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Popular Article

## Environmental Hygiene - a Key Intervention Strategy in Fighting Against Antimicrobial Resistance

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### Introduction:

The therapeutic and non-therapeutic use of antimicrobials has grown rapidly in past few decades. Easy availability, abuse and no proper regulations on their usage has led to antimicrobial resistance, evolution of superbugs and superinfections. AMR is driven by antibiotic misuse and overuse in various sectors, leading to the emergence of resistant microorganisms (Sirwan Khalid Ahmed *et al.*, 2024). AMR is one of the top global threats and the situation will become worse in coming years. Around 700,000 people losing battle to antimicrobial resistance (AMR) per year and another 10 million projected to die from it by 2050 (Taneja N *et al.*, 2019). AMR problem severely affects the health care quality, recovery rate and indirectly growth and GDP of country. If not tackled, AMR could force 24 million people into severe poverty by 2030 and hinder progress on Sustainable Development Goals (SDGs) (Rehab A. Rayan, 2023).

Regardless from which sector the waste is generated, it will be eventually released into the environment. It consists of pollutants and chemicals which drive the microorganisms to acquire resistance by selection pressure, that includes antimicrobials (as most of the dose taken will be excreted and enters into environment). Countering Antimicrobial resistance requires a multi-sector collaboration from human healthcare, livestock & poultry sectors and by maintaining environmental hygiene & health. Although awareness and control programs are currently established in human and veterinary health care, the environment part in acquiring and transmission of resistance is complex and not well studied.

Concept of tackling antimicrobial resistance via environmental hygiene include breaking transmission cycle and cutting-off the sources, prevention, and control measures, educating society etc. Actions of Environmental hygiene plays a key role in decreasing the chances of resistance in environment thus decreasing the load of super bugs that can potentially infect other organisms.

**Keywords:** Antimicrobial Resistance (AMR), WASH, Sanitation, One health, Antimicrobial Resistant Bacteria (ARB), Antimicrobial Resistant Genes (ARG)

**What is Environmental Hygiene?** This hygiene concept mainly focuses on certain prevention and control

measures that can be followed in order to control the environmental factors which affects the human and animal's health and well-being.

**Environmental Hygiene and Environmental Health:** both are the discipline of public health where environment health is a broader term. The former one consists concept of hygiene, waste management sanitation etc. and later one also includes climate change, greenhouse gases, disasters etc. According to Brian King, 2015., The field of environmental health examines how human health is affected by the natural and physical environment. The disciplines of environmental epidemiology, toxicology, and exposure science are often recognized as central to environmental health.

	Factor	Mechanism responsible for AMR spread	Action promoting AMR spread by the factor	Reason of occurrence of the factor in the environment
1	Antibiotics	Mutations of DNA caused by selection pressure	Contamination with antibiotics	Usage in agriculture, aquaculture, medicine, veterinary and industry
2	ARB	HGT	Contamination with ARB/ARGs	Soil fertilization with manure, biosolids or treated wastewater
3	ARGs	HGT	Contamination with ARB/ARGs	Soil fertilization with manure, biosolids or treated wastewater
4	Bacteriophages	HGT	Contamination with ARB/ARGs	Soil fertilization with manure, biosolids or treated wastewater
5	Heavy metals	Co-selection	Contamination with heavy metals	Usage in agriculture, medicine, veterinary and industry
6	Microplastic	Sorption process of antibiotics, heavy metals and ARB; Co-selection; HGT	Contamination with ARB/ARGs, heavy metals, proliferation of ARB	Usage in agriculture, medicine, veterinary and industry
7	Organic carbon content above 5%	HGT	Proliferation of ARB	Soil fertilization with manure, biosolids or treated wastewater
8	Temperature above 30°C	HGT	Proliferation of ARB	Global warming

ARB, Antibiotic resistant bacteria; ARGs, Antibiotic resistance genes; ARB/ARGs, Antibiotic resistant bacteria or Antibiotic resistance genes; HGT, Horizontal gene transfer.

**Table 1 - Factors promoting AMR dissemination.**

(Table reference; Goryluk-Salmonowicz A and Popowska M (2022) Factors promoting and limiting antimicrobial resistance in the environment – Existing knowledge gaps. *Front. Microbiol.* 13:992268. Doi: 10.3389/fmicb.2022.992268.)

### Components and Strategies:

- 1) Safe drinking water, Sanitation and Hygiene (**WASH**)
- 2) Water sanitation and management
- 3) Sewage and Effluence management
- 4) Personal and house hold hygiene

### WASH, Water Sanitation and Management:

Low hygiene standards, low quality drinking water and poor sanitation are the key contributors of many diseases (especially enteric diseases and infections that follows faecal-oral transmission). They are directly proportional to the morbidity, use of antimicrobial drugs and resistant infections. Water based infections are very common in developing countries. In 2019, 1.4 million preventable deaths were attributed to unsafe water, sanitation and hygiene (WASH), and 1.27 million deaths were traced to infections with antimicrobial resistance (AMR) pathogens (Weets CM *et al.*, 2024).

Wastewater from agricultural practices, pharmaceutical manufacturing plants, and hospital effluents was established to promote AMR. Furthermore, stress factors such as the presence of antibiotics, heavy metals, pH, and temperature initiate and propagate AMR in bacteria living in wastewater. AMR in bacteria from wastewater was established to be either natural or acquired (Shepherd Sundayi Sambaza *et al.*, 2023). The used antimicrobials from human and animal's again re-enter the environment and further contribute to development of resistant genes and microbes.

WASH is a basic requisite for healthy lifestyle and it offers a good solution to break the source point in transmission cycle, that means if one follows proper sanitation and hygiene practices, has adequate knowledge regarding drinking quality water can highly decrease the chances of falling sick and can potentially decrease the use of antimicrobials (about 60-70%), thereby reducing emergence of superinfections. Although the scenario is changing in 21<sup>st</sup> century (regarding WASH) by implementing various schemes and standards in national level but still many countries are currently lacking in having quality water (due to pollution, water scarcity and improper water-based waste management), poor hygiene habits (due to lack of awareness and infrastructure).

According to Pinto Jimenez CE *et al.*, 2023; Most WASH interventions are implemented in 'open' systems at a community level and focus on providing infrastructure for clean water and sanitation or changing hygiene practices by humans, primarily aiming to reduce enteric infections by preventing faecal-oral transmission of pathogens between humans and decreasing human exposure to human faeces. These interventions do not commonly recognise the added benefit of WASH to reduce exposure to pathogens coming from/to animals other than those associated with diarrhoea, despite being implemented in agricultural communities mainly composed of smallholders and subsistence farmers in close contact with animals.

#### **Control strategies -**

- **Healthy drinking water:** providing quality drinking water, proper storage and disinfection of water (chlorination), waste water treatment, quality pipeline system, providing potable water to remote places.
- **Hygiene practices:** good personal hygiene practices, proper cleaning of dishes and hands (safe hand wash), having only indoor defaecation, proper immunization, eating good quality and quantity of food (food safety and security) etc.
- **Sanitation:** providing more national wide sanitation schemes, preventing open defaecation, treatment of septic tank contents & waste management strategies.

#### **Sewage and Effluence Management:**

Sewage from communities and effluence from manufacturing industries contains excretions, traces of antimicrobials, toxic chemicals and waste that can potentially drive microbes to become resistant

following exposure. Wastewater treatment plants (WWTPs) are key sources of antimicrobial resistance genes (ARGs) that could influence the resistomes of microbial communities in various habitats of the receiving river ecosystem. However, it is currently unknown which habitats are most impacted and whether ARGs, like certain chemical contaminants, could be accumulated or enriched in the river ecosystem (Lee, J., Ju, F., Beck, K. *et al.* 2023)

According to Chau KK *et al.*, 2022; Overall concordance of wastewater-human AMR prevalence estimates was reasonably high for both phenotypic (CCC = 0.85 [95% CI 0.8–0.89]) and genotypic approaches (CCC = 0.88 (95% CI 0.84–0.9)) despite diverse study designs, bacterial species investigated and phenotypic/genotypic targets.

### **Control strategies –**

- The key solutions include proper effluent treatment prior to disposal, proper segregation of waste, following 3R principles (reduce, recycle and reuse), photocatalytic processing, careful landfilling, avoid mixing to waste with nearby natural waste bodies, separate pipelines for water inflow and waste outflow – regularly checking pipelines to avoid leakages & mix of water.
- Solar photocatalytic processes were chosen considering the context of developing tropical countries. Among these processes, solar photo-Fenton has been proved effective for the elimination of antibiotic resistance genes (ARGs) from municipal wastewater treatment plant effluent (MWWTPE) at neutral pH in bench and pilot scale and also under continuous flow. Yet, ARG removal varies as according to the gene. Irradiation intensity and matrix composition play a key role on treatment efficiency for this purpose. The use of sulphate radical in modified solar photo-Fenton is still incipient for antibiotic resistant bacteria (ARB) and ARG removal. (Maria Clara V. M *et al.*,2021).

### **Sources For Potential Harmful Waste & Effluence (Sources for AMR Emergence):**

#### **Agri-production Industries:**

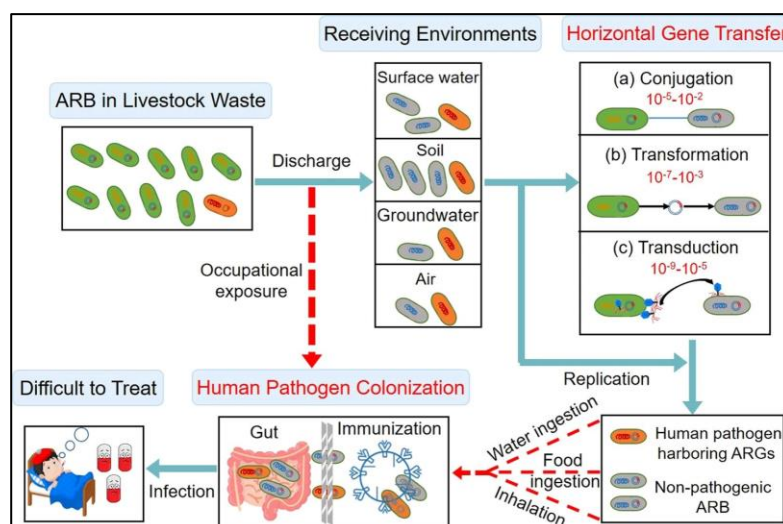
It includes agriculture and other food related sectors – livestock, poultry, crop production and aquaculture etc. Use of antibacterial and antiprotozoal antimicrobials are common in animal production industries and the use of antifungals is more in crop production. Improper treatment by farmers and quacks without sufficient knowledge, using antibiotics as growth promoters (to increase growth & production), improper biosecurity measures, easy over the counter availability, unnecessary inclusion of antibiotics to every clinical case led to abuse affecting both animal's health and environments.

Livestock sector has huge impact on AMR prevalence due to severe antibiotic abuse (especially in poultry industry). Most the antimicrobials used will be excreted and enters the environment (the soil and water) along with resistant bacteria and genes, they replicate and further infect other animals in environment and nearby human livelihood via drinking water, food and air (diffuse contamination and pollution). Antimicrobial residuals in livestock products & animal transport also transmit the AMR in

environment (Koutsoumanis K *et al.*, 2022). Aquaculture waste is one of the largest water pollution sources and in spread of ARG, ARB. The use of antimicrobials in aquaculture is very high and after harvest when the water is released in to natural bodies it will contaminate the environment. Antimicrobial residual in fishes and prawns severely impact the gut health in nearby by habitants (by entering food chain) especially children, pregnant women and immuno-compromised people.

### Control strategies –

- Regulations on using Antibiotics in production industry, treatment should be only done by qualified professionals, following proper withdrawal period, good animal husbandry practices, waste generated from the farms should not be released in to soil or nearby waste bodies or into drains without treatment, promoting healthy and organic farming, educating farmers regarding AMR and its impact on health, promoting good manufacturing practices, using alternative growth promoters (enzymes, pre and probiotics, immunization, organic acids, phytochemicals etc.), setting onsite waste treatment techniques, vermicomposting (Masaru Usui *et al.*, 2024), restricting aquaculture and livestock rearing near human habitats and at nearby water bodies etc.



**Figure 1: Potential transfer pathways of ARGs from livestock waste to human pathogens.**

(Picture Reference - Ya He *et al.*, 2020; He, Y., Yuan, Q., Mathieu, J. Et al. Antibiotic resistance genes from livestock waste: occurrence, dissemination, and treatment. *Npj Clean Water* 3, 4 (2020). <https://doi.org/10.1038/s41545-020-0051-0>.)

### Pharmaceutical Industries:

The need of antimicrobials is spiked in recent decades and because of demand there is severe rise in pharmaceutical industries. Though these industries are major players in fighting against the microbes, they in turn contribute to development of resistance mainly by the effluent produced while manufacturing (contains active antimicrobial ingredients). Pharmaceutical wastewater, loaded with antibiotics and resistance genes, poses a significant environmental risk, mainly due to inadequate treatment and irresponsible disposal. The pharmaceutical industry is a notable contributor to environmental antibiotic pollution, with varying effluent management practices (Rehab A. Rayan, 2023).

Many pharmaceutical companies will dispose the waste without proper neutralization and inactivation, they simply dump in nearby water bodies and in pits or dump yard. Continuous exposure to the active ingredients from waste will drive the microbes to acquire resistance. Once pharmacological waste is dumped, the pollutants also enter into the food chain (into different trophic levels), this is a serious health threat to people and animals who are exposed and outbreaks of resistant infections can be expected in nearby livelihoods. According to Kotwani A *et al*, 2023., The presence of antibiotic residues in the pharmaceutical effluent was considered inconsequential by State Pollution Control Boards (SPCBs) and small and medium-scale pharmaceutical companies (SMPCs) and majority of stakeholders imputed other causes as major contributors to AMR. However, the MNCs were well aware of the contribution of pharmaceutical effluent to AMR and CPCB also considered Antibiotic residues (ARs) as direct source of AMR.

### **Control strategies –**

- Rules and regulations on dumping waste from the pharmacological effluent, transparency in disposal of waste and regular inspection of manufacturing plants, Predicted No Effect Concentrations (PNECs), thorough treatment of waste water from these industries, adequate testing of water bodies which are situated nearby company, still requires more research & development of new technologies for aiding in disposal of active antimicrobials in effluent.
- **Predicted No Effect Concentrations (PNECs)**; A PNEC represents the concentration of a substance (in water, sediment, soil, or air) that is not expected to induce adverse effects in most organisms, in an ecosystem that is chronically exposed. For the majority of substances, ecotoxicity data are scarce and represent only a small number of species and effects (CEPA 1999). Currently a limited amount of pharmaceutical compounds has PNEC values (for limited no. of antibiotics), but there is need of PNEC values of all other antimicrobials manufactured including antifungals, antivirals.
- Controlling wastewater effluents to the default PNEC is expected to result in a significant reduction of antibiotic discharge, especially for antibiotics where specific PNECs have not been defined. The default PNECs may then be applied in a site-specific manner that considers characteristics of the local situation (e.g., wastewater treatment capabilities, stream flow, location of receptors). (Vestel J *et al*, 2022).

### **Hospitals, Health Care Facilities and Biological Labs:**

Human and veterinary hospitals act as a source of transmission of AMR by many ways (from hospital generated waste, disposed sewage, hospital waste water etc.)

- 1) Excretions & secretions (includes resistant microbes), antimicrobial metabolites & residues from sick patients entering into sewage.
- 2) Improper disposal of unused and old/expired antimicrobials.
- 3) Iatrogenic resistant infections

WASH and proper hygiene practices are key methods to be followed by medical professionals and staff in order to prevent transmission of infections (esp. resistant pathogens). Proper disinfection protocols and sanitation of medical equipment is necessary before using them for another patient (like forceps, endoscope etc.), it will decrease the load of resistant organisms in hospital environment and also decreases the chance of Hospital Acquired Infections (HAIs).

*Hospital Acquired Infections:* AMR was more with hospital acquired organisms and against commonly used antibiotics that are available since long period. Variation of resistance and sensitivity pattern with time and geographical location (Saravanan R *et al.*, 2013). The consistent emergence of antimicrobial resistant bacteria, particularly Gram-negative bacteria is contributing to the challenge of Hospital Acquired Infections (HAIs) (Molly Kukua Abban *et al.*, 2023).

### **Control strategies –**

- Establishing WASH guidelines in every healthcare facility, medical staff and health care workers should follow proper hygiene practices like hand washing, using sanitizers & masks, separate disposal of waste (colour based biomedical dustbins), organic waste and infectious waste should be properly disposed, faecal material should be properly treated before disposal. Toilet wastes should not be connected directly to sewage and should be collected separately, clean hospital premises, regularly conducting AMR & epidemiological studies, antimicrobial stewardship, establishments of technologies at every health care facility for treatment of generated waste, PPE kits for waste handlers, minimising the waste generation by educating the staff etc.
- These same measures are can also implemented in biological labs (those in which mainly works on pathogenic and resistant microbes, antimicrobials, chemicals etc.)
- **Antimicrobial Stewardship:** The term antimicrobial stewardship includes comprehensive quality improvement activities of antimicrobial use in reducing or containing the transmission of antimicrobial-resistant pathogens through optimum selection, dosing, route, and duration of treatment (O.J. Dyar *et al.*, 2017). Antimicrobial stewardship (AMS) programs have shown to reduce the emergence of antimicrobial resistance (AMR) and health-care-associated infections (HAIs), and save health-care costs associated with an inappropriate antimicrobial use (Al-Omari, A *et al.*, 2020).

### **Animal Manure:**

Fertilization with natural products is one of the main routes responsible for the introduction of antibiotic residues, ARG and zoonotic bacteria from animals to soil and, for the possible further dissemination into drinking water (Marutescu LG *et al.*, 2022). Animal manure application (as a bio fertilizer) in agriculture is a traditional approach to increase the growth & production from the crops, but the overuse of antibiotics in animals (ranging from cattle to poultry) and the manure of these animals when used in fields the resistant bacteria and genes contaminate the soil and water. Chicken and swine manure

also exhibit greater ARG diversity than cow manure (Qian, X *et al.*, 2018). The application of commercial organic fertilizer and composted manure significantly increased the abundance of ARGs and pathogens compared with mineral fertilizer, especially for the surface soil (Houyu Li *et al.*, 2022). The texture of soil to which manure was applied determined the persistence of the targeted ARGs (clay < peat < sand), thus affecting the fate of AMR in the environment (Gonçalo Macedo *et al.*, 2020).

Plant-based substrates which are used in bio-gas plant were found to be associated with AMR contamination, including culturable Gram-positive ARB (mainly Gram-positive *Bacillus* spp.), and Gram-negative pathogenic bacteria-associated ARGs and plasmids (He Sun *et al.*, 2022). Humans on eating raw and unclean food or by improper cooking, there is a high chance of getting sick because of these resistant microbes [the ARG in agricultural field (by transformation process) can make the bacteria resistant]. Similarly, it also happens when the poultry excreta are used in aquaculture to fertilize ponds. The residues and ARB may enter to fish and further infect the humans.

#### **Control strategies –**

- Separating manure of sick and animals undergone treatment and disposed properly. Anaerobic digestion of food, regulating use of poultry excretions in aquaculture, Composting seems to reduce or eliminate most of antibiotics residues, enteric bacteria, ARB and different representative ARG in manure more rapidly and effectively than lagoon storage (Marutescu LG *et al.*, 2022), there is requirement in research for efficient treatment of manure before agriculture application and to decrease the load of ARB and ARG in manure.

#### **Use of Biocides in various sectors:**

- Biocides are widely used in healthcare and industry to control infections and microbial contamination (Jones IA *et al.*, 2021). It is pertinent to note that the development of antibiotic resistance as a result of the selective pressure exerted by their intensive use, and sometimes misuse, is well documented (WHO, 2000). The possible linkage between biocide and antibiotic resistance in bacteria and the role of biocides in the emergence of such resistance has provided more controversies in their extensive and indiscriminate usage (Maillard JY., 2005).
- Measures to be taken to optimize the use of biocides in healthcare services (especially for diagnostic equipment) and in industries. The usage should be as prescribed by the manufacturing company without fail (to control the load of residual bacteria and ARB). Education regarding the proper use to medical professionals.

#### **Personal Hygiene and AMR at House Hold Level:**

A person (regardless which profession) should always follow the proper hygiene norms not only for social well-being but also to decrease the load to microbes they are carrying from their work place or from travel or from schools etc. The carried organisms (including ARB) have potential to infect the other

family members, which can be avoided by following the simple hygiene practices.

### Key Notes:

- **Technology gap** – there is a huge gap between the current availability and requirement of technology especially regarding the treatment of effluent from industries, treatment of waste from livestock production farms, neutralizing antimicrobials in contaminated water bodies, availability of PNEC for all the antimicrobials produced, how to dispose the expired and unused antimicrobials etc. These are only few requirements that are addressed, there is a need of thorough research and knowledge dissemination regarding environmental hygiene and handling antimicrobials.
- **Monitoring and surveillance** – regular monitoring and surveillance is necessary to understand the scenario of AMR in environment so it can improve the healthcare provided to the humans and animals and to understand about the future catastrophes due to the antimicrobial abuse. Surveillance for AMR in the environment provide perspectives on knowledge of the resistant organisms and resistance genes present in whatever population is contributing to that environment and knowledge of the resistant organisms that a receptor may encounter through exposure in that environment (Hart A *et al.*, 2023).
- **Education and awareness** – educating the healthcare professionals and general public is necessary to optimize the use of antimicrobials with appropriate dosage and duration, about withdrawal period to farmers, public health officers, in production industry & slaughter house technicians is necessary. General public should behave responsible regarding sewage, handling water, personal hygiene, septic tank and sanitation. These are small topics when followed together there will be a huge impact in decreasing ARB and ARG in environment.
- **Governance** – regulating the use of antimicrobials and there is necessary to have a rule to avoid pharmacists to give antimicrobials over the counter without prescription, schemes to provide quality water and public toilets (to avoid open defaecation), strict rules to prevent dumping septic tank content directly into drains and natural water bodies, on pharmaceutical industries and other chemicals industries about the processing of effluent, on collection of expired drugs from households & communities etc.
- **Quadripartite One Health Approach:** In 2015, a global action plan on AMR was among the first attempts to coordinate global action on AMR (WHO, 2015). Subsequently, multiple additional resolutions and strategies have been adopted by international organizations, such as the World Health Organization (WHO), the World Organization for Animal Health (WOAH, formally known as OIE), and the Food and Agriculture Organization of the United Nations (FAO). More recently, the United Nations Environment Program (UNEP) formally joined these efforts against AMR under the Quadripartite agreement. (Pinto Ferreira J *et al.*, 2022).

- The research agenda focus on five pillars:
  1. Transmission
  2. Integrated Surveillance
  3. Interventions
  4. Behavioural insights and change
  5. Economics and policy (WHO, 2023)

### Conclusion:

It is evident that following prevention & control measures can decrease the load of infectious organisms and need of antibiotic use. Set of practices on daily basis like water sanitation, proper industrial effluent management, waste management can decrease the load of pathogenic organisms, pollutants and chemicals entering into the environment and further infect humans and animals. Thus, concept of hygiene helps in countering the emergence of resistant organisms and transfer of genes through environment. AMR cannot be alone countered by controlling antibiotic use in healthcare sector and protection system and it is also required to break the transmission cycle so that no need or minimise the use of antibiotics. Sanitation and hygiene may be considered as small topics but the impact of them in our lives and on AMR control is huge. Though the current knowledge regarding the extent of AMR & it's impact on the environment is scarce, there is necessity to understand how environmental hygiene impact the acquiring resistance. Further research on environmental hygiene is necessary and regulations to be laid in order to control the AMR globally.

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**Table 1 -**

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**Figure 1 -**

He, Y., Yuan, Q., Mathieu, J. Et al. Antibiotic resistance genes from livestock waste: occurrence, dissemination, and treatment. *Npj Clean Water* 3, 4 (2020). <https://doi.org/10.1038/s41545-020-0051-0>. Copyright © 2020. Publisher: Springer Nature. <https://www.nature.com/articles/s41545-020-0051-0>.