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## A One Health Approach to Prevent Antimicrobial Resistance for Sustainable Livestock Production in India

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### Abstract

Antimicrobial resistance (AMR) is emerging as one of the greatest challenges to global health security, and livestock production systems have been identified as a key hotspot for its emergence and spread. This review summarizes the available evidence on the epidemiology, drivers, and control of AMR at the human, animal, and environmental interfaces, with a focus on AMR in India's livestock sector. The development of the One Health concept and its institutionalization within the FAO-OIE-WHO (now Quadripartite) framework are discussed. In-depth detail is provided on the degree of antimicrobial use in food animals, antimicrobial resistance trends from global and national surveillance networks, and the major drivers of antimicrobial use in both intensive and smallholder food production systems, including antimicrobial use at sub-therapeutic levels, inadequate biosecurity measures, the management of effluent, and inadequate regulation implementation. Spread within the food chain and directly from organisms, as well as from the water and manure-amended soils, is discussed, and problems with placing the responsibility for the burden of resistance on one side or the other of the food chain are outlined. Surveillance architecture and policy instruments, specifically India's National Action Plan on AMR, are discussed. Promising One Health interventions are evaluated, and the structural, economic, and governance barriers to their implementation in Low- and middle-income countries are identified. This article reveals that simultaneous, coordinated action across all areas of the health sector, including human, animal, and environmental health, is necessary to slow AMR. This requires context-specific research, farmer-level behavior change, and improved intersectoral governance. The antimicrobial

resistance and One Health themes focus on zoonoses involving poultry and livestock production.

**Keywords:** Antimicrobial resistance, One Health, Zoonoses, Poultry, Livestock production.

### Introduction:

The recent scenario of antimicrobial resistance (AMR) in India is alarming, and health authorities have emphasized the need to slow the rising burden of antibiotic-resistant infections and the importance of antimicrobial stewardship in managing AMR in food animals and other zoonoses. AMR has become a tangible and quantifiable burden on morbidity and mortality in both human and veterinary medicine. Around five million deaths are estimated to occur each year due to conditions related to bacterial AMR, and AMR is recognized as one of the threats to the capacity of health systems, particularly in resource-limited contexts in the South Asian region (Laxminarayan et al., 2013; Jindal et al., 2015; Antimicrobial Resistance Collaborators, 2022). India is one of the major antibiotic-consuming and producing nations in the world and has a high incidence of antimicrobial resistance among clinically important human pathogens (Van Boeckel et al., 2015; Laxminarayan & Chaudhury,

2016). In both industries, resistant organisms could be generated and shared between sectors due to increased livestock and poultry stocking density, high levels of human-animal-environmental contact, inadequate veterinary regulatory oversight, and easy access to informal antimicrobials (Kakkar et al., 2017).

Today, the One Health vision and framework are agreed upon, conceptually and operationally, to monitor and control AMR globally (Zinsstag et al., 2011; Mackenzie & Jeggo, 2019). This article discusses AMR as a One Health problem and highlights a global picture in the Indian epidemiological and policy context in the livestock sector. The objectives of this article were to review the conceptual evolution of the One Health paradigm and its applicability to tackle AMR; to understand the magnitude and drivers of AMR in livestock production systems; to understand how AMR is transmitted from animals to humans and from humans to their

environment; to review the AMR surveillance and policy architecture; to critically appraise intervention strategies and barriers to their implementation, with particular attention to the Indian context; and to identify research and policy priorities.

### **Historical development and basic theory behind the one health concept:**

The principles of One Health began in the nineteenth century with the understanding that infectious diseases in humans and animals were interconnected and evolved into "One Medicine" in the 1960s through the work of Calvin Schwabe, who identified a connection between human and animal health (Gibbs, 2014). The concept was greatly extended over the coming couple of decades to encompass the health of the ecosystem and of the environment, and, in fact, by the emergence of highly pathogenic avian influenza (H5N1) and other zoonotic epidemics in the early 2000s, the current "One Health" paradigm was established, which is now more 'institutionalized' (Destoumieux-Garzón et al., 2018). Growing awareness that the different environmental compartments are reservoirs and carriers of resistant organisms has generated

formalization of collaborative mechanisms among the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE, now WOAH), and the World Health Organization (WHO) in the Tripartite Agreement that was extended to a Quadripartite Agreement (Ruegg et al., 2019). AMR is an example of the One Health problem type: resistant bacteria and resistance genes emerge in human, animal, and environmental compartments and readily spread among them, and interventions limited to a single sector are unlikely to succeed if they affect the other sectors (Robinson et al., 2016; McEwen & Collignon, 2018). Livestock systems are an excellent example in this regard, as animals are used for therapeutic, prophylactic and growth promotion uses of antimicrobials; farm workers and communities are in close and repeated contact with animals and their waste; and manure, effluent and abattoir discharge are released into soil and water systems where resistant organisms can subsequently be re-introduced to human food and drinking water (Hernando-Amado et al., 2019).

### **The global and Indian scenario of the use and resistance to antibiotics:**

The global consumption of antimicrobials in food animals, estimated to be above 63,000 tonnes in 2010, is projected to grow markedly by 2030, primarily driven by the growing demand in the developing world in middle-income nations as they become more livestock-intensive, such as India, China, and Brazil (Van Boeckel et al., 2015). The percentage of tested food-animal bacteria showing resistance to antimicrobials above 50 percent has increased significantly in low- and middle-income countries since 2000, and "resistance hotspots" have been identified in northern India, north-eastern China, and the Nile Delta (Van Boeckel et al., 2019). The resistance of Enterobacteriaceae to 3rd-generation cephalosporins, fluoroquinolones, and, more recently, carbapenems has remained high, as reported by the hospital- and community-based surveillance system of the Indian Council of Medical Research Antimicrobial Resistance Surveillance Network (ICMR-AMRSN) (Walia et al., 2019; Taneja & Sharma, 2019). On the veterinary side, high levels of multidrug-resistant

(MDR) *Escherichia coli* (*E. coli*), *Salmonella*, and *Staphylococcus* species from poultry, dairy, and small ruminant production systems have been reported, as well as high levels of antimicrobial residues detected in milk, meat, and eggs in some of the states, as reported through ICAR's All India Network Program and related institutional surveillance. Many other countries in South and South-East Asia also have similar patterns, with the informal distribution of antimicrobial agents and limited access to diagnostic services compounding the difficulty of making reliable estimates of antimicrobial use and resistance (Chereau et al. 2017, Van et al. 2020).

### **The role of factors in the emergence of antimicrobial resistance in livestock production systems Antimicrobial use practices:**

The use of antimicrobials for sub-therapeutic and prophylactic purposes – traditionally in poultry and swine – continues to be a major selection pressure in intensive systems (Marshall & Levy, 2011; Manyi-Loh et al., 2018). The implementation of growth-promotant bans has been lacking in consistency, such as in low- and middle-income

countries; in parts of India, for instance, it has never been enforced (Chattopadhyay 2014), and antimicrobials are still easily available as over-the-counter drugs without veterinary prescription, including critically important ones like colistin and fluoroquinolones (Collignon et al. 2018).

#### **Production system intensification and the lack of biosecurity:**

Rapidly increasing the production of poultry and dairy products, frequently outpaced by biosecurity infrastructure, veterinary extension capacity, and waste management systems, increases disease pressure and thus the demand for antimicrobials and the density of animal–animal and animal-human contact in which resistant organisms can spread (Founou et al., 2016; Kimera et al., 2020). Smallholder systems (which make up the bulk of livestock keepers in India) face unique constraints: limited access to veterinary diagnostics can result in empirical, sometimes inappropriate, antimicrobial use, and the informal supply chain of input suppliers creates fewer opportunities for traceability of the products used (Grace 2015).

#### **Aquaculture and related industries:**

Aquaculture in India is a fast-growing sub-segment of the country where there is correlated antimicrobial resistance selection in aquatic bacterial communities, and it is an under-evaluated component of the One Health antimicrobial resistance burden (Cabello, 2006; Ma et al., 2021).

#### **Transmission pathways between humans, animals, and the environment:**

There are several routes of transfer of mobile genetic elements and resistant determinants between the compartments and resistant bacteria. The food chain is a direct route followed by resistant organisms that may be found in raw milk, meat, eggs, and fish, which then enter the food of consumers when the food has not been processed or cooked sufficiently (Landers et al., 2012). A second pathway is direct contact between farm workers, veterinarians, slaughterhouse workers, and colonized or infected animals, which has repeatedly been shown to confer a higher carriage of resistant organisms than the general population (Woolhouse et al., 2015). Even environmental pathways are on the rise in terms of quantity, with manure, etc. being applied to farmland,

effluent from antimicrobial manufacturing facilities discharged to water bodies, resistant bacteria and resistance genes in seed soil and aquatic ecosystems, that may return to the food and drinking water systems (Booton et al., 2021; Rahman et al., 2020). Wildlife and peri-domestic animals, such as rodents, wild birds, and stray dogs, which are commonly seen in Indian urban and peri-urban areas, can be additional poorly quantified reservoirs and vectors between these compartments (Sharma et al., 2019). Assessing the contribution of each pathway, and each sector to the overall burden of human resistance is methodologically complex and is a work in progress – recently, modelling studies indicated that, for many resistance phenotypes, the burden of human-to-human transmission and human antimicrobial use is more important than the burden of livestock-associated transmission and that the latter is more important in contexts where there is intense human–animal contact (Booton et al. 2021, Mughini-Gras et al. 2019 as cited in Hernando-Amado et al. 2019). This is an indicator of the need to conduct pathogen- and context-specific risk assessment and

intervention design, rather than a uniformly generalized approach.

### **Surveillance systems & policy frameworks Global architecture:**

The key international surveillance architecture includes the Global Antimicrobial Resistance and Use Surveillance System (GLASS) of the WHO and the OIE Antimicrobial Use in Animals database (WOAH, 2019), the World Health Assembly Global Antimicrobial Resilience Action Plan of 2015, which includes commitments of the member states to multisectoral national action plans (WHO, 2015). The Jim O'Neill Independent Review on Antimicrobial Resistance had an influential impact by providing an economic estimate of the human and economic consequences of leaving AR unabated and by building momentum for political commitment at the global level (O'Neill, 2016).

### **Current Indian policy landscape:**

Indian policy is a work in progress. In 2017, the Government of India implemented a National Action Plan on Antimicrobial Resistance (NAP-AMR) that closely aligns with the WHO Global Action Plan (Kakkar et al., 2018) and adopts six strategic priorities: awareness, surveillance, infection prevention, antimicrobial

optimization, research and innovation, and collaborative leadership. These have since been trailed by a few states declaring their own state action plans, and the Food Safety and Standards Authority of India (FSSAI) has set Maximum Residue Limits (MRLs) for antimicrobials in food of animal origin (Sharma et al., 2020). Despite this, implementation is still not consistent: the veterinary and agricultural components of the plan are still funded less than the human health components; coordination with inter-ministerial is still weak (including Ministries of Health, Fisheries, Animal Husbandry and Dairying and Environment); the capacity in the states to monitor veterinary surveillance is still limited, especially for the monitoring of resistance genes by whole genome-sequencing, according to (Gandra et al., 2017; Walia et al., 2019).

#### **One health intervention and mitigation strategies - The use of antimicrobials in veterinary care:**

Evidence in other countries shows that veterinary antimicrobial use reduction programmes (VAPs) have led to measurable decreases in antimicrobial use and for prevalence of antimicrobial resistance in food animals and meta-analytical evidence

has indicated that a reduction in antimicrobial use in food animals is associated with a reduction in prevalence of antimicrobial resistance in bacteria from animal associated animals, and in a smaller, but measurable, impact of antimicrobial resistance in human associated animals (Tang et al., 2017; Chandy et al., 2014).

#### **Vaccination, biosecurity, and alternatives to antimicrobials:**

Improved vaccination coverage for key bacterial and viral diseases of poultry, dairy cattle, and small ruminants will decrease the incidence of these diseases, and as a result, antimicrobial use; best practices in biosecurity, such as all-in-all-out management, controlled access of visitors, and good ventilation, will reduce baseline infection pressure (Robinson et al., 2016). Other feed additives, such as probiotics, prebiotics, organic acids, and, in the early stages of development, bacteriophage therapy, are being explored as alternatives to antimicrobials to prevent disease; however, limited evidence of consistent efficacy and cost-effectiveness for these alternatives in Indian smallholder systems exists (Manyi-Loh et al., 2018).

### **Integrated surveillance and genomic approaches:**

Surveillance of human, animal, food and environmental sampling having a One Health lens for antimicrobial resistance (AMR) is increasingly reliant on whole genome sequencing and metagenomic approaches that have the capacity to track the movement of AMR resistance genes from one compartment of the One Health enterprise to the other (previously not possible to do so by phenotypic surveillance) and is a priority for investment in India through ICMR, ICAR and state veterinary laboratory networks (Queenan et al., 2016; Hernando-Amado et al., 2019).

### **Challenges to implement the one health approach in India:**

While the Indian livestock sector is working towards implementing One Health, a significant number of structural barriers have been identified that hinder its effective implementation. Smallholder farmers who constitute majority of livestock holders lack access to affordable veterinary services and there are limited formal coordination mechanisms across ministries/ departments to coordinate use of antimicrobials in the field;

weak veterinary regulatory capacity to ensure that only professionals prescribe antimicrobials; and limited capacity for diagnostic microbiology across the district and block level, giving farmers economic reasons to rely on informal use of antimicrobials rather than professional use (Prasad et al., 2018; Sharma et al., 2020). There is ongoing limited data sharing between human and animal health surveillance systems; the numbers of which are required to be working together as a single team to undertake joint risk assessment exercises, similar to what is proposed with the One Health approach (Kakkar et al., 2017); and funding for veterinary and environmental aspects of AMR containment remains limited compared to funding for human health aspects of containment (Kakkar et al., 2017).

### **The future directions and research**

#### **Priorities:**

Future research and investment needs include developing representative quantitative attribution models for the Indian context to share the burden of resistance amongst sources of human, animal and environmental origin; scaling up the One Health approach to genome sequencing and metagenomics

surveillance from existing reference laboratories to district veterinary and public-health laboratories; rigorously testing non-antimicrobial alternatives in the field under smallholder production conditions; studying the behavioural drivers of use of antimicrobials in informal production systems, and developing strategies to reduce this use; and strengthening institutional mechanisms for One Health data sharing and joint risk communication between ministries responsible for Health, animal husbandry, fisheries and environment (Rahman et al. 2020, Chandra Bhusan Singh et al. 2021). It will be essential that political commitment, multisectoral coordination with adequate resources, and a context-appropriate response come from within India, rather than being uncritically imported from elsewhere, if the livestock sector is to play a significant role in curbing antimicrobial resistance.

### Conclusion:

The issue of antimicrobial resistance in the livestock sector can only be understood through a multisectoral approach that helps monitor and manage it, and is a human, animal, and environmental health issue that requires multisectoral actions grounded in science. India's high livestock density and its growing livestock sector, with high levels of interactions between humans, animals, and the environment, make the country highly susceptible to, and could play an important role in tackling, the global AMR burden. To achieve sustainable containment, the most credible approach is veterinary stewardship, intersectoral governance, and integrated One Health surveillance.

### References:

Please contact the corresponding author.