# Antibiotic Resistance in Zoonotic Bacteria: No Action Today, No Cure Tomorrow for People and Animals

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## Abstract

Antibiotic resistance (ABR) in zoonotic pathogens is a global challenge to animals, the environment, and human health and wealth. The misuse of antibiotics for the treatment of animal and human diseases, along with poor waste disposal, has increased resistant zoonotic bacterial strains. These bacteria cannot be killed with conventional antibiotics and the infections caused by these bacteria result in high death rates, and treatment costs and lead to incurable diseases. Zoonotic pathogens are transmitted via contact with animals, contaminated water, food, and environmental sources highlighting the connection between human, animal, and environmental health. This chapter examines the causes of ABR and its effects on public and animal health and the world's economy. It also discusses challenges in addressing ABR and alternative solutions like antimicrobial peptides, CRISPR-Cas technologies, nanoparticles, phage therapy, and plant-based antimicrobials. Furthermore, it emphasizes the significance of coordinated global efforts, based on the 'One Health' (OH) idea, to reduce the effect of ABR on food production, healthcare, and economic stability.

Keywords: Antibiotic resistance, Alternative therapies, One Health, Public health, Zoonotic bacteria

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## Introduction

Zoonoses refer to diseases that are capable of being transmitted between humans and animals, moving in either direction (Erkyihun and Alemayehu, 2022). These diseases are categorized based on their causative agents, including bacterial, viral, parasitic, fungal, rickettsial, chlamydial, mycoplasma, and protozoal zoonoses, as well as those caused by acellular non-viral pathogens (Rahman et al., 2020). However, the landscape of infectious diseases today is dominated by multidrug-resistant (MDR) pathogens such as *P. aeruginosa*, methicillin-resistant *S. aureus*, or *Acinetobacter* species, and emerging pan-resistant strains (Christou, 2011; Haq et al. 2024).

Antimicrobial resistance (AMR), often called a silent pandemic, has become a serious global concern in the twenty-first century, harming people, animals, and the environment (Ahmad et al., 2021). According to estimates, AMR causes 700,000 fatalities globally each year (Ahmed et al., 2017). AMR is viewed as a One Health (OH) concern because environmental factors and human and veterinary practices are combined to spread it (Delesalle et al., 2022). The excessive use of antimicrobials in medical prescriptions, and their misuse and improper usage have greatly contributed to the development and dissemination of AMR in humans.

The chapter focuses on the connection between zoonotic pathogens and the development of antibiotic resistance and why this is a One Health matter. This section also explains the main reasons for antibiotic resistance and how it affects people's health and wealth. The chapter also evaluates how different approaches may help fight resistance, including changing behavior through stewardship programs; unifying global rules to govern antibiotic use; and looking into alternative treatments. The goal is to discuss new ways to fight ABR, raise awareness, promote collaborations, and give important information to decision-makers who could work to avoid the postantibiotic era.

### 1. Mechanisms of Antimicrobial Resistance in Zoonotic Pathogens

The ABR develops when bacterial cells interact with antimicrobial agents. To avoid being killed by antimicrobial agents, bacteria use two main mechanisms; intrinsic and/or acquired resistance, and these mechanisms are acquired by bacteria through the evolution of millions of years (Blair et al., 2015; Ndagi et al., 2020).

#### 1.1 Intrinsic Antibiotic Resistance

Many bacteria can withstand antibiotics naturally, without needing to have past exposure to antimicrobials. Bacteria naturally develop resistance because of their physical qualities as explained by Wand (2017). Bacteria can avoid antimicrobials in four natural ways: inactivating antibiotics, changing their site of action, pumping antibiotics out of cells, and making their cell membranes less permeable (Figure 1) (Mc Dermott et al., 2003; Haq et al., 2024).

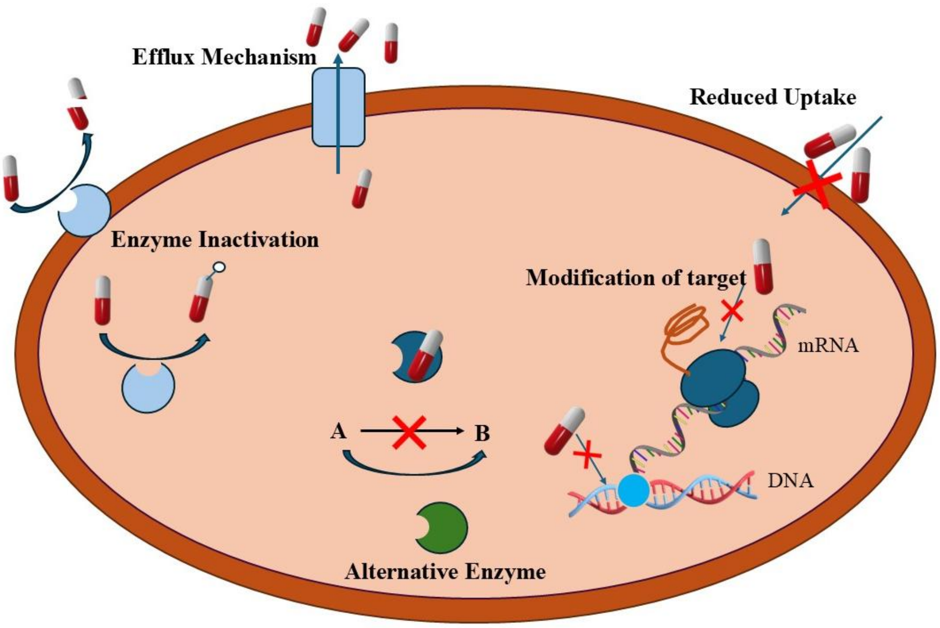


Fig. 1: Mechanism of intrinsic antibiotic resistance (PowerPoint)

### 1.2 Acquired Antibiotic Resistance and its Mechanism

Zoonotic bacteria acquire genetic materials in three main ways that make them drug-resistant. The first way bacteria share genetic material happens through plasmids, which transfer from one bacterium to another. The second way genetic materials move between bacteria comes from phages that deliver them to other bacteria. The third way is when bacteria naturally pick up genetic material from their environment and incorporate it into their DNA. The resistance acquired through the transfer of plasmid is the most common acquired resistance in clinical isolates (Blahová et al., 2000; Mc Dermott et al., 2003).

## 2. Drivers of ABR in Zoonotic Bacteria

Being a One Health issue ABR is an intricate health problem that affects people, livestock, and the planet's health alot (White and Hughes, 2019). Antibiotic-resistant zoonotic bacteria move from one area to another when animals pass the organisms to humans directly, when humans eat contaminated food, and when pathogens travel through environmental sources (Holmes et al., 2016). The factors responsible for the transmission of pathogens are interdisciplinary, complex, and disparate. Animals and people live together in shared surroundings, making them vulnerable to diseases that originate in animals (Collignon and McEwen, 2019). The spread of bacteria occurs most often when people touch animals carrying them or eat contaminated food (Koch et al., 2017).

### 2.1 Antibiotic Misuse in Human Medicine

Antibiotics are among the most commonly used drugs not only for the treatment of humans but also animals (Laxminarayan et al., 2013). Antibiotics are misused either by its overuse or underuse without the proper guidelines. This misuse of antibiotics is believed to be the main driver of ABR in zoonotic bacteria (Costelloe et al., 2010; Holmes et al., 2016). Only 50% of all the antibiotics used globally can be justified (Iskandar et al., 2020). In the hospital the excessive use of antibiotics is linked to various factors including time constrains in emergencies, lack of leadership and policy enforcement, prophylactic use of antibiotics, fear of hospital-acquired infections, and the lack of rapid diagnostic facilities to properly guide prescriptions (Holmes et al., 2016).

### 2.2 Antibiotic Misuse in Animal Health and the Agricultural Sector

To improve food production and satisfy the increasing consumer demand antibiotics are widely used in the agriculture sector. In the animal husbandry antibiotics are used to cure bacterial infections, increase growth, improve hygiene, and prevent illnesses (Page and Gautier, 2012). There is strong evidence that link the ABR to the misuse of antibiotics in the animals (Chatterjee et al., 2018). Resistant bacteria are mainly transmitted from animals to humans through the consumption of contaminated food, other routes include transmission through pets, from agriculture manure runoff and in the meat industry. Antibiotic resistant bacteria also transfer from humans to animals in the aquatic environment, due to the contamination of water by the sewage and industrial wastes (Iskandar et al., 2020).

### 2.3 Socioeconomic and Environmental Factors

Multiple environmental and socioeconomic aspects are associated with disseminating antibiotic resistance genes (ARGs) that result in the development of ABR. These aspects include the quality of healthcare systems, hygiene infrastructure, water and sanitation facilities, GDP per capita, and climate conditions (Reverter et al., 2020). Behavioral factors that further worsen the conditions are improper prescribing of antibiotics for viral diseases, and patient-specific conditions like obesity, smoking, and alcohol consumption that make the person susceptible to infections or affect the antibiotic's efficacy (Sun et al., 2022). AMR is easily transferable between ecosystems through mobile hosts such as humans and animals, movement of surface water runoff, and animal products trading (Allel et al., 2023).

## 3. Mechanisms of Zoonotic Transmission

### 3.1 Direct Transmission

When infections are directly transmitted between animals and people through the air (Rahman et al., 2020) or through body fluids such as saliva, urine, blood, and feces this is known as direct zoonosis. The way bacteria pass from animals to people causes infections like brucellosis and leptospirosis. People can also catch zoonotic diseases by encountering bacteria from bites, scratches, or breathing in germs released in aerosols from sick animals, such as bovine tuberculosis (Skowron et al., 2023).

### 3.2 Indirect Transmission

Indirect zoonosis occurs when animals pass bacterial infections to humans through vectors or food rather than direct contact. Foodborne transmission is the main mode in which the consumption of raw meat or raw milk results in the spread of zoonotic pathogens (*E. Coli, Salmonella*, *Staphylococcus aureus,* and *Campylobacter*). Bacteria may also be spread by insect vectors (ticks and fleas), causing diseases like plague (*Yersinia pestis*) and Lyme disease (*Borrelia burgdorferi*) (Lubna et al., 2023; Fong, 2017).

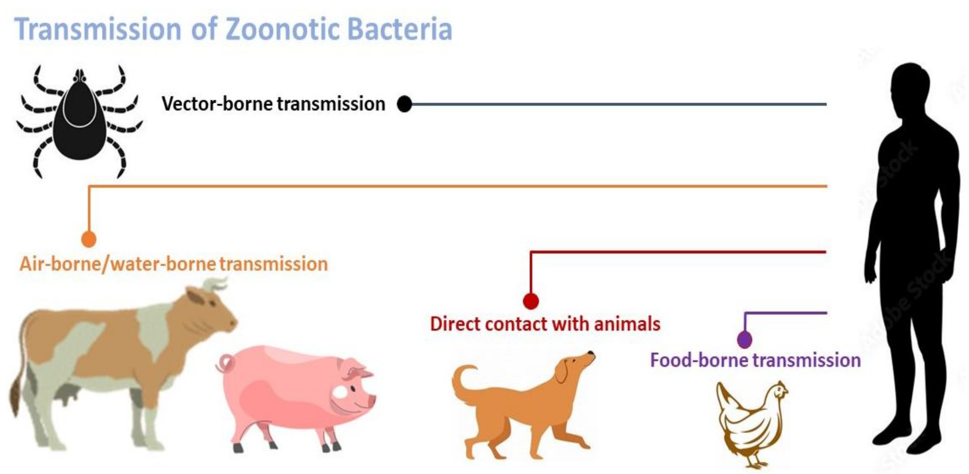


Fig. 3: Mechanism of transmission of zoonotic bacteria (PowerPoint)

## 4. Impacts of Antibiotic Resistance

### 4.1 Human Health Impacts

The ABR is still one of the most significant challenges to effective management and elimination of bacterial infections, posing important challenges to the healthcare systems worldwide (World Health Organization, 2023). Some of the consequences include increased mortality, increased healthcare costs, and longer hospitalization. Also, AMR results in more than 50,000 fatalities per year in the US and Europe only, while in the rest of the world, a significantly greater number of people die (O'Neill, 2014). Antimicrobial resistance is predicted to cause over 2.4 million deaths in Australia, Europe, and North America, between 2015 and 2050 if it is not addressed properly (Poudel et al., 2023).

### 4.2 Economic Impact

According to estimates, antimicrobial resistance would cost the world economy between $300 billion and $1 trillion by 2050 (Burki, 2018). The combined economic impact for countries in the Organization for Economic Co-operation and Development (OECD) might result in lost output of $20–$35 trillion by the same year (O'Neill, 2014). According to Ventola (2015), the AMR crisis is predicted to cost the healthcare industry up to $20 billion in the United States alone, with an extra $35 billion lost as a result of lower productivity. World Bank research suggests that antimicrobial resistance would exacerbate poverty, particularly affecting the poorest nations. Furthermore, a continuous rise in antimicrobial resistance could lead to an 11% reduction in livestock production by 2050, causing losses in animal production, which further suffers the economic position (World Bank, 2017).

### 4.3 Impact on Animal Health and Welfare

The issue of AMR will also affect livestock productivity by indefinitely disrupting animal mortality and morbidity rates (Hao et al., 2014). MDR bacteria pose a significant challenge to antibiotic treatment (Kamal et al., 2025). As frequently used antibiotics in agriculture become less effective, treatment efficacy for livestock will decrease, leading to higher infection rates and wider disease spread. As a result, decreased livestock production and trade would raise the cost of protein sources such as meat, milk, and eggs (World Bank, 2017). This lack of protein sources is concerning because of the increasing demand for animal-based protein to feed the world's expanding population (Van Boeckel et al., 2015). As reported by Lekagul et al. (2019), the World Bank has predicted that the AMR problem will significantly affect the yield of cattle, especially in middle and lower-income countries.

## 5. Current Efforts to Combat AMR

### 5.1 Role of International Organizations in Addressing AMR

In the fight against AMR, various international organizations are playing their role. These organizations can lead joint projects and contribute to efforts that address the AMR. The below table shows these organizations and their contributions to tackling the issue of AMR.

| Organization | Primary Role | Key Strategies/Initiatives | Focus Area(s) | Key Contributions | Reference |
|---|---|---|---|---|---|
| World Health Organization (WHO) | UN agency for global public health | Developed Global Action Plan | Public health, Surveillance, Development of new antimicrobials, Sanitation | Improving access to clean water, sanitation, and novel antimicrobials | (World Health Organization, 2016) |
| Food and Agriculture Organization (FAO) | Improving food security and nutrition | Guidelines for responsible antimicrobial use in animal agriculture, Enhanced surveillance and data collection in the livestock sector | Livestock and agriculture, antimicrobial use regulation | Improving food security while addressing AMR in agriculture | (Pinto Ferreira et al., 2022; Food and Agriculture Organization of the United Nations, n.d (2015) |
| World Organization for Animal Health (WOAH) | Promotes animal health and welfare | Guidelines for antimicrobial use in animal health, strengthening surveillance and data collection | Animal health and welfare, AMR in veterinary medicine | Leading initiatives to prevent animal diseases | (World Organisation for Animal Health, n.d; Góchez et al., 2019) |
| World Bank | Financial institution for economic development | Funding for AMR-related projects, supporting surveillance and new antimicrobial development projects | Economic impact of AMR, AMR project funding | Enhancing AMR surveillance, funding research, and promoting antimicrobial innovation | (World Bank, 2016; World Bank, 2024) |
| Group of 20 (G20) | Economic and political cooperation among major economies | Commitment to address AMR | International policy and collaboration | Mobilizing global action on AMR | (G20, 2017; World Health Organization, 2017; G20, 2022) |
| Global Antimicrobial Resistance Partnership (GARP) | Multi-sectoral partnership to tackle AMR | Multi-disciplinary expert collaboration | Multi-sectoral approach, Policy development | Bringing experts together for AMR strategy development | (Kamere et al., 2022; Global Antibiotic Research and Development Partnership, 2024) |
| International Council of Nurses (ICN) | Represents nurses globally | Promotion of antimicrobial stewardship, Guidelines for antimicrobial use in healthcare settings | Healthcare, Nursing | Ensuring responsible antimicrobial use in healthcare through nursing leadership | (International Council of Nurses, 2017; Wilcock et al., 2019) |
| Global Antimicrobial Resistance Surveillance System (GLASS) | WHO initiative for AMR surveillance | Strengthening global AMR surveillance | Surveillance, Data sharing | Providing accurate global data on AMR for better policymaking | (Seale et al., 2017; World Health Organization, 2021) |

### 5.2 One Health Approach

An OH approach is necessary to successfully combat the spread of AMR, which is regarded as a One-Health challenge. To promote scientific interest in AMR, improve funding, and inform AMR policy, the tripartite organizations (WHO, WOAH, and FAO) have developed an OH priority research agenda (World Health Organization, 2021). One Health encompasses a single, joined-up approach to improve various sectors (ecosystems, human and animal health) efficiently and sustainably (World Health Organization, 2021). WHO, FAO and WOAH began the AMR Multi-Stakeholder Partnership Program in November 2022 within the quadripartite partnership. The goal of this strategy is to improve OH-integrated surveillance, focusing on the food, animal, human, and environment (World Health Organization, 2022).

### 5.3 The Global Political Strategies of AMR Control

The political sector has provided attention to AMR from 2014 onwards, which has enabled the agenda to progress well in terms of policy making, resource mobilization, and policy functioning (General Assembly of the United Nations, 2016). The WHO World Health Assembly endorsed the Global Action Plan on AMR in May 2015 turning a new page in the combat against AMR. It was one of the significant initiatives that have been taken in recent years. Other major activities include the finalization of National Action Plans in many countries (World Health Organization, 2016), the launch of the Global Antimicrobial Resistance Surveillance System (GLASS) (World Health Organization, 2015), the creation of World Antibiotic Awareness Week in November 2015, and the decision of the G20 Leaders in July 2017 on the creation of the AMR Global Collaboration Hub (G20, 2017). To sustain and expand such initiatives, political support has been crucial, alongside adequate funding and policies (Inoue and Minghui, 2017).

## 6. Challenges in Addressing AMR in Zoonotic Bacteria

There is a worldwide issue of antibiotic resistance that is closely associated with animal, human, and environmental health; that is why the OH approach to intervention is required. Still, many open issues concern the nature of the emergence and the dispersion of ABR in the environment. It is, therefore, crucial to understand these knowledge gaps, which must inform further research on ABR in the environment (Yadav and Kapley, 2021).

Human actions also influence the distribution and diversification of antibiotics and ARGs in various environmental niches specifically aquatic environments (Yadav and Kapley, 2019). Sources like aquaculture, wastewater treatment plants, and the pharmaceutical industry are relevant contributors. Thus, it is still unknown how these sources affect the selection of antimicrobial resistance even though they are considered essential (Sabri et al., 2020). Lack of resources alongside poor stewardship has been linked to a rise in antibiotic resistance on a regional and global level. The spread of drug-resistant bacteria is made worse in poor countries because they don't have good monitoring systems, and don't give enough money for responsible research (Zellweger et al., 2017).

## 7. Future Directions and Solutions

### 7.1 Development of Alternative Therapies

Antibiotic-resistant strains such as MDR, XDR (extensively drug-resistant), and PDR (pandrug-resistant) bacterial strains have emerged, making us concerned about the arrival of the post-antibiotic period where most bacterial diseases cannot be treated effectively. We should study alternative ways to treat bacterial infections before we lose our best weapon (antibiotics) against them (O'Neill, 2014).

#### 7.1.1 Phage Therapy

Bacteriophages have been used to fight bacterial infections for many years even before the discovery of antibiotics. Since more bacteria have grown resistant to antibiotics, using phages as a therapy has attracted more attention in recent years (Knoll & Mylonakis, 2014). Phages are considered better than conventional antibiotics in different ways. It does not affect human cells, does not influence normal microbial populations, and is specific to bacteria. Bacteriophage therapy has several drawbacks, such as the potential for bacterial resistance and immunological reactions, difficulty in separating phages from bacterial endotoxins and exotoxins, and issues with formulation and stability during systemic distribution. However, these challenges could be overcome, making phage therapy the best option for treating bacterial infections (Pires et al., 2015).

#### 7.1.2 Medicinal Plants and Phytochemicals

Through the use of natural phytochemicals present in leaves, seeds, stems, flowers, fruits, and roots, plants have developed special defenses against microbes (AlSheikh et al., 2020). Additionally, plants produce a wide variety of structurally distinct compounds that each play a distinct part in how they react to microbial invasion (Gupta and Birdi, 2017). Therefore, the scientific and pharmaceutical sectors have developed attention to the potential effectiveness of chemicals originating from plants as therapeutic candidates (Savoia, 2012).

#### 7.1.3 Essential Oils (EOs)

EOs are combinations of volatile chemicals that are produced during secondary metabolism from various plant sections. Examples of EOs include aldehydes, terpenes, terpenoids, phenolics, and other aromatic compounds with promising antimicrobial properties (Swamy et al., 2016). Whether used alone, in combination with other essential oils, or in conjunction with antibiotics, EOs have shown effective antibacterial activity against a range of microorganisms, including MDR bacteria. We need researchers to investigate a wider range of essential oils and their antibacterial effects to treat resistant bacterial infections (Yang et al., 2021).

#### 7.1.4 CRISPR-Cas System

The bacterial adaptive immune system, known as CRISPR-Cas (Clustered Regularly Interspersed Short Palindromic Repeats-CRISPR Associated Protein), protects bacteria from invasion by mobile genetic elements like phages, plasmids, and foreign genetic material by using RNA-mediated, DNA-encoded, or DNA-targeting mechanisms. As sequence-specific, programmable antimicrobials, CRISPR-Cas systems provide exciting options for creating new antimicrobial and genomic engineering solutions (Palacios Araya et al., 2021; Fu & Xianyu, 2023). To decrease or eradicate antibiotic resistance and develop novel therapeutic options for MDR illnesses, these gene-editing technologies can quantitatively, precisely, and selectively target bacterial genomes (Aslam et al., 2020).

#### 7.1.5 Antimicrobial Peptides (AMPs)

AMPs are amphipathic, widely distributed, and have an overall cationic charge. When compared to conventional antibiotics, they exhibit comparable or even better antibacterial properties (Sheard et al., 2019). A variety of bacterial cells, including Gram-positive and Gram-negative, can be targeted by AMPs by using the same methods as conventional antibiotics. Following their penetration of the bacterial cell wall, AMPs target nucleic acids, protein biosynthesis, and/or the development of membranes and the cell wall to produce further antimicrobial action (Nguyen et al., 2011).

#### 7.1.6 Nanoparticle-Based Strategies

Nanoparticles (NPs) are nano-scaled particles with sizes between 1 and 100 nm (Hanif et al., 2024). These NPs are finding increasing use as bacterial growth inhibitors in various applications, including coatings for medical devices and materials, as well as antibiotic delivery systems. Additionally, they can function directly as antibacterial agents (Wang et al., 2017). While some metals in their bulk form exhibit antibacterial properties against Gram-negative bacteria and Gram-positive, others only demonstrate this activity when in NP form (Slavin et al., 2017).

7.2 The Role of Stakeholders in the Control of AMR

Addressing AMR requires more than just the efforts of medical experts and researchers. Although continuous education is essential for healthcare professionals to understand the significance of evidence-based and logical prescribing procedures (Bhutta and Balchin, 1996), other stakeholders and the public are also very important. AMR should be a top priority for governments worldwide, and regulations and procedures must be set in place to guarantee that antimicrobials are used and accessed responsibly (Blakely et al., 2006).

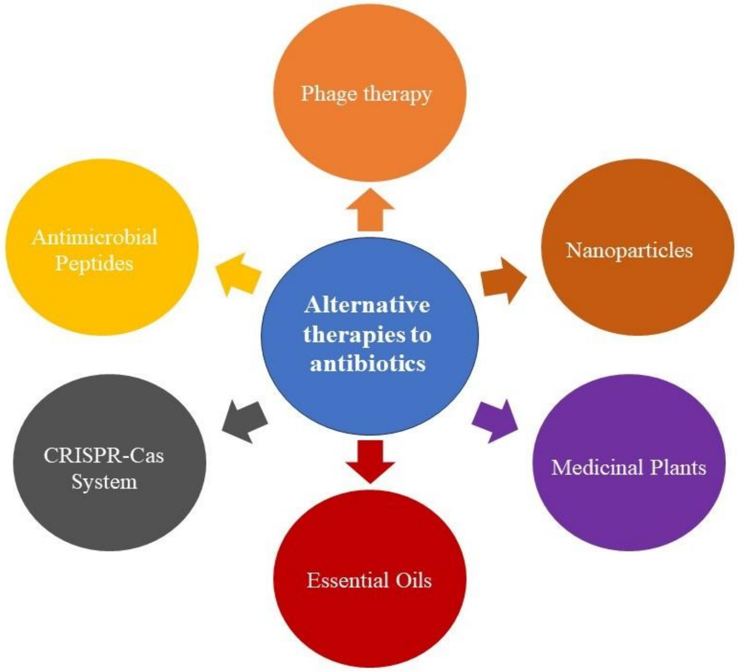


Fig. 5: Novel strategies to fight antibiotic resistance. (PowerPoint)

7.3 Public Awareness and Education

Educating the public on the risks posed by AMR is crucial. Media workers should have sufficient training to convey scientific and medical information in a comprehensible way on different kinds of media. Public education regarding the actions and behaviors that lead to the emergence and dissemination of AMR zoonotic pathogens is crucial (Blakely et al., 2006). Because education programs for journalists have proved effective in dealing with AIDS/HIV in many underdeveloped countries, it can be inferred that the same strategy can also give promising results in confronting AMR (Martinez-Cajas et al., 2008).

Conclusion

The spread of resistant bacteria from animals to humans poses a serious threat to our environment as well as animal and human health. Bacterial drug resistance develops from factors like poor waste management systems and antibiotic misuse in both human and animal healthcare. Antibiotic resistance causes treatment failure resulting in increased death rates and medical expenses and poses a great threat to food safety. The battle against antibiotic resistance faces many difficulties despite the efforts of global organizations. These challenges include poor surveillance systems, gaps in research, and a lack of public awareness. More research needs to be done to develop alternatives such as NPs, AMPs, bacteriophages, and CRISPR technology to combat AMR issues impacting global health. Additionally, it is important to raise public awareness to use antibiotics wisely and the government needs to create proper guidelines to use them. Finally, it is recommended that preventing AMR and preserving access to effective medicines requires interdisciplinary, cooperative, and persistent One Health efforts.

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