Antibiotics or Probiotics: Reducing Antibiotic Resistance

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ABSTRACT: Antibiotics are important to successful livestock production. Unfortunately use of antibiotics applies selection pressure that results in antibiotic resistance in exposed populations of bacteria and can also result in antibiotic residues in meat and milk from treated animals. Of major current concern is the risk of transfer of antibiotic resistant bacteria and genes encoding resistance from people to animals. A greater appreciation of the need to reduce antibiotic resistance in bacteria in animals is essential for the future of livestock industries.

Key Words: Antibiotics, Livestock Industries, Probiotics, Resistance

ANTIBIOTICS AND ANTIBIOTIC RESISTANCE

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INTRODUCTION

Modern husbandry practices can expose livestock to infectious diseases that require use of antibiotics for treatment and prevention. In addition, compounds with antibacterial activity are used in intensive livestock industries to control coccidiosis or as growth or production enhancers. Of 700 tonnes of antibiotics imported into Australia each year about one-third is used in human medicine and the rest in animals, with the bulk being used for prophylaxis, coccidiosis control or growth promotion (JETACAR, 1999).

CURRENT ISSUES

Antibiotics

Antibiotics are chemical agents that selectively damage or kill bacteria. Since the introduction of penicillin in the late 1940s, a large number of compounds with antimicrobial activity have been discovered and used to treat infections. Many of these compounds are metabolites produced by bacteria and fungi and some are synthetic molecules.

Use of antibiotics has led to concerns about antibiotic residues in the tissues of treated food animals and about antibiotic resistance.

Antibiotic residues

Many countries including Australia have put significant resources into minimising the occurrence of antibiotic residues in meat and milk. Extensive monitoring programs exist. The concerns relate principally to allergies to antibiotics such as penicillin and whether or not ingestion of residues will select for antibiotic resistant organisms in the intestinal tract of people.

Antibiotic resistance

Even before penicillin had been released as therapeutic agent, a bacterial β-lactamase enzyme capable of inactivating penicillin had been described (Abraham and Chain (1940). Some bacteria are intrinsically resistant to particular antibiotics and others acquire resistance from transfer of genes encoding antibiotic resistance. Exposure of what were previously sensitive bacterial populations to antibiotics applies selection pressure and results in the emergence of populations of bacteria resistant to those antibiotics (Table 1).

Table 1. Detection of antibiotic resistance in human isolates of bacteria

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Antibiotic</th>
<th>First used</th>
<th>Resistance reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>Penicillin</td>
<td>1940</td>
<td>1954</td>
</tr>
<tr>
<td>S. aureus</td>
<td>Methicillin</td>
<td>1960</td>
<td>1968</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>Gentamicin</td>
<td>1964</td>
<td>1968</td>
</tr>
</tbody>
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(Prescott and Baggot, 1993)

In animals, more information is available for enteric bacteria than for isolates from other sites and overall Escherichia coli is the most-studied organism. As early as 1954 Smith reported resistance in calf strains of E coli to sulphonamides, streptomycin, chloramphenicol and tetracyclines. As more antibiotics have been introduced and more animals have been treated with antibiotics, so the range of antibiotics in which resistance has been reported and the extent of resistance described has increased (Wray et al., 1993). Smith and Crabb (1957) found tetracycline resistance was common where low levels of tetracycline were used as a growth promotant but was not seen where tetracycline was not used in this way. With some antibiotics such as tetracyclines, once antibiotic resistant populations of bacteria have been established in a herd, they can persist for a long time (Rollins et al. 1976). In addition, Salyers and Amábile-Cuevas (1997) pointed out that in many situations even though resistance may drop initially, once an antibiotic is withdrawn, there is a rebound effect if the same antibiotic is used again.

There are also differences between antibiotics and between organisms in the development of resistance. Some serotypes of salmonella readily acquire resistance (eg Salmonella Typhimurium) whereas others do not (eg S Dublin) even when apparently exposed to the same antibiotic treatment regime.
Sources of antibiotic resistance

Antibiotic resistance arises from mutation of microbial genes and also by the uptake heterologous resistance genes from external sources (Davies, 1996). DNA from antibiotic producing micro-organisms encoding antibiotic resistance has been detected in antibiotic preparations and this could contribute significantly to the rapid emergence of antibiotic resistance (Webb and Davis, 1993). It has been speculated that vancomycin resistance genes now causing such a problem in human strains of enterococci may have originated in lactobacilli used in the production of fermented milk products such as yoghurt, as lactobacilli are intrinsically resistant to glycopeptides (Johnson et al., 1990). It is interesting to note that Boon and Cattanach (1999) reported more widespread resistance in native bacteria than in faecal bacteria isolated from various water systems in south-eastern Australia.

Link between antibiotic use in animals and resistance problems in people

Overuse and poor control of use of antibiotics in hospitals and community medical practices have led to the major antibiotic resistance problems in people: MRSA, extended spectrum β-lactamase (ESBL) producing enteric bacteria, penicillin resistant pneumococci and multi-resistant Mycobacterium tuberculosis, for example. However, as salmonella and campylobacters are spread to people via the food chain, antibiotic resistant strains of these organisms can also infect people by this route. Generally, infections with these organisms cause relatively mild self-limiting disease in normal healthy adults, but in the very young or the elderly or immunocompromised patients, life-threatening infections can occur. A recent paper (Smith et al., 1999) has reported treatment failure in patients infected with fluoroquinolone resistant campylobacters acquired from chickens. S. Typhimurium DT 104 (resistant to 5 classes of antibiotics) has spread from cattle to people (Fone and Barker, 1994) and is now of major concern in the UK, Europe and the USA (Akkina et al., 1997) and has implications for Australia (Cerrara et al., 1999).

Although the Swan Report (Report, 1969) drew attention to the risk of spread of antibiotic resistance from bacteria in animals to human pathogens, it was the emergence of vancomycin resistance in enterococci that focussed attention on the implications to human health of antibiotic use in animals (Report, Danish Veterinary Laboratory, 1995; Aarestrup et al., 1995; Jensen et al., 1998). It would seem that one type of vancomycin resistance, VanA resistance, is associated with the use of avoparcin as a growth promotant but the full picture is not yet clear. There is also concern about the use of other growth promotants such as tylosin, virginiamycin, zinc bacitracin and avilamycin (CAFA, 1997; MAFF, 1998; JETACAR 1999). In all cases it is easy to demonstrate resistance in animal isolates and generally in human isolates as well. In addition, in some cases the identical genes encoding resistance have been found in human and animal isolates (Jensen et al., 1998; Hammerum et al., 1998). Some of the most telling evidence comes from the detection in human isolates of resistance to antibiotics that have never been used in people, such as apramycin (Wray, 1986) and nourseothricin (Witte, 1997).

CONCLUSIONS

There are several reasons to be concerned about use of antibiotics in animals. Firstly, there is the issue of widespread resistance (including multiple resistance) in bacterial isolates from animals. This
restricts the range of effective antibiotics for therapeutic and prophylactic against infectious diseases in animals. Secondly, there is the issue of transfer of resistant bacteria and genes to people and their pathogens. While it is clear that most of the medical problems relate to medical overseuse and misuse, use of antibiotics in animals does impact on human health.

There is an urgent need for livestock industries to have a greater understanding of the problems associated with antibiotic use. In addition, one must question the wisdom of using compounds that have the known capacity (or potential capacity) to treat or prevent infectious disease in animals as growth promotants. There are a number of recommendations in the JETACAR report (JETACAR, 1999) which if adopted could see significant improvements in both medical and veterinary/animal husbandry use of antibiotics and a reduction in resistance problems in bacterial pathogens in people and animals.

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ANTIBIOTICS IN THE LIVESTOCK INDUSTRIES – THEIR ROLE, CURRENT USE AND ALTERNATIVES

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ABSTRACT: With the introduction of intensive husbandry systems the increased exposure of livestock to infectious diseases meant that the use of antibiotics was required to maintain animal health and productivity. As new husbandry techniques in livestock production systems improve the health and well being of livestock, the need for antibiotics as production aids is now declining. Public health perceptions of problems with antibiotic residues in food, and more recently international concerns that antibiotic use in animals may lead to transfer of resistance to human pathogens, has placed pressure on the livestock industries to find alternatives to antibiotics where they are used routinely in animal production. The current use of antibiotics in animal production systems is discussed and alternatives to antibiotic use considered. It is concluded that good disease prevention measures and vaccinations for infectious diseases should be implemented wherever possible. Additional research is required to demonstrate the value of other proposed alternatives to antibiotic use.

Keywords: Animal Production, Antibiotics

INTRODUCTION

Antibiotics have played an important role in livestock production over the last 40 to 50 years. To improve productivity intensive husbandry systems were developed for poultry, pigs, cattle and aquaculture. These systems have increased the propensity for introduction of infectious diseases in the livestock due to increased stress, high animal to animal contact levels and feedstuffs that are not consistent with the traditional diet of the animal. In addition to managing animal health problems antibiotics have become an important tool for improving feed efficiency.

The use of antibiotics in livestock production has become a sensitive issue for consumers and public health officials. Their main concerns relate to the likelihood of residues being present in edible animal products and the possibility of antibiotic resistance developing in organisms with animals as a host being transferred to human pathogens via the food chain. These concerns, coupled with the economic need to reduce the costs of production inputs, have encouraged the livestock industries to seek alternatives to antibiotics in livestock production.

There are technical definition differences in the common use of the words antibiotic and antibacterial. For the purposes of this paper antibiotics will be considered to include those antimicrobial agents with bactericidal or bacteriostatic effects. The ionophore (polyether) group of antibacterial agents is included in this definition and anti protozoal agents are excluded.

Use of antibiotics

There are three common ways that antibiotics are used. These are known as therapeutic where a particular condition has developed and requires treatment; prophylactic where the condition is likely to develop and the antibiotic is used as a preventative measure; and as a growth promontor or growth enhancer where the antibiotic acts on the ecology of the intestinal microflora to improve productivity of the livestock in terms of growth rate and feed efficiency.

Administration methods for antibiotics generally relate to the husbandry system. In intensive systems for poultry and pigs administration via water or feed is commonly used. For therapeutic treatment of pigs individual animals may be treated using injectable antibiotics. Feedlot cattle may receive antibiotics in feed where a mob of cattle is treated; otherwise the cattle tend to be treated individually using injectable antibiotics.

Extensive production systems generally involve individual animal treatment. Prophylactic use of antibiotics is rare in extensive production systems. Where supplementary feeding is practiced in extensively raised cattle or sheep inclusion of antibiotics in the feed to avoid lactic acidosis or bloat is often practised.

An important feature of treatment of livestock for any condition is the economic aspect of the decision to treat. Understandably poultry and young pigs will often be euthanased rather than treated if the cost of treatment is not economically justified. Sheep are generally not treated with a course of antibiotics unless they are important as breeding animals. Cattle on the
other hand are generally worth treating because of the high individual animal value.

**Therapeutic use of antibiotics**

In an ideal situation, before implementing antibiotic therapy to an individual animal or a flock or herd with an infectious condition, the following steps would be taken: identification of the pathogen including the sensitivity to different antibiotics; selection of a suitable antibiotic based on site of infection and nature of lesion; determination of the dose, route of administration, frequency of treatment and the duration of treatment; and additional supportive therapy to assist the animals to recover (Merck Veterinary Manual, 1998).

In practice however it is not realistic to apply the first step and the choice of antibiotic is generally determined based on the diagnostic skills and experience of the veterinarian or, for common conditions, the person responsible for the husbandry of the animals. Bovine respiratory disease is a good example of where the livestock manager can readily identify the disease. It is known to be most commonly associated with a Pasteurella haemolytica secondary respiratory infection and animals respond to therapy with tetracyclines, tilmicosin or tylosin.

Similar situations occur with other conditions affecting pigs and poultry. Ideally a veterinarian is directly involved in the initial diagnosis. However this is not always possible and a telephone consultation with the veterinarian who regularly attends to the livestock may be required.

**Prophylactic use of antibiotics**

Prophylactic use of antibiotics is a common practice in the intensive animal industries and in the dairy industry. It may involve a long-term low dose treatment regime or a short-term treatment.

Long term low dose prophylaxis involving in feed (or water) administration of antibiotics is used in poultry (avoparcin for necrotic enteritis), pigs (olaquindox for proliferative enteritis) and feedlot cattle (tylosin for liver abscesses, ionophores or virginiamycin for lactic acidosis and bloat control). While this form of therapy is effective against the target organism it has the disadvantage that resistance may be selected for in non-target organisms.

Short-term treatment regimes are common in the dairy and feedlot industries. In dairy cattle a dry cow therapy for mastitis is often administered to a whole herd. This effectively reduces the likelihood of cows developing clinical or sub-clinical mastitis at the time of calving. In feedlot cattle injectable oxytetracycline or tylosin is often used at induction of animals into the feedlot to prevent the onset of bovine respiratory disease.

**Antibiotics as growth enhancers**

The means by which antibiotics increase feed efficiency and promote growth is not entirely clear. It is known that the compounds used have little or no effect on gram negative organisms. There is a stabilisation of the intestinal flora in animals receiving antibiotic growth promoters (Report, 1998). This results in a decrease in the number of micro-organisms involved in the use of nutrients for the production of toxic metabolites such as amines and ammonia. The well being, feed efficiency and growth rate of the animal is therefore enhanced.

There are various reports of the extent of the increase in growth resulting from antibiotic use. They range from no effect to 20% improvement for poultry pigs and cattle depending on the species, age of the animal and the conditions under which they are kept (Report 1998; JETACAR, 1999; CAFA 1997). Beef cattle and calves were reported to have a 6 to 7% increase in daily weight gain with a corresponding 4 to 6% increase in feed conversion efficiency (Verbeke and Vlaene, 1996).

The benefits of antibiotic growth promotants have been declining in recent years due mainly to improved feed formulation, hygiene in production systems and genetics (Gropp and Schumaker 1997, CAFA 1997).

Environmental benefits associated with the use of antibiotics as growth promotors in animals have also been reported. These include reduced manure production and nitrogen output in pig production (Gropp and Schumaker 1997) and a reduction in greenhouse emissions through the use of monensin in cattle where methane production is reduced by up to 16% (Thornton et al 1976).

**Extent of antibiotic use in Australia**

There are no detailed records of actual antibiotic use by species and purpose of use in Australia. As antibiotics are not manufactured in Australia the information collated on antibiotic imports provides a base level of overall antibiotic use in humans and animals (JETACAR, 1999).

Import figures for antibiotics (excluding anti protozoals and polyethers) over the last five years show that on average 48.2% of antibiotics are destined for human use with 43.2% being used in animal feed and 8.6% for other veterinary uses (JETACAR 1999). The stockfeed and other veterinary uses include all animals not only food animals. The average yearly imports for all antibiotics (excluding anti protozoals and polyethers) over the five years was 521867 kg of active ingredient.

The polyethers have been excluded from these figures, as they are generally not regarded as a significant risk to the transfer of antibiotic resistance to humans. The polyethers account for a further 168,264.3 kg of active ingredient or 24.4% of antibiotics imported (JETACAR 1999).

The majority of in feed antibiotic use in livestock will be for prophylactic or growth enhancing purposes. This highlights an opportunity to substantially reduce overall antibiotic use in livestock through improved production practices and techniques.

**Antibiotic residues and antibiotic resistance**

Antibiotic residues in edible products derived from livestock have been an issue of concern to consumers since the early 1980s. They have been included in the Australian National Residue Survey since that time and the results show that there is a high...
level of compliance with Australian food standards for antibiotics (BRS, 1998).

Antibiotic resistance was identified as an issue of concern in 1969 in the Swann Committee report to the UK Government (Report 1969). The Australian regulatory system has essentially been guided by the principles of the Swann report in the registration of antibiotics for use in livestock since the early 1980s (JETACAR, 1999). International interest in the potential for transfer of antibiotic resistance from animals to humans heightened in the mid 1990s with the emergence of vancomycin resistant enterococci and concerns about the possibility of cross resistance arising from the use of avoparcin in livestock. Many countries are now moving to reduce or restrict the use of antibiotics as growth promoters in livestock.

The outcome of these changes is that pressure is now on the livestock industries to introduce alternative production practices that do not require extensive use of antibiotics.

**Alternatives to antibiotics in livestock**

There are many opportunities to reduce the use of antibiotics in livestock, particularly for growth promotant and prophylactic uses. These alternatives include: introduction of stringent disease preventative measures in production systems; developing vaccines against infectious agents requiring prophylactic or widespread therapeutic use of antibiotics; use of organic acids, prebiotics, probiotics and enzymes to modify intestinal flora and function (European Commission, 1999; Report, 1998).

Improved health and disease control in intensively reared livestock by using batch production (all-in-all-out systems), age segregation, effective biosecurity routines and optimal nutrition and environmental conditions (temperature, ventilation and humidity) provides an effective means of reducing the reliance on antibiotics. Outbreaks may not be eliminated but may be of such a low frequency that therapeutic use of antibiotics at the time an outbreak occurs may well be a more cost effective option. This has apparently been the experience of the poultry industry in Sweden following the ban on using virginiamycin and other antimicrobials as growth promoters (European Commission, 1999). Similar experiences were reported in pig production.

Some production systems overseas do not lend themselves to reducing antimicrobial use because the production method itself results in increased susceptibility to infection. White veal production is a case in point. The calves become anaemic and susceptible to infection resulting in unusually high levels of antimicrobials being used (Franken et al., 1990). Such production systems may need to be significantly modified or even abandoned in countries where continued prophylactic use of antibiotics is not permitted.

Vaccines can be effective in preventing bacterial infection in livestock. Vaccination against coliform infection in piglets has virtually eliminated piglet diarrhoea thereby reducing substantially the need for prophylactic antimicrobials in pig production (European Commission, 1999; JETACAR, 1999). In Australia vaccines are available for erysipelas in pigs and poultry, mycoplasma in pigs and poultry, fowl cholera, poultry coryza, duck infectious serositis and salmonellosis in poultry (JETACAR, 1999). Vaccination of feedlot cattle for infectious bovine rhinotracheitis at induction into a feedlot has reduced the need for prophylactic injections of antibiotics at induction to counter bovine respiratory disease.

Organic acids such as propionic acid, acetic acid, formic acid, citric acid and tartaric acid have often been added to piglet feed in Europe. They are believed to improve digestion and influence the intestinal flora in a positive way (Report, 1998). They also improve feed hygiene and have an intrinsic energy value in their own right (European Commission, 1999).

Prebiotics are indigestible carbohydrates that selectively promote the growth of favourable microorganisms in the intestinal tract. They are often referred to as NDOs or non-digestible oligosaccharides. They are understood to influence the intestinal ecosystem through improving lactic acid fermentation (Report, 1998).

Probiotics are effectively one or more species of living organisms that, when administered orally to animals (generally in the feed), will modify the intestinal flora and improve feed utilisation. There is an improvement in animal health and growth as a result of their use (Report, 1998). Live yeast products have been used in cattle production. Variable results have been observed for the productivity of dairy cattle fed yeast supplements as a means of improving growth and feed efficiency (Kung, et al., 1997).

Enzymes are added to feeds to assist in the digestion of particular components of the grains and meals used in production of the feed. In Australia they are used in broiler feeds to improve the digestion of wheat and barley based feeds (JETACAR, 1999). In Europe a range of enzymes are used in broiler and piglet feeds to improve the nutritional yields of soya, peas, rapeseed meal, sunflowers, copra, rice bran and sorghum (European Commission, 1999).

The use of competitive exclusion products is another means of reducing the need for antibiotics for prophylactic or growth enhancer reasons. These products involve seeding the gastrointestinal tract of newborn animals with beneficial flora from the gut of a healthy adult animal (JETACAR, 1999).

Overall there is much more research required before these alternatives in the form of feed additives can replace antibiotics as growth enhancers in animal production.

**CONCLUSIONS**

Antibiotic use, particularly therapeutic and prophylactic use, remains an important part of animal production at this point in time. However, given the consumer and public health concerns, it is imperative that the livestock industries and government regulators work together to implement animal production practices that reduce our reliance on antibiotics for prophylaxis and growth enhancing purposes.
The livestock industries can effectively reduce the need to continue with many of the prophylactic uses of antibiotics if good disease prevention measures and available vaccines are used.

Other alternatives appear to require considerably more research and development work before they could be implemented on a wide scale. Australian industries need to be aware of this need and to encourage the implementation of the required research and development programs to ensure Australia is well placed to introduce alternatives to routine antibiotic use in livestock.

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SPECIFICALLY TARGETED PROBIOTICS CAN REDUCE ANTIBIOTIC USAGE IN ANIMAL PRODUCTION

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ABSTRACT: Live microbial feed supplements, probiotics, have been trialled in almost all fields of animal production to decrease disease and to improve productivity. Progress in probiotic development was slowed with the introduction of antibiotics, however, probiotics are once again receiving attention since there is a concerted effort to decrease antibiotic usage in agriculture in many countries. While there are many non-conclusive or contradictory probiotic studies, it is agreed that if one specifically selects the probiotic strains, improvements in health and performance of animals can be obtained. The probiotic supplements include single strains as well as simple and complex mixtures of microbial types. Specifically selected probiotics have been shown to reduce numbers of enteric pathogens and/or diarrhoea and death linked to these pathogens in suckling pigs, lambs and calves. Probiotics are also being selected for use in fish farming to reduce fish diseases and for use with dogs and horses. Microbial supplements are also being used to improve milk and egg production, and to reduce caecal levels of Salmonella and Campylobacter in chicks to reduce carcass contamination by these food poisoning microbes. It is anticipated that specifically targeted probiotics can reduce pathogen levels in animals, and thereby decrease antibiotic usage.

INTRODUCTION

Gastrointestinal diseases in animals contributes to huge economic losses and has lead to excessive usage of antibiotics to control such diseases. Today, antibiotics are being used not only for therapeutic applications but also prophylactically as growth promoters. Many will argue that the latter application is also for disease prevention since if one can reduce sub-clinical levels of pathogens, an improvement in performance will be noted. Alternatives to antibiotics are being sort after. The term “Probiotics” was coined by Parker (1974) as the opposite of antibiotic i.e. “for life”, however, the concept dates back centuries to the time when the farmer used the cud from the health animal to heal the sick one. Today, the definition of Fuller (1992) is commonly used and refers to probiotics as live microbial feed supplements which improve the health of the host by beneficially influencing the indigenous microbes. Unfortunately, a veil of controversy still surrounds probiotics since over the years there have been many contradictory reports and non-conclusive studies (Atlas, 1999). In unravelling the mysteries associated with probiotics, it is essential to understand how they function and thus shed light on why they may fail to be efficacious. It is now established that probiotic strains need to be specifically selected using a stringent selection criteria in order to obtain functional strains with known modes of function. The most consistent success with the control of pathogens using microbial preparations has been achieved using a complex mixture of microbes of gut origin, referred to as the Nurmi concept (Nurmi and Rantala, 1973). However, recent developments in the strain selection for pigs and poultry has shown that with careful attention to strain selection, pure cultures and simple mixtures can also provide probiotic benefits. One can envisage that the combination of probiotics with other dietary supplements e.g. enzymes
PROBIOTIC PREPARATIONS

Both single strains and mixtures of microbes are used as probiotics. Traditionally, probiotics were frequently pure strains of lactobacilli (Conway, 1989). Today lactic acid bacteria, especially lactobacilli, bifidobacteria and enterococci, are used either alone or together with other microbes such as non-pathogenic enteric bacteria, *Saccharomyces* spp, *Aspergillus oryzae* and anaerobic bacteria such as *Bacteroides*, *Clostridium* and *Veillonella*. *Carnobacterium* (Jöborn et al, 1997) and *Pseudomonas* spp (Gram et al, 1999) are being investigated for use as fish probiotics. There is also an emerging interest in the use of *Bacillus* since there have been some reports on improved performance in pigs, rabbits, chickens, turkeys, calves, horses and lambs with the oral administration of a preparation of *Bacillus* (Lestradet, 1995).

The mixtures of microbes vary and the following have been trialled: (a) defined mixtures of a specified number of strains which are combined after production of the individual strains; (b) semi-defined mixtures which often includes a number of species of the same genus which may be co-cultured and hence there is no control over the numbers of each strain; (c) undefined mixtures which can be sourced directly from caecal contents, mucosal scrapings or faeces and then either used directly or after the mixture is cultured. The latter step can alter dramatically the composition since there is no guarantee that these fermentation conditions favour all the microbes present. The more complex the mixture used, the more difficult it is to address the safety issue of the preparations to ensure that it is free from hazardous microbes.

Since there are always economic considerations in animal production, not only do the probiotic preparations need to be efficacious they need to be of a moderate cost, and need to be easily stored, transport and administered. As the complexity of the mixture increases, the cost for production and use can become an issue. The probiotic preparations have been administered to animals via the drinking water, by spray or droplet application, in ovo prior to hatching and by incorporation into feeds. It is desirable to ensure the probiotic preparation can be introduced into the digestive tract as soon as possible after birth/hatching since this can prevent the establishment of the less desirable microbes in the tract, a concept referred to as colonization resistance (van der Waaij et al 1971).

Microbial preparations are administered to animals to improve the health of the host by reducing pathogen levels directly or indirectly as consistent with the definition of probiotics according to Fuller (1992). The probiotic effect is monitored either directly as a decrease in levels of pathogens, or indirectly by studying a symptom of the infection e.g. diarrhoea, or by monitoring a production parameter such as weight gain, milk or egg production or feed utilization. In addition, microbial preparations are used to reduce the levels of human pathogens in the digestive tract of the poultry since at slaughter, the carcass becomes contaminated with microbes from the gut. The complex mixtures have been used effectively to reduce carriage of human pathogens in poultry, and while this is not a probiotic effect according to the definition of Fuller, many loosely refer to these microbial preparations as probiotics.

MECHANISMS OF FUNCTION OF PROBIOTICS

At birth, the digestive tract of animals is sterile and is subsequently successively colonised by microbes from the mother and from the environment until a very complex and diverse population exists in the tract. These microbes contribute to the health of the host in a number of ways including protecting the host from invasion of pathogens (Barrow et al, 1977; Blomberg and Conway, 1989), contributing to digestion and by producing valuable metabolites such as vitamins and short chain fatty acids. While most of the microbes are desirable, potential pathogens can enter the tract and may establish. The stability and composition of these indigenous microbes is affected by stress to the host and by dietary changes e.g. weaning, and thus may allow the increase in the undesirable microbes which may be present in low numbers. Probiotics ensure the establishment or re-establishment of a healthy microbial population which prevents the growth of pathogens (Fuller 1986). This can occur by competitive exclusion whereby the desirable microbes outcompete the pathogens for either nutrients or colonization sites (Nurmi and Rantala, 1973), or by the production of metabolites which are inhibitory to the growth or adhesion of the pathogen (Blomberg et al, 1993), thus preventing their establishment in the gut. The metabolites can include short chain fatty acids which are either inhibitory to growth of many pathogens, or lower in situ pH such that the pathogens grow poorly (Fox, 1988). In addition, some probiotic microbes produce bacteriocins which inhibit the growth of the pathogen (Lindgren and Dobrogosz, 1990), and others have immunomodulating properties (De Simone et al, 1995). It is propose that the respiratory nature of the yeast strains, mostly *Saccharomyces*, influences its effectiveness in stimulating beneficial effects in the ruminants most probably because as the yeast respires it consumes traces of oxygen thus allowing the more anaerobic rumen bacteria to develop (Wallace and Newbold, 1995). It should be noted that even if the yeast does not grow well in the rumen, it can be metabolically active. *Aspergillus oryzae* is also used in ruminants and most probably functions because of its associated enzymes (Beharka et al, 1991).

CRITERIA USED FOR PROBIOTIC STRAIN SELECTION

Many of the probiotic products of by-gone years were ineffective. It is agreed that in some cases the viability of the preparation was very poor, often the particular strain used was not specified, and field trials often overlooked that control animals may become contaminated with the probiotic microbe and invalidate the study (Havenaar et al, 1992; Conway, 1996). It is

(McGilliard and Stallings, 1998) will provide added benefits for pathogen reduction.
agreed that a stringent selection criteria should be used since the selected strains must be biologically active against the identified target, have the capacity to colonise and be metabolically active in the host, and must be evaluated under strict scientifically controlled conditions. Furthermore the desirable properties of the strains must be stable during production, storage and when used. It is envisaged that there will be particular probiotic strains for specific applications and that ideally the strains should originate from the host for which it is developed.

**PROBIOTICS FOR PIGS AND POULTRY**

Probiotic usage for pigs has been extensively reviewed (Jonsson and Conway, 1992; Stewart et al, 1993; Conway, 1999) and it is interesting to note the extensive use of lactic acid bacteria for pigs, either as pure cultures or as simple mixtures of a limited number of strains. This could be due to the dominance of these microbes in the gut, especially in the pars oesophagus region which seeds the rest of the tract with lactobacilli and enterococci. Using the stringent selection criteria for probiotics described above, it was possible to gain significant improvements in weight gain, feed conversion and a decrease in the incidence of post weaning diarrhoea in pigs fed from birth via a creep feed and the normal feed, a single strain of Lactobacillus inhibitory to enterotoxigenic E. coli (Conway 1999). Furthermore, a mixture of Bifidobacterium, Enterococcus and Lactobacillus improved carbohydrate utilization and decreased ammonia levels by pig caecal bacteria (Sakata et al, 1999). Some workers have also investigated the use of Bacillus spp and *Lodrundium butyricum* for piglets with some success. Using *B. toyoi* or *B. licheniformis*, significant reductions in the incidence and severity of post weaning diarrhoea were noted in a dose dependent way. No enterotoxigenic *E. coli* were noted in pigs dosed the highest level of *B. licheniformi* (log 7 per g of feed). Other workers (Adami and Cavazzoni, 1999) were able to decrease faecal coliform levels in pigs fed *B. coagulans*.

The application of probiotics to poultry has focussed extensively on reducing caecal levels of *Salmonella* and *Campylobacter* in order to reduce the spread of these food poisoning organisms in the human food chain. There has been less focus on the promotion of good health of poultry, however, there are some suggestions that egg production can be enhanced with probiotic administration and growth of broilers is enhanced. Interesting the crop of the chick is densely colonised by lactobacilli as is *pars oesophagus* of pigs, however, probiotic preparations for chicks have favoured complex mixtures of microbes after the Nurmi concept (Nurmi and Rantala, 1973) and there are many complex mixtures as commercial products today. However, one group of workers have specifically selected a single strain of *Lactobacillus salivarius* and prevented Salmonella colonization of chicks with it (Garriga et al, 1998; Pascual et al, 1999).

**PROBIOTICS FOR RUMINANTS**

Mixtures of lactic acid bacteria have effectively been used to reduce carriage of enteric pathogens in sucking calves (Wallace and Newbold, 1995; Zhao et al, 1998), however, once the rumen function is established, such preparations have been less effective. There is more extensive use of *Saccharomyces* and *Aspergillus oryzae* alone or together with lactic acid bacteria after weaning, and in fact, these microbes have been shown to assist in the development rumen structure, thus accelerating weaning (Beharka et al 1991). These workers showed that *A. oryzae* dosage stimulated rumen development with higher counts of total, amylolytic, pectinolytic, cellulolytic and hemicellulolytic bacteria in calves. Using a mixture of *A. oryzae*, *B. subtilis*, *L. acidophilus* and a yeast, some improvement in milk production has been noted (McGilliard and Stallings, 1998), however other workers using the yeast alone or with *A. oryzae* have not noted an increase in milk productin but do report increased feed digestibility (Holden, 1999).

**CONCLUSIONS**

It can be concluded that targeted probiotics can be used to improve health and performance of a wide range of animals and thus will result in a reduction of antibiotic usage. For effective application to animal production, attention to strain selection and evaluation is essential.

**REFERENCES**


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