

## Research Opportunities for Antimicrobial Resistance Control in China's Factory Farming

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Antimicrobial resistance (AMR) is well recognized as a major threat to public health worldwide.<sup>1,2</sup> Infections caused by antimicrobial-resistant bacteria are more difficult and take longer time to cure, and result in higher rates of disability and death.<sup>1,2</sup> Various public health authorities, including the World Health Organization and U.S. Centers for Disease Control and Prevention, have advocated for reducing antimicrobial use to prevent the emergence and spread of AMR. After imposing the most stringent decree against the overuse and misuse of antimicrobials in human health care in 2012, China banned the nontherapeutic use of 227 drugs, including 150 antimicrobials, in food animal production recently. The ban opens new research opportunities for studying the development and spread of antimicrobial-resistant bacteria in animal husbandry and controlling AMR to protect public health. We believe scientists and researchers can significantly accelerate the AMR control in China by developing alternatives to antimicrobials for disease prevention and growth promotion, surveillance programs to assess the contribution of antimicrobial use in livestock production to AMR development, and animal waste processing technologies to prevent environmental spread of resistant bacteria, as well as by outreaching to animal producers.

Besides human misuse and overuse, the ubiquitous use of antimicrobials in food animal production, particularly the nontherapeutic use, also contributes to the selection and propagation of resistant bacteria.<sup>1,2</sup> As illustrated in Figure 1, AMR developed in animal populations can spread easily to

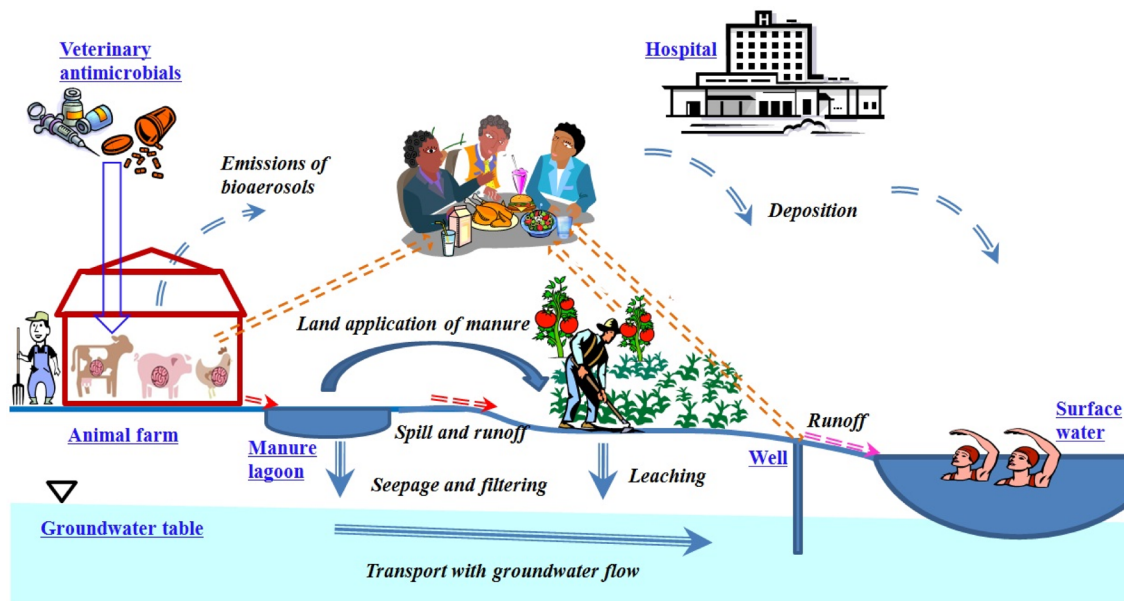
humans through direct contact with these animals and animal products, as well as through food chain, air, water, and manure-fertilized soils.<sup>2</sup> As the world's largest livestock meat producer (over 80 million tonnes in 2013), China has experienced a major shift toward factory farming operations over the past decade. Animal agriculture is estimated to consume about 97 000 tonnes of antimicrobials annually, and overuse and abuse of veterinary drugs have resulted in many food safety scandals in China. Meanwhile, the emergence of AMR as a "hidden" side-effect from the extensive use of antimicrobials in factory farming has not caught much public attention. A total of 70 types of antimicrobial resistance genes (ARGs) have been found in the gut microbiota from over half of the samples of Chinese individuals, compared to 49 and 45 types in Spanish and Danish individuals, respectively.<sup>3</sup> Significant increases in the abundance of ARGs for antimicrobials used in food-producing animals and for those with a longer history of use were observed in human gut microbiome, indicating antimicrobials used in animal husbandry contributed to AMR development in human commensal bacteria.<sup>4</sup> A recent survey detected a total of 149 ARGs in the manures of swine farms across China, which use all major classes of antimicrobials except vancomycins, with the top 63 ARGs being enriched 192 (median) up to 28 000 (maximum) folds compared to the antimicrobial-free manures and soils.<sup>5</sup>

The experience from the European countries (e.g., Sweden and Denmark) and a large and growing body of scientific evidence support that the environmental load of ARGs can be diminished by stopping the nontherapeutic use of antimicrobials in food animal production.<sup>1</sup> A total of 150 medically important antimicrobials have become available only by prescription for the control and treatment of animal diseases in China since March 1, 2014. While the regulatory ban presents animal producers with emerging challenges, scientific research community can contribute significantly to controlling antimicrobial abuse, and development and spread of AMR in China's factory farming, as discussed below:

Antimicrobials are used in livestock production for multiple purposes, including treatment or prophylaxis of infections, growth promotion, and feed efficiency improvement.<sup>1,2</sup> Collaborative research with pharmaceutical industry should be conducted to develop new antimicrobials, vaccines, and alternatives to antimicrobials for growth promotion and disease prevention in animal husbandry. In particular, significant effort should be made toward the development of vaccines against common infectious diseases of farmed animals.

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**Figure 1.** Schematic illustration on environmental transport of microorganisms carrying AMR emerged from antimicrobial misuse in animal husbandry and the pathways of human exposure. AMR can be transmitted to humans through contact with animals and their manure, consumption of contaminated food products, contact with contaminated environmental media, and hospital-acquired infections.

The impact of veterinary antimicrobial use on human health, including the development of AMR in livestock and its transfer to humans, has not been closely studied in China. Little is known about the type, dosage, and duration of antimicrobials applied during animal production, and comprehensive monitoring of the changes in AMR in animal husbandry is lacking, which make it difficult to assess the extent of abuse and their contribution to AMR development. Nationwide surveillance programs need to be established to evaluate the relationship between veterinary antimicrobial use and the development of antimicrobial-resistant bacteria in food animals and humans, and guide relevant public health policy.

The animal wastes are often discharged into lagoons for temporary storage and biological treatment before being applied on farmlands as a fertilizer, even though spills and intentional releases to soils and local rivers also occur. Many bacteria in the animal manure, some carrying AMR, can survive in the lagoons and soils for long periods of time. Little research has been conducted on disinfection of the bacteria in animal wastes from factory farms. Thus, there is a significant need to study the survival of resistant bacteria in anaerobic digestion and other treatment processes, and develop effective disinfection technologies to minimize their contamination of surface water, soil, and groundwater.

Instead of antimicrobials, the health of animals raised in factory farms can be safeguarded with right and good veterinary medical care, such as regular check-ups, vaccinations, and prompt medical treatment of diseases, and supported by probiotics that can strengthen their immune systems.<sup>1</sup> Education and outreach to animal producers can help ensure the safe and effective use of antimicrobials in livestock production. Furthermore, animal nutrition and health can be improved by following the experts' practical guidance on alternatives for growth promotion, and prevention of animal diseases with safe, cost-effective, and hygienic production techniques, which contributes to reduced antimicrobial use in animal disease treatment.

The scientific community should address these important issues and contribute to the effective control of AMR during the

transition toward veterinary oversight of antimicrobial use in Chinese factory farms. Based on the experience of European countries,<sup>1</sup> termination of use of antimicrobials as growth promoters is expected to result in a major reduction in AMR without causing significant negative impact on food animal production in China.

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### Notes

The authors declare no competing financial interest.

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