Meat Consumption as Source of Zoonotic AMR

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Abstract

Since one of the main ways that resistant organisms spread is by zoonotic transmission, the global rise in antimicrobial resistance (AMR) poses a serious threat to public health. Consuming meat, especially from animals that have received antibiotic treatment, has been found to be a significant factor in the development and spread of microbes resistant to antibiotics. Examining how antimicrobial usage in animal production results in resistant bacteria that can be spread to people by direct contact, ingestion of contaminated meat, or environmental exposure, this chapterdelves into the intricate relationship between meat consumption and zoonotic AMR. The dangers of various meats, including beef and chicken, are assessed, as is the contribution of proper food handling and cooking techniques to reducing these dangers. Furthermore, the efficiency of several regulatory measures, including prohibitions on the use of antibiotics in animal husbandry, in lowering the spread of zoonotic AMR is examined. Knowing how zoonotic AMR spreads via the food chain is essential for creating plans to lessen its negative effects on human health while the world's demand for meat keeps growing.

Keywords: Antimicrobial Resistance (AMR Zoonosis, Transmission, Meat, Animal health, Antibiotics, Food safety

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Introduction

Since antimicrobial resistance (AMR) is thought to cause hundreds of thousands of deaths annually, all international organizations, including the WHO, agree that it is a serious global concern. One of the most significant medical advances of the 20th century was the discovery of antimicrobial chemicals, which opened the door for the use of antibiotics to treat and cure bacterial infections. This innovation was considered a watershed in the medical field. Due to the quick development of antibiotic resistance in numerous microbiological species, which has become a global issue, its usage has been limited (Thukar et al., 2019). Before antibiotics were discovered, developed, and made available for purchase, there was antibiotic resistance. In fact, bacteria isolated from glacial streams more than 2,000 years ago had ampicillin resistance, but germs from permafrost more than 30,000 years ago displayed Bactrim resistance (Zembower and Morrison, 2020).

Human society has changed more quickly in the last fifty years than at any other time in history due to technical developments that have enhanced and stabilized the food supply, improved sanitation and health, and other facets of human life. The food supply has altered as a result of the adoption of new agricultural and livestock systems. In many places, livestock production systems have become more intensive in terms of the use of land, water, and feed in order to increase overall production and generate higher productivity in terms of output per animal, land, and labor unit. Particularly in lower- and middle-income nations, these factors have resulted to an exceptionally rapid population growth during this time, with many of these newcomers residing in urban areas (Alemayehu Tegegn, 2024).

Population Growth Effect
(1) A sizable portion of the population still goes without enough food.
(2) A fast-growing population that consumes excessive amounts of calories; and
(3) Access to micronutrients is limited for certain individuals (Bongaarts, 1996)

Although different populations may be impacted by this triple burden, the rural-to-urban transition has occurred so swiftly that it has also been observed in the same family and, in the worst cases, in the same individual (Keino et al., 2014; Dominguez-Salas et al., 2016). These nutrition-related problems are contributing to a rise in the total number of noncommunicable diseases (NCDs) as well as their relative importance (Murray et al., 2012; Black et al., 2013). In low- and middle-income countries LMICs, metropolitan regions are particularly affected by NCD issues. This study represented that NCDs are an area that needs careful consideration when thinking about animal feeding systems, even if it will not particularly address them. Intensification of cow agriculture has also led to the problems of disease reemergence and introduction. Many of these pathogens only affect animals, and some of them have an impact on the food supply due to their contagiousness, the harm they cause, and the steps taken to control the illness (Knight-Jones and Rushton, 2013; (Knight-Jones et al., 2017). Other viruses, on the other hand, have a major impact on human health because they are zoonotic, meaning they may spread from other animals. Eating contaminated food or coming into contact with animals and their byproducts, including influenza viruses, can cause food-borne illnesses and the spread of zoonotic diseases (Havelaar et al., 2015). Pharmaceutical drugs' efficacy in treating these infections in humans may be harmed if the animals from which they originate have previously received treatment with certain antimicrobials, as selection pressures may cause antimicrobial resistance (AMR) to develop (Aarestrup et al., 2008; Marshall and Levy, 2011a). The setting of escalating livestock systems will be discussed in this chapter along with the zoonotic infections found in the related value chains. In order to address current problems and prevent future ones from emerging while maintaining steady and secure supplies of livestock products, this process will assist in guiding how the Consultative Group for International Agricultural Research (CGIAR) can use research innovation and policy influence (Rushton et al., 2018).

Food and Nutrition Security

Food is defined as "adequate access to food for all people at all times for an active, healthy life," whereas food security is defined as "a substance consumed or consumed to sustain growth and life." However, it is believed that nutrition security goes beyond this simple concept. Nutrition security is only considered achieved when there is a enough supply of food in a form that is always readily available for everyone to use in order to live a happy and healthy life. It entails having enough readily available food that a population can use to maintain good health, not just having food on hand (Pangaribowo et al., 2013).

Increasing the Intensity of Livestock Systems

Animal systems refer to the improved use of external services and inputs to increase the volume or value of output per unit for animal production. To increase output per labor unit and per animal, this usually means applying specialist management approaches, such as changes to housing, food, and husbandry. This is typically brought on by growing consumer demand for meat, dairy, and eggs (Udo et al., 2011).

Deficiency

Accessibility is the extent to which an individual, group, or population is unable to anticipate, control, endure, and recover from the consequences of natural or man-made disasters. This is a dynamic process that is frequently connected to poverty (Bebe,et al., 2002).

Food Chain/Food System

"The full range of fields and industries and their successive organized valuable activities that provide particular agricultural supplies while transforming them into specific food products that sell to final consumers" is how the Food and Agriculture Organization (FAO) describes a food system (FAO, 2014a).

AMR and Antimicrobials

Antimicrobials are compounds that either kill or prevent the spread of bacteria, viruses, fungi, and parasites. Antimicrobial resistance (AMR) occurs when these microorganisms adapt in ways that make antimicrobial drugs useless against them. Despite the fact that AMR is believed to be a natural adaptation mechanism for microbes, antibiotic abuse and negligent use increase the risk of resistance.AMR increases morbidity and mortality rates in both human and animal species by making infections harder to treat and cure. This can therefore increase healthcare costs and therefore affect livelihoods and food security. Since antibiotics are antibacterials that either kill or inhibit the growth of germs, antibiotic resistance specifically refers to bacterial resistance (FAO, 2016; WHO, 2018).

Foodborne Illnesses and Zoonotic Infections

The term "zoonotic disease" refers to a disease that naturally infects humans from vertebrate animals, including domestic pets, livestock, or wildlife (Rahman et al., 2020).. These illnesses are thought to account for more than 60% of all developing diseases and 58% of all human infections (Jones et al., 2013). Consuming contaminated food, whether from a chemical agent, parasite, virus, or bacterium, can result in a foodborne illness (Tauxe et al., 2010). An estimated 33 million DALYS were lost in 2010 as a result of foodborne illnesses, with diarrheal causative agents accounting for more than half of these cases (Havelaar et al., 2015).

Animal Welfare

The condition of an animal and how it adjusts to its environment are referred to as animal welfare. If an animal is safe, healthy, fed properly, able to exhibit its natural behaviors, and not in pain, fear, or discomfort, then its wellbeing is seen to be up to par. Positive animal wellbeing requires compassionate handling and killing, appropriate housing, management, and nutrition, as well as disease prevention and treatment (OIE, 2016a).

Mechanisms of Antibiotic Resistance

New transmission vectors are being uncovered at the same time that new resistant mechanisms and resist-associated genes are emerging. The pathogen's ability to block access to drug targets, structural alterations to antibiotic targets, and the modification or deactivation of potentially impacted medications are some of the mechanisms.(Moo et al., 2020). Certain antibiotic resistance in bacteria can be acquired through HGT, gene mutations, or intrinsic resistance. Because of inherent structural or functional characteristics, bacterial species that exhibit intrinsic resistance are able to withstand the effects of specific antibiotics. Intrinsic resistance is created using the inherent structural or functional characteristics of the molecular target. Daptomycin is effective against Gram-positive bacteria but ineffective against Gram-negative ones due to the differences in the makeup of their cytoplasmic membranes. Gram-negative bacteria's cell membrane has less anionic phospholipids than the cytoplasmic membrane of Gram-positive bacteria. This reduction in the proportion of anionic phospholipids affects the Ca2+-dependent insertion efficiency of daptomycin into the cytoplasmic membrane, which is essential for its antibacterial activity. Recent studies have shown that some genes produce innate resistance to particular antibiotic families, including as aminoglycosides, βlactams, and fluoroquinolones (Moo et al., 2020).

Thioredoxin reduction (trxB), thioredoxin A (TrxA), SapC, DacA, FabI, and D-Ala-D-Ala carboxypeptidase are the main resistance genes. Therefore, the combined antagonism of these gene products may assist increase the effectiveness of current medications for treating infections, including rifampin, aminoglycosides, and certain β-lactams. A high level of genome a mutated libraries and high volumes screening methods were used to identify the genes causing innate resistance. Either targeted insertion or random transposon insertion mutagenesis was used to produce the libraries in bacteria involving *Pseudomonas aeruginosa, Escherichia coli,* and *Staphylococcus aureus*. Finding potential innovative medication combinations that will allow for the suppression of intrinsic resistance mechanisms is made achievable by this library screening method. As a result, other antibiotics' range of action can be expanded to include diseases other than their typical target species. Apart from inherent resistance, bacteria can also develop a number of additional resistant mechanisms, which can be divided into three main categories: blocking access to the target, altering the antibiotic target through mutation, and altering the target itself. Over the past few decades, these modalities of action have been thoroughly examined. This study will therefore provide an up-to-date summary of the most recent findings on each type of antibiotic resistance mechanism (Moo et al., 2020).

Prevention of Access to Target

An example of how an antibiotic may be prevented from reaching its target is the resistance of Enterobacteriaceae to carbapenems, which arises from a reduction in the permeability of the bacterial membrane. Hydrophilic antibiotics enter the bacterial cell through the porin proteins in the outer membrane. OmpC and OmpF from *E. coli* are typical examples of the principal porins found in most Enterobacteriaceae. This study indicate that bacteria may employ resistance strategies include downregulating porin protein synthesis or replacing key porins with more selective membrane channels (Zhu et al., 2022). As a result, Enterobacteriaceae resistance to carbapenems in the clinical setting continues even when the bacteria do not produce carbapenemase; instead, important changes either reduce porin production or result in the expression of mutant porin alleles. Access to the drug's target can be blocked by increasing the antibiotic's efflux. Antibiotics are actively transferred out of the cell in bulk by the bacterial efflux pump. This plays a significant role in Gram-negative bacteria's natural resistance to numerous drugs used to treat bacterial infections. The five primary groups of efflux pumps that have been identified are the ATP-binding cassette family (ABC), the resistance-nodulation-cell-division family (RND), the major facilitator superfamily (MFS), the multidrug and toxic compound extrusion family (MATE), and the small multidrug resistance family (SMR). Multidrug-resistant (MDR) efflux pumps transport a broad range of structurally different substrates (Zhu et al., 2022).

Numerous genes that encode the MDR efflux pumps are found on bacterial chromosomes; however, because they are mobilized onto plasmids, some of these genes can be transferred from one bacterium to another. The IncH1 plasmid, derived from Citrobacter freundii, has been shown to include a gene cassette encoding a novel resistance modulation division (RND) pump and New Delhi metallo-β-lactamase 1 (NDM1). This discovery raises serious concerns since it suggests that these particular resistances can be passed from one bacterium to another via plasmids, thereby promoting the spread of novel, clinically significant resistances to other bacterial diseases. Gram-negative bacteria include the best-characterized RND family pump with clinical significance (Zhu et al., 2022). When the RND is overexpressed, a wide variety of substrates can be exported more quickly. The inner membrane contains RND pumps, which combine with the outer-membrane channels TolC or OprM and the periplasmic adaptor proteins AcrA or MexA to form a tripartite complex. Among the known RND pumps is the homotrimeric protein AcrB. Computational studies and co-crystallization of E. coli AcrB in association with transported substrates have revealed two binding pockets in AcrB. The pumps' resistance to a wide range of antibiotics can be explained by the binding pockets' capacity to retain substrates with different sizes and chemical properties (Zhu et al., 2022). Enterobacteriaceae, *P. aeruginosa, and S. aureus* all overexpress the RND efflux pump. The overexpression of the efflux pumps is regulated by both global and local regulators, including QacR from *S. aureus* and EmrR from *E. coli*. One important regulator of global expression is the transcription factor family AraC-XyIS. MtrA promotes the transcription of mtrCDE in *N. gonorrhoeae*. The regulator family Arac-XyIS is encoded in conjunction with a repressor of the various antibiotic resistance proteins MarR family (Zhu et al., 2022).

Importance of Relationship between AMR and Zoonoses

The formation of resistance is significantly strained by the inappropriate and growing use of antimicrobial drugs in livestock production because of the short reproduction period and the higher quantity of intestinal bacteria. Antimicrobial-resistant bacteria are produced in the gut as a biological reactor and are thereafter continuously released into different ecosystems. These antimicrobial-resistant bacteria disperse resistant genes throughout local flora via quorum sensing, carriers, and horizontal gene transfer pathways. Pathogenic zoonotic organisms may carry genes that are resistant to antibiotics and could be transmitted to humans (Dafale et al., 2020). The development of resistance in humans is significantly influenced by these antibiotic-resistant genes, which enter the human gut through zoonotic infections. Understanding zoonotic disease, including the transfer of ARBs, early detection, and management techniques are necessary to prevent the development of antimicrobial resistance in the ecosystem and eventually to humans through animals and the food chain (Hannan et al. 2023).

Mitigating AMR Emergence and Transmission

AMR can be prevented from emerging and spreading by a number of actions. A better knowledge of the burden of resistance and the ability to take setting-specific actions to stop future spread can result from strengthening AMR surveillance and research both within and across sectors. This can only be accomplished by expanding diagnostic capabilities, creating trustworthy integrated systems for reporting AMR data across nations, labs, and industries (such as data from food, environmental, animal, and human samples), and guaranteeing funding access for carrying out these initiatives, especially in LMIC. Making sure the data are representative and accurately depict the local/regional AMR landscape is also essentiel (Koutsoumanis et al., 2021).In a similar vein, trustworthy data on animal AMU is required to guide legislation and develop educational initiatives aimed at changing behavior and lowering AMU. The establishment of resistance to these antimicrobials might be less detrimental to human health if new antimicrobial classes and systems (such as phages and plasmids) were developed that are exclusively utilized in food production (Hernando-Amado et al., 2019). Additionally, enhancing cleanliness in veterinary care, education, and animal-rearing facilities, together with proper sewage treatment and waste disposal, would stop AMR determinants from entering the food chain, contaminating the environment, and spreading from animal to animal (Nadimpalli et al., 2018).

Finding out how and where food production and commercialization involve contamination with resistant organisms, as well as how it is spread to and from humans, would also help researchers create mitigation measures. One promising weapon in the fight against AMR is the vaccine. These work indirectly by lowering AMU and directly by lowering the prevalence of infections in general and resistant infections in particular. Pigs vaccinated against Lawsonia intracellularis, for example, showed a significant decrease in AMU and increased productivity. Although vaccines for high-value Atlantic salmon have been produced and are being used in aquaculture to combat illnesses, there is still a need for or underutilization of vaccinations for low-value fish that are mostly raised in LMIC (Bak and Rathkjen 2009). The future of antimicrobials would be protected by laws and policies that limit and manage the use of antibiotics that are essential for human health, the unregulated acquisition of antimicrobials, and their use to promote animal growth (Nadimpalli et al., 2018). Farmers may be encouraged to lower AMU by promoting the labeling of animal products based on the use of antibiotics in food production.

Research and Development of New Antimicrobial Agents and Vaccines

The US FDA and/or the EMA only approved 12 novel antimicrobials between 2017 and 2022, despite the fact that finding new antibiotics is an essential step in the fight against the AMR crisis. About 80% of the most recently approved antibacterial drugs are from antibiotic families that are already in use and have resistance mechanisms known (Zasheva et al., 2024). The majority of these drugs also exhibit minimal therapeutic improvement over existing treatments. As of late 2021, there were 217 antibacterial candidates and 77 antimicrobial or combination medications in clinical and preclinical research targeted at the 13 WHO critical infectious pathogens, including *Mycobacterium tuberculosis and Clostridium difficile* (Eisinger et al., 2023). Finding new drugs within a well-established class of antibiotics is crucial because it can lead to improved safety features, more realistic dosage schedules, and the collection of data for diseases or populations that have not yet been studied for the drug class. The antibacterial spectrum may also progressively change as new drugs are created within an existing class (compare cefazolin, ceftriaxone, and cefepime, for instance). However, the development of new classes of antibiotics with distinct mechanisms of action is the only way to effectively address the growing drug resistance in common diseases and the possible concern of mutant, multidrug-resistant pathogens in bioweapons (Spellberg et al., 2004).

Because vaccination reduces illnesses caused by bacteria that are both susceptible to and resistant to antimicrobial agents, it reduces the overall requirement for antimicrobial agents, making it a crucial part of the fight against antimicrobial resistance. *Hemophilus influenzae type b (Hib), Bordetella pertussis, Neisseria meningitidis,* and *Corynebacterium diphtheriae* outbreaks have all significantly decreased during the last century, proving that vaccines are successful in lowering the prevalence of disease. Pneumococcal vaccinations have reduced invasive illness and nasopharyngeal carriage of S. pneumoniae (including isolates resistant to antibiotics), suggesting that vaccinations can counteract the effects of antimicrobials. Vaccines have been demonstrated to improve human health and decrease the need for antibiotics in a number of animals, including fish, pigs, and poultry (Zhang et al., 2007). The capsular polysaccharides (CPS) of the bacterial species *S. pneumonia* and *H. influenza* are the targets of the pneumococcal and Hib vaccines, respectively. The effectiveness of the pneumococcal conjugate vaccine against invasive pneumococcal illness ranges from 86% to 97%. As a result, the capsular polysaccharides are one of the most powerful and often targeted bacterial antigens in vaccine development, and as of 2021, a number of vaccines, including the 12-valent vaccine for extra-intestinal pathogenic *E. coli*, are being tested in clinical trials against bacterial strains that attack capsular polysaccharides and have high antimicrobial loads (Mullins et al., 2023).

Innovations in Diagnostics for Timely Identification of Zoonotic Infections

Traditional methods for identifying zoonotic infectious agents, like those based on bacterial culture, polymerase chain reaction, and immune-mediated techniques, have some advantages, but they also have some drawbacks, like a long turnaround time and the requirement for difficult tasks, expensive materials, and specialized equipment in some cases. Therefore, biosensors seem to be one of those innovative, useful diagnostic tools for this aim. These elements are very reliable, effective, and have good specificity and sensitivity. Their usefulness in medical systems for diagnostics can be further increased when they are backed by nanoparticles (Ahangari et al., 2023). Liposome-based nanotechnology has mostly enhanced animal diagnostics and therapeutic compounds. Liposomes have been employed for imaging, targeted drug administration, and gene delivery. For disease management and surveillance, nanotechnology's ability to increase sensitivity, exclusivity, and efficiency is essential. The ongoing study of influenza and HIV-1 viruses has led to the discovery of applications for nano-diamonds, nano-traps, and nano-fibers. The majority of avian influenza detection methods rely on immunochromatography, which uses colloidal particle-conjugated antibodies and antiretroviral nuclear protein antibodies; preliminary research has been done on a fluorescent monochromatic test strip for hemagglutinin-specific europium nanoparticles (NPs) with a threshold of detection (LOD) of ng/ml. A colloidal immunochromatographic strip test using two MAbs has been developed as an experimental gold-related diagnostic to identify the H7 N9 avian influenza viral antigen; this test demonstrated a 71.40% sensitivity and a 98.6% accuracy in comparison to other tests (Arshad et al., 2022).

There are numerous uses for phage display technology in broad-spectrum antibody identification of various illnesses. However, the equipment being used for study is costly and time-consuming. For unambiguous genomic identification, especially for unknown illnesses, high throughput sequencing—also known as next-generation sequencing—is employed. Risk assessment is also made possible by this method. NGS techniques are being used to monitor the spread of viruses, i.e., their ongoing spread as opposed to their reemergence within a population. These diseases include the Heartland virus, Bas-Congo virus, Sosuga virus, and SFTS virus. Methicillin-resistant Staphylococcus aureus (MRSA) colonization in sinus cavities and Marburg virus in a bat reservoir are two examples of microorganisms that can be quickly detected using NAAT (Nucleic Acid Amplification Test), which comprises Quantitative Real-time PCR/RT-PCR (Mehmood et al., 2023).

Future Perspectives and Challenges

Growing Demand for Sustainable Products and Consumer Awareness:

As awareness of AMR increases, consumers may desire meat made without antibiotics and using sustainable practices. This could encourage the market for more ethical meat production practices and force the industry to employ less antibiotic-dependent techniques. Labeling schemes such as "antibiotic-free" or "antibiotic stewardship certified" might become more common, allowing consumers to make informed decisions about how much meat they eat (WHO 2022c).

International Cooperation and Monitoring

Since AMR is a global problem, controlling it will necessitate international collaboration. In the future, more advanced global surveillance systems for tracking AMR in humans and animals might be created. Data sharing and study on AMR patterns can help guide policies and practices that reduce the formation of resistant bacteria in the food chain (Bungau et al. 2021; Abdellatif and Mohammed 2023).

Different Strategies for Livestock Health

Probiotics, bacteriophages, and plant-based antimicrobial treatments are examples of potential future antibiotic alternatives. By reducing the need for antibiotics in meat production, these methods may reduce the risk that consuming beef will expose people to AMR. Improvements in veterinary medicine, like vaccines and advanced diagnostics, may reduce the need for antibiotics in livestock care (Rupasinghe et al. 2022).

Conclusion

One of the biggest threats to public health is zoonotic antimicrobial resistance (AMR), which is greatly accelerated by meat consumption. The overuse and misuse of antibiotics in cattle production is a major factor in the development of resistant bacteria, which can then enter the food chain and infect humans. Although other factors like food handling, cooking procedures, and regulations can help, the major option to prevent these hazards is to strictly regulate the use of antibiotics in animal husbandry. Reducing the use of antibiotics in animal husbandry, enhancing surveillance, and educating consumers about safe meat consumption practices are all essential to halting the spread of AMR. As the world's meat consumption rises, governments, the agricultural sector, and the general public must collaborate to address this new threat and guarantee that antimicrobial treatments remain effective for future generations.

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