The Rising Threat of Antibacterial Resistance: Zoonotic Implications in the Context of One Health

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Abstract

Being one of the most successful forms of chemotherapeutic agents, antibiotics have been used to cure the ailment and infectious diseases of animals and humans since ancient times. The global consumption of antibiotics is linked to the regular emergence of microbial infections and the development of new antimicrobial drugs. Elevated levels of antibiotics, that is, antibiotic pollution due to excessive consumption may force the microbial community to develop resistance, with *Escherichia coli* being the first discovered showing penicillin resistance. Many zoonotic diseases are being discovered, neglected worldwide showing a need to raise awareness by the masses. Their transmission occurs through direct and indirect contact (vector, food, water, air-borne), climatic changes, displacements, and immunosuppression. To tackle antimicrobial resistance, One Health approach is essential which combines human, animal and environmental health using different campaigns. Several steps like education and awareness campaigns, cross-sector collaboration, research and development of novel antibiotics, bacteriophage therapy, immunotherapies and unconventional genomic surveillance approaches can reduce the disease risks. Taking precautionary measures, infection prevention and hand hygiene practices can even considerably lessen the need for antibiotics shaping the health of the future generations.

Keywords: Zoonosis; Antimicrobial resistance; AMR; One Health; Microbes

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Introduction

Antibiotics are one of the most successful forms of chemotherapeutic agents used to cure the ailment and infectious diseases of animals and humans since ancient times (Aminov, 2010). The presence of tetracycline traces in the skeletal remains of humans from classical times (350-550 CE) and in the femoral midshafts of skeletons from the late Roman period indicated that the exposure of living organisms to antibiotics is not merely confined to the modern "antibiotic era" (17^{th} -20^{th} century) (Nelson et al., 2010; Aminov, 2017). In ancient times, the practice of using Traditional Chinese Medicines (TCM) which contained natural compounds (e.g. tetracycline) with antimicrobial properties for the treatment of infections would have led to its presence in the bones (Cui & Su, 2009). From the modern era of antibiotics, Louis Paster was the first to observe the inhibition of anthrax bacteria using saprophytic bacteria (Aminov, 2017). Paul Ehrlich and Alexander Fleming are the prominent names in the modern antibiotic era. After approximately six years (1904-1909) of trials, Ehrlich successfully synthesized an organic compound (salvarsan) by systematic screening approach that could cure syphilis, a sexually transmitted disease, caused by spirochete *Treponema pallidium* (Ehrlich & Hata, 1910). Later on, in 1929 Alexander Fleming discovered the antimicrobial properties of *Penicillium,* a fungus (Fleming, 1929; Aminov, 2010). The foundation laid by Ehrlich and Fleming acts as a paradigm for all research in drug discovery today, resulting in the number of new antibiotics (Aminov, 2010), either synthetic, semi-synthetic, or organic.

All the present classes of antibiotics such as aminoglycosides, tetracyclines, lipopeptides, oxazolidinones, glycopeptides, streptogramins, and quinolones, were discovered during the "Golden Era of Antibiotics" (1950-1970) and since then new drugs have been made by the modification of existing drugs (Chopra et al., 2002; Chin et al., 2023). Since their discovery in the 20^{th} century, antibiotics have significantly reduced the mortality rates of many infectious diseases. For example, antibiotics in the United States of America (USA) led to an 8.2% decrease in mortality caused by pneumonia, tuberculosis, and influenza infections between 1938 and 1952 (Cohen, 2000). This reduction was attributed to streptomycin, sulphonamides, penicillin, para-aminosalicylic acid, and isoniazid antibiotics (Baldry, 1976).

1.1. Global Consumption and Antibiotic Resistance

The global consumption of antibiotics is linked to the regular emergence of microbial infections and the development of new antimicrobial drugs (Chin et al., 2023). In 2000, the worldwide use of antibiotics was 2.11 billion defined daily doses (DDD's) which then increased to 34.8 billion DDD's in 2015 (Klein et al., 2018). The class of antibiotic mostly used varies among countries, for example, in Japan, the consumption of quinolones showed an increase of 20.78% from 2009-2013 (Muraki et al., 2016). Inside living organisms i.e. humans or animals, antibiotics are degraded by enzymatic actions, as a result, an active ingredient that has antimicrobial properties is produced while the remaining residues are excreted outside the body in urine or feces which in turn increase the level of antibiotics in the environment. Elevated levels of antibiotics, which is known as, antibiotic pollution due to excessive consumption may force the microbial community to develop resistance (Kollef et al., 2017). Antibiotic or antimicrobial resistance (AMR) is the failure of therapy because of the reduced ability of a substance (antibiotic or antimicrobial agent) against the disease-causing bacterium (Ema & Efsa, 2017). Alexander Fleming was among the earlier cautioners about the resistance in bacteria to penicillin (Aminov, 2010). The *Escherichia coli* bacterial strain was the first to be found with penicillin resistance in the 1940s. The bacteria degraded the antibiotic through the penicillinase enzyme (Abraham & Chain, 1940). AMR may develop due to resistant genes either through mutation or the exogenous antibiotic-resistant genes transfer from other bacterial strains and the induction of resistance mechanism through specific metabolic cascade activation (Ema & Efsa, 2017).

1.2. Zoonosis and Pathogenic Organisms

According to Taylor et al. (2001), there are approximately 1415 species of pathogenic organisms that are infectious to human beings. It encompasses 217 viral species (including prions), 307 fungi species, 66 protozoan species, 287 helminths, and 538 species of bacteria and rickettsia. Out of 1415 species, about 868 (61%) are zoonotic, i.e. these pathogenic organisms can be transferred between animals and humans either through direct physical contact with food-producing or companion animals or through the contaminated environment being shared (Taylor et al., 2001; Cantas & Suer, 2014). Food-borne zoonotic pathogens include 31 species of microorganisms encompassing bacteria such as *Staphylococcus aureus, Escherichia coli, Salmonella* species, *Pseudomonas*, *Klebsiella* species, (Hemalata & Virupakshaiah, 2016) *Campylobacter* species (Epps et al., 2013), and *Listeria monocytogen* (Peiris, 2011), presence of these pathogens in the food causes food safety issues and human health problems (Zhao et al., 2014). Other zoonotic pathogens such as *Yersinia pestis* (plague), *Bacillus anthracis* (anthrax), *Vibrio cholerae* (severe diarrhea), and *Brucella* species (brucellosis) cause vector-borne, airborne, waterborne, and direct contact-borne illness, respectively, in humans (Corbel, 1997; Ahmed et al., 2010; Barbieri et al., 2020; Chen et al., 2022).

1.3. Use of Antibiotics in Animals and Emergence of Antibiotic Resistance

Zoonotic diseases caused by bacterial pathogens have re-emerging potential even after their eradication mainly due to changing lifestyle and increased contact with animals (adoption of small animals as pets), for example, leptospirosis, which is caused by *Leptospira* species and transmitted through the water contaminated with urine of infected animals (Higgins, 2004; Haake & Levett, 2015), such diseases affect the tourism, travel, commerce and economy worldwide (Acha, 2001). About 8 million kilograms of antibiotics are being fed to farm animals or livestock to eradicate any potential pathogen (or as a growth promotor) and around 1 million kilograms of antibiotics are used by humans globally (Roe &Pillai, 2003). This extensive use of antibiotics in the veterinary practice, results in increased antibiotic resistance in pathogenic zoonotic bacteria (such as *Salmonella*, *Campylobacter, Shigella, Yersinia, Listeria*, *Enterococcus* species, and *E. coli*) as well as in fecal flora of animals (Corpet, 1988; Cantas & Suer, 2014). Zoonotic pathogens have been identified to have resistance against broad-spectrum antibiotics such as β-lactams, carbapenems, fluoroquinolones, and aminoglycosides (Cloeckaert et al., 2017).

1.4. Mechanisms of AMR Transmission

Antimicrobial resistance (AMR) spreads from bacteria to bacteria through horizontal gene transfer (HGT) through mobile genetic elements such as plasmids, transposons, gene cassettes, integrative and conjugative elements, etc. The horizontal transfer of the resistance genes facilitates the faster spread of multiple drug resistance (MDR) among animals, humans, and the environment (Cloeckaert et al., 2017). Younger, older, pregnant, and immune-compromised individuals are at greater risk for acquiring antibiotic-resistant bacterial zoonotic diseases (Acha, 2001). Healthcare facilities serve as the main repository of MDR pathogens including methicillin-resistant staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE) (Boyce, 2007). For instance, *Salmonella* species have *tet* gene for tetracycline, *sul* gene for sulfonamides, *cat*, *cm1,* and *floR* for chloramphenicol and *aph*, *aac* for aminoglycosides are observed which impart MDR to bacteria (Adesiji et al., 2014). The bacterial flora that persists in the gastrointestinal tract of humans is the major reservoir of antibiotic-resistance genes, and here the transmission of genes between clinical bacterial pathogens and commensal bacteria takes place (Djordjevic et al., 2013). So, the industrialized countries are allocating a big part of their healthcare budget in the screening of such potential reservoirs of bacteria and products obtained from animals. Companion animals (or pets) transfer most commonly encountered zoonotic diseases through their paws scratch and bite. These diseases include cat scratch disease and bartonellosis caused by *Bartonella henselae.* Transfer of zoonotic pathogens has also been observed through the fecal-oral route i.e. *Salmonella* sp., c*ampylobacter* sp., S*higella* sp., and *E. coli*. Pathogenic bacteria (*Coxiella burnetiid*) cause Q-fever in Europe, which is the most disastrous disease originating from farmhouses and livestock mainly (Cantas & Suer, 2014). This intricate interaction between the animals, humans, and the shared environment calls for the 'One Health' approach, which provides an integrated and unifying framework for their interconnected well-being and health (Calistri et al., 2013).

2. Bacterial Zoonotic Diseases

For a few decades, scientists have been greatly focused on zoonosis. Studying the causative agent its mode of transmission, symptoms and preventive measures can help in wiping out or at least controlling the pandemic in the future. A detailed overview of zoonotic bacterial diseases is given in Table 1 and figure 1 summarizes the types and routes of bacterial diseases.

3. Transmission

Zoonotic disease transmission primarily occurs through direct and indirect contact. Transmission through indirect routes encompasses vector-borne, food-borne, water-borne, and air-borne pathways. Furthermore, climatic changes, displacements, and immunosuppression contribute to wider and recurrent transmission of bacterial zoonotic diseases.

Table 1: Zoonotic bacterial diseases and their types, mode of transmission, symptoms and preventive measures

Diseases	Causative Agents	Sources & Transmission	Types	Symptoms	Prevention	Treatment	References
Anthrax	▪ *Bacillus anthracis* (genus *Bacillus)* ▪ Exists in two forms i.e. vegetative and spore form (virulent form)	▪ Contaminated soil, water, animal's contact.	1. Cutaneous Anthrax (through skin) 2.Gastrointestinal Anthrax (through GI tract/ undercooked meat) 3.Inhalation anthrax (inhalation of spores) 4.Injection anthrax (injecting illegal drugs)	▪ Painless sore, fever, headache, ▪ Nausea, vomiting, fever, abdominal pain ▪ Flu-like symptoms, sore throat, mild fever, muscle aches, shortness of breath, nausea ▪ Redness at injection site, swelling, shock, organ failure, meningitis	▪ Vaccination, Sanitization ▪ Preventing the slaughter of ill animals ▪ Raising awareness	▪ Penicillin G, amoxicillin, ciprofloxacin, doxycycline are used in treatment. ▪ Human immunization is available only in UK and US only for occupational and military zones.	Ahmed et al., 2010; Sweeney et al., 2011; Doganay et al., 2023; Mayo Clinic, 2023a
Bovine Tuberculosis	▪ *Mycobacterium tuberculosis Mycobacterium bovis*	▪ Cattle, bison, elk, and deer. ▪ Using unpasteurized dairy products. ▪ Person to person through air by coughing and sneezing.		▪ Prolonged cough, Chest discomfort Weakness, Fatigue, Weight loss, Fever ▪ Night sweats. (symptoms appear in active TB)	▪ Pasteurization of dairy products ▪ TB skin and fluid tests ▪ Seeking medical advice ▪ Using face masks ▪ Adopting hygiene practices ▪ Adopting TB preventing treatment (TPT)	▪ Using antibiotics such as isoniazid, rifampicin, ethambutol	Admassu et al., 2015
Plague (Black Death)	▪ *Yersinia pestis* bacterium (enterobacteria family)	▪ Rodents and fleas ▪ Human activities like trading ▪ Cuts, aerosols, contaminated food ▪ Inhalation of infected particles ▪ Handling *Y. pestis* in laboratories.	1.Bubonic plague (most widespread) weakness, headache, fever, painful lymph node 2.Septicemic plague (fever, overtiredness, abdominal distress, bleeding into the skin and various organs.) 3.Pneumonic plague (fever, headache, systematic pneumonia, chest pain, bloody cough)		▪ Diagnosed by observing blood, fluid from buboes, brain, spinal cord or taking mucus from the lungs. ▪ Preventing rodents to wander around your home. ▪ Wearing gloves and use sanitizers while handling rodents mostly the infected ones. ▪ Keep fleas off the pets.	▪ Treatment is usually done in the hospital. ▪ Antibiotics include gentamicin, doxycycline, ciprofloxacin, levofloxacin moxifloxacin	Butler, 2009; Raoult et al., 2013; Barbieri et al., 2020; Glatter & Finkelman, 2021; Mayo Clinic, 2023b
Tetanus	▪ *Clostridium tetani* a bacterium ▪ Exists as spores or vegetative form	▪ Soil, feces, dust. ▪ Spores can enter by minute crack in skin injury, burns, ulcers. ▪ Spores (germinate in the wound anaerobically) ▪ Vegetative bacteria (produce tetanospasmin, also called tetanus toxin)		▪ Lock jaw, muscle spasms, seizures, headache, fever. ▪ Fluxes in blood pressure or heart rate	▪ Using medicine human tetanus immune globulin (TIG) ▪ Aggressive wound care ▪ Drugs to control muscle spasms ▪ Antibiotics ▪ Vaccination.	▪ Vaccination e.g. diphtheria and tetanus vaccines	Becker et al., 2003
Salmonellosis	▪ Members of the genus *Salmonella.* ▪ *Salmonella choleraesuis, Salmonella typhisuis*	▪ Live in animal and human intestines and are shed through stools. ▪ Spread by contaminated food and water.		▪ Diarrhea ▪ Stomach aches ▪ Fever ▪ Nausea ▪ Vomiting ▪ Chills ▪ Headache ▪ Blood in the stool (in extreme cases)	▪ Proper sanitation and sewage dumping.	▪ Antibiotics such as cefixime, chloramphenicol, amoxicillin, aztreonam, cefotaxime to prevent death. ▪ Dexamethasone for problems like coma or shock occurs	Adesiji et al., 2014; Gut et al., 2018; Griffith et al., 2019; Mayo Clinic, 2022
Campylo-bacteriosis	▪ Causative agent belongs to the genus *Campylobacter*	▪ Raw and undercooked poultry, pork, and beef ▪ Unpasteurized milk ▪ Untreated drinking water		▪ Diarrhea ▪ Cramping ▪ Abdominal pain ▪ Fever ▪ Nausea or vomiting ▪ Headache	▪ Bio security measures ▪ Water purification ▪ Programs to control insects	▪ Fluid replacement ▪ Symptomatic treatment ▪ Antibiotic medication	Amin et al., 2023

		▪ Fecal-oral transmission ▪ Homosexual contact ▪ Congenital transmission					
Brucellosis	▪ *Brucella* bacterium	▪ Contaminated foods ▪ Occupational contact ▪ Placental barrier ▪ Lactation ▪ Sexual contact ▪ Infected tissues such as blood & bone marrow		▪ Fever ▪ Headache ▪ Weakness ▪ Sweating ▪ Chills ▪ Weight loss ▪ General aching ▪ Joint and muscle pain ▪ Inflammation of the liver and spleen ▪ GI or respiratory symptoms	▪ Exercise of hygienic precautions ▪ Heating of dairy products	▪ Antibiotics intake for a minimum of 6–8 weeks	Pappas et al., 2005
Cat-Scratch Disease	▪ Causative agent belongs to *Bartonella* species	▪ Through a scratch, bite, ▪ Contamination of a wound ▪ Mucous membrane from a cat infected with Bartonella henselae		▪ Swollen lymph nodes ▪ Aching ▪ Malaise, ▪ Anorexia ▪ Low-grade fever	▪ Using flea control products ▪ Avoiding rough play ▪ Adopting mature cats	▪ Treatment has not been evaluated, but a combination of erythromycin or doxycycline & rifampin for 4 to 6 weeks may be effective	Klotz et al., 2011 ▪
Mycoplasma Pneumonia	▪ Caused by bacterium *Mycoplasma pneumoniae* relevant to cold agglutinin disease.	▪ Through respiratory droplets from coughing and sneezing		▪ Fever ▪ cough ▪ Headache ▪ Sore throat ▪ Shortness of breath ▪ Feeling tired ▪ Chills ▪ Sweating ▪ Runny or stuffy nose ▪ Watery eyes ▪ Wheezing	▪ No vaccine is currently available. ▪ Cover a cough or sneeze ▪ Hand washing procedures.	▪ Antibiotics ▪ Macrolides	Pappas et al., 2005; Christian et al., 2016
Lyme Disease (Lyme borreliosis)	▪ Caused by species of *Borrelia* bacterium	▪ Transmitted to humans by the bites of infected ticks of the genus *Ixodes*		▪ Fever ▪ Rash ▪ Chills ▪ Headache ▪ Fatigue ▪ Muscle and joint aches ▪ Swollen lymph nodes ▪ Facial paralysis ▪ Irregular heartbeat ▪ Arthritis ▪ Nerve problems, ▪ Heart problems	▪ By avoiding or reducing time in likely tick habitats	▪ Antibiotics are the primary treatment	Steere et al., 2004
Leptospirosis (LPS) Fort Bragg fever, Rice field fever, Weill's disease	▪ caused by gram-negative bacterium of genus *Leptospira*	Transmitted by: ▪ Direct contact with contagious secretions (blood, urine, aborted fetus). ▪ Indirectly with contaminated water, soil, feed and uterine discharge of infected animal.		▪ In humans: fever, headache, myalgia, acute heart failure and hemoptysis. ▪ In animals: reproductive issues in bovines.	▪ Improving sanitary conditions ▪ By raising awareness	▪ In humans LPS is treated with antibiotics including ampicillin, ceftriaxone and cefotaxime ▪ In hamsters, swine and cattle antibiotics like ampicillin, ofloxacin, enrofloxacin, ciprofloxacin, doxycycline are used	Ja Al-orry et al., 2016
	▪ Caused by	Transmitted by:		▪ Fever	▪ By raising	▪ Antibiotics	

Bartonellosis	gram negative bacterium of *Bartonella* species	▪ Arthropod vector (mites, fleas, ticks and lice). ▪ Scratches ▪ Bites ▪ Exposure to contaminated bodily fluids.	▪ Fatigue ▪ Joint pain ▪ Headache ▪ Memory loss ▪ Muscle pain	awareness ▪ Controlling vector population. ▪ By maintaining good hygiene.	such as doxycycline, azithromycin, rifampin, gentamicin are used	Breitschwerdt, 2014
Listeriosis	▪ Caused by gram positive bacterium *Listeria monocytogenes*	▪ Transmitted by: Direct exposure with infected animal, through contaminated food. ▪ Vertical transmission during pregnancy.	▪ Bacteremia ▪ Gastroenteritis ▪ Meningitis ▪ Miscarriage ▪ Stillbirth ▪ Neonatal infections	▪ Maintaining proper food handling ▪ Hygiene practices ▪ Washing vegetables and fruits. ▪ Cooking food ▪ properly.	▪ Antibiotics such as ampicillin with or without gentamicin, trimethoprim, sulfamethoxazole	Koopmans et al., 2023
Tularemia	▪ Caused by gram negative bacterium *Francisella tularensis*	▪ Transmitted by: Infected animals, arthropod vectors, skin abrasions and aerosolized particles.	▪ Fever ▪ Ulcer ▪ Sore throat ▪ Weight loss ▪ Fatigue ▪ Pharyngitis	▪ Avoid direct contact with vectors and contaminated materials. ▪ Vaccination	▪ Antibiotics such as tetracycline, doxycycline, streptomycin and gentamicin	Hepburn & Simpson, 2008
Melioidosis	▪ Caused by gram negative bacterium *Burkholderia pseudomallei*	▪ Direct contact with contaminated soil or water. ▪ Inhalation of aerosols. ▪ Ingestion of contaminated water or food	▪ Septicemia ▪ Pneumonia ▪ Organ abscesses ▪ Arthritis ▪ Persistent fever.	▪ Avoid contact with contaminated soil or water. ▪ Wear boots and gloves. ▪ Chlorination of water.	▪ Oral antibiotics like co-trimoxazole and intravenous antibiotics such as ceftazidime or carbapenems are used.	Cheng & Currie, 2005

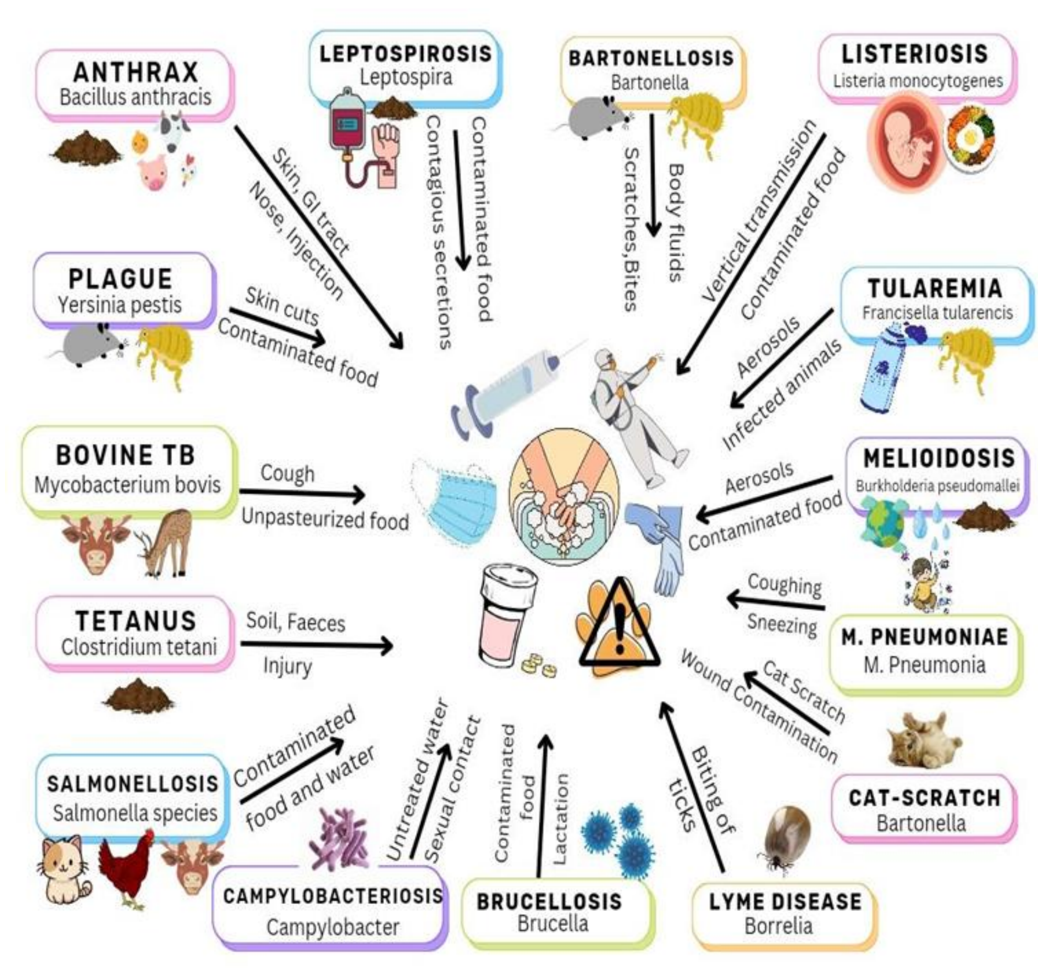

Fig. 1: Types of bacterial zoonotic diseases

A CDC (Centers for Disease Control and Prevention) case-control research study identified a correlation between visiting a farm with cows within five days before the onset of illness, which marks the inaugural report of animal contact as a risk factor in the United States in 1997 (Kassenborg et al., 2004). This demonstrates that zoonotic infections can transmit directly when individuals come into close contact with animals. On the contrary, when individuals encounter contaminated water, soil, food, or infected urine, they contract the disease indirectly. An instance of which is leptospirosis, a bacterial zoonotic disease that spreads through wild rodents and domesticated animals. Typically, human illness results from contact with urine, water, or soil contaminated by bacterial pathogens (Al-orry et al., 2016). Additionally, some zoonotic illnesses are spread by vectors. For instance, fleas served as a vector for the bubonic plague, popularly referred to as the Black Death, which killed an estimated 25 million people in Europe (Glatter & Finkelman, 2021). Given that vectors are ectothermic, variations in the climate and environment (temperature, precipitation, and humidity) can have an impact on their capacity to reproduce, survive, spread geographically, and subsequently spread illnesses (de Souza & Weaver, 2024).

Foodborne transmission refers to the ingestion of meat and eggs contaminated with bacteria such as *Clostridium*, *Staphylococcus*, *and Salmonella*, which reside in reservoirs like cattle and poultry. Inadequate food preparation facilitates the transfer of these bacteria from animals to people (Tajkarimi et al., 2013). Waterborne diseases transmit to humans mostly through the use of contaminated water and recreational activities involving polluted water. Likewise, numerous epidemiological studies indicated a correlation between airborne transmission and zoonotic diseases. Bovine tuberculosis (BTB) is induced by *Mycobacterium bovis*, which can be transmitted from animals to humans through aerosol inhalation (Rupasinghe et al., 2022). Presently, there are more than 108 million individuals forcibly displaced worldwide, primarily comprising refugees, asylum seekers, and internally displaced persons. These migrations correlate with heightened susceptibility to infectious zoonotic illnesses, especially in areas where living circumstances are congested (Oakley et al., 2024). Individuals with reduced immunity elevate the likelihood of repeated and prolonged persistence of zoonotic infections. Numerous bacteria are capable of long-term infection and persistence within their hosts. This may result from the pathogen's immune evasion, the host's immunosuppression, or ineffective antibiotic killing (Fisher et al., 2017). The modes of transmission of bacterial diseases are given in figure 2.

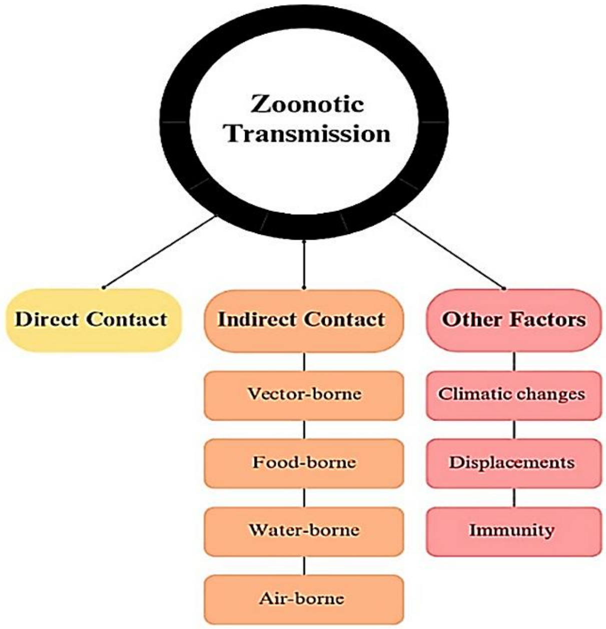

Fig. 2: Modes of zoonotic transmission of bacterial diseases

4. Fighting Antimicrobial Resistance: A One Health perspective for Global Health Defense

In treating infections, AMR poses major challenges, if left unaddressed and forecasts 10 million deaths annually by 2050 (Mudenda et al., 2023). To tackle AMR, the One Health perspective is compulsory which combines human, animal and environmental well-being. This approach promotes intersectoral alliance, antibiotic stewardship and interdisciplinary research to fight resistance. As depicted in One Health, effective antibiotic use reduces the selective pressure that drives resistance. The One Health perspective safeguards a more extensive response to AMR by encouraging alliance among healthcare providers, veterinarians, farmers and policymakers. It also emphasizes the need for inventive treatments, for instance new diagnostics and vaccines, coupled with healthy antimicrobial guidelines (Cella et al., 2023)

Along with promoting responsible antibiotic use, AMR stewardship includes global initiatives like the WHO's Global Antimicrobial Resistance Surveillance System (GLASS) and national plans, for instance, the US Department of Health and Human Services 2020-2025 policy. To enhance antibiotic use in animals' control, the use of medically important antibiotics for growth promotion and guide stakeholders on responsible antibiotic practices are the main aims of these programs. In reducing resistance by ensuring careful antimicrobial use, hospital, outpatient and community pharmacy-based AMS programs are important. The advocacy of such implementations coupled with global alliance is essential for addressing the AMR crisis and ensuring the benefits of antimicrobials in both human and animal health (MaArthur & Tsang, 2017).

Establishing One Health governance to make joined policies, forming inclusive monitoring systems like the National Antimicrobial Resistance Monitoring System (NARMS), and applying stewardship programs across all sections are included in primary goals. These policies must be adjustable and informed by scientific evolution. Education and guidance campaigns targeting healthcare professionals, farmers, and the public are also essential in promoting careful antibiotic use. Global initiatives, for example, the EU's ban on nonmedicinal antibiotics in animals and inflexible management in the USA, highlight the importance of policy execution. A One Health perspective, coupled with antibiotic stewardship, education and cross-sector corporation, is essential to mitigating AMR and securing global health defense. (MaArthur & Tsang, 2017) (Figure 3).

In fighting antibiotic resistance, research and development of new antibiotics, substitute therapies, and rapid diagnostic tools are compulsory. The studying of bacteriophage therapy, immunotherapies, and unconventional genomic monitoring strategies, such as whole-genome sequencing (WGS) and metagenomics, is important to understanding and overcoming resistance. Alongside these, precautionary measures for infection prevention and hand hygiene practices, can considerably lessen the need for antibiotics (Cella et al., 2023). Some of the major points of global plan of action to fight antimicrobial resistance are depicted in Table 2.

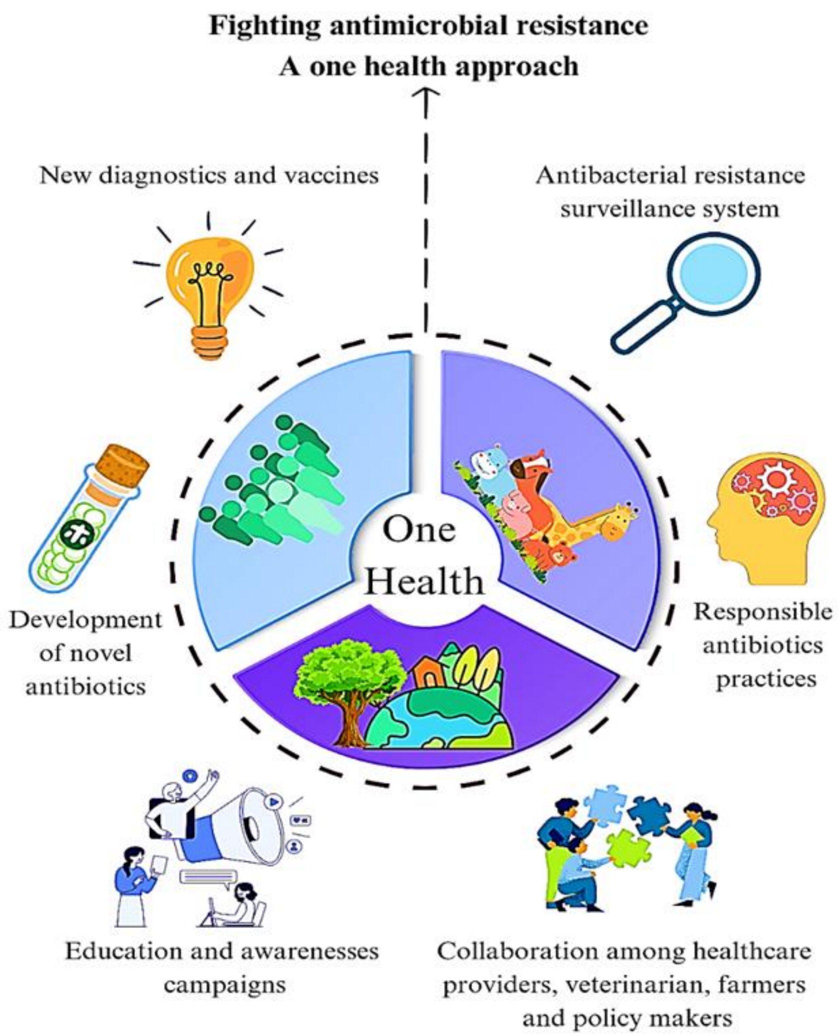

Fig. 3: Fighting Antimicrobial Resistance: A One Health Approach

Table 2: Global plan of actions to fight antimicrobial resistance (AMR) (Mudenda et al., 2023)

Plan of action	Plan depiction
Global Action Plan (GAP) on AMR	World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO) and World Organization for Animal Health (OIE) started GAP to address AMR through a "One Health" perspective in May, 2015.
Aims of GAP	Enhancing education and guidance on AMR, increasing research and supervision, decreasing infections through hygiene, upgrading careful antimicrobial use in human and animal health and providing aid for sustainable investment in novel medicines.
Antimicrobial Stewardship (AMS) Programs	It was designed to uplift rational antimicrobial usage by upgrading choice, dose, duration and frequency to certify the best clinical results and reducing AMR.
Actions for public well being	It includes campaigns for instance World Antimicrobial Awareness Week (WAAW) to improve understanding about AMR globally. It is held yearly from the 18^{th} to the 24^{th} of November.
Animal Healthiness	Animal health is also included in AMS programs, stimulating careful antimicrobial use and the formation of alternative treatments. The use of antimicrobials in animal feed is controlled by the US Veterinary Feed Directive (VFD) Rule, predominantly reducing the use for growth promotion.

Conclusion

The world is advancing with each passing age and so are the disease-causing pathogens like *Brucella* , *Leptospira* , *Clostridium tetani* , *Campylobacter*. These pathogens pose a significant public health threat. These can get stepped up to the complex levels, difficult or even impossible to be controlled. So, these emerging and re-emerging diseases, raise the opportunity of having more preventive and collaborative measures for the masses. Inter- sectoral campaigns and integrated awareness programs like the One Health approach, Global Action Plan on Antimicrobial Resistance and Antimicrobial Stewardship are needed at different levels like primary school children, family to community levels paving their ways with fruitful steps preventing zoonotic transmission. Further researches and modern technologies are required sideways to wipe out the old and new emerging pathogenic strains, developing the novel use of antibiotics and vaccines, leading the world towards sustainable and a healthy future - a future that guarantees masses health from childhood at the community level.

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