Zoonoses and AMR: Silent Spreader of Superbug Pandemic

14

Abdul Hannan[1],*, Mayra Ihsan[1], Md Atiqul Haque[2] and Xiaoxia Du[3,]*

ABSTRACT

The accelerated and indiscriminate use of antimicrobial agents in livestock, driven by their short reproduction period and abundant intestinal microbes intensifies the emergence of resistance. Livestock gut serves as a breeding ground for antimicrobial-resistant bacteria, perpetually disseminating them across diverse ecosystems. Through horizontal gene transfer and quorum sensing, resistant genes proliferate within native flora. Zoonotic pathogens, acting as carriers, may transmit antibiotic-resistant genes to humans, underscoring their pivotal role in human resistance development. To mitigate this threat, a comprehensive understanding of zoonotic illnesses, early detection, and effective management strategies are imperative. The one health approach integrates diverse disciplines to achieve optimal medical outcomes by acknowledging the interconnectedness of humans, animals, and their shared environments. According to new speculation from the Center for Disease Control and Prevention, the globe is about to break into a "post-antibiotic era" in which illness caused by bacteria will be the leading cause of death instead of tumor. Over 2 million incidents of serious diseases, which comprise 23,000 fatalities annually in the United States, are brought on by bacteria that are resistant to antibiotics. Over 95% of all emerging infectious diseases described in the second half of the 20th century are zoonotic and antimicrobial-resistant (AMR) infections. Each year, drug-resistant illnesses brought on only by tuberculosis (TB), HIV, and malaria claim the lives of almost 700,000 people. Drug-resistant diseases are predicted to imperil 10 million individuals annually by 2050 if nothing is accomplished. This chapter underscores the urgency of curbing antimicrobial resistance in ecosystems and its potential impact on human health and the collaborative endeavors of global authorities such WHO, CDC, and OIE and other pertinent health and agriculture agencies are crucial in addressing and mitigating the challenges posed by the zoonosis in spread of superbug pandemic.

CITATION

Hannan A, Ihsan M, Haque MA and Du X, 2023. Zoonoses and AMR: Silent spreader of superbug pandemic. In: Altaf S, Khan A and Abbas RZ (eds), Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan, Vol 4: 186-201. https://doi.org/10.47278/book.zoon/2023.147

CHAPTER HISTORY Received: 20-March-2023 Revised: 21-May-2023 Accepted: 20-June-2023

[1]Department of Pharmacy, University of Agriculture, Faisalabad, Pakistan
[2]Department of Microbiology, Faculty of Veterinary and Animal Science, Hajee Mohammad Danesh Science and Technology University, Dinajpur 5200, Bangladesh
[3]Shandong Vocational Animal Science and Veterinary College, Weifang, China
***Corresponding author:** abdulhannan720@gmail.com (AH); duxiaoxia0931@126.com (XXD)

1. INTRODUCTION

The groundbreaking development of antimicrobial agents, which provided the cornerstone of antibiotic treatment to cure and manage infections caused by bacteria, was seen as a turning point in the field of medical discipline and is one of the most important medical discoveries of the 20th century. Due to the advent and rapid growth of antibiotic resistance among many microbial species, which has turned into a worldwide problem, its usefulness has since been constrained (Kumar 2019). Before antibiotics were discovered, created, or made available for purchase, antibiotic resistance already existed. In actuality, bacteria collected from glacier waters over 2000 years ago had ampicillin resistance, and microbes from permafrost more than thirty thousand years ago have vancomycin resistance. (Morrison and Zembower 2020). In accordance to a World Health Organization (WHO) research from 2019, antimicrobial resistance caused 7 million fatalities, and it's predicted that in the year 2050, that number is expected to increase to 20 million, incurring more than $2.9 trillion. The majority of antimicrobial agents were produced in the "golden era" of antimicrobial studies, which spanned the years 1950 to 1960. The first "superbug" in the past was eventually referred to as methicillin-resistant *Staphylococcus aureus* (MRSA) and it is transmitted to humans via zoonotic animals (Uddin et al. 2021). Antimicrobial resistance bacteria are becoming more prevalent within zoonotic pathogens and typical bacterial species as a result of the overuse of antibiotics in veterinary treatment and food-producing animals.

2. IMPORTANCE OF RELATIONSHIP BETWEEN AMR AND ZOONOSES

Owing to the short reproduction period and the greater abundance of the intestinal microbes, the inappropriate and increased use of antimicrobial agents in livestock production places substantial strain on the emergence of resistance (Fig. 1). The gut serves as a biological reactor for the generation of antimicrobial resistance bacteria, which are then constantly discharged in various ecosystems. Through horizontal gene transfer processes, carriers, and quorum sensing, these antimicrobial resistant bacteria spread resistant genes across native flora. Antimicrobial resistant genes that could be spread to human beings may be carried by pathogenic zoonotic organisms (EFSA Panel 2009). These antibiotic resistant genes reach the human gut via zoonotic pathogens and therefore, plays an important role in development of resistance in humans. To limit the development of antimicrobial resistance in the ecosystem and ultimately to humans via livestock and food chain, understanding of zoonotic illness, encompassing ARBs transfer, early detection, and management strategies must be established (Dafale et al. 2020).

3. UNDERSTANDING ANTIMICROBIAL RESISTANCE

According to the European Committee on Antimicrobial Susceptibility Testing (EUCAST), pathogenic antibiotic resistance in bacteria can be described in 2 distinct manners: first, in terms of the usual microbe population that exists prior to being exposed to the antibacterial agent, and secondly, in the context of the negative clinical consequences associated with an unregulated illness if an individual gets that antibiotic (MacGowan 2008). Since penicillin was first used in medicine, *Staphylococcus aureus* has been documented to be resistant to β-lactam medications (Yoshii et al. 2017; Ahmed et al. 2019).

3.1. MICROBIAL

a) The majority of microorganisms have a quick growth rate, ensuring favorable alterations,
b) Gene mutation/change in genetic sequence,

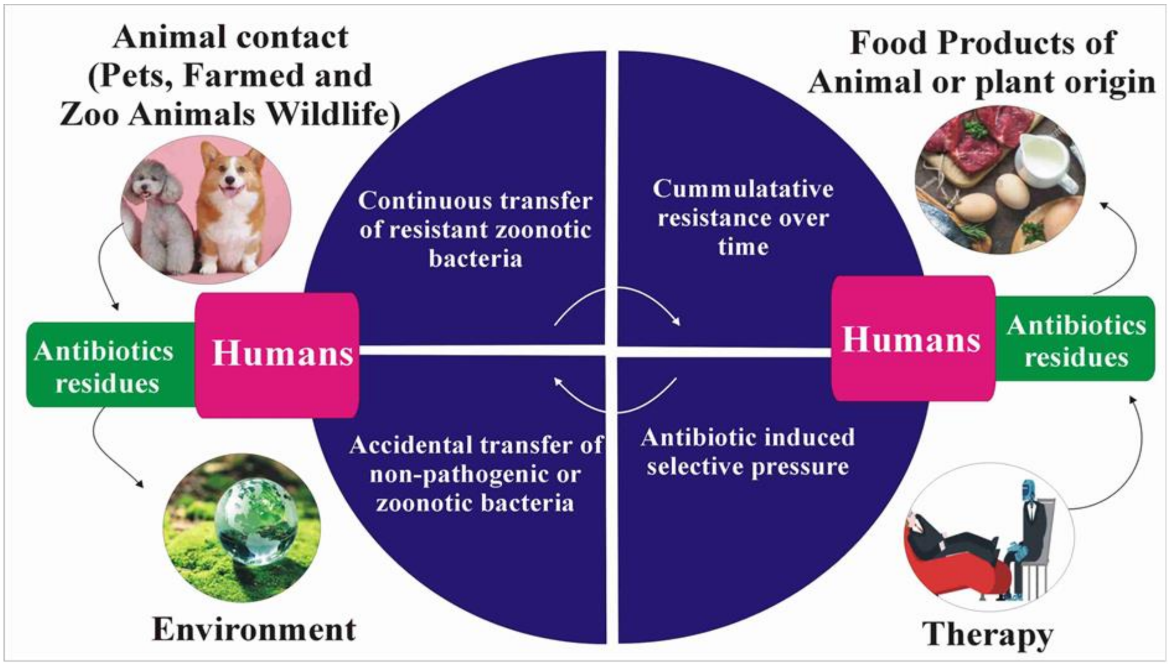

Fig. 1: The transfer of antibiotic residues form animal to human and then to environment. On the other side the treatment of human being and transfer of these residues to food products of animal and plant origin. Zoonotic resistance bacteria are transfer and results in cumulative resistance, similarly the antibiotic selective pressure and transfer into nonpathogenic zoonotic bacteria.

c) The influence of selective pressure on the population of microbes, and

d) Applied selective stress: Humans use antibiotics extensively and intensively, creating an aggressive and polarized selective stress that is going to persist to elicit a powerful adaptive response in the microorganisms (Michael et al. 2014; Nadeem et al. 2020).

3.2. HUMAN

a) Increase in population also provides bacterial culture with ample nutrients and suitable conditions and exhibits exponential growth,

b) The quick propagation of infectious illnesses is greatly facilitated by a large percentage of people residing nearby, and

c) Rapid travel can carry diseased people, causing infections to spread over the world even prior to the manifestation of visible symptoms (Michael et al. 2014).

3.3. OVERUTILIZATION OF ANTIBIOTICS

Antibiotic overuse has contributed to the current increase in AMR rates (Manohar et al. 2020; Tang et al. 2023).

3.4. THERAPEUTIC PRACTICES

a) Inappropriate prescription: Antibacterial recurrent use can culminate in excessive use of antibiotics and AMR,

b) Consecutive antimicrobial treatment: Combination of antibiotics results in the development of AMR, and

c) Established practices: Overall bacterial adaptive response is caused by the prescription of long-term antibiotics that have been prolonged up to 14 days, and also by the prescription of large doses (Michael et al. 2014; Cantón et al. 2022).

3.5. MASS PERCEPTION AND BEHAVIOR

Antibiotics are seen by the general population as a fast and effective cure for a wide range of illnesses, which has led to behaviors that successfully subvert the authority of a prescriber and therefore promote AMR (Michael et al. 2014; Lyall et al. 2023).

3.6. CULTIVATION APPLICATIONS

The productivity of farms can be considerably boosted by using antibiotics on both cattle and crops. The impact of farming practices on microbial ecology has led to the presence of numerous and diversified AMR genes in urbanized agricultural nature, and seemingly natural environments (Michael et al. 2014; Hassell et al. 2019; Nadimpalli et al. 2020; WHO 2022c).

4. ZOONOTIC ANIMALS

Implication of antimicrobials in livestock for growth promotion leads to the emergence of antibiotic resistance in humans towards bacterial species that can infect both animals as well as humans (Wassenaar and Silley 2008).

5. MECHANISMS OF ANTIMICROBIAL RESISTANCE DEVELOPMENT

Antibiotic pathways to resistance can be generally divided into Intrinsic or Acquired resistance.

5.1. INTRINSIC RESISTANCE

Certain particular genera of bacteria (or species) have distinctive structural/functional traits that lead towards the development of resistance to antibiotics (Impey et al. 2020). These bacterial populations typically lack a target site for the particular antibiotic, rendering it useless i.e., Resistance to β-lactam antibiotic towards Mycoplasma species due to the absence of cell wall (Maes et al. 2020). Moreover, the existence of an outer layer preventing an antimicrobial agent from entering cells of bacteria. Presence of efflux pumps i.e., the ATP-binding cassette (ABC) superfamily and inactivation of antibiotics by bacterial enzymes i.e., β-lactamase.

5.2. ACQUIRED RESISTANCE

In which ordinarily sensitive bacteria can acquire genes from different strains of bacteria in order to acquire resistance to specific drugs. Three mechanisms by which bacteria acquire resistance (Christaki et al. 2020; Biondo 2023).

a) Alteration of bacterial enzymes and inactivation of antibiotic
b) Decreased intrinsic antibiotic concentration

c) Modifications at the antibiotic agents' target sites
d) Resistance by propagation of resistance gene (Fig. 2).

6. RESISTANCE DUE TO QUORUM SENSING AND BIOFILM PRODUCTION

Bacterial quorum sensing, a technique that controls bacterial transcription of genes, is dependent on the adaptable chemical messengers referred to as auto-inducers. By employing auto-inducers for quorum sensing, microbes are able to interact both between and within species. Bacteria use quorum sensing both for the development of resistance as well as to increase each other's virulence in disease conditions. For example, *Vibrio cholerae*'s insidious releases auto-inducer which at lower concentrations functions as kinases and promotes the formation of LUXO-Phosphate from phosphate which promotes the development of biofilm as bacteria reproduces concentration of autoinducer increases and binds to its receptor and it results in alteration in activity of auto-inducer from kinase to phosphate and dephosphorylation of LUXO and halting of biofilm gene expression and start of new sequence of quorum sensing events. This ultimately results in the production of highly toxic cholera toxins and increases deaths (Holoidovsky and Meijler 2020; Ramamurthy et al. 2020).

There is a 1000-fold increase in the development of resistance in bacteria in biofilm and quorum sensing because it results in a better exchange of genetically altered information within and between bacterial strains (Athulya and Chaturvedi 2020).

7. CONSEQUENCES AND IMPLICATION OF AMR IN HUMAN AND ANIMAL HEALTH

According to research (de Kraker et al. 2016) by 2050 AMR might result in a 1% yearly Economic decline, with this number reaching as high as 5-7% in underdeveloped nations. This would result in loss of between 100 and 200 trillion euros globally. The frequency of antimicrobial intake in a given bacterial population is strongly connected with the degree of antibiotic resistance generated by the microorganisms in the population of animals. Overuse and long-term administration of antibiotics in livestock at sub-clinical concentration stimulates growth, changes in gut microflora and promotes cross resistance among different classes of antibiotics.

From the zoonotic spread of illnesses, antibiotic-resistant bacteria enter the human gastrointestinal tract where they disrupt the natural biodiversity of the gastrointestinal tract (Esposito et al. 2022). When zoonotic pathogens containing antibiotic-resistance genes enter in human body they spread the resistance genetic material to the gut microflora of the host, upsetting the balance of the ecology in the stomach (Adem 2022).

Additionally, human beings excrete ARGs (antibiotic resistance genes) or ARBs (antibiotic resistance bacteria), which then enter the ecosystem from soil or water from municipalities. ARBs penetrate the food chain through the soil or sewage and harm the well-being of animals, continuing the process of ARB dissemination (Dafale et al. 2020). The incorporation of antibiotics in pesticides in edible crops causes the contamination of antibiotics in soil and water ultimately dissemination of multidrug resistance bacteria via metabolic processes i.e. manure application in commercial swine farms results in resistant Salmonella serotypes (Pokharel et al. 2020).

8. CURRENT GLOBAL TRENDS AND CHALLENGES IN COMBATING AMR

AMR is among the 10 most prevalent worldwide public health concerns (Sanderson et al. 2019; Tang et al. 2023). The idea of "One Health" affirms that there exists a direct link between the health of human,

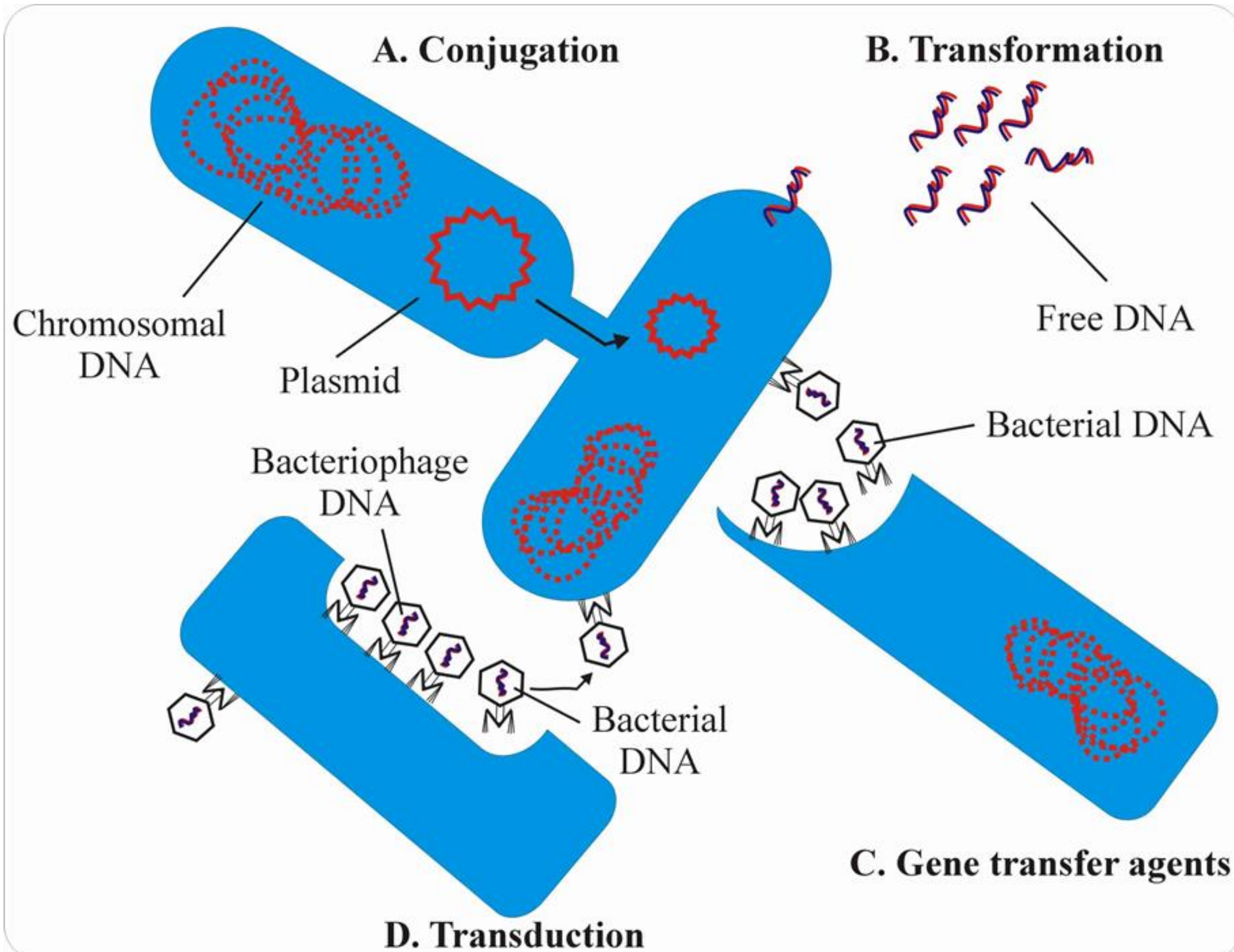

Fig. 2: Diagram representing the resistance by propagation of resistance gene A) Conjugation B) Transformation, C) Gene transfer agents, and D) Transduction (Von Wintersdorff et al. 2016).

animals, and their shared environment. The World Organization of Animal Health (OIE), the Food and Agriculture Organization of the United Nations (FAO), and the WHO have closely collaborated to make sure that viable measures are implemented in every field to reduce the potential hazards of antimicrobial resistance through this strategy (Tang et al. 2023).

Along with the "One Health Approach" the World Health Organization (WHO) introduced the Global Action Plan focused on AMR (GAP-AMR), an intervention program for AMR in 2015. By responsibly preserving antibiotics and providing proper accessibility and quality controls, this approach seeks to guarantee that infectious illnesses can always be effectively treated and managed. In order to accomplish the objectives of the general Global Action Plan, it is anticipated that nations would present their national plans in AMR. The Global Antibiotic Resistance and Use Surveillance System (GLASS) was the other strategy that was introduced. This initiative's main objectives are to promote worldwide antimicrobial monitoring and identify its underlying causes. This would entail giving guidance and suggestions to assist states in putting appropriate corrective measures into place. One must include social sciences like economics and politics to completely comprehend the scope of the antimicrobial resistance dilemma. Therefore, understanding how each person integrates with reality via mental models is crucial (Calvo-Villamañán et al. 2023).

9. ZOONOTIC DISEASES

In 1951 WHO defined zoonoses as "diseases and infections that are naturally transmitted between vertebrate animals and man". Whereas, Rudolph Virchow in the 19th century introduced the term “zoonosis” (plural zoonoses) which is derived from two Greek words “zoon” (animals) and “noson” (sickness) (Leal Filho et al. 2022; Singh et al. 2023). Zoonotic infections account for more than 75% of developing infections. The rapid appearance of influenza A/H1N1 in Mexico in late April 2009, the Nipah Virus in Southeast Asia in 1998, SARS in early 2003 and Highly Pathogenic Avian Influenzas (HPAI) first appeared in 2004 and reemerged in 2009 are a few examples of zoonotic infections (Cáceres and Otte 2009).

9.1. IMPACT OF ZOONOTIC DISEASES ON HUMAN AND ANIMAL POPULATIONS

Each year, zoonosis causes over 2.7 million fatalities and 2.5 billion cases of human disease while also having an effect on cattle production and the security of food. Animal goods were significantly reduced by more than 70% due to zoonotic diseases. The lack of high-protein foods of animal origin, such as milk, meat, and eggs, has an impact on both the health of humans and their nutrition. Zoonotic illnesses like toxoplasmosis and brucellosis can cause infertility, abortions, and poor progeny. Farmers and the entire nation may suffer significant financial losses as a result (de Silva et al. 2023).

Notably, the SARS pandemic and highly virulent avian influenza, which affected several industries notably tourism, had a major detrimental effect on the world GDP. According to the World Bank, outbreaks that affected sheep and beef caused Australia's livestock sector to lose 16% of its economic value. The latest COVID-19 pandemic has had a big effect on the world economy. All societal sectors, notably the tourism and hospitality, banking, educational and health services, and sports sectors, have been profoundly affected by COVID-19 (Rahman et al. 2020). The consequences of zoonotic diseases extend beyond the negative effects on human and animal health to include significant economic loss as a result of decreased livestock productivity, environmental disruption, and the expense of human disease.

9.2. EMERGING ZOONOTIC DISEASES AND THEIR POTENTIAL FOR GLOBAL SPREAD

An average of more than 3 novel viral species that harm people are identified annually. Some of the common emerging diseases include Ebola, MERS, HIV, SARS, etc. Variations in human demographics and the community, along with shifts in the utilization of land and agricultural practices, were recognized by Woolhouse and Gowtage-Sequeria as the 2 kinds of variables most frequently linked to the reemergence of infectious diseases among humans.

When efficient control and biosecurity protocols are not effective, the intensification of farming for livestock, which is linked to rising animal population and assists in the spread of diseases by encouraging invasion into wildlife habitats and creating new possibilities for encounters among humans, livestock, wildlife, and vectors (Otte and Pica-Ciamarra 2021).

9.3. INTERPLAY BETWEEN ANTIMICROBIAL RESISTANCE AND ZOONOSES

The majority of developing illnesses have penetrated virtually every ecosystem and breached transboundaries. Animals are the most typical biological carriers for the propagation of pathogens with resistance (Vidovic and Vidovic 2020; Sivagami et al. 2020). Microbial populations found in animal guts

work in concert to benefit their hosts. By passing the resistant gene to other pathogens in the gut, the introduction of a drug-resistant pathogen changes the microbial community structure. Opportunistic diseases travel from animal to human either directly (via zoonoses) or indirectly (through vectors), which has an impact on human health (Gnat et al. 2021; Mohamud et al. 2023). The majority of antimicrobial agents that enter the bodies of humans and animals are not fully metabolized, causing the release of metabolized forms into the environment. Antibiotic resistance genes (ARGs) are becoming more prevalent as a result of the presence of antimicrobial agents in the atmosphere (Zhuang et al. 2021). The widespread presence of ARBs in the surroundings is increased by the spread of ARGs via related mobile genetic elements (MGEs) such transposons, plasmids, and genomic islands to other microbial populations. These ARBs develop into powerful pathogenic zoonotic agents that may sicken the global population of people severely (Dafale et al. 2020).
Moreover, both direct contact with animal feces having resistant microbes and indirect contact with polluted water or food can result in the spread of resistant germs from animals to humans. For instance, a significant fraction of the bacteria in the fecal ecology of hens are resistant to antibiotics. This has resulted in the development of resistance against most critical and remarkably important antibiotics (Table 1) i.e., streptomycin, gentamicin, ampicillin, sulfamethoxazole, sulfisoxazole, trimethoprim, chloramphenicol, spectinomycin, tetracyclines) in animals as well as in humans (Roug et al. 2013).

Table 1: Resistant antibiotic classes and resistant bacterial species

Sr.no.	Resistant Drugs		Bacterial species	Zoonosis Occur via species
1	a.	Nalidixic acid, Ciprofloxacin	*E. coli*	Poultry, Swine, Cattle
	b.	Amino penicillin (amoxicillin and ampicillin)		
	c.	Cephalosporin i.e. cefotaxime		
2	a.	Glycopepetide i.e. vancomycin	*E. faecium*	Poultry, Swine, Cattle
	b.	Macrolide	*E. faecalis*	
	c.	Quinupristin and delfopristin		
3	a.	Fluoroquinolones	*Campylobacter jejuni* *Campylobacter coli*	Broiler, Pig
4	a.	Carbapenem	*Acinetobacter baumannii*	Cattle, Pig
5	a.	Methicillin	Staphylococcus aureus,	Dogs, Cats
	b.	β-lactams, lincosamide and fluoroquinolones	*Staphylococcus pseudintermedius*	

10. CASE STUDIES ILLUSTRATING THE INTERCONNECTION BETWEEN AMR AND ZOONOSES

E. coli resistance to cefotaxime, a third-generation cephalosporin, became more prevalent in poultry in the Netherlands after 2003, reaching an extent of over 20% in 2007; this resistance incidence reduced significantly following the utilization of ceftiofur. A one more 3rd generation cephalosporin, was banned in hatching facilities in 2010, reaching a degree of 2.9% in 2014. The first cases of livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA) in pig farms were identified in the beginning of the 2000s. Contact directly between cattle and humans is the main threat for MRSA transmission, which happens often. Exposure can result in colonization, and LA-MRSA can then be detected asymptomatically on the epidermis or in the nasal cavity. LA-MRSA can result in a local skin infection (such as an abscess) if it enters the body through the skin (for example, through a wound or cut). There are times when it can result in severe illnesses like pneumonia or bloodstream infections (BSIs).

The WHO which classifies vancomycin as a crucial AM for the well-being of humans, says that avoparcin is a glycopeptide that was formerly utilized in veterinary treatment as an antibiotic growth promoter. After learning that the application of avoparcin as an antibiotic growth promoter predisposed vancomycin-resistant enterococci (VRE) to occur, Denmark became one of the earliest nations to outlaw it in 1995 (Bennani et al. 2020).

11. POLICY AND REGULATORY INTERVENTIONS AT THE NATIONAL AND INTERNATIONAL LEVELS FOR COMBATING AMR

This set of public health problems includes global epidemics, antibiotic-resistant bacteria (AMR), food-borne illnesses, and recurrent zoonotic infections. A collaborative and integrated multi-sectoral competence is needed for the mitigation, early detection, and efficient response, and to minimize the consequences. This strategy is commonly known as One Health. Initial calls for a One-Heath policy were made following the H5N1-caused avian influenza epidemic.

One Health, according to the World Bank, is an approach for improved cooperation in fields of mutual concern (intersections), with a focus initially on zoonotic diseases and AMR, that will lower threat, strengthen public health worldwide, and combat poverty and economic expansion in developing nations (Gebreyes et al. 2014). Two primary objectives for implementing One Health include improving national capacity for zoonotic illnesses and AMR for avoidance, identification, and response, as well as improving collaborative cooperation and communication among key stakeholders for combating zoonoses and antimicrobial resistance (WHO 2022a).

India's National Action Plan on AMR is a great illustration of the One Health strategy and may be utilized as a reference to create a practical outline for a nation's efforts to deal with other comparable public health issues, particularly in the event of future outbreaks of disease India’s National Action Plan includes

a) The use of antimicrobials for the purpose of promoting poultry production has been outlawed.

b) Need for cross-sectoral collaboration for the establishment of a national policy for antimicrobial resistance containment that includes approaches that are largely focused on using antibiotics in the human health sector.

c) A regulation for livestock encouraging the responsible application of antimicrobial agents in livestock.

d) Defining the duration of the antimicrobial discontinuation period for poultry, livestock, and seafood.

e) Guideline about the discontinuation period and residual cap for antibiotics in meat and related products.

Moreover, agricultural, food and environmental sectors should be listed as crucial bodies in mitigating AMR. The national action plan’s objectives include raising information through effective interaction, instruction, and training, enhancing monitoring methods, reinforcing the control and prevention of infections, research and development, supporting investments, and cooperative actions to fight antimicrobial resistance (Biswas et al. 2023).

12. PROGRAMS ADVANCING THE ONE HEALTH PARADIGM AT THE NATIONAL AND INTERNATIONAL LEVEL INCLUDES

a) Global congress on influenza and birds (El Mellouli et al. 2022)

b) Collaborative partnership between UNESCO, World Health Organization, Food and Agriculture Organization, World Organization for Animal Health (Ossebi et al. 2022)

c) Quadripartite agreement for combating AMR, rabies, TB, and SARS (WHO 2022b)
d) OH alliance comprising the globe healthcare and animal associations (Otu et al. 2021)
e) Functional ecological, individual, and veterinary healthcare outline for boosting One Health

13. RESEARCH AND DEVELOPMENT OF NEW ANTIMICROBIAL AGENTS AND VACCINES

The discovery of new antibiotics is a crucial step in combating the AMR epidemic, yet from 2017 to 2022, the US FDA and/or the EMA only granted approval for 12 novel antimicrobials. The bulk of the most recently licensed antibacterial shows only little therapeutic improvement over current therapies, and about 80% of these medications come from families of antibiotics that are currently in use and where resistance mechanisms have already been identified. In the clinical and preclinical research, there were as of late 2021, 77 antimicrobial or combination medicines and 217 antibacterial candidates, respectively, intended for the 13 WHO essential infectious agents, notably *Mycobacterium tuberculosis* and *Clostridium difficile* (Eisinger et al. 2023).

It is important to discover novel medications within an established antibiotic class since this can result in enhanced safety characteristics, more practical dosing regimens, and the gathering of information for pathologies or populations that have not yet been researched for the drug class in question. When new medications are developed within an established class, the antibacterial spectrum may also evolve gradually (for example, compare cefazolin to ceftriaxone to cefepime). However, the escalating resistance to drugs in ordinary diseases and the potential worry of mutated, multidrug-resistant agents in bioweapons can only be adequately addressed by the creation of novel classes of antibiotics with unique modes of action (Spellberg et al. 2004).

Vaccination is a key component of antimicrobial resistance prevention because it decreases infections brought on by bacterium that are equally vulnerable to and resistant to antimicrobial agents, which lowers the total need for antimicrobial agents. It is evident that vaccines have been successful in minimizing the incidence of diseases over the past century; outbreaks of *Corynebacterium diphtheriae*, *Neisseria meningitidis*, *Hemophilus influenzae* type b (Hib), and Bordetella pertussis have all decreased significantly. Pneumococcal vaccinations have reduced both invasive illness and nasopharyngeal carriage of S. pneumoniae (including isolates resistant to antibiotics), suggesting vaccination's ability to tackle antimicrobials in action. The use of vaccines has been proven to minimize the use of anti-microbial over a wide range of species, including fish, pigs, and poultry, in addition to improving human well-being.

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 for invading pneumococcal illness ranges from 86% to 97%. The capsular polysaccharides are among the most effective and commonly targeted antigens of bacteria in vaccine development as a result. Clinical studies are underway for a number of vaccinations for strains of bacteria with substantial antimicrobial burdens that attack capsular polysaccharides as of 2021, including the 12-valent vaccine for extra-intestinal pathogenic *E. coli* (Mullins et al. 2023).

14. INNOVATIONS IN DIAGNOSTICS FOR TIMELY IDENTIFICATION OF ZOONOTIC INFECTIONS

Since traditional approaches for identifying zoonotic infectious agents, such as those centered on bacterial culture, polymerase chain reaction, and immune-mediated methods, offer certain benefits they also have some disadvantages, such as a lengthy timeframe for outcomes and the need for challenging tasks, costly supplies, and specialized tools in some situations. Thus, biosensors appear to be considered among those cutting-edge, effective instruments of diagnosis for this purpose. These components are highly efficient and trustworthy with excellent specificity and sensitivity, and when supported by nanoparticles, their practicality can further be enhanced in medical systems for the diagnosis (Ahangari et al. 2023).

Nanotechnology which is based on liposomes has mostly improved animal medicinal molecules and diagnosis. Liposomes have been used for targeted medication and delivery of genomes as well as for imaging purposes. Enhancing sensitivity, exclusivity, and efficiency using nanotechnology is crucial for disease management and surveillance.

The ongoing study of HIV-1 and influenza viruses has identified applications for nano-diamonds, nano-traps, and nano-fibers. Frequently affecting both humans and species of birds, avian influenza is now a threat to both individuals and the worldwide financial system. The majority of avian influenza detection methods employ immunochromatography, which makes use of colloidal particle-conjugated antibodies and antiretroviral nuclear protein antibodies. Early research on a fluorescent monochromatic test strip with a threshold of detection (LOD) of ng/ml for hemagglutinin-specific europium nanoparticles (NPs) has been reported. Currently, a colloidal immunochromatographic strip test with two MAbs for H7 N9 avian influenza viral antigen identification has been invented as an experimental gold-related diagnostic. Compared to other tests, this strip test had a 98.6% precision and a 71.40% sensitivity (Arshad et al. 2022).

The phage display technology has a lot of applications for broad-spectrum antibody identification of different diseases. However, it is a pricy and labor-intensive technology being employed for research. High throughput sequencing, commonly referred to as next-generation sequencing, is utilized for unambiguous genomic identification, particularly for unidentified infections. This approach also enables risk evaluation. The surveillance of virus dissemination, i.e., continuous propagation vs reappearance in a population, is being done using NGS approaches. Heartland virus, Bas-Congo virus, Sosuga virus, and SFTS virus are among the diseases that have been identified.

NAAT (Nucleic Acid Amplification Test) which includes Quantitative Real-time PCR/RT-PCR is a quick detection method for already identified microorganisms like methicillin-resistant Staphylococcus aureus (MRSA) colonization in the sinus cavities as well as Marburg virus in a bat reservoir (Mehmood et al. 2023).

15. FUTURE PERSPECTIVES AND CHALLENGES

15.1. ANTICIPATED TRENDS IN AMR AND ZOONOTIC DISEASE DYNAMIC

The propagation of resistance genes is significantly influenced by intricately related environmental and socioeconomic variables. The effectiveness of healthcare frameworks, the facilities for water, sanitation, and hygiene (WASH), per-capita GDP, and weather have all been highlighted as key contributors to the development and spread of antimicrobial resistance**.**

Antibiotics are used improperly and excessively for purposes other than for consumption by humans (Bungau et al. 2021; Abdellatif and Mohammed 2023). The anticipated global sales of antimicrobials for use in livestock raised for human consumption in 2017 totaled 93309 tons. By 2030, this amount is anticipated to increase to 104079 tons. The growing need for meat-based goods and over-the-counter sales, especially in countries with low or middle incomes (LMICs), where demographics are expanding and becoming economically advanced, is the cause of this rise in the consumption of antibiotics. A variety of variables, such as the migration of people and animals, surface water runoff, and the trading of agricultural goods, contribute to the fast dissemination of AMR across ecosystems. Numerous anthropogenic variables, including population growth (urban density) and increasing wealth, have been determined to be linked to AMR at the human-animal interface by higher preferences for animal-based foods and goods (Allel et al. 2023).

15.2. POTENTIAL IMPACTS OF CLIMATE CHANGE AND URBANIZATION ON THE SPREAD OF AMR AND ZOONOSIS

Ecological changes impacting infectious disease prevalence and spread are linked to climate change. Sand flies, mosquitoes, and ticks are examples of species of arthropods that carry vector-borne diseases. Being ectothermic, vectors of arthropods are directly affected by temperature, which also has an impact on the growth, existence, and replication of infectious agents within vectors as well as the dissemination, prosperity, environmental suitability, frequency, and chronological cycle of vector behavior (such as biting rates). Heavy rains create more potential hatching grounds for mosquitoes and other vectors. Additionally, the lush vegetation that develops after rain offers vectors with cover and rest places Fields (Rupasinghe et al. 2022).

New ecosystems with an elevated human population concentration are upsetting widespread ecotones. As a result, there is greater potential for zoonotic diseases and resistance to spread between organisms, particularly as there is more interaction between people and wild animals. The function of ecosystems in the human-animal health interaction is further affected by human-induced stresses such as land use change, biodiversity loss, climate change, and environmental damage (WHO 2022c).

15.3. RESEARCH GAPS AND AREAS FOR FUTURE EXPLORATION

The development of One Health studies shows an increase in international involvement by comparing the study ecosystems among the first and sixth world one health congresses (ten years later). Despite increased awareness of the challenges facing global sustainable development, there is presently little representation of "Environmental and Ecological issues" and "Sustainable Food Systems" inside the World One Health Congress. In order to monitor disease outbreaks and respond quickly to them, it can be helpful to determine the main animal groups that could be the cause of outbreaks of disease. Additional investigation is required to pinpoint the environmental reservoirs and carriers for zoonosis, which include a diverse array of African bats, apes, and bird species. The methods and modes of transmission, notably the function of vectors, should also be covered in such investigations. It is necessary to identify the kind, degree, and gene mutations of antibiotic resistance in pathogenic zoonotic bacteria in distinct environmental niches. By implementing national laws, developed nations are able to keep the spread of antibiotic resistance to a minimum (Ahmed et al. 2023).

Tragically, due to insufficient laboratory resources and insufficient funding for health services, monitoring of antimicrobial-resistant organisms is often minimal or nonexistent in nations with low incomes. This is especially concerning when taking into account the increased likelihood of the spread of infectious diseases in LICs due to their restricted availability of sanitary facilities and clean water. Nevertheless, with international collaboration, exchange of information, and modifications to policy, these problems can be resolved (Gwenzi et al. 2022).

In epidemiology, investigations involving infections caused by bacteria, whole genome sequencing has come to be regarded as the gold standard because it allows for strain differentiation at the point of single nucleotide polymorphism. Utilizing a structure-based drug discovery approach has sped up the development of new antimicrobial drugs, pharmaceuticals, and vaccine candidates. In order to lessen the impending threat of resistance to antibiotics in the future, there is a need for multidisciplinary investigation and strategic thinking to enhance awareness of genetic variation (Sharma et al. 2023).

16. CONCLUSION

Antimicrobial resistance (AMR) has now become a significant global public health issue, with ten million annually fatalities predicted by 2050. AMR happens when viruses, bacteria, fungi, and parasites in people and animals do not respond to antibiotics, thereby allowing microbes to survive inside the host's body. The One Health Approach is a system including a variety of disciplines in order to attain the optimal medical outcome by recognizing the obvious interactions among humans, animals, and their common surroundings. The Sustainable Development Goals (SDGs), to address the issue of antimicrobial resistance. As a part of both regional and global action strategies, it is still necessary to underline the significance of awareness among the public and lay audiences' understanding of health issues. The 21st century's biggest public health challenge is still resistance to antibiotics. The Group of Seven nations (G7 nations) have already made significant political contributions to this issue, and it is still on the radar of many political summits. It is estimated that if AMR is not fully addressed, we will soon revert to the pre-antibiotic age, when routine diseases related to childbirth, surgery, and open shattered limbs may be fatal. The COVID-19 pandemic has clearly established the need to understand the relationship between human-animal disease patterns as well as the spread of zoonotic diseases and antimicrobial resistance globally among human-animals, animal-animal and human-human disease, and antimicrobial resistance transmission. In order to guarantee that the globe has access to a substantial stockpile of potent antibacterial substances that will support human and animal health both currently and in the future, people, communities, and governments must collaborate (Tang et al. 2023).

REFERENCES

Abdellatif AO and Mohammed KA, 2023. A review of the effects of excessive antibiotic prescription on public health. International Journal of Research and Analytical Reviews 10: 284-289.

Adem J, 2022. Review of the zoonotic importance of salmonellosis and associated risk factors. Veterinary Medicine Open Journal 7(2): 62-69.

Ahangari A et al., 2023. Advanced nano biosensors for rapid detection of zoonotic bacteria. Biotechnology and Bioengeering 120: 41–56.

Ahmed et al., 2019. Evaluation of the role of bla genes in beta lactam and methicillin resistant Staphylococcus aureus. Egyptian Journal of Botany 59(1): 29-38

Ahmed T et al., 2023. Future directions for One Health research: Regional and sectoral gaps. One Health 17: 100584. https://doi.org/10.1016/j.onehlt.2023.100584

Allel K et al., 2023. Global antimicrobial-resistance drivers: an ecological country-level study at the human–animal interface. Lancet Planet Health 7: e291–e303.

Arshad R et al., 2022. Nanotechnology for Therapy of Zoonotic Diseases: A Comprehensive Overview. Chemistry Selection 7: e202201271.

Athulya KS and Chaturvedi S, 2020. Approach to Quorum Sensing and Functions of Signal Molecules in Biofilms. International Journal of Pharmacology Research and Health Sciences 8: 3192–3194.

Bennani H et al., 2020. Overview of evidence of antimicrobial use and antimicrobial resistance in the food chain. Antibiotics 9: 49.

Biondo C, 2023. Bacterial Antibiotic Resistance: The Most Critical Pathogens. Pathogens (Basel, Switzerland) 12(1): 116. https://doi.org/10.3390/pathogens12010116

Biswas R et al., 2023. One Health approaches adapted in a low resource setting to address antimicrobial resistance. Science in One Health 1: 100011. https://doi.org/10.1016/j.soh.2023.100011

Bungau S et al., 2021. Aspects of excessive antibiotic consumption and environmental influences correlated with the occurrence of resistance to antimicrobial agents. Current Opinion in Environmental Science & Health 19: 100224.

Cáceres SB and Otte MJ, 2009. Blame apportioning and the emergence of zoonoses over the last 25 years. Transboundary Emerging Diseases 56: 375–379.
Calvo-Villamañán A et al., 2023. Tackling AMR from a multidisciplinary perspective: a primer from education and psychology. International Microbiology 26: 1–9.
Cantón R et al., 2022. Relevance of the Consensus Principles for Appropriate Antibiotic Prescribing in 2022. The Journal of Antimicrobial Chemotherapy 77(Suppl_1): i2–i9. https://doi.org/10.1093/jac/dkac211
Christaki E et al., 2020. Antimicrobial Resistance in Bacteria: Mechanisms, Evolution, and Persistence. Journal of Molecular Evolution 88(1): 26–40. https://doi.org/10.1007/s00239-019-09914-3
Dafale NA et al., 2020. Zoonosis: an emerging link to antibiotic resistance under "one health approach. Indian Journal of Microbiology 60: 139–152.
de Kraker et al., 2016. Will 10 million people die a year due to antimicrobial resistance by 2050? PLOS Medicine 13(11): 02184. https://doi.org/10.1371/journal.pmed.1002184
de Silva B et al., 2023. Zoonoses: The Rising Threat to Human Health. One Health: Human, Animal, and Environment Triad, Wiley Online Library, pp: 49–62.
EFSA Panel 2009. EFSA Panel on Biological Hazards: Joint opinion on antimicrobial resistance (AMR) focused on zoonotic infections. EFSA Journal 7: 1372. https://doi.org/10.2903/j.efsa.2009.1372
Eisinger RW et al., 2023. A call to action—stopping antimicrobial resistance. JAC-Antimicrobial Resistance 5: dlac142.
El Mellouli F et al., 2022. Molecular detection of avian influenza virus in wild birds in Morocco, 2016–2019. Avian Diseases 66: 29–38.
Esposito AM et al., 2022. Phylogenetic Diversity of Animal Oral and Gastrointestinal Viromes Useful in Surveillance of Zoonoses. Microorganisms 10: 1815.
Gnat S et al., 2021. A global view on fungal infections in humans and animals: opportunistic infections and microsporidioses. Journal of Applied Microbiology 131(5): 2095-2113.
Gebreyes WA et al., 2014. The global one health paradigm: challenges and opportunities for tackling infectious diseases at the human, animal, and environment interface in low-resource settings. PLoS Neglected Tropical Diseases 8: e3257.
Gwenzi W et al., 2022. Grappling with (re)-emerging infectious zoonoses: Risk assessment, mitigation framework and future directions. International Journal of Disaster Risk Reduction 82: 103350. https://doi.org/10.1016/j.ijdrr.2022.103350
Hassell JM et al., 2019. Deterministic processes structure bacterial genetic communities across an urban landscape. Nature Communications 10(1): 2643. https://doi.org/10.1038/s41467-019-10595-1
Holoidovsky L and Meijler MM, 2020. Synthesis and evaluation of indole-based autoinducers on quorum sensing in vibrio cholerae. ACS Infectious Diseases 6(4): 572-576.
Impey RE et al., 2020. Overcoming intrinsic and acquired resistance mechanisms associated with the cell wall of gram-negative bacteria. Antibiotics 9(9): 623. https://doi.org/10.3390/antibiotics9090623
Kumar Y, 2019. Antimicrobial resistance: a global threat. Intech Open.
Leal Filho W et al., 2022. Climate change and zoonoses: a review of concepts, definitions, and bibliometrics. International Journal of Environmental Research and Public Health 19(2): 893.
Lyall B et al., 2023. Antibiotics online: digital pharmacy marketplaces and pastiche medicine. Medical Humanities. https://doi.org/10.1136/medhum-2022-012574
MacGowan AP, 2008. Clinical implications of antimicrobial resistance for therapy. Journal of Antimicrobial Chemotherapy 62: ii105–ii114.
Maes D et al., 2020. Antimicrobial treatment of Mycoplasma hyopneumoniae infections. Veterinary Journal 259-260: 105474. https://doi.org/10.1016/j.tvjl.2020.105474
Manohar P et al., 2020. Will the overuse of antibiotics during the Coronavirus pandemic accelerate antimicrobial resistance of bacteria?. Infectious Microbes & Diseases 2(3): 87.
Mehmood M et al., 2023. Detection of Emerging Zoonotic Pathogens: An Integrated One Health Approach. In: Khan A, Abbas RZ, Aguilar-Marcelino L, Saeed NM and Younus M (eds), One Health Triad, Unique Scientific Publishers, Faisalabad, Pakistan, Vol. I, pp: 175-181. https://doi.org/10.47278/book.oht/2023.26

Mohamud AK et al., 2023. Magnitude of opportunistic infections and associated factors among adult people living with human immune deficient virus on art at selected public hospital, mogadishu somalia: cross-sectional study. Annals of Medicine and Surgery 85(7): 3364-3371.

Michael CA et al., 2014. The antimicrobial resistance crisis: causes, consequences, and management. Frontiers in Public Health 2: 145.

Morrison L and Zembower TR, 2020. Antimicrobial resistance. Gastrointestinal Endoscopy Clinics 30: 619–635. https://doi.org/10.1016/j.giec.2020.06.004

Mullins LP et al., 2023. Vaccination is an integral strategy to combat antimicrobial resistance. Plos Pathogens 19: e1011379.

Nadeem SF et al., 2020. Antimicrobial resistance: more than 70 years of war between humans and bacteria. Critical Reviews in Microbiology 46(5): 578-599.

Nadimpalli ML et al., 2020. Urban informal settlements as hotspots of antimicrobial resistance and the need to curb environmental transmission. Nature Microbiology 5(6), 787–795. https://doi.org/10.1038/s41564-020-0722-0

Ossebi W et al., 2022. One health training needs for Senegalese professionals to manage emerging public health threats. Science in One Health 1: 100005.

Otte J and Pica-Ciamarra U, 2021. Emerging infectious zoonotic diseases: The neglected role of food animals. One Health 13: 100323.

Otu A et al., 2021. Africa needs to prioritize One Health approaches that focus on the environment, animal health and human health. Nature Medicine 27: 943–946.

Pokharel S et al., 2020. Antimicrobial use in food animals and human health: time to implement 'One Health'approach. Antimicrobial Resistance and Infection Control 9: 1–5.

Rahman MT et al., 2020. Zoonotic diseases: etiology, impact, and control. Microorganisms 8: 1405.

Ramamurthy T et al., 2020. Virulence regulation and innate host response in the pathogenicity of Vibrio cholerae. Frontiers in Cellular and Infection Microbiology 10: 572096.

Roug A et al., 2013. Zoonotic fecal pathogens and antimicrobial resistance in county fair animals. Comparative Immunology, Microbiology and Infectious Diseases 36(3): 303–308. https://doi.org/10.1016/j.cimid.2012.11.006

Rupasinghe R et al., 2022. Climate change and zoonoses: A review of the current status, knowledge gaps, and future trends. Acta Tropica 226: 106225.

Sanderson H et al., 2019. Antimicrobial resistant genes and organisms as environmental contaminants of emerging concern: addressing global public health risks. In: Management of Emerging Public Health Issues and Risks, Academic Press, pp: 147-187.

Sharma P et al., 2023. Computational biology: Role and scope in taming antimicrobial resistance. Indian Journal of Medical Microbiology 41: 33–38.

Singh BB et al., 2023. Zoonosis–Why we should reconsider "What's in a name?". Frontiers in Public Health 11: 1133330.

Sivagami K et al., 2020. Antibiotic usage, residues and resistance genes from food animals to human and environment: An Indian scenario. Journal of Environmental Chemical Engineering 8(1): 102221.

Spellberg B et al., 2004. Trends in antimicrobial drug development: implications for the future. Clinical Infectious Diseases 38(9): 1279–1286. https://doi.org/10.1086/420937

Tang KWK et al., 2023. Antimicrobial Resistance (AMR). British Journal of Biomedical Science 80: 11387.

Uddin TM et al., 2021. Antibiotic resistance in microbes: History, mechanisms, therapeutic strategies and future prospects. Journal of Infections and Public Health 14: 1750–1766.

Vidovic N and Vidovic S, 2020. Antimicrobial resistance and food animals: Influence of livestock environment on the emergence and dissemination of antimicrobial resistance. Antibiotics 9(2): 52.

Von Wintersdorff CJH et al., 2016. Dissemination of antimicrobial resistance in microbial ecosystems through horizontal gene transfer. Frontiers in Microbiology 7: 173.

Wassenaar TM and Silley P, 2008. Antimicrobial resistance in zoonotic bacteria: lessons learned from host-specific pathogens. Animal Health Research and Reviews 9: 177–186.

WHO, 2022a. Strategic framework for collaboration on antimicrobial resistance: together for One health. Food &

Agriculture Organization. https://www.who.int/publications/i/item/9789240045408

WHO, 2022b. One health joint plan of action (2022–2026): working together for the health of humans, animals, plants and the environment. https://www.who.int/publications/i/item/9789240059139

WHO, 2022c. A health perspective on the role of the environment in One Health. World Health Organization. Regional Office for Europe. https://www.who.int/europe/news-room/fact-sheets/item/environment-and-one-health

Yoshii Y et al., 2017. Norgestimate inhibits staphylococcal biofilm formation and resensitizes methicillin-resistant Staphylococcus aureus to β-lactam antibiotics. NPJ Biofilms and Microbiomes 3(1): 18.

Zhuang M et al., 2021. Distribution of antibiotic resistance genes in the environment. Environmental Pollution 285: 117402.