

Research Progress on the Distribution Characteristics, Ecological Risks, and Removal Technologies of Antibiotic Residues and Resistance in the Environment

Haojun Zhao

*Kaiping Kaiqiao Middle School, Jiangmen, China
1170213468@qq.com*

Abstract. Antibiotic residues and resistance have emerged as pervasive environmental pollutants because of extensive use in medicine, agriculture, and aquaculture. A review of recent literature reveals a lack of comprehensive analyses which integrate distribution characteristics, ecological risks, and the full spectrum of removal technologies across environmental matrices. This study synthesizes recent research on distribution patterns, ecological and public health risks, and removal technologies in relation to antibiotic residues and resistance. The results reveal significant ecological impacts: inhibiting microbial and primary producer activity, altering community structures, and reducing biodiversity, while potentially undermining the efficacy of antibiotics in medicine. Various technologies have been explored and implemented to remove antibiotic contaminants and mitigate antibiotic resistance in environmental matrices, each employing different mechanisms and exhibiting varying efficacy in eliminating antibiotics or antibiotic resistance genes. To combat antibiotic pollution effectively, integrated strategies under a One Health framework are essential.

Keywords: Antibiotics, Quantifying Ecological Risks, Wastewater Effluents, Agricultural Runoff and Waste, Pharmaceutical Manufacturing

1. Introduction

Antibiotic residues and resistance are widespread pollutants resulting from long-term use in medicine, agriculture and aquaculture [1,2]. Releases from wastewater, agricultural run-off, manure and pharmaceutical discharges create burdens in water, soil and biota [3]. Surface waters hold ng/L–µg/L levels, although manufacturing hotspots can reach mg/L [4-5]. Agricultural soils accumulate residues because most veterinary drug mass is excreted unmetabolised, yielding µg/kg–mg/kg burdens [6]. These contaminants move among compartments; residues bioaccumulate in wildlife and crops [7]. Notably, sub-inhibitory exposures select antibiotic-resistant bacteria and resistance genes, enlarging environmental reservoirs relevant to clinics [8-10]. Co-pollutants such as heavy metals and microplastics can intensify selection and transport [11-12].

Wastewater treatment incompletely removes residues and genes; advanced oxidation, activated carbon, optimised biology and combined approaches achieve higher removal, while emerging phage

and CRISPR tools target resistance directly [13-15]. Nevertheless, comprehensive reviews integrating distribution characteristics, ecological risks, and the full spectrum of removal technologies across environmental matrices remain limited. This review, therefore, systematically examines the global distribution patterns of antibiotic residues and resistance in environmental compartments, evaluates their ecological risks to ecosystems and human health, and critically assesses current and emerging removal technologies. By synthesizing recent advances, this review aims to identify knowledge gaps and inform integrated management strategies under a One Health approach [16].

2. Methodology

This review employed a comprehensive literature survey to assess the distribution, ecological risks, and removal technologies of environmental antibiotic residues and resistance. Academic databases were systematically reviewed, using keywords such as “environmental antibiotics,” “antibiotic residues,” “antibiotic resistance genes (ARGs),” “ecological risk,” and “antibiotic removal.” Chinese-language studies were also examined to incorporate regional data. Over 300 publications were screened, and about 100 key sources (research articles and reviews) were chosen for detailed analysis based on relevance and quality. From these sources data on antibiotic concentrations across environmental media (water, soil, biota) were extracted. For ecological risk assessment, this article compiled studies reporting toxicity thresholds (e.g., median effective concentration EC_{50} or no-observed-effect concentration NOEC values) and calculated risk quotients ($RQ = \text{measured concentration} / \text{predicted no-effect concentration}$) for antibiotics in various ecosystems [17].

To address human health implications, the study included recent high-impact studies quantifying the risks of environmental ARGs to clinical outcomes (e.g., horizontal gene transfer of ARGs to human pathogens). In evaluating removal technologies, the article reviewed conventional and advanced treatment methods and compiled reported antibiotic removal efficiencies from wastewater treatment studies covering physical, chemical, and biological processes [14,18]. The article also focused on emerging remediation approaches such as biochar amendments, phage therapy, and CRISPR-based tools highlighted in recent research. Throughout the review, data from different studies were compared and synthesised to identify consensus findings and knowledge gaps.

3. Distribution characteristics of antibiotic residues and resistance

3.1. Water

Water bodies are major recipients of antibiotic pollution and serve as conduits dispersing these contaminants. Antibiotics have been detected in virtually all types of aquatic environments – rivers, lakes, groundwater, and even oceans – typically at ng/L to low $\mu\text{g/L}$ concentrations [19]. However, much higher levels occur near points of intense pollution. Concentrations tend to be elevated in regions with intensive antibiotic use or limited wastewater treatment. Major sources include wastewater discharges (municipal and hospital effluents), agricultural runoff from manure-fertilised lands, pharmaceutical manufacturing effluent, and aquaculture inputs [13,20]. Conventional wastewater treatment plants reduce but do not fully eliminate these drugs, so treated effluent still releases many antibiotics in the high ng/L to low $\mu\text{g/L}$ range [21,22]. For example, urban WWTP effluent often contains common antibiotics such as sulfamethoxazole, ciprofloxacin, and azithromycin between 90 to 6000 ng/L [23]. In some cases, extreme point-source pollution occurs near pharmaceutical factories: effluents have contained antibiotics at mg/L concentrations, causing

downstream waters to reach levels thousands of times above safe benchmarks [24]. A well-known incident in India found ciprofloxacin in a drug manufacturing plant effluent above 1 mg/L, with downstream river water around 2.5 mg/L [4,5]. Aquaculture (fish and shrimp farming) is another significant source, as antibiotics used in ponds are directly released into surrounding waters, particularly where usage is poorly regulated [25]. Sediments often accumulate higher antibiotic concentrations than the overlying water due to sorption of compounds like fluoroquinolones to particulates, which limits their dispersion in water columns. Even trace concentrations (ng–µg/L) of antibiotics in surface waters are ecologically relevant: chronic exposure at these sub-inhibitory levels can still select for resistant microbes [26]. A recent global survey found that antibiotic concentrations in many rivers worldwide exceed thresholds known to promote resistance or harm aquatic life [27]. Consistently, water bodies receiving antibiotic pollution harbour elevated levels of ARGs and resistant bacteria compared to cleaner upstream sites [28].

3.2. Soil

Soil is a major sink for antibiotic residues, especially in agricultural settings. Across land uses, soil residues span microgram-per-kilogram to occasional milligram-per-kilogram spikes, with tetracyclines and fluoroquinolones showing the highest persistence (Appendix A. Table 1). Agricultural soils receive antibiotics primarily through land application of animal manure and sewage sludge (biosolids), as well as irrigation with contaminated water. Because a large fraction of veterinary antibiotics is excreted unmetabolised, manure-amended soils tend to accumulate antibiotic residues over time [6,29]. Heavily fertilised farm soils commonly contain antibiotics in the tens of µg/kg to low mg/kg (dry weight) range, with some intensive livestock farming sites reporting total antibiotic levels in the high mg/kg (thousands of µg/kg) [6]. Antibiotic distribution in soil is often heterogeneous: concentrations are highest at points of manure deposition (e.g., feedlots, manure storage areas) and decrease with distance and depth due to dilution, sorption, and degradation processes [30]. Many antibiotics adsorb strongly to soil particles, which limit vertical leaching into groundwater [31]. However, more mobile compounds like certain sulphonamides can occasionally percolate into subsoils under conducive conditions [32]. Land use and management practices strongly influence soil antibiotic burdens. Studies show that soils with long-term manure application have significantly higher antibiotic and ARG concentrations than soils with minimal anthropogenic influence. For example, one comparison found soils near intensive animal farms had over 20 times higher antibiotic and ARG levels than soils with little human impact [10]. Likewise, vegetable fields irrigated with reclaimed wastewater can accumulate human-use antibiotics to levels above those in rain-fed fields [33]. Known “hotspots” include manure lagoons, compost piles, and chronically fertilised plots. Composting manure can reduce antibiotic content but often does not eliminate residues or ARGs completely [34]. Certain persistent antibiotic classes tend to accumulate in soil due to strong binding to organic matter and clay, whereas others degrade relatively quickly [6]. Soil conditions also affect degradation rates [29]. Importantly, co-pollutants in manure can influence antibiotic persistence and resistance selection. Manure often contains heavy metals and disinfectants; these can co-select for resistant microbes and sometimes inhibit antibiotic biodegradation, prolonging the persistence of both antibiotics and ARGs in soil [11,35].

3.3. Biota

Antibiotic residues also accumulate in living organisms, serving as another distribution vector through food webs. Aquatic biota in contaminated waters – including fish, shellfish, and other fauna

– can bioaccumulate antibiotics in their tissues [36,37]. Uptake occurs via ingestion of contaminated water and food, or by direct absorption across gills. For example, fish living downstream of wastewater outfalls have shown sub- $\mu\text{g/g}$ antibiotic levels in muscle and liver, while in severely polluted sites fish tissues reached tens of $\mu\text{g/g}$ [38,39]. Bivalves (e.g., mussels) likewise accumulate antibiotics via filter-feeding [40]. In aquaculture, antibiotic use can leave residual drugs in farmed fish and shrimp; if harvest withdrawal times are not observed, a few $\mu\text{g/g}$ of the drug may remain in edible tissues [40], thereby exposing consumers and releasing antibiotics via processing or waste. Terrestrial livestock treated with antibiotics can carry residual antibiotics in meat or milk, though regulations and withdrawal periods usually keep these residues below safety limits [41]. Plants grown on contaminated soil or irrigated with antibiotic-tainted water can also take up these compounds [7]. For example, leafy vegetables from manure-fertilised fields have been found to contain sulfonamides and fluoroquinolones at tens of ng/g [42,43]. Under extreme conditions – such as irrigation with pharmaceutical manufacturing wastewater – plant tissues have even reached $\mu\text{g/g}$ levels of antibiotics [44]. Terrestrial wildlife and scavengers near human activity can likewise be exposed; studies have found antibiotic residues or resistant bacteria in wild birds and mammals around polluted sites [45]. Even though these residual levels in biota are generally low (far below therapeutic doses for animals), their presence raises concerns about subtle ecological effects (e.g., disrupted gut microbiomes in exposed animals) and provides additional pathways for resistance dissemination. Humans may indirectly ingest antibiotics or resistant microbes by consuming contaminated fish, shellfish, or produce, linking environmental antibiotic pollution to food safety. Ongoing monitoring of antibiotic residues in biota is critical for evaluating these exposure pathways and managing the associated risks.

3.4. Source analysis

The major pathways introducing antibiotics (and associated ARGs) into the environment are well known. Key sources include wastewater effluents from human use (municipal and hospital sewage), agricultural runoff and waste from livestock operations, industrial discharges from pharmaceutical manufacturing, and aquaculture activities [13,20]. Human sewage is a primary source since many antibiotics are excreted unmetabolised; even after conventional treatment, sewage effluent still contains numerous antibiotics that enter surface waters [13]. Hospitals contribute concentrated multi-antibiotic waste, elevating antibiotic levels in urban sewage [46]. In agriculture, the widespread use of antibiotics in livestock means manure and farm runoff are major contributors [47,48]. Regions with intensive poultry or swine farming often show heightened antibiotic residues and ARGs in nearby soils and waterways [10]. Aquaculture (fish/shrimp farming) also releases antibiotics directly into water, particularly where use is unregulated [40]. Pharmaceutical manufacturing is another severe (though localised) source when factory wastewater contains extremely high antibiotic concentrations [4,5]. In practice, multiple sources often converge in one watershed – for example, a river might receive both urban wastewater and agricultural runoff in different reaches. Therefore, effectively managing environmental antibiotics requires a multipronged approach targeting each major pathway. Improving wastewater treatment, better managing animal waste, treating industrial effluents, and proper drug disposal should all be pursued in parallel to reduce overall contamination levels, as each intervention contributes to curbing the environmental antibiotic resistance problem [20].

3.5. Co-occurrence of antibiotics with other pollutants

In real-world scenarios, antibiotics often co-occur with other contaminants, and such combined pollution can amplify the development of antibiotic resistance [35]. One important co-pollutant group is heavy metals. Heavy metals (e.g., copper, zinc, arsenic) commonly accumulate in the same settings as antibiotics (such as manure-amended soils and certain wastewaters), and they can co-select for antibiotic-resistant bacteria [11]. Bacteria under chronic metal stress may develop cross-resistance to antibiotics via shared defence mechanisms or genetic linkages between metal resistance genes and ARGs. Consequently, sites with high heavy metal contamination often have elevated ARG levels even without exceptionally high antibiotic concentrations [35,49]. For example, long-term fields with heavy manure and metal inputs show ARG abundances correlating strongly with soil metal content [10]. Reducing heavy metal pollution in the environment (e.g., limiting copper and zinc additives in animal feed) could help lower this ancillary selection pressure for resistance.

Another notable co-pollutant is microplastics. Microplastic particles (now ubiquitous in water and soil) can adsorb antibiotics on their surfaces and quickly develop biofilms enriched with ARGs. In essence, microplastics can ferry antibiotic compounds and resistant microbes together, allowing ARGs to disperse beyond their original sources [12,50]. Studies have found that microplastics from polluted sites (e.g., aquaculture ponds) carry higher ARG loads than the ambient water, indicating that microplastics can concentrate and transport resistance elements [12,50]. This suggests microplastics facilitate the co-dispersal of antibiotics and ARGs, effectively linking pollution sources to far-field environments. Other pollutants can also interact with antibiotics to encourage resistance. For instance, the antimicrobial biocide triclosan (commonly used in soaps) can co-select for antibiotic-resistant bacteria in the environment [51].

4. Ecological risks and health hazards

4.1. Ecotoxicity to non-target organisms

The presence of antibiotic residues in the environment can adversely affect a range of non-target organisms. Many antibiotics are designed to kill or inhibit bacteria, but at environmental concentrations they can also impact algae, aquatic plants, invertebrates, and higher fauna. Ecotoxicological studies indicate that even low levels ($\mu\text{g/L}$ range) of certain antibiotics can inhibit algal growth and photosynthesis [52]. For example, *Lemna minor* (duckweed) exposed to fluoroquinolone antibiotics showed significant growth inhibition at concentrations below 0.1 mg/L [53]. Similarly, chronic exposure to macrolide or sulfonamide antibiotics has been reported to impair algal reproduction and reduce chlorophyll production at tens of $\mu\text{g/L}$ levels [54]. Antibiotics can also affect aquatic invertebrates: crustaceans and insect larvae have exhibited developmental delays or reproductive toxicity when continuously exposed to certain antibiotics in the low $\mu\text{g/L}$ range [54].

In soil ecosystems, antibiotic residues may disrupt soil microbial activity and nutrient cycling, indirectly affecting soil fauna such as earthworms or nematodes. For instance, earthworms in soil with antibiotic contamination have been found to bioaccumulate the compounds and experience changes in their gut microbiota and growth rates [55,56]. Pharmaceutical pollutants have even been linked to broader ecological consequences: a classic case is the veterinary drug diclofenac (an anti-inflammatory, not an antibiotic) which caused catastrophic vulture population declines in South Asia when vultures fed on treated livestock carcasses [57]. This example underscores that pharmaceuticals in the environment can have food-web-scale effects. While most antibiotics are less acutely toxic to vertebrates than pesticides or heavy metals, chronic exposure can still cause subtle

harms such as altered fish behaviour and immune function. Risk assessments often find that measured environmental concentrations of antibiotics approach or exceed predicted no-effect concentrations (PNECs) for sensitive species in hotspot areas. For example, antibiotic levels in some wastewater-impacted rivers yield RQ values above 1 for algae and cyanobacteria, indicating a high potential for ecological impact [27,55].

4.2. Effects on microbial communities and ARGs

Beyond individual species effects, antibiotics can significantly alter microbial community structure and function in water, soil, and even air. In environmental settings, microbial communities are complex and diverse, but antibiotic exposure tends to suppress susceptible bacteria and select for resistant strains, often reducing overall microbial diversity and disrupting ecosystem processes like decomposition and nutrient cycling. For example, long-term exposure to manure containing antibiotics has been shown to shift soil microbial communities toward more resistant taxa and to decrease populations involved in nitrogen cycling [48,58]. Field studies report that soils fertilised with antibiotic-laden manure have different community profiles and reduced microbial evenness compared to control soils [58]. In river microcosms, even low doses of antibiotics have altered community composition within days, favouring bacteria that carry ARGs and diminishing more sensitive competitors. Antibiotic pressure not only changes which species are present, but can also induce physiological stress responses.

Many bacteria under sub-lethal antibiotic stress activate the SOS response, which increases mutation rates and can mobilise genetic elements (transposons, integrons) that carry ARGs [59,60]. This phenomenon can accelerate the development and horizontal transfer of resistance. In one classic laboratory study, sub-inhibitory antibiotic exposure led to a ~10-fold increase in the rate of horizontal gene transfer of a resistance plasmid, due to SOS-mediated stimulation of conjugation functions [61]. In natural settings, co-occurring stressors can amplify these effects (see Section 3.2.3): for example, the presence of heavy metals or biocides alongside antibiotics can further enrich multidrug-resistant strains [35]. Environmental monitoring has revealed that ARGs are ubiquitous in human-impacted habitats. High-throughput DNA analyses find dozens to hundreds of distinct ARGs in sediments, soils, and even air samples near sources like wastewater plants and farms [8,62]. Importantly, ARG abundances (e.g., copies of resistance genes per gram of soil or per mL of water) often correlate with antibiotic concentrations in those environments, reflecting the selective pressure effect [28].

4.3. Human health risks

Antibiotic resistance is not only an environmental issue but also a public health threat, as environmental reservoirs of ARGs and ARB can potentially transfer into human populations. The propagation of resistance in nature increases the baseline reservoir of resistance determinants that pathogenic bacteria can acquire. There are several pathways by which environmental antibiotic pollution and resistance can impact human health:

Contaminated water and food: Humans can be exposed to antibiotics or ARB through contaminated drinking water, recreational water use, or food. Studies have found that swimmers in rivers with high faecal pollution are at elevated risk of acquiring antibiotic-resistant bacteria (e.g., resistant *E. coli*) compared to non-swimmers [63]. Irrigation of crops with inadequately treated wastewater can introduce antibiotics and ARGs to produce; consuming raw vegetables from such fields has been linked to ingestion of bacteria carrying ARGs [37]. Seafood from aquaculture or

coastal areas near effluent discharges can also carry antibiotic residues and resistant bacteria, which may colonise the human gut when consumed.

Occupational and community exposure: People living near intensive livestock operations or manure-fertilised fields may inhale or come into contact with resistant bacteria. A study in Pennsylvania found that community members in high-density swine farming areas – especially those near fields where swine manure was applied – had significantly higher rates of MRSA (methicillin-resistant *Staphylococcus aureus*) infections [64]. The analysis attributed approximately 11% of community-acquired MRSA cases in the region to exposure from swine operations and manure-fertilised crop fields [64]. This suggests that environmental dissemination of ARB from farms contributes measurably to human infection risks. Similarly, airborne spread of resistant bacteria from animal facilities has been documented: for instance, resistant *Staphylococcus* and *E. coli* have been captured in air samples kilometres downwind of farms [45], indicating a potential route of community exposure via air.

Gene transfer to human pathogens: Perhaps the most insidious risk is the transfer of ARGs from environmental bacteria into human pathogens. Environmental bacteria (often non-pathogenic) can act as reservoirs of resistance genes that, through horizontal gene transfer, end up in pathogenic strains. The discovery of the NDM-1 carbapenemase gene in environmental bacteria exemplifies this concern. NDM-1 (New Delhi metallo- β -lactamase) was initially identified in clinical isolates, but subsequent surveys found NDM-1-producing bacteria widely present in New Delhi surface waters and drinking water supplies, likely due to sewage contamination [65]. This indicated that a critical resistance gene had spread into the environment, from which it could continually re-enter the clinic. Other studies have found similar overlap between environmental resistomes and clinical resistance [13]. The risk is that ARGs that evolve or amplify in the environment can make infections harder to treat.

Global public health burden: Antibiotic-resistant infections already cause significant mortality and morbidity (an estimated 1.27 million deaths in 2019 were directly attributable to drug-resistant bacterial infections, with many more associated deaths) [66]. Environmental pathways contribute to this burden by spreading resistance across geographic and ecological boundaries. For instance, international travel and trade can distribute ARB/ARGs found in water or food to new regions. Environmental hotspots like WWTPs have been termed “reservoirs and reactors” of antimicrobial resistance, where multi-resistant organisms can proliferate and eventually reach humans [22]. Inadequate sanitation infrastructure globally means that millions of people come into daily contact with water contaminated by antibiotics and ARB, heightening infection risks.

5. Removal technologies for antibiotics and resistance

A variety of technologies have been explored and implemented to remove antibiotic contaminants and mitigate antibiotic resistance in environmental matrices. These range from conventional treatment processes to advanced and emerging methods. Each technology category has different mechanisms and efficacy profiles for eliminating antibiotics or ARGs.

5.1. Conventional treatment

Conventional wastewater treatment (e.g., activated sludge biological processing in municipal WWTPs) achieves only moderate removal for many antibiotics, typically reducing around 20–75% of the total antibiotic load across a treatment plant [24]. For example, tetracyclines are effectively removed (>80%) largely by sorption to sludge, whereas fluoroquinolones and macrolides often show

lower removals (~0–50%) because they persist through standard biological treatment [22,67]. Sulfonamides and trimethoprim tend to have intermediate removals (roughly 30–60%). Since conventional treatment is not specifically designed to target micropollutants, removal often relies on incidental biodegradation and adsorption; effluent concentrations on the order of hundreds of ng/L can remain [21]. Importantly, conventional WWTPs do reduce the load of resistant bacteria to some extent (via physical settling and disinfection), but many ARB and ARGs survive and are released. Typically, a 1–2 log unit (90–99%) reduction in culturable bacteria occurs through secondary treatment and disinfection, yet studies find ARG copies in treated effluent only about one order of magnitude below influent levels, indicating only partial ARG removal [68,69].

5.2. Advanced treatment

Advanced physicochemical treatments show much higher removal potential for antibiotics. Advanced Oxidation Processes (AOPs) – such as ozonation, UV/H₂O₂, or Fenton reactions – generate highly reactive radicals that degrade antibiotic molecules. Full-scale ozonation of WWTP effluent has demonstrated removal rates of 70–99% for many antibiotics [67]. For instance, ozonation at a dose of ~5 mg/L O₃ can remove >90% of ciprofloxacin, sulfamethoxazole and macrolide antibiotics within minutes [67,70]. Ozone effectively breaks down antibiotic structures (though it may form transformation products which are usually less bioactive or toxic than the parent compounds). Chlorine disinfection, a common tertiary step, can also oxidise certain antibiotics: chlorination has been reported to eliminate ~93–99% of trimethoprim and significantly reduce tetracyclines, sulfonamides, and macrolides in wastewater [71,72]. However, chlorination by-products and the potential selection for chlorine-resistant bacteria (some of which carry ARGs) are noted concerns. UV irradiation alone is generally less effective for antibiotic removal (often <20% reduction at standard disinfection doses) because many antibiotics are not highly photosensitive [71]. UV can damage extracellular DNA, potentially helping to reduce free ARGs, but many ARGs in wastewater are carried within cells or protected in particles and thus survive typical UV exposure [69,73]. Among adsorption-based methods, activated carbon (either granular or powdered) can adsorb a broad range of antibiotics very effectively, often removing >80% of compounds that are hydrophobic or have aromatic structures [74]. Adsorption, however, is a phase-transfer process rather than destruction – the antibiotics are concentrated on the carbon, so the spent carbon must be regenerated or disposed of safely to avoid secondary release.

6. Conclusion

Environmental contamination with antibiotic residues and the proliferation of antibiotic resistance in ecosystems pose a multifaceted challenge at the interface of environmental and public health. This review has highlighted that antibiotics are now detectable across virtually all environmental media. Hotspots such as wastewater outfalls and pharmaceutical manufacturing sites can reach extremely high antibiotic levels, driving the local accumulation of antibiotic-resistant bacteria and genes. These pollutants have demonstrable ecological impacts, from inhibiting microbial and primary producer activity to altering community structures and reducing biodiversity. They also contribute to an expanded environmental resistome that can potentially transmit into pathogenic bacteria, undermining the efficacy of antibiotics in medicine. Critically, conventional infrastructure and practices are not fully containing the issue. Wastewater treatment plants, while removing the bulk of organic matter and pathogens, are not explicitly designed to eliminate micropollutants like

antibiotics or completely halt the release of ARGs. As a result, treated effluents often still carry a residual cocktail of drugs and resistant microbes into downstream environments.

Addressing this complex problem requires a concerted One Health approach, recognising the interconnectedness of human, animal, and environmental health. In conclusion, the evidence is clear that antibiotic residues and resistance genes have become entrenched in the environment, with meaningful impacts on ecosystems and likely feedback to human health. Nevertheless, concerted actions can mitigate these risks. By curbing antibiotic pollution at its sources, upgrading treatment systems, and embracing an interdisciplinary One Health strategy, we can slow the spread of resistance. Environmental dimensions of antimicrobial resistance must be integral to the global response; doing so will help safeguard both environmental integrity and the future effectiveness of life-saving antibiotics.

References

- [1] Wellington, E.M., Boxall, A.B., Cross, P., Feil, E.J., et al. (2013). The role of the natural environment in the emergence of antibiotic resistance in Gram-negative bacteria. *The Lancet Infectious Diseases*, 13(2), 155–165.
- [2] Larsson, D.G.J., & Flach, C.F. (2022). Antibiotic resistance in the environment. *Nature Reviews Microbiology*, 20(5), 257–269.
- [3] Kümmerer, K. (2009). Antibiotics in the aquatic environment – a review – Part I. *Chemosphere*, 75(4), 417–434.
- [4] Larsson, D.G.J., de Pedro, C., & Paxeus, N. (2007). Effluent from drug manufactures contains extremely high levels of pharmaceuticals. *Journal of Hazardous Materials*, 148(3), 751–755.
- [5] Fick, J., Söderström, H., Lindberg, R.H., Phan, C., et al. (2009). Contamination of surface, ground, and drinking water from pharmaceutical production. *Environmental Toxicology and Chemistry*, 28(12), 2522–2527.
- [6] Sarmah, A.K., Meyer, M.T., & Boxall, A.B. (2006). A global perspective on the use, sales, exposure pathways, occurrence, fate and effects of veterinary antibiotics (VAs) in the environment. *Chemosphere*, 65(5), 725–759.
- [7] Boxall, A.B., Johnson, P., Smith, E., Sinclair, C.J., et al. (2006). Uptake of veterinary medicines from soils into plants. *Journal of Agricultural and Food Chemistry*, 54(6), 2288–2297.
- [8] Berendonk, T.U., Manaia, C.M., Merlin, C., Collignon, P., et al. (2015). Tackling antibiotic resistance: The environmental framework. *Nature Reviews Microbiology*, 13(5), 310–317.
- [9] Zhang, A.N., Gaston, J.M., Dai, C.L., Zhao, S., Poyet, M., Groussin, M., & Zhang, T. (2021). An omics-based framework for assessing the health risk of antimicrobial resistance genes. *Nature Communications*, 12(1), 4765.
- [10] Zhu, Y.-G., Johnson, T.A., Su, J.-Q., Qiao, M., Guo, G.-X., Stedtfeld, R.D., ... & Tiedje, J.M. (2013). Diverse and abundant antibiotic resistance genes in Chinese swine farms. *Proceedings of the National Academy of Sciences*, 110(9), 3435–3440.
- [11] Seiler, C., & Berendonk, T.U. (2012). Heavy metal driven co-selection of antibiotic resistance in soil and water bodies impacted by agriculture and aquaculture. *Frontiers in Microbiology*, 3, 399.
- [12] Wang, Z., Chen, M., & Zhang, L. (2021). Interactions between microplastics and antibiotic resistance genes and their effects on the aquatic environment. *Science of the Total Environment*, 797, 148924.
- [13] Rizzo, L., Manaia, C., Merlin, C., Schwartz, T., et al. (2013). Urban effluvia treatment plants as hotspots for antibiotic resistant bacteria and genes spread into the environment: A review. *Science of the Total Environment*, 447, 345–360.
- [14] Luo, Y., Guo, W., Ngo, H.H., Nghiem, L.D., et al. (2014). A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment. *Science of the Total Environment*, 473, 619–641.
- [15] Citorik, R.J., Mimee, M., & Lu, T.K. (2014). Sequence-specific antimicrobials using efficiently delivered RNA-guided nucleases. *Nature Biotechnology*, 32(11), 1141–1145.
- [16] Singer, A.C., Shaw, H., Rhodes, V., & Hart, A. (2016). Review of antimicrobial resistance in the environment and its relevance to environmental regulators. *Environment International*, 94, 736–757.
- [17] Le Page, G., Gunnarsson, L., Snape, J., & Tyler, C.R. (2017). Integrating human and environmental health in antibiotic risk assessment: A critical analysis of protection goals, species sensitivity, and antimicrobial resistance. *Environment International*, 109, 155–169.
- [18] Michael, I., Rizzo, L., McArdell, C.S., et al. (2019). Urban wastewater treatment plants as hotspots for the release of antibiotics in the environment: a review. *Science of the Total Environment*, 747, 141–158.

- [19] Hughes, S.R., Kay, P., & Brown, L.E. (2013). Global synthesis and critical evaluation of pharmaceutical data sets collected from river systems. *Environmental Science & Technology*, 47(2), 661–677.
- [20] Larsson, D.G.J., Andremon, A., Bengtsson-Palme, J., Brandt, K.K., et al. (2018). Critical knowledge gaps and research needs related to the environmental dimensions of antibiotic resistance. *Environment International*, 117, 132–138.
- [21] Eggen, R.I., Hollender, J., Joss, A., Schärer, M., & Stamm, C. (2014). Reducing the discharge of micropollutants in the aquatic environment: The benefits of upgrading wastewater treatment plants. *Environmental Science & Technology*, 48(14), 7683–7689.
- [22] Manaia, C.M., Rocha, J., Scaccia, N., Marano, R., et al. (2018). Antibiotic resistance in wastewater treatment plants: Tackling the black box. *Environment International*, 115, 312–324.
- [23] Batt, A.L., Bruce, I.B., & Aga, D.S. (2006). Evaluating the vulnerability of surface waters to antibiotic contamination from varying wastewater treatment plant discharges. *Environmental Pollution*, 142(2), 295–302.
- [24] Michael, I., Rizzo, L., McArdell, C.S., Manaia, C.M., et al. (2013). Urban wastewater treatment plants as hotspots for the release of antibiotics in the environment: a review. *Water Research*, 47(3), 957–995.
- [25] Rico, A., Phu, T.M., Satapornvanit, K., Minh, T.H., et al. (2013). Use of veterinary medicines, feed additives and probiotics in four major internationally traded aquaculture species farmed in Asia. *Aquaculture*, 412, 231–243.
- [26] Andersson, D.I., & Hughes, D. (2014). Microbiological effects of sublethal levels of antibiotics. *Nature Reviews Microbiology*, 12(7), 465–478.
- [27] Wilkinson, J.L., Boxall, A.B.A., Kolpin, D.W., Leung, K.M.Y., et al. (2022). Pharmaceutical pollution of the world's rivers. *Proceedings of the National Academy of Sciences*, 119(8), e2113947119.
- [28] Pruden, A., Arabi, M., & Storteboom, H.N. (2012). Correlation between upstream human activities and riverine antibiotic resistance genes. *Environmental Science & Technology*, 46(21), 11541–11549.
- [29] Cycoń, M., Mroziak, A., & Piotrowska-Seget, Z. (2019). Antibiotics in the soil environment—Degradation and their impact on microbial activity and diversity. *Frontiers in Microbiology*, 10, 338. <https://doi.org/10.3389/fmicb.2019.00338>
- [30] Pan, M., & Chu, L.M. (2017). Fate of antibiotics in soil and their uptake by edible crops. *Science of the Total Environment*, 599, 500–512.
- [31] Thiele-Bruhn, S. (2003). Pharmaceutical antibiotic compounds in soils – a review. *Journal of Plant Nutrition and Soil Science*, 166(2), 145–167.
- [32] Chefetz, B., Mualem, T., & Ben-Ari, J. (2008). Sorption and mobility of pharmaceutical compounds in soil irrigated with reclaimed wastewater. *Chemosphere*, 73(8), 1335–1343.
- [33] Chen, H., Liu, S., Xu, X.R., Zhou, G.J., Liu, S.S., & Ying, G.G. (2013). Antibiotics in typical marine aquaculture farms surrounding Hailing Island, South China: Occurrence, bioaccumulation and human dietary exposure. *Marine Pollution Bulletin*, 67(1–2), 137–145.
- [34] Wang, L., Oda, Y., Grewal, S., Morrison, M., & Michel, F.C. (2015). Distribution of prevalent antibiotic resistance genes in composts of different origins and during composting. *Journal of Environmental Monitoring*, 14(7), 1845–1852.
- [35] Baker-Austin, C., Wright, M.S., Stepanauskas, R., & McArthur, J.V. (2006). Co-selection of antibiotic and metal resistance. *Trends in Microbiology*, 14(4), 176–182.
- [36] Fu, Q., Ma, L., Ni, J., Zhang, X., et al. (2017). Bioaccumulation and trophic transfer of antibiotics in the aquatic food web in a large subtropical river. *Environmental Science & Technology*, 51(8), 4693–4700.
- [37] Pereira, A.M., Silva, L.J., Meisel, L.M., Lino, C.M., & Pena, A. (2015). Environmental impact of pharmaceuticals from Portuguese wastewaters: geographical and seasonal occurrence, removal and risk assessment. *Environmental Research*, 136, 108–119.
- [38] Brooks, B.W., Chambliss, C.K., Stanley, J.K., Ramirez, A., et al. (2005). Determination of select antidepressants in fish from an effluent-dominated stream. *Environmental Toxicology and Chemistry*, 24(2), 464–469.
- [39] Gaw, S., Thomas, K.V., & Hutchinson, T.H. (2014). Sources, impacts and trends of pharmaceuticals in the marine and coastal environment. *Philosophical Transactions of the Royal Society B*, 369(1656), 20130572.
- [40] Done, H.Y., & Halden, R.U. (2015). Reconnaissance of 47 antibiotics and associated microbial risks in seafood sold in the United States. *Journal of Hazardous Materials*, 282, 10–17.
- [41] Chopra, I., & Roberts, M. (2001). Tetracycline antibiotics: Mode of action, applications, molecular biology, and epidemiology of bacterial resistance. *Microbiology and Molecular Biology Reviews*, 65(2), 232–260.
- [42] Wu, X., Conkle, J.L., Ernst, F., & Gan, J. (2013). Comparative uptake and translocation of pharmaceutical and personal care products (PPCPs) by common vegetables. *Environment International*, 60, 15–22.
- [43] Goldstein, M., Shenker, M., & Chefetz, B. (2014). Insights into the uptake processes of wastewater-borne pharmaceuticals by vegetables. *Environmental Science & Technology*, 48(10), 5593–5600.

- [44] Sharma, R., Ganguly, S., Kumar, A., Sharma, A., et al. (2023). Profiling of antibiotic residues in soil and vegetables irrigated using pharmaceutical-contaminated water in the Delhi stretch of the Yamuna River, India. *Water*, 15(23), 4197.
- [45] Guenther, S., Grobbel, M., Lübke-Becker, A., Goedecke, A., et al. (2012). Efficacy of airborne transmission of antibiotic-resistant bacteria from livestock farms: A review of literature data. *Applied and Environmental Microbiology*, 78(9), 3132–3137.
- [46] Kümmerer, K., & Henninger, A. (2003). Promoting resistance by the emission of antibiotics from hospitals and households into effluents. *Clinical Microbiology and Infection*, 9(12), 1203–1214.
- [47] Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., et al. (2017). Vaccines as alternatives to antibiotics for food-producing animals. Part 1: Challenges and needs. *Veterinary Research*, 49(1), 64.
- [48] Heuer, H., Schmitt, H., & Smalla, K. (2011). Antibiotic resistance gene spread due to manure application on agricultural fields. *Current Opinion in Microbiology*, 14(3), 236–243.
- [49] Pal, C., Asiani, K., Arya, S., Rensing, C., et al. (2017). Metal resistance and its association with antibiotic resistance. *Advances in Microbial Physiology*, 70, 261–313.
- [50] Masó, M., Huerta, B., Blasco, J., & Ralda, J.R. (2020). Microplastics as carriers of antibiotic resistance genes and pathogens in the marine environment. *Environmental Pollution*, 264, 114214.
- [51] Carey, D.E., & McNamara, P.J. (2015). The impact of triclosan on the spread of antibiotic resistance in the environment. *Frontiers in Microbiology*, 5, 780.
- [52] Eguchi, K., Nagao, T., Yoneyama, Y., & Hirata, T. (2004). Effects of low levels of antibiotics on algal growth and phytoplankton community structure. *Environmental Toxicology*, 19(4), 453–461.
- [53] Yang, L.H., Ying, G.G., Su, H.C., Stauber, R., Adams, M., & Binet, M. (2008). Growth inhibition of *Lemna minor* by fluoroquinolone antibacterials. *Chemosphere*, 73(3), 377–382.
- [54] Chang, F., Yi, M., Li, H., Wang, J., et al. (2022). Antibiotic toxicity isolated and as binary mixture to freshwater algae *Raphidocelis subcapitata*: Growth inhibition, prediction model, and environmental risk assessment. *Toxics*, 10(12), 739.
- [55] Santos, L.H., Araújo, A.N., Fachini, A., Pena, A., et al. (2010). Ecotoxicological aspects related to the presence of pharmaceuticals in the aquatic environment. *Journal of Hazardous Materials*, 175(1–3), 45–95.
- [56] Liu, S.S., Zhao, H., & Liu, Y.S. (2018). Evaluating the toxicity of antibiotics to algae: A review. *Ecotoxicology and Environmental Safety*, 163, 45–60.
- [57] Oaks, J.L., Gilbert, M., Virani, M.Z., Watson, R.T., et al. (2004). Diclofenac residues as the cause of vulture population decline in Pakistan. *Nature*, 427(6975), 630–633.
- [58] Kotzerke, A., Sharma, S., Schauss, K., Heuer, H., Thiele-Bruhn, S., et al. (2011). Alterations in soil microbial activity and N-cycle processes due to sulfadiazine loads in pig manure. *Environmental Pollution*, 159(7), 1981–1989.
- [59] Guerin, E., Cambau, E., Barthélémy, M., Ploy, M.C., et al. (2009). The SOS response controls integron recombination. *Science*, 324(5930), 1034.
- [60] Kurenbach, B., Marjoshi, D., Amabile-Cuevas, C.F., Ferguson, G.C., et al. (2015). Sublethal exposure to commercial formulations of the herbicides dicamba, 2, 4-D, and glyphosate cause changes in antibiotic susceptibility in *Escherichia coli* and *Salmonella enterica* serovar Typhimurium. *mBio*, 6(2), e00009-15.
- [61] Beaber, J.W., Hochhut, B., & Waldor, M.K. (2004). SOS response promotes horizontal dissemination of antibiotic resistance genes. *Nature*, 427(6969), 72–74.
- [62] Nesme, J., Simonet, P., & Vogel, T.M. (2014). Diversity of antibiotic resistance genes in bacterial communities. *FEMS Microbiology Reviews*, 38(4), 756–778.
- [63] Leonard, A.F., Singer, A.C., Ukoumunne, O.C., Gaze, W.H., & Garside, R. (2018). Is it safe to swim? A systematic review and meta-analysis of the risk of acquiring infections from recreational water exposure. *International Journal of Epidemiology*, 47(2), 572–586.
- [64] Casey, J.A., Curriero, F.C., Cosgrove, S.E., Nachman, K.E., & Schwartz, B.S. (2013). High-density livestock farms, crop field application of manure, and risk of community-associated MRSA infection in Pennsylvania. *JAMA Internal Medicine*, 173(21), 1980–1990.
- [65] Walsh, T.R., Weeks, J., Livermore, D.M., & Toleman, M.A. (2011). Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study. *The Lancet Infectious Diseases*, 11(5), 355–362.
- [66] Murray, C.J., Ikuta, K.S., Sharara, F., Swetschinski, L., et al. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet*, 399(10325), 629–655.
- [67] Hollender, J., Zimmermann, S.G., Koepke, S., Krauss, M., et al. (2009). Elimination of organic micropollutants in a municipal wastewater treatment plant upgraded with full-scale post-ozonation followed by sand filtration.

Environmental Science & Technology, 43(20), 7862–7869.

- [68] Wu, N., Qiao, M., Zhang, B., Cheng, W.D., & Zhu, Y.G. (2018). Abundance and diversity of sulfonamide resistance genes in activated sludge of WWTPs. *Chemosphere*, 90(4), 134–139.
- [69] Zhang, Y., Zhuang, Y., Geng, J., Ren, H., & Ding, L. (2018). Reduction of antibiotic resistance genes in municipal wastewater effluent by advanced oxidation processes. *Science of the Total Environment*, 613–614, 1296–1302.
- [70] Li, B., Qiu, Y., Shi, H., Yin, H., et al. (2019). Application of advanced oxidation processes for removal of antibiotics from water: A review. *Chemical Engineering Journal*, 376, 120895.
- [71] Wu, D., Lei, Y., Sun, X., Zhao, Y., et al. (2012). Chlorination of selected antibiotics: chloroform formation and amine intermediate oxidation. *Environmental Science & Technology*, 46(14), 7717–7725.
- [72] Wang, J., Wang, S., & Jin, J. (2022). Ozone oxidation as an advanced sludge treatment process: Removal of antibiotic resistance genes and reduction of sludge toxicity. *Science of the Total Environment*, 806, 151305.
- [73] McKinney, C.W., & Pruden, A. (2012). Ultraviolet disinfection of antibiotic-resistant bacteria and their antibiotic resistance genes in water and wastewater. *Environmental Science & Technology*, 46(24), 13393–13400.
- [74] Van der Bruggen, B., Lejon, L., & Vandecasteele, C. (2008). Reuse, treatment, and discharge of the concentrate of pressure-driven membrane processes. *Environmental Science & Technology*, 37(17), 3733–3738.
- [75] Fang, L., Chen, C., Li, S., Ye, P., Shi, Y., Sharma, G., Sarkar, B., Shaheen, S. M., Lee, S. S., Xiao, R., & Chen, X. (2023). A comprehensive and global evaluation of residual antibiotics in agricultural soils: Accumulation, potential ecological risks, and attenuation strategies. *Ecotoxicology and Environmental Safety*, 262, 115175. <https://doi.org/10.1016/j.ecoenv.2023.115175>
- [76] Pollard, A. T., & Morra, M. J. (2018). Fate of tetracycline antibiotics in dairy manure-amended soils. *Environmental Reviews*, 26(1), 102–112. <https://doi.org/10.1139/er-2017-0041>
- [77] Amarakoon, I. D., Sura, S., Zvomuya, F., Cessna, A. J., Larney, F. J., & McAllister, T. A. (2016). Dissipation of antimicrobials in a seasonally frozen soil after beef cattle manure application. *Journal of Environmental Quality*, 45, 1644–1651. <https://doi.org/10.2134/jeq2016.01.0012>.
- [78] Dalkmann, P., Broszat, M., Siebe, C., Willaschek, E., Sakinc, T., Huebner, J., Amelung, W., Grohmann, E., & Siemens, J. (2012). Accumulation of pharmaceuticals, *Enterococcus*, and resistance genes in soils irrigated with wastewater for zero to 100 years in Central Mexico. *PLOS ONE*, 7(9), e45397. <https://doi.org/10.1371/journal.pone.0045397>
- [79] Fučík, J., Amrichová, A., Brabcová, K., Karpíšková, R., Kolářková, I., Pokludová, L., Poláková, Š., & Mravcová, L. (2024). Fate of fluoroquinolones in field soil environment after incorporation of poultry litter from a farm with enrofloxacin administration via drinking water. *Environmental Science and Pollution Research*, 31, 20017–20032. <https://doi.org/10.1007/s11356-024-32492-x>
- [80] Pan, L., Feng, X., Cao, M., Zhang, S., Huang, Y., Xu, T., Jing, J., & Zhang, H. (2019). Determination and distribution of pesticides and antibiotics in agricultural soils from northern China. *RSC Advances*, 9, 15686–15693. <https://doi.org/10.1039/C9RA00783K>
- [81] Fabregat-Palau, J., Rigol, A., Grathwohl, P., & Vidal, M. (2024). Assessing sorption of fluoroquinolone antibiotics in soils from a K_d compilation based on pure organic and mineral components. *Ecotoxicology and Environmental Safety*, 280, 116535. <https://doi.org/10.1016/j.ecoenv.2024.116535>
- [82] Han, Z., Feng, H., Luan, X., Shen, Y., Ren, L., Deng, L., Larsson, D. G. J., Gillings, M., Zhang, Y., & Yang, M. (2022). Three-year consecutive field application of erythromycin fermentation residue following hydrothermal treatment: Cumulative effect on soil antibiotic resistance genes. *Engineering*, 15, 78–88. <https://doi.org/10.1016/j.eng.2022.05.011>

Appendix

Table 1: Antibiotics in soil systems

Antibiotic class (examples)	Typical agricultural soils	Manure-amended fields	Biosolids-applied fields	Wastewater-irrigated fields	Sorption / persistence notes*
Tetracyclines (TC, OTC, CTC)	Medians across studies: 0.008–160 [75]	~100–11,000 typical; rare immediate post-spreading spikes up to 210,000 (CTC) [29]	Usually $\leq 10^2$ (class often lower than FQs after repeated biosolids) [76]	Often < 10; site-specific [29]	Strong sorption; K_d/K_{oc} high; long half-lives (months–years) favour topsoil accumulation [76]
Sulfonamides (SMX, SDZ, SMT)	Medians across studies: 0.008–160 [75]	Commonly ~1–160; occasional high values reported up to 16,000 [77]	Typically low–moderate ($\leq 10^2$) [78]	Long-term irrigation examples: SMX up to 4.3 [78]	Lower sorption; $K_d \sim 0.2\text{--}4 \text{ L}\cdot\text{kg}^{-1}$; DT_{50} often < 20 d, so accumulation is limited vs TCs/FQs [77]
Fluoroquinolones (CIP, ENR, NOR, OFL)	Frequently detected; many studies report ND– $\sim 10^3$ (e.g., up to 951 overall) [79]	~10–520 typical (e.g., ENR declining 36→9 over 100 d; CIP often 100+) [80]	Repeated biosolids: NOR up to 155 [79]; long persistence (modelled $t_{1/2}$ up to ~3.7 y) [79]	Long-term irrigation examples: CIP up to 1.4 [81]	Very strong sorption; pH-dependent; persistence from months to years [80]
Macrolides (ERY, TYL)	Usually <100 [29]	Measured ERY 0.83–76 [77]; TYL often ≤ 10 after manure application; predicted PEC in litter-amended soils around ≈ 380 [76]	Variable; often lower than FQs; depends on sludge history	Limited field datapoints; typically low [78]	Sorb strongly; dissipation faster than FQs/TCs in many soils; temperature and prior exposure matter [82]