

ONE HEALTH SOLUTION TO THE PROBLEM OF ANTIMICROBIAL RESISTANCE; IT'S MUCH MORE THAN ONE

DEBJIT CHAKRABORTY^{1*}, FALGUNI DEBNATH² AND SHANTA DUTTA³

Antimicrobial Resistance (AMR) is a rapidly emerging public health concern as antimicrobial medicines are becoming increasingly ineffective against the disease-causing microbes. The problem has magnified in the recent years, mainly because common people do not only consume antibiotics through prescribed or self-purchased medicines, but also through their daily intake of food and water. Antibiotics enter the food chain and environmental resources through more than one pathway such as animal farming, fishery and agriculture, and through hospital, pharmaceutical and household waste streams. AMR bacteria from various sources, like pharmaceutical effluents, biomedical waste and effluents, litter and manure from poultry and livestock farms, aquaculture, plant agriculture, household sewage, and slaughterhouse waste either directly contaminate the aquatic environments or contaminate the soil. 'One Health' approach to AMR recognizes the interlinkages between human health, animal health and the environment. Considering the increasing human, animal, environment interfaces and interactions, concept of One Health has been conceptualized to protect the health of all sectors together. In 2021 definitions of One Health came in place globally. India developed its first National Action Plan (NAP) on AMR in April 2017 but environmental dimensions were included in the second NAP -AMR in 2022. While all these efforts reflect the intent of the country to address the policy gaps in AMR mitigation, enforcement of all these will only be feasible and consistent if these interventions are backed up by a comprehensive, cross-sectoral institutional framework where different actors in these three sectors will come together and work on a common, collaborative platform.

The Problem of AMR

Antimicrobial Resistance (AMR) is a rapidly emerging public health concern as antimicrobial medicines are becoming increasingly ineffective against the disease-causing microbes. While the human

health sectors such as hospitals, clinics, physicians, and pharmacies are primarily responsible for the issue, unknowingly, the larger society is also contributing to the problem equally and thus leaving our future generations with no options but to suffer from common infections in greater severity. Consequently, it is of utmost importance that the larger social responsibilities are realized and addressed systematically to mitigate the risks of AMR.

In recent years, there is a rise in AMR across all the sectors, as inappropriate use of antibiotics has increased. Finally, the consumed antibiotics enter the food chain through interconnecting pathways involving different users such as animal farming, fishery, agriculture, hospital, pharmaceutical and household waste streams.

1 Scientist- E, Division of Epidemiology, ICMR- National institute for Research in Bacterial Infections, Kolkata, West Bengal, India. e-mail: drdebjitepi@gmail.com

2 Scientist- E, Division of Epidemiology, ICMR- National institute for Research in Bacterial Infections, Kolkata, West Bengal, India. e-mail: falgunidebnath@yahoo.in

3 Director & Scientist- G, Division of Bacteriology, ICMR- National institute for Research in Bacterial Infections, Kolkata, West Bengal, India. e-mail: drshantadutta@gmail.com

* Corresponding Author:

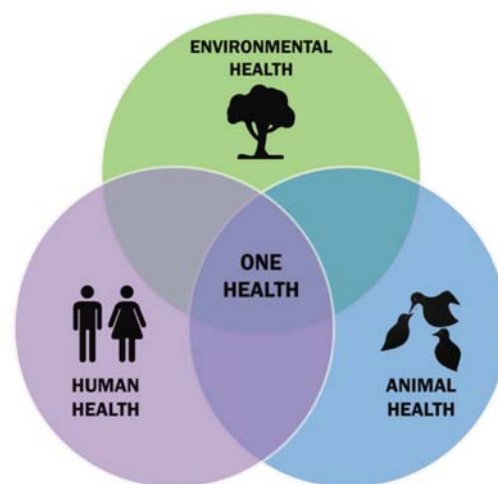
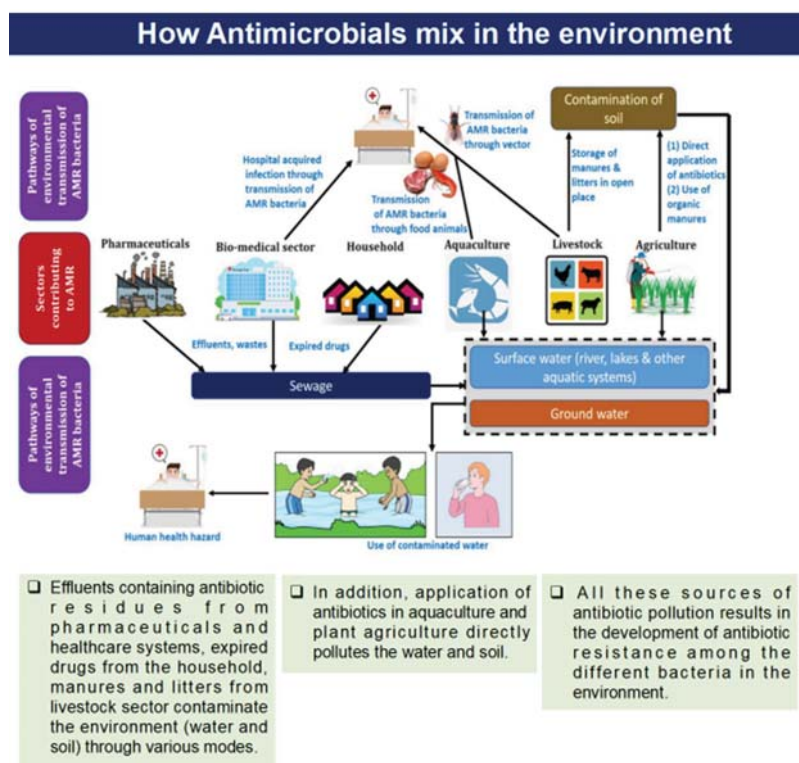


Fig. 2: Concept of One Health

Fig. 1: Environmental Pathways of Antimicrobial Pollution



Fig. 3: Role of individual and community in One Health AMR movement:

Table 1a: Programmatic & Technological Challenge in Environmental AMR

Type of challenges	Water Treatment & Sanitation	Soil Testing and Treatment	Waste handling and Disposal
Programmatic 	The existing policies on environment do not include aspects of AMR, similarly the health policies do not cover environmental pathways of AMR, Inadequate regulations on OTC sale of antibiotics		
	Poor WASH system allows indiscriminate mixing of disposed end of life antibiotics in the effluent streams	- Inadequate soil testing and treatment guidelines for detection and segregation of traces of antibiotics in soil - No standards around soil remediation for residual antibiotics	- Injudicious handling of antibiotics waste in terms of collection, segregation, treatment and disposal - No mention of collection, segregation, treatment and disposal of residual antibiotics in existing soil waste or biomedical waste management rules
Technological 	- Lack of laboratory-based strong surveillance on AMR - Methods of measuring traces of antibiotics in different environmental streams, guidelines on allowable thresholds, instrumentation needed for such measurements etc. are either not clearly laid out in any environmental standards or not field tested for validation and large-scale adoption - Lack of innovation on cost-effective alternatives to antibiotic growth promoters		

Table 1b: Institutional & Financial Challenge in Environmental AMR

Type of challenges	Water Treatment & Sanitation	Soil Testing and Treatment	Waste handling and Disposal
Institutional 	- Inadequate capacity with the environmental regulators (in terms of resources and skill sets) to develop and implement guidelines around prevention of AMR in environmental streams - Lack of research and development on monitoring and containing AMR in different environmental streams - Absence of collaboration amongst State Pollution Control Boards, Departments of Environment, Livestock, Aquaculture, Agriculture and Public Health - Inadequate awareness amongst farmers on use and benefits of non-antibiotic growth promoters and adverse impacts of AMR bacteria on human health		
Financial 	Absence of incentivization (e.g., subsidies) mechanism to take up costlier alternatives to antibiotic growth promoters leads to rampant use of antibiotics in livestock and aquaculture sectors		

Irresponsible application and overuse of antimicrobials in different sectors (human medicine, agriculture, livestock farming) adds to the problem by developing selection pressure, i.e., repetitive and unnecessary use of antibiotics, resulting into AMR^{1,2}.

Improper application of antimicrobials, inadequate infection prevention and control, unmanaged effluents in the environment from agricultural, pharmaceutical and biomedical activities, and migration of human and animals infected with resistant bacteria from one place to the other favour the spread of resistance bacteria and resistant genes^{2,3}.

Environmental Pathways of AMR:

Environmental health plays an important role in preventing the spread of many infectious diseases, including the spread of AMR bacteria. [Fig. 1] Water and soil are the major environmental reservoirs and modes of transmission of AMR bacteria in humans and animals. Water (groundwater and surface water), especially, is getting more attention for spreading antibiotic-resistant bacteria (ARBs) and antibiotic-resistant genes (ARGs). AMR bacteria from various sources, like pharmaceutical effluents, biomedical waste and effluents, litter and manure from poultry and livestock farms, aquaculture, plant agriculture, household sewage, and slaughterhouse waste either directly contaminate the aquatic environments or contaminate the soil. AMR bacteria present in the soil is eventually transferred to surface water through runoff or groundwater through leaching. Again, the resistant bacterial strains get transferred to crops and vegetables through this contaminated water and soil. The subsequent consumption of drinking water and food or contaminated surface water leads to human morbidity and mortality. Not only the administration of antibiotic medicines in food-producing farm animals facilitates AMR, but it also leads to the presence of antibiotic residues in animal-derived food products further available for wider human consumption¹⁰

The existing challenges of AMR – Policy, programs, technology, institutional and financial:

The existing challenges that need to be addressed to reduce the risk of AMR are discussed in the table below: [Table 1a & 1b]

One Health; Bringing All Together

On an average, one new disease has emerged or re-emerged each year since 1640, and 75% of these newly

emerged diseases have been from an animal source. From 1940 to 2018, more than 340 pathogens emerged, with 60% being zoonotic origin⁴. Thus 'One Health' approach to AMR recognizes the interlinkages between human health, animal health and the environment. Given the interdependence of human, animal, and environmental pathways of antimicrobial resistance, One Health approach is highly logical towards addressing AMR⁵.

This is quite pertinent to India where incidences of antimicrobial resistance are gradually increasing in all three sectors⁶. Considering the increasing human, animal, environment interfaces and interactions concept of One Health has been conceptualized to protect the health of all sectors together. In the year 2021 following definitions of One Health came in place globally [Fig. 2]

One Health High-Level Expert Panel (OHHLEP) Definition (2021)⁷:

One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent.

The approach mobilizes multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for clean water, energy and air, safe and nutritious food, taking action on climate changes and contributing to sustainable development

US CDC and One Health Commission (OHC) definition (2021)⁸

One Health is a collaborative, multisectoral, and trans-disciplinary approach - working at local, regional, national, and global levels - to achieve optimal health (and well-being) outcomes recognizing the interconnections between people, animals, plants and their shared environment

One Health at the UN Environment Assembly:

Connections between ecosystem health and human health were on the agenda of the second segment of the fifth UN Environment Assembly (UNEA-5.2), held in February 2022 in Nairobi. The concluding Ministerial Declaration recognized the risk for future pandemics and other health risks if humanity does not overhaul its patterns of interaction with nature by adopting a holistic approach such as One Health.

In this context, there is a resolution on animal welfare, taken by the UN Member States (FAO, UNEP, WOA, WHO) that highlights the need for protecting animals, safeguarding their habitats and meeting their welfare requirements (UNEP/EA5/L10/REV.1) Another resolution by the UN Member States on biodiversity and health recognizes the importance of the One Health approach to address the impacts of environmental crises on global health (UNEP/EA5/L11/REV.1)⁹.

Policies, Programs, Regulations and Guidelines Related to Environment and AMR in India

The sixty-eighth World Health Assembly (WHA) came up with the Global Action Plan on AMR (GAP-AMR) in 2015¹¹. This action plan delineated the major objectives and outlined the activities to be adopted by the nations. India developed its first National Action Plan (NAP) on AMR in April 2017 and second NAP -AMR in 2022. In the first NAP, the environmental dimensions were missing which were considered in the second version. In addition to this, several other policies, guidelines, and programs related to human health, animal health and the environment were introduced at the national level.

In terms of environmental policies and regulations around prevention of AMR, though in January 2020, the Ministry of Environment Forest and Climate Change (MoEFCC) came up with limiting values for concentration of antibiotic residues in the treated effluent of bulk drug and formulation industries, those limits were subsequently dropped in the next amendment of guidelines in August 2021 and a reference to Hazardous and Other Wastes (Management and Transboundary Movement) Rules, 2016 was made. Discussions on the need for more specific residual values of antibiotics in the effluents from bulk drug and formation manufacturing units is still a matter of discussion under the purview of the judiciary system. It is also to be observed that these regulations are currently focused on residual antibiotics in the effluent streams of the antibiotic manufacturing facilities and not addressing the issues of AMR contamination in effluents in the sectors where antibiotics are used e.g., households, livestock and aquaculture farms, veterinary facilities etc.

However, in the human health sector, multiple policies and programs have been introduced for prevention of AMR. The National Programme on AMR Containment by the National Centre for Disease Control (NCDC), the Antimicrobial Stewardship

Program (AMSP), 2018, the Treatment Guideline for Antimicrobial Use in Common Syndromes (ICMR), 2019, and the National Guidelines for Infection Prevention and Control in Healthcare Facilities, 2020, are some of the key ones to name¹².

Similarly, in the animal health sector, there have been significant efforts towards containment of AMR. Some of the key interventions are Coastal Aquaculture Authority (CAA) guidelines on antibiotic use, the National Policy for Containment of Antimicrobial Resistance, 2011, the National Animal Disease Reporting System (NADRS), 2014, the National Residue Control Plan (NRCP), and the Pre-harvest testing (PHT) by Marine Products Export Development Authority (MPEDA), the Indian Network of Fisheries and Animal Antimicrobial Resistance (INFAAR) in 2018.

The Coastal Aquaculture Authority (CAA) put restrictions on the use of twenty antibiotics and pharmacologically active substances in aquaculture. The Drug and Cosmetics Rules, 2012, emphasizes labeling withdrawal periods on medicine being used for treating animals¹³. National Policy for Containment of Antimicrobial Resistance focuses on the development of suitable protocols for antibiotic use in food animals. It regulates the use of non-therapeutic antibiotics in animals, and control the selling of antibiotics, especially Schedule H1, without prescriptions issued by registered practitioners. Under the National Animal Disease Reporting System (NADRS) surveillance program, different animal diseases in India can be monitored and data can be recorded and collected¹⁴.

The Marine Products Export Development Authority (MPEDA) has developed the National Residue Control Plan (NRCP) and Pre-harvest testing (PHT) of antibiotic residues in exportable aquaculture products to European countries but residual testing in marine products for domestic consumption is still a distant reality¹⁵. The Export Inspection Council (EIC, 2011 and 2019) has surveillance over antibiotic residues in animal food, especially milk¹⁶ and honey¹⁷.

The UN Food and Agriculture Organization (FAO) is collaborating with ICAR (Indian Council of Agriculture Research) set up a national network of laboratories in veterinary sector to generate data on antimicrobial resistance (AMR) among animals in India. This is known as Indian Network for Fishery and Animals Antimicrobial Resistance (INFAAR) who has recently published their first report.

While all these efforts reflect the intent of the country to address the policy gaps in AMR mitigation, enforcement of all these will only be feasible and consistent if these interventions are backed up by a comprehensive, cross-sectoral institutional framework where different actors in these three sectors – environment, human health and animal health will come together and work on a common, collaborative platform. Not only policymakers and health providers, but also individual households and community have important role to play in mitigating AMR through One Health approach [Figure 3] as simple, small quantum of effort by the population at large promises to bring significant impact. The “oneness” of the diverse needs of different sectors needs to be understood and a common way forward needs to be delineated clearly articulating the roles and responsibilities of each stakeholder to achieve “One Health” and prevent AMR. □

**Bottom line: AMR means All Measures
Required.**

References:

1. M.E. Velazquez-Meza, M. Galarde-López, B. Carrillo-Quiróz and C.M. Alpuche-Aranda, *Vet World* 15:743-749 (2022).
2. P. Collignon, J.J. Beggs, T.R. Walsh, S. Gandra and R. Laxminarayan, *Lancet Planet Heal.* 2:398–405 (2018).
3. H. Bürgmann, D. Frigon, W.H. Gaze, C.M. Manaia, A. Pruden, A.C. Singer, B.F. Smets and T. Zhang, *FEMS Microbiol Ecol.* 94:1–14 (2018)
4. <https://timesofindia.indiatimes.com/city/nagpur/center-for-one-health-approved-for-nagpur-icmr-director/articleshow/68326643.cms>
5. S.A. McEwen, P.J. Collignon, *Microbiol Spectr*, 6:10.1128 /microbiol spec.arba-0009-2017 (2018).
6. N. Taneja and M. Sharma, *Indian J Med Res.* 149:119-128 (2019)
7. <https://www.fao.org/one-health/overview/one-health-overview/en>
8. https://www.onehealthcommission.org/en/why_one_health/what_is_one_health/#:~:text=US%20CDC%20and%20One%20Health,plants%20and%20their%20shared%20environment.
9. <https://www.unep.org/resources/resolutions-treaties-and-decisions/UN-Environment-Assembly-5-2>
10. C. Manyi-Loh, S. Mamphweli, E. Meyer, A. Okoh, *Molecules*, 23:795 (2018)
11. World Health Organization. Monitoring and Evaluation of the Global Action Plan on Antimicrobial Resistance: Framework and Recommended Indicators. 2019.
12. R.K. Srivastava, National Policy for Containment of Antimicrobial Resistance India; Ministry of Health & Family Welfare: New Delhi, India, 2011
13. Coastal Aquaculture Authority. Guidelines for regulating Coastal Aquaculture (Annexure-I), CAA Rules. 2005.
14. H.C. Kumar, J. Hiremath, R. Yogisharadhya, V. Balamurugan, S.S. Jacob, G.M. Reddy, K.P. Suresh, R. Shome, M. Nagalingam, R. Sridevi, et al. *Indian J. Med. Res.* 153; 299–310 (2021)
15. Marine Products Export Development Authority (MPEDA). National Residue Control Plan (NRCP). Available online: https://mpeda.gov.in/?page_id=1088
16. Export Inspection Council. Milk Product: Residue Monitoring Plan (RMP) for Export to EU, Year 2011-12; Export Inspection Council, Ministry of Commerce & Industry, Government of India: New Delhi, India, 2011
17. Export Inspection Council. Honey: Residue Monitoring Plan (RMP), Year 2019-20; Export Inspection Council, Ministry of Commerce & Industry, Government of India: New Delhi, India, 2019