International Association of Hydrogeologists Technical Insight Series:

Antimicrobial Resistance – A Growing Global Groundwater Challenge

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Abstract

Antimicrobials are composed of medications such as antibiotics and antivirals which are widely used to ensure human and animal health. However, inappropriate use of antimicrobials is a major driver of antimicrobial resistance in groundwater or other aquatic systems. AMR arises from complex interactions between humans, animals, microbial organisms, medicines, wildlife and the environment. Antibiotics are only partially removed by most wastewater treatment plants and are frequently detected in both effluent water and sludges. Bacteria can develop antibiotic resistance through several mechanisms such as genetic mutations or by acquiring antibiotic resistance genes (ARGs) from other bacteria via horizontal gene transfer. Based on studies worldwide, hundreds of ARGs have been detected in various aquatic systems, posing significant environmental and public health concerns. Once in the environment, ARGs can disseminate within bacterial populations from which some species could re-enter human and animal systems via contaminated water, food, or recreational activities. This environmental reservoir of resistance undermines the effectiveness of antibiotic therapies, complicates the treatment of infectious diseases, and increases the risk of outbreaks caused by multidrug-resistant pathogens. The current strategy of preventing AMR is to protect aquatic environments from pharmaceutical contamination, especially antibiotics. But because of the difficulty and expense of detecting compounds associated with AMR, most countries do not have national, legally enforceable water quality standards. Further developments in affordable screening and treatment solutions will be necessary to tackle this insidious contamination.

Technical Insight Series

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Thick foam carpeting the Yamuna River downstream from a sewage channel in New Delhi, India (T.Boving URI)

Antimicrobials have been used for decades and are an essential part of modern medicine. Antimicrobials are composed of medications such as antibiotics, antifungals, antivirals, anthelmintics, etc., widely used to ensure human and animal health. However, inappropriate use of antimicrobials is known to be a major driver of antimicrobial resistance (AMR)[1]. AMR arises from complex interactions between humans, animals, microbial organisms, medicines, wildlife and the environment (Figure 1).

A recent study estimated the proportion of inappropriate antibiotic use globally to be on average 30% (~13,000,000 kg) equivalent to the annual consumption of antibiotics in China[2]. AMR is a chronic public health problem globally, set to account for 10 million deaths each year by 2050[3].

Animal usage of antibiotics varies considerably, for example in the USA it accounts for around 70% of antibiotic sales, while in the UK this figure is around 30%, indeed across Europe between 2011-2018 there was a 33% reduction in the sales of antibiotics for livestock[4]. However, in Asia, the far East and Oceania, antibiotic use per unit livestock remains around 4 times higher than Europe[4].

To manage the threat of AMR a 'One Health' Approach is required which integrates efforts to reduce inappropriate use across multiple sectors and disciplines. Rapid advances in genomic surveillance for AMR have enabled monitoring of persistence and abundance of AMR genes and mutations within microbial organisms[5] and forms a central tool for monitoring AMR spread globally.

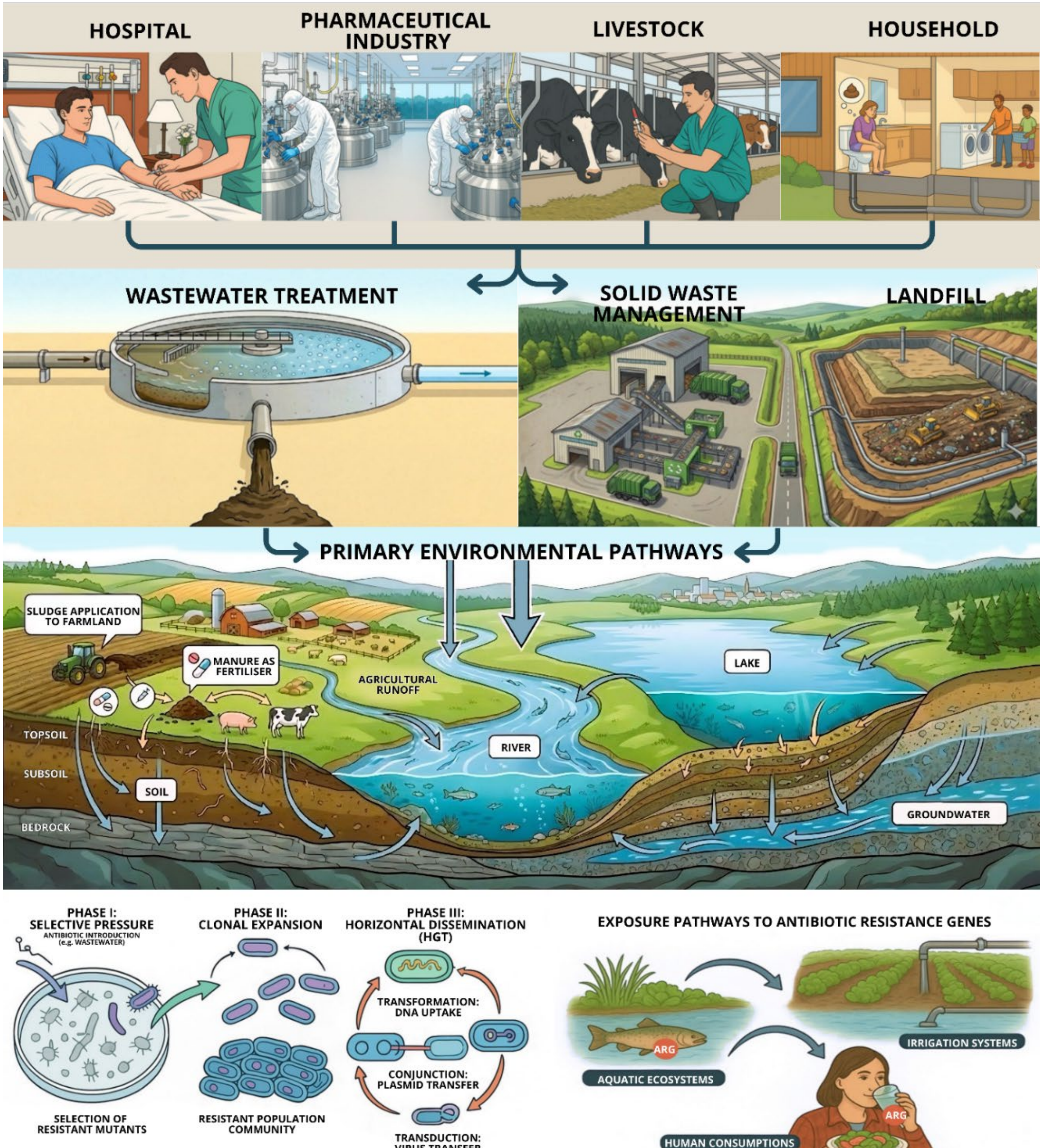

Figure 1: Environmental releases and pathways of chemical compounds that can cause antimicrobial resistance (AMR). (AI Generated. Design by B.P. Vellanki IIT-R; M. Lenczewski NIU)

Antimicrobial Pharmaceuticals and Their Detection in Waters

Most modern antibiotics are synthetic derivatives of various natural compounds and encompass a diverse range of chemical structures. Of the many antibiotics on the market, ciprofloxacin, tetracycline, sulfamethoxazole, and amoxicillin are among the most frequently detected antibiotic residues in rivers, groundwater, and wastewater[6,7]. Notably, most antibiotics were first discovered decades ago with very few new ones developed since.

The global surge in antibiotic consumption for both medical and livestock applications has inadvertently introduced these bioactive compounds into aquatic environments[8]. Importantly, antibiotics are not completely metabolized when administered to humans and animals. In the case of antibiotics administered to animals, approximately 90% are excreted in original form or as metabolites[9]. Once in the wastewater stream, antibiotics are incompletely removed by most wastewater treatment plants (WWTPs) and are frequently detected in both effluent water and sludges. Sulfamethoxazole, ciprofloxacin, and trimethoprim are among the most persistent antimicrobics, with overall aqueous removal efficiencies typically below 40%. Untreated municipal sewage may contain as much as 10 μg L^{-1} antibiotics, whereas typical antibiotic concentrations in treated municipal sewage range from non-detects to approximately 1 μg^{L-1} [10]. Once AMR causing compounds enter the groundwater, they pose a high risk to human health, as indicated in a study of private drinking water wells in Ireland[11]. A study of groundwater in China showed that 47 antibiotics, mainly sulfonamides and fluoroquinolones, have been detected and that these antibiotics in groundwater will induce the production of resistance genes, causing ecological harm[12].

Antibiotic Resistance Genes (ARG)

WWTPs are hot spots for the transfer and proliferation of AMR bacteria in the environment[26]. Especially during biological treatment of domestic sewage, conditions are conducive for the emergence of AMR bacteria via horizontal gene transfer. A recent study showed that full scale WWTP in a metropolitan city in India could not remove the clinically relevant antimicrobial resistant genes (AMG) from wastewater and anaerobically digested sludge[13]. Another study revealed that the agricultural soils amended with sewage sludge had higher abundance of ARGs than normal agricultural soils[14]. Elevated levels of AMR-indicating class 1 integron-integrase gene, *intI1*, and a wide range of emerging contaminants in urban surface waters and lower levels in groundwaters were found in Bengaluru, India [15]. Risk quotients indicated potential AMR development caused by high concentrations of azithromycin, fluconazole, and sulfanilamide in surface waters due to sewage inflows.

Bacteria can develop antibiotic resistance through several mechanisms[16]. These traits in antibiotic-resistant bacteria can arise through genetic mutations or by acquiring antibiotic resistance genes (ARGs) from other bacteria via horizontal gene transfer, occurring mainly through conjugation, transformation, and transduction.

Urban water systems (Figure 2) contribute to the dissemination of resistance determinants between bacterial species, thereby making aquatic environments reservoirs and routes that facilitate the spread of ARGs and the emergence of antibiotic-resistant pathogens[17]. To date, hundreds of ARGs have been detected in various aquatic systems, posing significant environmental and public health concerns[18].

Box 1

The Potomac River sewage spill, 2026

The 2026 Potomac River sewage spill was a massive raw sewage release caused by a major sewer line collapse north of Washington, D.C. Estimates put the spill at roughly 240–300 million gallons of raw sewage discharged into the river, one of the largest wastewater spills in U.S. history. Persistently elevated E. coli and Staphylococcus aureus, including antibiotic-resistant strain of this bacterium known as MRSA, were reported in river water and nearby soils weeks after the break, with contamination detected several miles downstream. Because many first-line antibiotics no longer work, MRSA infections can be harder to treat, may require stronger or intravenous drugs.

AMR indicators in groundwater and surface water in urban India

Urban groundwater and surface water in the South Indian city of Bengaluru was investigated for antimicrobial resistance (AMR) indicators and emerging organic contaminants (EOC)[15]. Out of 125 EOCs detected in this study, 62 were present in groundwaters and a number of these compounds could be linked directly to distinct recharge sources. Risk quotients were computed to evaluate the level of risk associated with the concentrations of EOCs to contribute to AMR development. Of the nine detected antimicrobials that could have RQs calculated, three were found at concentrations posing a risk of AMR development: azithromycin, fluconazole and sulfanilamide. The ubiquitous detection of the sweetener sucralose indicated recent groundwater recharge and a contribution of imported Cauvery River water for recharge. This study highlights the need for monitoring and water protection and the role of EOCs as potential drivers of AMR.

Figure 2: Untreated sewage is discharging in a channel that drains wastewater into the Yamuna River in New Delhi, India. Once released into the surface water, compounds like antimicrobial pharmaceuticals can migrate into the groundwater (T. Boving – URI)

Once in the environment, ARGs can disseminate within bacterial populations from which some species could re-enter human and animal systems via contaminated water, food, or recreational activities (Figure 1). This environmental reservoir of resistance undermines the effectiveness of antibiotic therapies, complicates the treatment of infectious diseases, and increases the risk of outbreaks caused by multidrug-resistant pathogens[17, 19, 20].

Regulations

The current strategy of preventing AMR is to protect aquatic environments from pharmaceutical contamination, especially antibiotics. However, monitoring pharmaceuticals is insufficient to fully assess the threat associated with AMR. Rather, additional indicators are needed, such as monitoring the presence of antibiotic-resistant bacteria and analyzing the transfer of resistance genes[21]. But because of the difficulty and expense of detecting compounds associated with AMR, most countries do not have national, legally enforceable water quality standards for it.

In the United States, the Environmental Protection Agency (USEPA) issues a list of unregulated drinking water contaminants that are known or anticipated to occur in public water systems but currently are not subject to national primary drinking water regulations. Compounds used in pharmaceuticals or byproducts of their use, such as estrogenic hormones (estradiol, estriol, estrone) and antibiotics (erythromycin), were proposed, but were not considered for further regulations when the 4th Contaminant Candidate List (CCL) was finalized in 2021[22]. The current CCL5 list includes 81 contaminants or contaminant groups; none are antibiotics.

In the European Union (EU), the Water Framework Directive (WFD) is the main tool to reduce the emissions of priority substances that harm the aquatic environment. Updated lists of these substances have been published since 2001, but pharmaceuticals were not included in any of these lists [21]. In 2013, the EU established the first Surface Water Watch List, which, like the EPA's CCL, lists compounds suspected of posing a risk to aquatic environments but lack sufficient data to be included in the WFD. Updated every 4 years, the Watch List includes several antibiotics, hormones and other drugs.

The Indian Government proposed a bill on pollution limits for antibiotics at manufacturing sites. The proposed limits were based on measured concentrations in treated effluents. However, the bill passed in 2020 without antibiotic discharge limits due to critiques primarily from manufacturers[23].

The AMR Industry Alliance, an industry group headquartered in Switzerland, formulated Antibiotic Manufacturing Standard (AMS), which is a set of minimum requirements for evaluating risks in antibiotic supply chains to prevent the release of antibiotic residues into the environment and mitigate AMR [24]. The voluntary standard requires that the manufacturer of an antibiotic must have an effective environmental management system and that the antibiotic's Predicted No-Effect Concentrations (PNEC), or the level at which a substance will not have an adverse effect on its environment, are met[24]. The PNEC below which AMR is not likely to develop ranges from about 0.1 to 2.0 μg L^{-1} for many antibiotics[9]. For comparison, typical antibiotic concentrations in untreated hospital effluent and industrially polluted surface water can be orders of magnitude higher than PNEC and can even reach the minimal inhibitory concentration which is the lowest concentration of an antimicrobial drug that prevents the visible growth of a microorganism in a laboratory setting[10].

Figure 3: As part of a complex mixture of pharmaceuticals and personal care products (PPCPs), antimicrobial compounds are being released into the environment via many pathways where they can pollute groundwater and surface water bodies. Sampling and testing of wastewater in the field is a first step towards studying the environmental impacts of AMR. Here, students from IIT Roorkee in India studying an artificial lake fed by partially treated wastewater. (T. Boving – URI).

Future Outlook

AMR and the presence of pharmaceuticals in general is a major groundwater quality issue in the coming decades. The ubiquitous distribution of AMR around the globe has the potential to significantly affect the quality and therefore limits the availability of water resources in many regions. While groundwater AMR presence typically is significantly lower than in surface waters, the pervasive presence of AMR in the environment raises concerns about impacts to the ecosystem and human health. Further developments in affordable screening and treatment solutions will be necessary to tackle this insidious contamination.

Box 2

Further Information

The global reach of the AMR problem is reflected in numerous guidance documents prepared by national and international organizations. In response to growing concerns of AMR the World Health Organization launched Global Antimicrobial Resistance and Use Surveillance (GLASS) in 2015, which includes annual reporting on AMR and antimicrobial consumption data. In 2024, the WHO published the Guidance for Responsible and Sustainable Manufacturing of Antibiotics[23] in which it provides a framework for manufacturers to reduce antibiotic pollution from their facilities by setting human health-based targets. It also established a risk management process for wastewater and solid waste. The United Nation's General Assembly High-Level Meeting on Antimicrobial Resistance[25] is an international effort to address AMR. This initiative responds to "drug-resistant infections know no borders", meaning no single country can respond to AMR alone. However, it must be noted that the water quality regulations of many countries so far pay little attention to the growing AMR problem. Drivers of AMR in groundwater and groundwater dependent ecosystems clearly remains an understudied area of research and there is a need for more detailed studies to fill this knowledge gap.

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