naturally occurring (or acquired via genetic mutation) capability to withstand treatment without any previous exposure to the antibiotics
- previous exposure to the antibiotics
- transfer of resistance from other bacteria (pathogenic or non-pathogenic) that have already acquired resistance.

Why are experts concerned about it?

The concern is that existing antibiotics will become ineffective in treating bacterial infections and that new antibiotics may not be found in time to prevent a return to the situation where bacterial

infections routinely become life-threatening. This was the case up until the discovery of antibiotics in the 20th century.

Does the use of antibiotics in animals cause resistance in human bacterial pathogens?

Except for specific instances involving particular antibiotics, antibiotic use in animals is not considered to be a significant contributor to the development of antibiotic resistance in human bacterial pathogens. However, most countries including New Zealand are taking a prudent or cautious approach.

With regard to human health, the significance of bacterial resistance depends on:

- whether the bacteria in question can cause disease
- whether they can transfer resistance
- whether there is likely to be exposure to humans
- whether the bacteria are infectious to humans.

Is it possible for antibiotic resistance to pass from animals to people?

It is not the antibiotic resistance that may pass from animals to people. It is the possibility that antibiotic resistance may pass from bacteria in animals to bacteria in people or that resistant animal bacteria may infect people.

In many cases the bacteria in animals are the same as, or very similar to those in people. Resistant and non-resistant bacteria can transfer from animals to humans, either through direct contact or through contaminated food. The reverse (transfer of bacteria from humans to animals) can happen too. Some of those bacteria can cause disease in animals or people – or both. Others may not cause any harm, but may still be resistant to some antibiotics and could pass that resistance on to harmful bacteria.

Resistance to particular antibiotics develops in bacteria. Some animal bacteria can be transferred to people and, at times, result in disease. Bacterial genetic material that confers resistance to a particular antibiotic can be transferred to another bacterial species. This can occur in animals and the resistant bacterial genetic material can be passed on to bacteria in humans.

What combination of events would have to happen for that to occur?

For antibiotic resistance to be significant, two events must occur:

- resistance must develop in bacteria
- the bacteria must cause disease in the host or their presence would not be noticed, or could in fact be beneficial to the host, making resistance irrelevant.

For antibiotic resistance to be transferred from animals to people and for it to be significant to human health, the following would need to occur:

- the resistance must develop in the bacteria
- people must be exposed to the bacteria in the animals
- the bacteria must be able to thrive in or on humans
- the bacteria must be able to either cause disease in humans or transfer its resistance to bacteria that can cause disease in people.

The same steps would be required for transfer from humans to animals.

Are there any recorded instances anywhere in the world where it has happened?

Absolute confirmation of the transfer of antibiotic resistance from animals to humans is difficult. There have been cases where it is suspected that people have been infected with antibiotic-resistant pathogenic bacteria from animals. In some instances, a change of antibiotic use in animals has led to an apparent effect on the resistance patterns of bacteria affecting people. Other studies have shown that resistant bacteria found in people are genetically very similar or identical to bacteria in animals. No clinical cases have been reported where human pathogens have been found in people and the source of the resistance has been confirmed to have been transferred from resistant bacteria of another species in animals.

What was the outcome?

Restriction of the use of particular antibiotics appears to have reduced the prevalence of resistant bacteria.

What is the likelihood of animal to human transfer occurring in New Zealand?

Some resistance to particular antibiotics has developed in animals. However, given that the effectiveness of antibiotic therapy in animals overall has not been seriously jeopardised by present practices, the probability that a person in New Zealand will develop a disease caused by a human pathogen that is resistant to antibiotics due to transfer of resistance from an animal bacteria species appears low.

How does this compare with other potential pathways?

None of the existing cases of limited effectiveness of antibiotic therapy in people in New Zealand can be confirmed to have been associated with transfer of resistance from animal bacteria species. To date the most common association with unresponsive cases is related to hospitals or intensive health care situations.

If a transfer occurred, what would happen next?

The response would be managed by the existing protocols for antibiotic resistance and infectious diseases in the health system. If it was confirmed that transfer from animal bacteria was the cause, the response would depend on the case. At this stage, it is impossible to predict what the circumstances might be and what antibiotic might be involved and what disease organism might be involved.

Is there a link between antibiotic resistance and superbugs?

Yes. Superbugs describe strains of bacterial pathogens that are resistant to a wide range of antibiotics. The superbugs discovered to date have been found in people primarily associated with hospital and health care services in which patients who have been exposed to repeated or long-term treatment with antibiotics are cared for. In effect they are ‘hospital acquired’ infections.

Most of the bacteria that become resistant remain susceptible to a wide range of antibiotics and respond well to conventional treatment. Even though antibiotics use in animals has been common practice for as long as it has in people, so far there have been no distinctly animal pathogen superbugs found.

How are antibiotics used in animals?

Like humans, animals need antibiotics to fight off bacterial infections. At times antibiotics are also used to prevent bacterial infections when there's a likelihood of an infection, in much the same way as they are in humans (for example, to prevent the spread of bacterial meningitis).

The use of antibiotics in cattle and sheep is relatively low because of the pastoral farming systems used in New Zealand (as compared with 'feed lots' in many other countries). Use tends to be higher in the intensive rearing industries, mainly the pig and poultry industries.

Antibiotic use in animals in New Zealand falls into two areas:

- **for medicinal or therapeutic use** when the individual animal or groups of animals are ill and show symptoms of disease. Most antibiotics are used for this purpose.
- **for preventative or prophylactic use** when it's highly likely that animals will contract diseases and when a disease appears among a group of animals. For example, antibiotics may be used to treat an entire group for conditions such as pneumonia and diarrhoea when it becomes obvious that they are all likely to become ill.

What antibiotics are used on animals?

A wide range of antibiotics are used therapeutically, depending on the disease. Routine use is limited to those antibiotics that are of least significance to human health, such as ionophores or zinc bacitracin. These two make up the majority of all antibiotics used in animals. Of the antibiotics that may be associated with human use, only a small amount of the total kilograms used has a high or critical significance to human health.

What is being done about concerns?

Current actions taken by the Ministry for Primary Industries (MPI) recognise that antibiotic resistance could occur. Controls are designed to minimise any chances of this happening while ensuring that antibiotics are still available to meet the health and welfare needs of animals.

If production animals are treated with antibiotics a certain amount of time must elapse – the withholding period – before they can be sent for slaughter and enter the food chain. This ensures that the medicine has done its job and passed out of the animal's system so that any remaining antibiotics will be less than the maximum residue level (MRL) allowed in the Maximum Residue Levels for Agricultural Compounds (notice under the Food Act 2014). Compliance with this notice ensures that there is no safety concern over any residual trace present in the food produced. Coincidently, normal residue management ensures that any small amount of antibiotic that might still be present will not be enough to contribute to resistance.

All the antibiotics that are registered for mass medication of animals in New Zealand have been assessed against thorough review criteria. They have been reviewed for veterinary use and human health significance and agreed with the Ministry of Health.

If the potential for resistance has been identified in antibiotics that are of high or critical importance in human health, action has been taken – such as imposing the need for a veterinary prescription before sale or use to ensure that they are used only when needed.

New Zealand has taken a conservative and prudent position on the issues surrounding antibiotic resistance. In a country so dependent upon our reputation as a producer of safe food, protecting our animal welfare and human health must be priorities. MPI is confident that the actions taken in regard to antibiotic resistance have us well positioned to continue to safeguard this reputation of New Zealand and the public health of all those who live here.

MPI continues to monitor antibiotic use in New Zealand animals, and changes can be made to requirements as necessary to ensure we meet international standards in this regard.

Why isn't antibiotic use in animals stopped?

Antibiotics are essential for the health and welfare of animals. The livestock industry is investigating alternatives, but in many cases antibiotics must still be used to ensure the health and welfare of animals. Some antibiotics pose no risk of antibiotic resistance development in human pathogens: those are the sorts of antibiotics that are not or cannot be used in or on people and, because of the way they work, they do not cause cross-resistance in antibiotics that are significant to human health.

Can antibiotic use in animals be limited to therapeutic use?

Because some animals are reared in large groups in constant contact with each other, one sick animal means that all will have been exposed to the disease and, depending on the illness, are also likely to fall ill within days of each other. In some cases the disease organism (such as the bacteria that causes necrotic enteritis in chickens) is already present in the animal and the use of antibiotics prevents sickness in large groups of animals.

In terms of resistance, what kind of antibiotic use is of most concern?

General opinion is that antibiotics ‘in-feed’ (known as oral administration) is probably the most likely pathway for the development of antibiotic resistance because of the number of people who would have contact with food produced from those animals. However other pathways, such as direct contact with sick animals, are possible. No matter which pathway is relevant, the concern is greater for some antibiotics. These particular antibiotics attract the most stringent regulatory control.

Has the volume of antibiotics used in animals in New Zealand increased in recent years?

The volume of antibiotics sold in New Zealand in recent years has increased, alongside a growth in the size of the livestock industries. There is a high level of support among industry for the principle of prudent use of antibiotics. Sales statistics show that, while total amounts sold have increased, the actual total rate of use (on a per animal basis) remains at a similar level.

How does MPI regulate the use of antibiotics in animals to ensure the risk of resistance is minimised?

All antibiotics must be registered and approved for use by MPI’s Agricultural Compounds and Veterinary Medicines Group. Except for those antibiotics that are not relevant to the resistance problem, antibiotics cannot be used unless there is a veterinary prescription. Conditions are placed on the registrations that specify the responsibilities on veterinarians to ensure that they prescribe these products in a prudent manner. The relevant antibiotics are only allowed to be sold by approved traders to ensure that access to them is effectively limited by the prescription condition.

Does intensive rearing of poultry lend itself to the spread of disease – isn’t free range better/safer?

Poultry that is intensively reared does have an increased potential for disease spread.

On the other hand improved quarantine, husbandry and security reduce the exposure to environmental pathogens and parasites that free-range chickens are exposed to. The management

systems in place to raise poultry in New Zealand are necessary to produce a cost-effective, safe product for consumers. They have also resulted in the one of the most efficient livestock production operations with the best health status in the world.

What does it mean if an antibiotic used in New Zealand has been ‘banned’ overseas?

It is absolutely essential to ensure that, when comparing regulatory control in different countries, that you are comparing the same thing. For example, the European Union banned use of certain antibiotic as ‘feed additives’. The EU did not ban those antibiotics for use in animals for disease control purposes, and they are still available as veterinary medicines.

How does antibiotic use in New Zealand compare with overseas?

New Zealand has always considered antibiotics as drugs rather than ‘feed additives’ and has never allowed the level of degree of unrestricted use that used to be common in other countries. New Zealand’s regulatory control of antibiotics remains one of the most stringent in the world. New Zealand encourages prudent use without imposing unjustifiably restrictive practices that would jeopardise the health and welfare of the animals. The New Zealand position is fluid and regulations may change depending on what our monitoring systems reveal.

How does New Zealand’s response to the threat compare with that of other countries?

New Zealand has one of the most stringent regulatory control programmes in the world for antibiotics. It also has the one of the lowest incidences of antibiotic resistance in the world for both animals and humans. It has one of the highest animal health statuses in the world, with very little dependence of antibiotics compared to other countries. Consequently, the threat is relatively small.