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Antimicrobial Resistance: the Reservoirs, Transmission, and Public Health Implications

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Abstract:

Antimicrobial resistance (AMR) has been recognized as one of the leading public health threats worldwide. The increasing resistance of microorganisms to existing antimicrobial agents poses a significant global health risk that results in increased mortality and morbidity, hospitalization rates and costs. Even with global endeavors to fight AMR, we continue to witness an ever growing prevalence notably in lower and middle income countries. A better understanding of the reservoirs, transmission, and public health concerns is crucial for the development of efficient strategies for tackling AMR. The fight against AMR isn't just a quest for new antibiotics, it involves a change in how we approach treating infections. Reducing the use of pharmaceuticals not only slows down resistance but provides a more secure, scientific way to tackle recurrent infections.

Keywords: Antimicrobial resistance, antimicrobial agents, microorganisms, public health.



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INTRODUCTION

Antibiotics are drugs used to control and cure infections caused by bacteria. The development of antibiotics in the 20th century represents a turning point in modern medicine (Begum *et al.*, 2021; ECDC, 2009; Elliott, 2015). The global threat of antimicrobial resistance (AMR), poses the greatest challenge to modern health systems and medicine (Ashraf and Iqbal, 2020; Ashraf *et al.*, 2020). The emergence and proliferation of multidrug-resistant organisms (MDROs) over the past 20 years (2000-2024) have accelerated at an unprecedented level and caused a public health emergency (CDC, 2023; Marino *et al.*, 2025). The warnings regarding AMR originating in the 1940's have now become reality with an emergent crisis-resistant bacteria is responsible for over 1.27 million deaths per year and affects healthcare globally (Murray *et al.*, 2022; Tosas Augustet *et al.*, 2025). The development of resistance mechanisms has risen sharply over time compared to the rate at which new antibiotics are created, leading to a rapidly widening treatment gap, undermining the foundations of modern medical practice (Akunne *et al.*, 2025). This opposition has also been strengthened by a lack of drug development innovation, the pursuit of health as a business commodity, and the absence of diagnostic testing prior to prescribing (Akram *et al.*, 2023).

Antibiotics, similarly to other essential medications, are greatly advantageous in a proper administration but can bring detrimental effects to patient care in improper usage-all without providing clinical benefit (Tamma *et al.*, 2017). A hidden and invisible pandemic is undermining gains in health care resulting from many years of medical advances on a global scale (Gajdács and Albericio, 2019; Uddin *et al.*, 2021). Furthermore, although many efforts of research and development have been conducted to deal with AR, there are still several gaps that hinder an effective control and prevention for this global threat. The existing studies have helped understand the causes of AR including genetic mutations, horizontal gene transfer (HGT) and biofilm formation. The main

causes of increasing resistance such as extensive use and misuse of antibiotics, farming, and environmental influences have also been reported (Rani and Saharawat, 2024).

Mechanisms of antibiotic resistance

Antibiotic resistance (AMR) is one of the most significant threats to contemporary medicine since most approved drugs are rendered useless against one or more microbial species. Bacterial resistance to the effect of antibiotics is typically due to the development of resistance mechanisms that allow the organism to bypass or inactivate them either inherently or by acquiring mechanisms of resistance (Abebe *et al.*, 2016; Alexander *et al.*, 2008; Giguère and Dowling, 2013). Most antibiotics are aimed against essential bacterial activities such as the synthesis of proteins, replication of DNA and formation of cell wall, but bacteria possess multiple molecular mechanisms of resistance to them. Such mechanisms include alteration of target site, induction of efflux pumps, enzymatic inactivation, decrease of membrane permeability, activation of metabolic bypasses, and formation of biofilms (Abebe *et al.*, 2016; Darby *et al.*, 2023; Wright, 2011). AMR arises as a result of adaptation of bacteria to counteract the action of antibiotics (caused mainly by misuse/overuse/selection pressure) using several mechanisms (Table 1) (Chinemerem Nwobodo *et al.*, 2022; Habboush and Guzman, 2023). A comprehension of these mechanisms will be crucial for guiding antibiotic development design, optimizing its therapeutic use, and engineering novel agents capable of evading or combating resistance (Darby *et al.*, 2023; Kapoor *et al.*, 2017).

Environmental reservoirs and transmission pathways

The selection and dissemination of resistant determinants in diverse niches, including aquatic environments, agricultural soils and food production, has been greatly enhanced by the indiscriminate and widespread usage of antibiotics in human medicine, veterinary

practice and agriculture (Larsson and Flach, 2022).

Table 1. Mechanisms of antibiotic resistance development (Chinemerem Nwobodo et al., 2022; Habboush and Guzman, 2023).

Method of resistance	Description	Examples
Mutation	The mutations on genes in the bacteria will change the structure of the protein molecule so the antibiotic will not bind to it.	RNA polymerase mutations confer Rifampicin resistance.
Efflux pumps	Bacteria are able to pump out antibiotics from the cell through efflux pumps, hence decreasing their intracellular concentration.	Efflux of tetracycline from Gram-negative bacteria.
Enzymatic degradation	Bacteria synthesize enzymes, which chemically alter or destroy the antibiotic.	Beta-lactamase enzymes that degrade penicillin.
Change of target sites	Alteration of the antibiotic target site by bacteria results in a reduced affinity for the drug, thereby lowering their function.	MRSA alters penicillin-binding proteins.
Reduced permeability	Altered cell wall or membrane decreases antibiotic uptake.	Porin mutations in <i>Pseudomonas aeruginosa</i> .
Horizontal gene transfer	Resistance genes may be transferred from other bacteria to the resistant bacteria via: transformation, transduction or conjugation.	<i>Streptococcus pneumoniae</i> taking on genes for capsular polysaccharides that may render it more pathogenic. Salmonella obtain AR genes in via transduction mediated by phages. Plasmids bearing AR genes (like R-plasmid) are transferred between cells of <i>Escherichia coli</i> .
Biofilm formation	Bacteria produce biofilms which resist the penetration of antibiotics as well as offering a protection mechanism against host immunity.	<i>Pseudomonas aeruginosa</i> in patients with cystic fibrosis.

Wastewater treatment plants as reservoir for transmitting AMR

The improper handling of wastewater leads to the environmental dissemination of AMR, exacerbating its spread (Mohamad and Bakon, 2025). Wastewater treatment plants (WWTPs) act as hotspots for the environmental dissemination of AMR, being a focal point where various bacterial communities originating from human waste, hospital effluents, agricultural runoff, and industrial waste converge under optimal circumstances for gene transfer to occur. Since numerous bacterial communities are enclosed within the activated sludge and biological treatment processes, there is a probability for horizontal gene transfer leading to novel resistance gene profiles that could be absent from any single incoming stream (Meradji et al., 2025; Su et al., 2024). Wastewater effluents serve as pathways for onward dissemination of resistant organisms to receiving

surface waters, and many genome surveillance studies have found WWTPs to harbor diverse populations of antibiotic-resistant bacteria (ARB) and resistance genes (ARGs), which has implications for human, animal, and ecosystem health (Al-Mustapha et al., 2025; Thakur et al., 2025).

The effectiveness of WWTPs at eliminating AMR bacteria is highly variable and often inadequate, particularly with regard to resistance genes. Even though treatment stages have a considerable impact on the load of total bacteria, comparing AMR gene load between influents and effluents from WWTPs has revealed that, with specific treatment design, effluents can contain similar or even higher loads of resistant bacteria and resistance genes (La Rosa et al., 2025; Owojori et al., 2024). The resistance profiles of surface water bacteria (located several km downstream of the WWTP discharge points) is very similar to those of WWTP isolates, demonstrating that the release of

WWTP effluent into surface water bodies leads to a downstream AMR contamination gradient (Esmaeili-khoshmardan *et al.*, 2024).

Agricultural and animal husbandry settings for resistance transmission

Antimicrobial resistance in agricultural systems poses a growing threat to food safety, public health, and environmental sustainability. The widespread use of antibiotics and subsequent AMR selection in agriculture is found in environments such as crop production, livestock farming, poultry production and aquaculture. The development of a high agricultural AMR load has been attributed to a lack of basic health infrastructure, non-therapeutic administration to promote growth in animals, widespread use and misuse, contaminated animal feed in contact with treated animal excreta, weak infection controlling measures, and unauthorized use of antibiotics (Enshaie *et al.*, 2025; Hosain *et al.*, 2021; Iqbal, 2024; Khan *et al.*, 2019; Manyi-Loh *et al.*, 2018). Soil associated bacteria moving from poultry farms into surface water system with the runoff at wet season such as monsoon has potential to be important routes which can transmit the resistance genes from farmland into aquatic systems (Liu *et al.*, 2024).

Irrigation water and surface water as basis for resistance transmission

Antibiotic resistance is not just confined to medical facilities – it is having ever larger and more dangerous implications for our future. Furthermore, recent research indicates that the environment plays a key role in not only the transmission of bacteria with resistance, but in the development of this resistance (Berendonk *et al.*, 2015; Karnwal *et al.*, 2025). In environmental settings, surface waters such as rivers, canals, ponds and irrigation channels into which inputs enter from hospital waste, agriculture and urban sewage, act as significant pathways for the transmission of AMR. The convergence of water used for crop irrigation, livestock and human use form successful pathways for the transference of AMR into the human population from environmental resistance

stores within river systems due to the contamination in such systems driven by high antibiotic usage in agriculture, raw sewage outputs, and poor regulation (Bengtsson-Palme *et al.*, 2018). The emergence of antimicrobial resistance in the environment, livestock, and humans increases the risk of human infection by resistant bacteria (Sachdeva *et al.*, 2025).

Public health implications of antimicrobial resistance

Infectious disease management over the past several decades has been a tremendous public health success, but has faced one of the most significant challenges of the twenty-first century: the rise of antimicrobial resistance (AMR) (Ashraf and Iqbal, 2021; Ashraf *et al.*, 2020; Ferdinand *et al.*, 2024; Sartorius *et al.*, 2024). The problem of AMR has evolved to be a complex phenomenon that poses threats to human and animal health (Edrees and Anbar, 2021; Shawish *et al.*, 2020). The emergence of resistance has health and clinical implications for the patient, but also implications for the healthcare practices. The high morbidity and mortality that result from these easily managed infections is one of the major consequences of the condition. Antibiotic-resistant organisms such as MRSA, and carbapenem-resistant Enterobacteriaceae (CRE), make infections more complicated, longer-lasting, and fatal (Xie *et al.*, 2018). These infections may turn into more severe complications and organ failure which requires intensive care and long recovery (Larsson and Flach, 2022). Furthermore, potent antibiotic might have adverse effects when used to fight resistance which can slow down the recovery, supported by the report from WHO and Nature (Maragakis *et al.*, 2008).

Cancer patients have a greater risk of AMR. Cancer patients undergoing chemotherapy generally have compromised immune systems and are therefore at an increased risk of contracting infections. Repeated infections often erode the effectiveness of preventative therapies, thereby requiring more powerful and toxic drugs. Side effects may be more likely and cancer therapy plan is therefore challenged, with

the success of cancer treatment and mortality rate also compromised (Marshall and Levy, 2011).

The interaction of human, animal, and environmental health systems increases the scale of the AMR problem. One Health is the underlying conceptual framework for understanding the genesis, persistence, and transmission of resistance among ecological compartments (Djordjevic *et al.*, 2024). In this framework, environment components such as surface waters, waste water, agricultural soil, and sediments are active environments that allow the selective, amplification, horizontal transfer and persistence of resistance genes rather than just passive recipients of resistant organisms. This paradigm shift has influenced both scientific and policy perspectives on AMR surveillance and management (Larsson and Flach, 2022; Zhai *et al.*, 2025).

Research into pathways of resistance is predominantly limited by available knowledge regarding global consumption. The total consumption of antimicrobials by food-animals has continued to rise to critically high levels, in low- and middle-income countries with high rates of consumption compared to the rest of the world (Van Boeckel *et al.*, 2020). Excessive over-the-counter purchase and excessive use coupled with a low level of infrastructure to cope with sewerage led to very good breeding conditions to generate and disseminate AMRs. High levels of MDR-Enterobacteriaceae found in water bodies including rivers, sewerage, irrigation water, farm poultry washings and clinical environment commonly express clinically relevant determinants of resistance (Ali *et al.*, 2016; Hasan *et al.*, 2014; Huda *et al.*, 2025).

AMR impacts the financial sector to a similar extent. The overall aim of environmental monitoring for AMR in the financial sector serve two purposes; 1: It generates the evidence base to support evidence-based One Health interventions that break chains of resistance transmission before human infection occurs. 2: It generates an early warning system that can signal the risks presented to the clinical sector

that may be apparent sometime in the future (Berendonk *et al.*, 2015; Hendriksen *et al.*, 2019). The One Health aspects of AMR spread in agricultural contexts are particularly well-illustrated by the epidemiology of resistance (Iryawati *et al.*, 2025).

CONFLICT OF INTEREST

The author declares no conflict of interest.

GENERATIVE AI STATEMENT

The author(s) declare that no Generative AI was used for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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