



EDITORIALS

End non-essential use of antimicrobials in livestock

A rational response by WHO to the crisis in antimicrobial resistance

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Tackling antimicrobial resistance (AMR) is a priority of the World Health Organization's public health agenda, and in November 2017 the organisation launched guidelines on the use of medically important antimicrobials in the food production industry. Their unambiguous recommendations were that their routine use for animal growth promotion and disease prevention in healthy animals should be discontinued (Boxed Text on page 2box 1).¹ In line with the global action plan on AMR,² the aim is to help preserve the effectiveness of antimicrobials critical for human medicine. As a supranational body, WHO has taken the opportunity to put independent pressure on healthcare policy makers to now respond to its challenge.

Box 1 Recommendations from WHO¹

1. An overall reduction in use of all classes of medically important antimicrobials in food producing animals
2. Complete restriction of use of all classes of medically important antimicrobials in food producing animals for growth promotion
- 3.3 Complete restriction of use of all classes of medically important antimicrobials in food producing animals for prevention of infectious diseases that have not yet been clinically diagnosed
- 4.4a Suggest that antimicrobials classified as critically important for human medicine should not be used for control of the dissemination of a clinically diagnosed infectious disease identified within a group of food producing animals
- 5.4b Suggest that antimicrobials classified as highest priority (see below) critically important for human medicine should not be used for treatment of food producing animals with a clinically diagnosed infectious disease

Evidence level (based on grade criteria) for 1, 2, and 3 is low, and for 4a and b is very low, reflecting the lack of high quality studies

Highest priority critically important antimicrobial: a critically important antimicrobial belonging to an antimicrobial class that meets three criteria:

1. It is used for treating infections in high absolute numbers of humans, or is commonly used in healthcare settings to treat patients with serious bacterial infections for which the antimicrobial class is the sole choice, or one of few choices, to treat serious infections in humans
2. It is often used for any indication in human medicine, or else is commonly used in patients with serious infections in healthcare settings
3. It is used to treat infections in humans for which there is evidence of transmission of resistant bacteria or resistance genes from non-human sources to humans

A complete list of highest priority critically important antimicrobials is available at www.who.int/foodsafety/cia/en

Although the guidelines were welcomed by world leaders,³ some organisations, particularly in the food producing industry, including the US Department of Agriculture, considered it to be too uncompromising and questioned the underpinning evidence. Others said the recommendations were insufficiently far reaching. A visibly more united interagency approach with the UN's Food and Agriculture Organisation and the World Organisation for Animal Health could have strengthened the message. Nonetheless, the recommendations are an important step forward.

It is widely accepted that antimicrobial exposure is the single most important driver for the emergence of, and increase in, AMR.⁴ Moreover, AMR bacteria or AMR-encoding genes may transfer from animals to humans through the environment, food chain, or by direct contact. Despite this, in some countries as much as 80% of the total consumption of antimicrobials is in the animal sector, with marked variation across nations.^{5,6} Within Europe, for example, use in Spain is over a 100-fold more per production unit than in Norway.⁵ Emerging economies are projected to increase their use of antimicrobials in livestock, contributing to a projected global increase of 67% from 2010 to 2030.⁶

Some countries have already successfully reduced antimicrobial use in livestock without compromising animal health or productivity.¹⁷ The WHO guidelines do not restrict any required treatment or the targeted prevention of specific diseases. An accompanying policy brief gives guidance on implementation

and actions to preserve the effectiveness of antimicrobials in veterinary medicine, including reduction targets, surveillance measures, and improving nutrition, hygiene, infection prevention, and the use of vaccines.¹ Healthy animals need fewer antimicrobials but many agricultural stakeholders see the push to reduce antimicrobial consumption as unwarranted interference, rather than a drive to improve animal health.

The new guidelines were shaped by published reviews commissioned by the WHO Advisory Group on Integrated Surveillance of AMR.^{8,9} This work reinforced the established understanding that reducing antimicrobial use in agriculture is associated with reductions in antimicrobial resistance in food producing animals, as well as the idea that, at minimum, the benefit appears to extend to farmers and those in direct contact with food producing animals.⁹ The authors clearly acknowledge the limitations in these reviews, and although there are few studies showing a direct effect on human health of antimicrobial use in animals, the overall body of evidence provided enough evidence to support WHO's recommendations.

The recommendations could have been more critical of the evidence supporting use of antimicrobials as growth promoters.¹⁰ Moreover, the focus on specific antimicrobial classes rather than a broader consideration of all antimicrobials could be questioned, as the use of one class may select for resistance to other classes, because of shared mechanisms of resistance and genetically linked resistance determinants.

AMR is complex; different bacterial species, resistance mechanisms, transferable plasmids, host populations, and environmental reservoirs contribute to direct and indirect transmission. Further studies to characterise the spread of AMR in both animals and humans are needed, supported by more sophisticated methodology and technology.

Bacterial genome sequencing shows a complex emerging picture, with evidence of an association between human infections and reservoirs of antimicrobial resistance in animals. Heavy use of colistin in Chinese livestock and the emergence and spread of colistin resistance led to the banning of colistin for growth promotion in China in November 2016.^{8,11}

But we also need to maintain perspective. Successful interventions to reduce antimicrobial use in livestock have not always resulted in AMR reduction in humans, and molecular studies of some bacterial species show that direct transmission of the organism or the resistance genes from livestock to humans may be less important than other sources, including human-to-human transmission.¹² WHO guidelines highlight the need for further research to tackle knowledge gaps and improve the quality of evidence, including more standardised methodology, better surveillance, and higher quality data.

Eliminating the non-essential use of antimicrobials in livestock is a rational and welcome response to the growing crisis in AMR. The overarching aims fall within the generally agreed principles of antimicrobial stewardship by veterinarians, industry, and government. As countries are often reluctant to phase out non-essential use, whether through uncertainty or because of commercial pressures, the guidelines provide a necessary external impetus. They may also encourage societal response, consumer expectation, and civil action to drive and sustain this agenda. Of course, action in animals must not distract us from action within human healthcare—antimicrobial stewardship, effective prevention of infections, and the need for clean water and sanitation—but must be seen as an essential additional requirement in our global response to AMR.

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