



The Role of Food-Producing Animals in the Transmission of Multidrug-Resistant (MDR) Bacteria to Humans: A One Health Approach

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ABSTRACT

Antimicrobial Resistance (AMR) is currently recognized as one of the most complex and acute public health challenges of the 21st century, having transcended geographical and species boundaries. Recent reports and scientific documentation indicate that infections caused by resistant bacteria are directly responsible for the deaths of millions of people worldwide. If current trends are not corrected, AMR-related mortality is projected to exceed 10 million people per year by 2050, surpassing the total deaths caused by cancer. In this context, the livestock industry and food-producing animals, which consume approximately 73% of all antibiotics produced globally, serve as a massive reservoir and driving force for the evolution and dissemination of resistant bacteria. The expansion of intensive farming systems to meet the global demand for protein has exacerbated this crisis. The aim of this review article is to provide a comprehensive and multilateral analysis of the pathophysiological mechanisms of resistance emergence, identify key zoonotic pathogens, and accurately delineate transmission pathways from farm-to-fork within the framework of the One Health approach. This study synthesizes current literature to examine gaps in epidemiological knowledge and evaluates the effectiveness of control strategies. The reviewed evidence indicates that the use of sub-therapeutic doses of antibiotics as growth promoters creates severe selective pressure for the survival of strains harboring antimicrobial resistance genes (ARGs). Priority pathogens such as ESBL-producing and carbapenemase-producing *Escherichia coli*, *Salmonella*, and *Campylobacter* are transmitted to human populations through the food chain, direct occupational contact (particularly among slaughterhouse workers), and environmental contamination (manure and water sources). The emergence of plasmid-mediated genes such as *mcr-1* (colistin resistance) and *bla*NDM indicates extensive genetic exchange between animal and human reservoirs. Managing the AMR crisis is impossible without a coordinated global approach. Integrated surveillance of drug consumption, the elimination of antibiotic growth promoters, the improvement of on-farm biosecurity, and the replacement of antibiotics with novel methods



such as phage therapy and probiotics are vital strategies for preserving human health and food security in the future.

Keywords: Animals, Multidrug-Resistant, bacterial, Humans

1. INTRODUCTION

In the current era, humanity faces a threat with the potential to revert modern medicine to the pre-antibiotic age. Antimicrobial Resistance (AMR) is no longer a scientific prediction for a distant future, but a stark and tangible reality pressuring global health and economic systems. According to statistics in authoritative literature, drug-resistant infections not only increase mortality rates but also drastically escalate treatment costs and prolong hospital stays. Studies have shown that by 2050, AMR could cause a 1.1% to 3.8% decline in global Gross Domestic Product (GDP) and push millions below the poverty line [1,2].

At the epicenter of this global crisis lies the increasing and relentless demand for animal protein. As the global population grows and dietary patterns shift toward higher consumption of meat, milk, and eggs, livestock and poultry farming systems have transitioned from traditional, low-density methods to intensive industrial farming. This structural shift has necessitated strategies to maintain herd health at high densities, which unfortunately has led to a heavy and systematic reliance on antibiotics. It is estimated that global antibiotic consumption in food-producing animals will reach 106,000 tons by 2030, representing a 67% increase compared to 2010 [3].

The significance of food-producing animals in the antibiotic resistance equation is critical and multifaceted. Antibiotics are used in the livestock industry at four main levels: Therapeutic (for sick animals), Metaphylaxis (to control outbreaks in herds where some members are sick), Prophylaxis (to prevent disease in healthy animals), and finally, as Growth Promoters. Although the use of antibiotics as growth promoters has been banned in the European Union and some other regions, it remains common in many developing countries and emerging economies. This non-therapeutic, long-term use at sub-therapeutic doses provides an environment where susceptible bacteria are eliminated, and resistant strains find the opportunity to proliferate and dominate the microbial population [2,4].

The concept of One Health is a framework essential for understanding and managing this complexity. This approach recognizes that the health of humans, domestic animals, wildlife, and the environment (including soil and water) are inextricably linked and cannot be managed in silos. Bacteria do not recognize geographical or species boundaries. A resistant bacterium that evolves in the gut of a pig on a remote farm can enter the soil through manure, contaminate groundwater, settle on crops, or find its way directly into a family's kitchen via meat. Furthermore, approximately 60% of all known infectious diseases in humans and 75% of emerging diseases are of zoonotic origin, doubling the importance of animal reservoirs [3,5].



Despite global awareness, deep gaps in our knowledge remain. Many studies focus on nosocomial infections, and the precise, quantifiable role of animal-to-human transmission in non-clinical settings has received less attention. Particularly in Low- and Middle-Income Countries (LMICs), where surveillance of drug consumption and animal waste disposal is weak, epidemiological data is limited. The objective of this study is to bridge part of this gap by comprehensively reviewing the current state of knowledge, closely examining biological mechanisms and transmission pathways to present a clear picture of the dimensions of this threat [6,7].

2. Mechanisms of Emergence and Pathophysiology of Resistance

Understanding how antibiotic resistance emerges and spreads requires deep knowledge of bacterial biology and the ecological pressures prevailing in livestock environments. The phenomenon of resistance is a natural evolutionary process, but human activities act as a powerful catalyst, exponentially accelerating its rate.

The most important mechanism driving resistance in livestock farming is the selective pressure resulting from continuous antibiotic use. When a bacterial population is exposed to antibiotics, susceptible cells are killed or their growth is halted. However, cells that naturally possess specific genetic mutations or have acquired resistance genes survive. In the gut environment of animals constantly receiving low doses of antibiotics (via feed or water), these resistant strains not only survive but, in the absence of competition from other bacteria, proliferate rapidly. This phenomenon is particularly prevalent regarding the use of tetracyclines, sulfonamides, and penicillins, which are inexpensive and readily available [2,3].

Although chromosomal mutations (Vertical Transmission) play a significant role in resistance, the most dangerous aspect of AMR is the ability of bacteria to share resistance genes with one another through Horizontal Gene Transfer (HGT). This process occurs through three main pathways: Conjugation (direct bacterial contact), Transformation (uptake of free DNA), and Transduction (transfer by bacteriophages). The role of Mobile Genetic Elements (MGEs) in this process is vital. Plasmids, transposons (jumping genes), and integrons (such as class 1 and 2 integrons) can carry resistance gene cassettes and move them between different bacterial species [8,9].

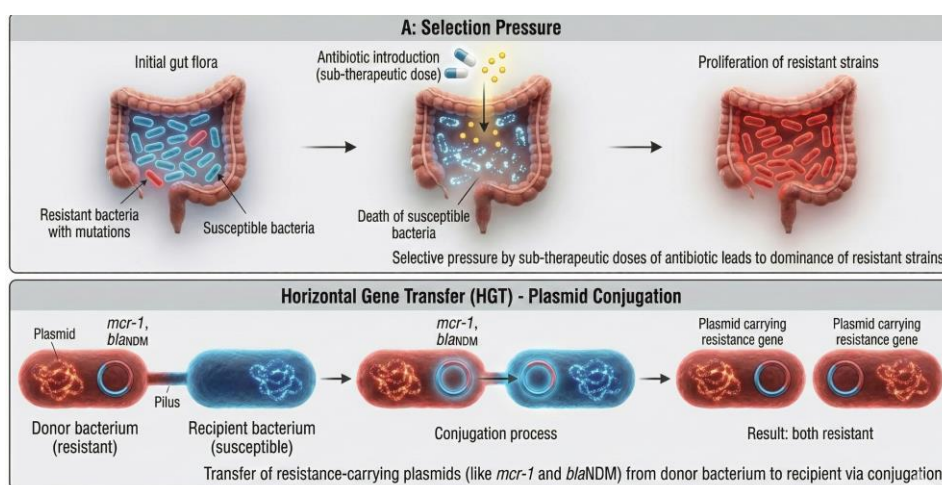




Figure 1. Mechanisms of resistance dissemination. (A) Clonal Expansion (Vertical Transmission): Under selective pressure, susceptible bacteria die, while resistant mutants survive and proliferate, passing resistance to their offspring. (B) Horizontal Gene Transfer (HGT): Resistance genes (e.g., *mcr-1*) are transferred laterally between different bacterial cells via conjugation, allowing resistance to spread rapidly across species boundaries.

Recent studies have focused on specific genes that pose a direct threat to human therapeutics. The gene *mcr-1*, first identified in China, encodes resistance to colistin. Colistin is a last-line defense antibiotic for treating carbapenem-resistant Gram-negative infections. The discovery of plasmid-mediated *mcr-1* in animals was a global alarm bell, as it demonstrated that resistance to the last available drug could also spread rapidly [2,10]. Genes such as the *bla*CTX-M family, *bla*TEM, and *bla*SHV, which produce Extended-Spectrum Beta-Lactamases (ESBLs), confer resistance to penicillins and third- and fourth-generation cephalosporins. These genes are found abundantly in animal isolates [11,12]. The identification of genes such as *bla*NDM (New Delhi metallo-beta-lactamase) and *bla*OXA-181 in livestock is highly concerning, as carbapenems are vital drugs for treating severe human infections [8,13].

Understanding the difference between Cross-resistance and Co-resistance is vital in AMR management. Cross-resistance occurs when a single resistance mechanism (e.g., an efflux pump) causes the expulsion of multiple similar types of antibiotics from the cell. However, co-resistance occurs when resistance genes for completely different antibiotics (e.g., tetracycline and chloramphenicol) are located on a single genetic element (such as a large plasmid). Co-selection occurs when resistance genes for different antibiotic classes are genetically linked on the same Mobile Genetic Element (MGE). Consequently, the use of tetracycline exerts selective pressure that maintains the plasmid, thereby preserving the associated chloramphenicol resistance gene even in the absence of chloramphenicol usage [3,14].

3. Key Pathogens and Epidemiological Evidence

In the One Health approach, certain bacteria are identified as key pathogens due to high prevalence, pathogenic potential, and the ability to transfer resistance. Epidemiological evidence suggests that these bacteria act as the primary bridge between animal reservoirs and human infections. *Escherichia coli* serves as a commensal bacterium in the gut of humans and warm-blooded animals and is the best indicator for assessing resistance status in a population. This bacterium can not only be a pathogen itself but also acts as a mobile reservoir of resistance genes, transferring them to other enteric pathogens such as *Salmonella*.

Global surveillance data indicates a rise in ESBL-producing Enterobacteriaceae. For instance, recent studies in North Africa have documented the emergence of *bla*NDM-1 and *bla*OXA-181 in livestock, highlighting the infiltration of high-level resistance into animal reservoirs previously thought to be free of such carbapenemases. Similarly, high prevalence rates have been observed in Sub-Saharan Africa. Results showed that 17% of cattle and 1% of sheep carried *E. coli* resistant to third-generation cephalosporins (3GC). A highly concerning point in this study was the identification of isolates simultaneously carrying *bla*NDM-1 (carbapenem resistance) and



*bla*OXA-181 genes. This was the first report of these dangerous genes in livestock in Africa, indicating the infiltration of high-level resistance into animal reservoirs. Furthermore, 85% of the isolates in this study exhibited a Multidrug-Resistant (MDR) pattern [8].

In another study in Nigeria, the prevalence of resistant *E. coli* among slaughterhouse workers was investigated. The results were shocking: 50% of the workers carried *E. coli* with an MDR pattern. This study showed that butchers had a higher resistant microbial load compared to other staff (such as cleaners), which is directly linked to prolonged contact with animal viscera. The genes *tetA* and *sulI* were the most abundant genes identified in these individuals [7].

Salmonella is one of the most important causes of food poisoning globally, and almost all cases of non-typhoidal salmonellosis are of zoonotic origin. Poultry and eggs are the main sources of serotypes *S. Enteritidis* and *S. Typhimurium*. The primary concern regarding *Salmonella* is the increase in resistance to fluoroquinolones (such as ciprofloxacin), which is the drug of choice for treating invasive infections in adults. Reviewed studies indicate that the use of enrofloxacin in the poultry industry has a direct correlation with increased ciprofloxacin resistance in human isolates. Additionally, monophasic *Salmonella* strains, which are often MDR, have spread within pig populations and caused human outbreaks [6,14].

Campylobacter jejuni and *C. coli* are the most common bacterial causes of gastroenteritis in developed countries, and the consumption of chicken meat is the primary factor in their transmission. Unlike *Salmonella*, which can survive in the environment, *Campylobacter* is highly sensitive, and transmission occurs almost exclusively through the food chain. Resistance rates to fluoroquinolones and tetracycline in isolates from broiler chickens have been reported to be very high (between 60% and 90%) in many countries. This level of resistance has practically rendered these drug classes ineffective for treating severe human infections [3,15].

Although MRSA was traditionally known as a nosocomial pathogen, the emergence of Livestock-Associated MRSA (LA-MRSA) strains, particularly the CC398 clone, has changed the equation. These strains are predominantly found in pigs, calves, and poultry. Unlike enteric pathogens, LA-MRSA transmission occurs mainly through direct contact and contaminated dust in farms. Studies have shown that pig farmers and veterinarians are at a very high risk for nasal colonization with this bacterium and can transmit it to their family members and ultimately to the community [5,6].

4. Transmission Routes from Animals to Humans

The transmission of antibiotic-resistant bacteria from animals to humans is a complex and multi-pathway phenomenon that can generally be classified into three main routes: the food chain, direct contact, and environmental transmission. Among these, the food chain (Farm-to-Fork) is recognized as the most significant route of general population exposure to zoonotic resistant bacteria, as contamination can occur at various stages of production, processing, and consumption. In slaughterhouses, during slaughter, skinning, and evisceration processes, the probability of gut rupture and the transfer of contents to the carcass surface is very high. This leads to meat contamination with resistant bacteria such as *Escherichia coli* and *Salmonella*; if these products are cooked inadequately, the bacteria can be transmitted to the consumer [7,16].

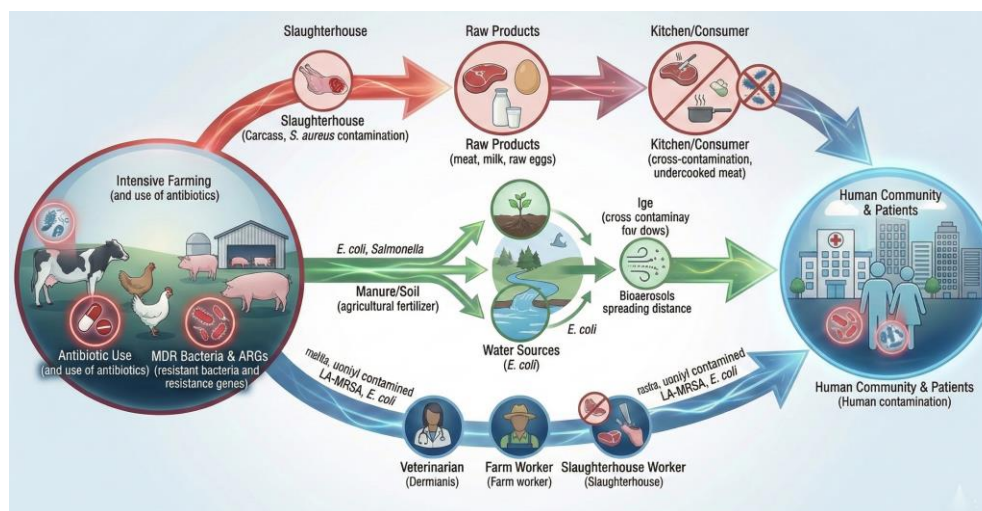


Figure 2. Schematic diagram of transmission routes of multidrug-resistant (MDR) bacteria from food-producing animals to humans within the framework of the One Health approach.

Consumption of raw or undercooked products, including unpasteurized milk and raw or soft-boiled eggs, carries a high risk of transmitting resistant bacteria, and evidence shows that raw milk can harbor pathogens such as resistant *Campylobacter* and *Listeria monocytogenes* [14,17]. A point that has received less attention is the role of lactic acid bacteria found in fermented foods such as cheeses and fermented meat products; although generally non-pathogenic, these bacteria can act as reservoirs for antibiotic resistance genes, including erythromycin and tetracycline resistance genes. Upon entering the human digestive tract, they can transfer these genes via horizontal transfer to the natural gut flora or opportunistic pathogens [14].

The Direct Contact route is mainly limited to specific occupational groups and is recognized as an occupational hazard. Farmers, farm workers, livestock transport drivers, veterinarians, and slaughterhouse staff are on the front lines. A study in Nigeria showed that the risk of carrying MDR bacteria is significantly higher in individuals who have direct contact with carcasses. Factors such as frequent hand cuts, lack of glove and boot usage, and eating in the contaminated slaughterhouse environment drastically increase the probability of transmission. Interestingly, this study identified handwashing with soap after work as a strong protective factor that significantly reduced the chance of contamination [7].

Environmental transmission of antibiotic-resistant bacteria is an important but often overlooked route in the resistance dissemination cycle, where the environment acts as a bridge between animals, humans, and the ecosystem. Animal manure contains high amounts of resistant bacteria and unmetabolized antibiotic residues. The application of untreated manure on agricultural land leads to the direct entry of these bacteria and antibiotic resistance genes into the soil. Reports indicate that the concentration of resistance genes in soils treated with animal manure can be up to 28,000 times higher than in pristine soils; these microorganisms and genes can settle on vegetables and crops consumed raw and be transmitted to humans [3,18].

In addition to soil, water sources also play a major role in environmental resistance dissemination; surface runoff from rainfall in livestock units and aquaculture ponds can enter surface and groundwater, facilitating



the widespread transfer of resistance genes. The identification of sulfonamide (*sul*) and tetracycline (*tet*) resistance genes in water sources distant from livestock farms indicates the persistence and mobility of these pollutants in aquatic ecosystems [2,9]. Furthermore, in intensive farming systems, particularly poultry farms and pig farms, bioaerosols containing resistant bacteria, endotoxins, and genetic residues are released via airborne dust particles. Evidence shows that these particles can be transported by air currents over long distances—sometimes up to about 10 kilometers and enter the human body through inhalation by residents of surrounding areas [2].

5. Control Strategies and One Health Integration

Combating the AMR crisis requires fundamental changes in veterinary and agricultural management practices. Single-dimensional solutions are doomed to fail and must give way to comprehensive One Health strategies. The first and most critical step is the reduction of overall antibiotic consumption. This includes a total ban on growth promoters and restricting the use of antibiotics that are Critically Important for Human Medicine (CIA), such as fluoroquinolones, in animals. Countries that have implemented these policies have observed a significant reduction in resistance rates without serious damage to production productivity [2,4].

Surveillance systems must move out of silos. Data regarding resistance in humans, animals, and food must be collected simultaneously and compared. The use of Whole Genome Sequencing (WGS) technology has revolutionized these systems. WGS makes it possible to determine precisely whether a specific resistant clone causing disease in a hospital is the same clone present in local farms [2,5].

Given the limitations and consequences of widespread antibiotic use in animal husbandry, the introduction and application of effective alternatives to maintain herd health have gained increasing importance. One prominent approach in this field is Phage Therapy, which is based on the use of bacteriophages as highly specific biological agents to target and eliminate pathogenic bacteria; due to high specificity, it has minimal impact on the host's natural flora. Alongside this, the use of probiotics and synbiotics aiming to strengthen and stabilize the gut microbial flora of livestock has been noted as a strategy to increase the host's natural resistance against infections, such that these interventions can reduce the risk of pathogen establishment [19,20]. Furthermore, gene-editing technologies such as CRISPR-Cas systems are gaining attention as precision antimicrobial tools. Unlike traditional antibiotics, these systems can be programmed to specifically target and degrade antimicrobial resistance genes (ARGs) carried on plasmids. This approach, known as 'plasmid curing', allows for the re-sensitization of bacteria to antibiotics and prevents the spread of resistance elements without disrupting the beneficial gut microbiota.

Other alternatives under investigation include Antimicrobial Peptides (AMPs), which are natural molecules and part of the innate immune system capable of inhibiting or killing a broad spectrum of bacteria via diverse mechanisms. Additionally, livestock vaccination is proposed as a fundamental preventive strategy, as the development and use of effective vaccines against common animal diseases can significantly reduce the incidence of infections, thereby radically limiting the need for antibiotic-based therapeutic interventions [21,22].



Implementing these strategies, however, faces significant economic barriers, particularly in Low- and Middle-Income Countries (LMICs). Many farmers rely on antibiotics as a low-cost substitute for hygiene and biosecurity measures. The sudden withdrawal of antibiotic growth promoters can lead to immediate productivity losses and increased mortality rates. Therefore, successful transition strategies must include financial incentives and subsidies to support farmers in upgrading farm infrastructure and biosecurity standards [20,23].

Prevention is always better than cure. Improving hygiene on farms, quarantining new animals, controlling the entry of personnel and vehicles, and proper management of manure and wastewater interrupt the infection transmission cycle. At the slaughterhouse level, modifying slaughter methods to minimize fecal contamination and continuous disinfection of carcasses is essential [7,24].

6. Conclusion and Future Perspectives

A review of existing scientific literature clearly indicates that food-producing animals are one of the main sides of the antimicrobial resistance triangle (Human-Animal-Environment). There is undeniable evidence of the transmission of resistance genes and MDR bacteria via food, direct contact, and the environment. Phenomena such as the horizontal transfer of *mcr-1* and *bla*NDM genes serve as a serious warning to the global community [10,25].

In the short term, priority must be given to enforcing strict laws to eliminate unnecessary antibiotic use in agriculture. However, in the long term, the future landscape requires leveraging novel technologies. Artificial Intelligence (AI) holds immense potential for analyzing genomic big data and predicting outbreak patterns [26,27]. Furthermore, the development of rapid diagnostic kits capable of determining bacterial type and resistance patterns on the farm in less than an hour could revolutionize disease management. Ultimately, fighting AMR is a shared ethical responsibility; preserving the efficacy of these drugs for future generations guarantees the survival of modern medical achievements [28,29].

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