Antimicrobial resistance in animals and impacts on food safety and public health

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Few issues in applied microbiology excite as much debate as the threatened transfer of antimicrobial resistance (AMR) from animals to cause disease in humans. Yet, almost four decades after the first warning of the potential risk to human health from the use of antimicrobials in agriculture [1], and after a plethora of national and international reports with similar conclusions [2-8], broad agreement is lacking on key elements of scientific fact, responsibilities and interventions. This article briefly considers some areas of concern and misunderstanding in the debate about public health impacts from the use of antimicrobials in animals. What is clear is that progress requires viewing the problem from the context of 'the whole system' rather than from the narrow confines of specific disciplines, professional groups, institutions, or commercial interests.

Science of resistance or resistance to science?

Popular debate about the public health impact of antimicrobial use in animals has often resulted in over-simplification of technical facts for marketing of information to the broader population. Inevitably this has distorted the accuracy of scientific arguments, propagated misconceptions amongst professionals, and blurred the boundary between science and politics. Most importantly, it has portrayed the subject as a single scientific issue when it is in fact a complex network of related issues. Within this network each issue is defined by a specific combination of factors including the type of antimicrobial, the species of animal being treated, how animals are managed and housed, antimicrobial usage practices (dose and route of administration), the likelihood and effectiveness of human exposure, genetic mechanisms for resistance and the nature and severity of the disease in humans possibly caused by the emergence of resistance in animals. The diversity of these possibilities ensures that AMR from animals cannot be dealt with by a single discipline or single profession and that expertise from a range of backgrounds is essential for progress. Diversity and complexity also provides conditions ideal for dissemination of pseudoscience, whether it be deliberate and motivated by vested interest, or unintentional and well meaning but founded on ignorance. Therefore, perhaps the greatest challenge for the joint management of AMR in animals, food and humans is to sift out what is genuinely known from what is unknown.

Drugs of high importance

With the demise in the use of antimicrobials as growth promoters the focus of attention in Australia has shifted to improving the management of those drugs used in animals that are also of 'high importance' in human medicine. Of greatest concern are third generation cephalosporins (specifically ceftiofur), streptogramins (virginiamycin), glycopeptides (vancomycin for humans, avoparcin for animals), gentamicin and fluoroquinolones. Avoparcin has been unavailable in Australia since 2000 and gentamicin and fluoroquinolone drugs have never been registered in this country for use in food animals. However, the use of ceftiofur in Australia is contentious because the analogous drugs in human medicine are highly valued as reserve agents and their use in healthcare is tightly controlled. In contrast, veterinarians are able to readily prescribe ceftiofur for use in food animals where it is typically targeted against infections having a substantial economic impact. Fears do exist that the use of ceftiofur in Australian livestock will escalate and promote emergence of extended spectrum beta-lactam-resistance in human pathogens in this country. In North America, epidemiological data for AMR in *Salmonella* suggests that that this has already occurred for some zoonotic strains, most notably serovars *typhimurium* and *newport* that typically already have resistance to five other antimicrobials [9,10]. The implications for human health where these organisms emerge in livestock are substantial because non-typhoidal *Salmonella* infections are one of the most common food-borne infections. A small proportion of these cases, develop an invasive form of disease where the pathogen escapes the gut to colonise blood and tissues. Resistance of these pathogens to third generation cephalosporins makes effective therapy highly problematic and mortality very likely [11].

There are additional concerns related to the frequency with which drugs of medium importance are administered, including for example, the inclusion of macrolide antimicrobials (e.g. tylosin) in the diet of intensively managed livestock. In some cases industries have made great progress in reducing reliance on these and other drugs by finding alternative control measures including, for example, vaccines for respiratory pathogens in poultry and by applying enhanced bio-security at the herd and flock level to prevent disease transmission on a large scale. Unfortunately, not all infectious diseases of livestock can be so effectively managed without antimicrobials and more solutions of this nature are needed.

AMR and food

Food can be a very efficient vehicle for bringing a large number of people into contact with a potential hazard. Thus, from a population perspective, food-borne exposure is regarded as the most critical pathway for transfer of AMR from animals to humans. Not all foods of animal origin pose an equal risk of exposure to the organisms of concern and not all antimicrobial resistance in food microflora should be attributed to use of antimicrobials in animals. In qualitative terms, there is a gradient of risk according to the antimicrobial use practices of each farm and industry, the extent of contamination of the raw food commodity with enteric bacteria, and the practices occurring within the food chain affecting the occurrence of cross-contamination and the effectiveness of any 'kill steps' prior to consumption (e.g. cooking and pasteurisation). Moreover, the consequences resulting from exposure are in most instances very difficult to quantify. This is especially so with respect to genetic determinants of resistance found in commensal organisms and which are often present in raw foods (e.g. enterococci and various Enterobacteriaceae). The literature is rich with assertions and counter assertions on the health threat posed by genetic determinants of resistance per se. Once again this highlights the need for each specific issue to be considered individually and divorced from the emotive, exaggerated reasoning that often characterises the debate.

Concerns about the safety of food and the widening gap between urban and rural Australia has allowed some damaging misconceptions about antimicrobial use in food production to proliferate. One of the most ludicrous and common implies that most farm animals receive antimicrobials on a daily basis – a contention that cannot possibly be supported by data on the amount of antimicrobials available for use in agriculture[3]. These misconceptions are very divisive and cause harm by drawing attention away from specific issues of antimicrobial use in animals and man where valuable progress is achievable. Establishing a system for reporting objective data on the amounts of antimicrobials (type, quantity, frequency and species) used in animals and man is one such area that desperately requires attention.

Economic drivers

Market forces can be a powerful incentive for farmers and food producers to meet higher standards of quality. However, there are presently few indications that Australian consumers are willing to place concerns about AMR above those of the price they pay for foods of animal origin. Further, many farmers are discouraged from using less antimicrobials in their livestock because it might feasibly increase the amount of disease, so raise the cost of production, and force their commodities to be less competitive. Most farm enterprises in Australia have low rates of return on capital and this combined with increased competition from global markets means that farmers must vigorously pursue efficiency to remain viable.

International markets may be a more important stimulus for raising quality than domestic markets. The decisions that some livestock owners make about antimicrobial use must strictly align with the expectations of consumers and regulators in foreign markets. One advantage that Australia has enjoyed in food safety is a red-meat and dairy sector based firmly on grazing. Under these conditions antimicrobials become less relevant to the health needs of livestock because animals do not acquire the bacterial diseases of their intensively managed counterparts. Historically, this natural tendency to avoid antimicrobial use has been of enormous benefit in meeting the requirement for low residues of antimicrobials in exported commodities. In the future it may also be useful for demonstrating superiority of product with respect to levels of antimicrobial resistant bacteria. Here farmers need to understand there are critical differences between residues and resistance. Residues can be immediately controlled once the source is detected by modifying the ways drugs are used. However, resistance is a persistent issue because reversion of pathogens and commensals to full susceptibility might only occur in the long term if at all. Therefore, many Australian farmers have an opportunity to distinguish their commodities in the international marketplace on the basis of quality by pursuing practices that place low reliance on antimicrobials and select less for resistance in a demonstrable way.

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