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Review Article

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Antibiotic Resistance: A Looming Global Threat and Urgent Call to Action

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Abstract Antibiotics have become essential for treating infectious illnesses and have played a crucial role in the substantial advancements in world health over the last 70 years. Millions of individuals today endure infections that were formerly considered life-threatening. Excessive use of antibiotics and irresponsible prescribing practices by physicians are significant factors contributing to the rise of antibiotic resistance in the population. More effective treatments, viable preventative methods, and a scarcity of new antibiotics must be needed. This necessitates the creation of innovative treatment alternatives and alternative antimicrobial medicines. This article highlights the main factors contributing to antibiotic resistance: overuse, resistance genes, and widespread use of antibiotics in agriculture. This article highlights the main factors contributing to antibiotic resistance: overuse, resistance genes, and widespread use of antibiotics in agriculture.

Keywords Antibiotic resistance, Infections, pneumonia

1. Introduction

Antibiotics are "chemical compounds generated by microorganisms that either eradicate or impede the development of other microorganisms.". [1] There is hope that diseases may be treated and avoided thanks to the discovery of antibiotics. On the other hand, infections continue to rank as the top killers in emerging nations. This is because of the rise of new illnesses, the return of old ones, and, most importantly, the development of antibiotic resistance. A significant public health concern in the past decade has been the rise of antimicrobial resistance (AMR). This phenomenon is widespread across many world regions, and there are significant gaps in the current surveillance systems. In April 2014, the World Health Organization (WHO) released its first global report on antimicrobial resistance (AMR) surveillance, which gathered data from national and international networks for the first time. [2]

Anatomy of bacterial cell

The intricate, mesh-like bacterial cell wall keeps most bacteria's cell shape and structural integrity. A network of polysaccharide strands cross-linked by brief peptide bridges connected to the MurNAc residues makes up most of the cell wall. This network is known as peptidoglycan (PG). The cell wall's rigidity is required to sustain high intracellular pressures and tolerate external stresses, while its flexibility is essential for cellular growth.

The bacterial cell envelope is a sophisticated layered structure shielding organisms from challenging surroundings. Most bacteria may be categorized into two types based on their cell envelopes. Gram-negative bacteria have a peptidoglycan cell wall enclosed by an outer membrane that contains lipopolysaccharide. Gram-positive bacteria do not have an exterior membrane but are enclosed by thick layers of peptidoglycan, which are denser than Gram-negative bacteria. [3]

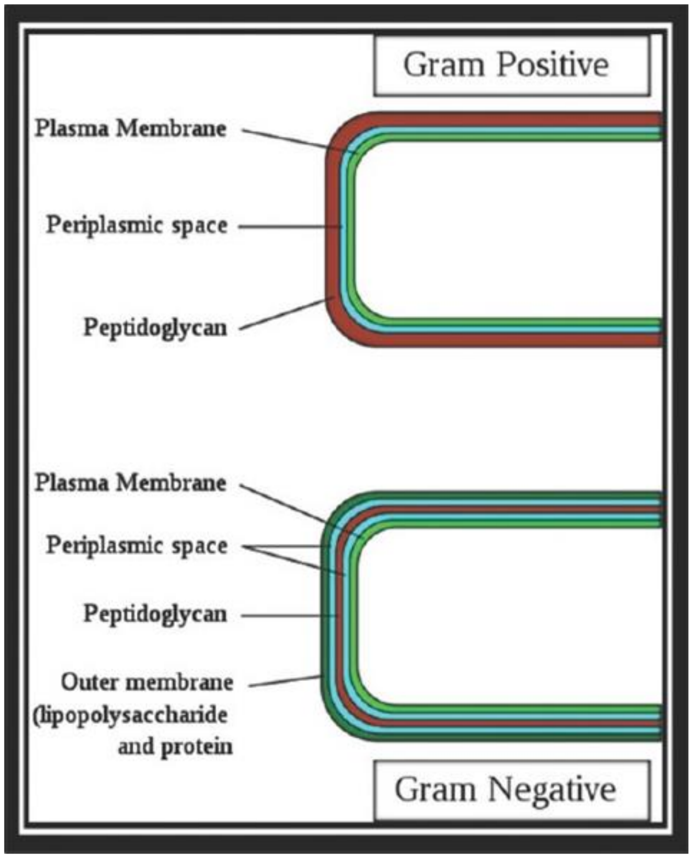
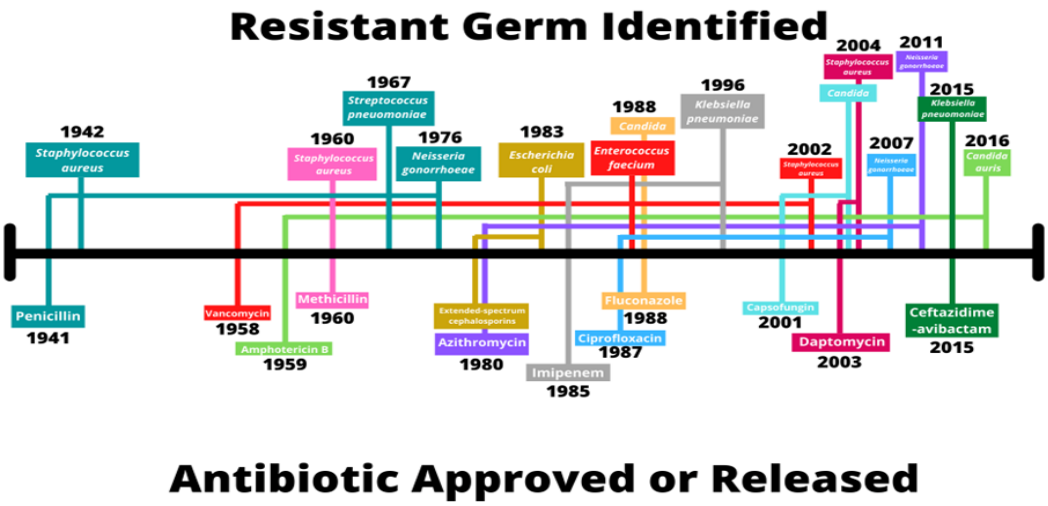


Figure 1: structure of bacterial Cell Envelope [4]

Development of Antibiotics

The addition of antibiotics into medical treatment was the most significant advancement in healthcare throughout the 20th century. [5] Sir Alexander Fleming discovered penicillin in 1928, marking the beginning of the current age of antibiotics. [6] Antibiotics have revolutionized contemporary medicine and saved millions of lives since then. Antibiotics were first recommended to treat severe illnesses in the 1940s. [7] Vancomycin was first used in clinical settings in 1972 to treat methicillin-resistant strains of S. aureus and coagulase-negative staphylococci. [6] Developing vancomycin resistance was considered improbable in a clinical environment due to the significant challenges involved. Vancomycin resistance was identified in coagulase-negative staphylococci in 1979 and 1983. The pharmaceutical industry developed several new antibiotics in the late 1960s and early 1980s to address resistance. [8] However, following that period, the introduction of new medications decreased as the antibiotic pipeline started to diminish. In 2015, many years after the first use of antibiotics to treat patients, bacterial infections have resurfaced as a significant concern. Antibiotics not only cure infectious diseases but also enable contemporary medical operations such as cancer therapy, organ transplants, and open-heart surgery. Yet, the improper use of these beneficial substances has led to a fast increase in antimicrobial resistance (AMR), rendering certain illnesses untreatable. [9]



Source: CDC

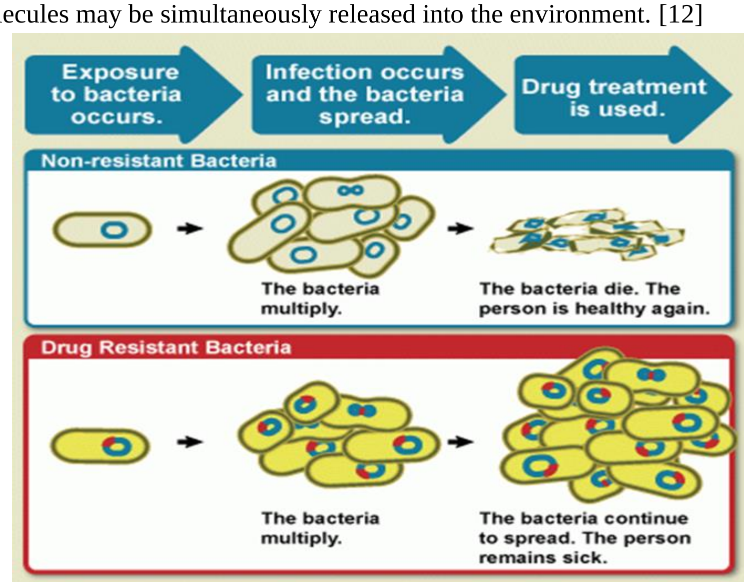
Causes of Antimicrobial (Drug) Resistance

Microbes, including bacteria, viruses, fungi, and parasites, are living entities that undergo evolution. Their primary purpose is to reproduce, flourish, and propagate rapidly and effectively. Microbes adapt to their habitats and evolve to secure their survival. An antibiotic may induce genetic modifications in microbes, allowing them to survive and continue growing. This occurs via several methods.

1. **Selective Pressure**

When antibiotic exposure occurs, microorganisms are destroyed or survive if they possess resistance genes. [10] The survivors will reproduce, and their offspring will soon become the prevailing kind in the microbial community.

Antibiotic pollution may promote the emergence and dissemination of antibiotic resistance. Antibiotics from human and veterinary medication may be introduced into the environment via several pathways, such as wastewater treatment plant discharges, hospital and processing plant discharges, agricultural waste and biosolids application, and leakage from waste storage containers and landfills. [11] One challenge in linking higher environmental resistance levels to antibiotic pollution is that antibiotic-resistance genes and antibiotic molecules may be simultaneously released into the environment. [12]



Source: NIAID

2. Overuse

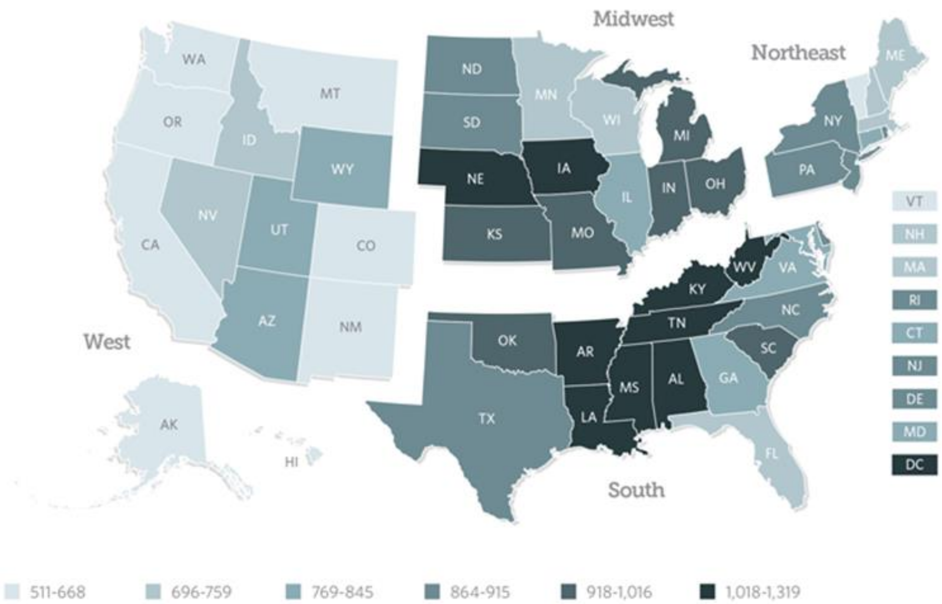
A prominent driver of antibiotic resistance development is their excessive usage. [13] According to epidemiological research, antibiotic use is directly associated with the development and spreading of microorganisms resistant to these drugs. [14] Bacteria may get genes from relatives or strangers on plasmids or other mobile genetic components. Bacterial species may acquire antibiotic resistance by horizontal gene transfer (HGT). [13] Resistance may also arise naturally because of mutation. [13]

There were 838 prescriptions for every 1,000 individuals in the United States in 2015, with approximately 270 million antibiotics written by providers in outpatient settings such as physician's offices and emergency rooms. [15] Trends in antibiotic prescriptions differ substantially among different types of providers. For instance, between 2011 and 2015, the prescription rates of physician assistants and nurse practitioners increased by 64%, while those of primary care physicians decreased by 18%. The second number needs to account for how physicians' caseloads may vary over time, such as seeing more patients with bacterial illnesses. Nevertheless, it is crucial to establish all-encompassing stewardship programs that include all kinds of providers to address these trend disparities.

Figure 1

Outpatient Antibiotic Prescriptions by State, 2015

Antibiotic prescriptions per 1,000 people



Source: Centers for Disease Control and Prevention, "Outpatient Antibiotic Prescriptions—United States, 2015," accessed Jan. 25, 2018, https://www.cdc.gov/antibiotic-use/community/pdfs/Annual-Report-2015.pdf

3. Inappropriate Antibiotic Use

It indicates that antibiotic usage is rising in this nation despite the link between overuse and the development of drug-resistant bacteria. According to nationwide office-based research, antibiotic prescriptions for children rose 48% from 1980 to 1992. [16] The elderly and the very young have a disproportionately high rate of antibiotic usage. One study found that by the time children were three and six months old, 70% had taken antibiotics, and by the time they were three and six months old, 37% had done so. [17] In vitro, resistance has developed in formerly vulnerable organisms when antibiotic usage has increased. This is true for S. pneumoniae in respiratory tract infections and Escherichia coli in urinary tract infections, for example.

It indicates that viruses or illnesses that resolve on their account for a significant share of antibiotic use. According to the CDC, doctors' offices write prescriptions for over 100 million courses of antibiotics annually, with around half of those prescriptions being superfluous. [18]In the ambulatory context, most antibiotic prescriptions are for respiratory infections. [19]Forty percent of patients with acute bronchitis and almost half of those with colds or URIs get antibacterial medication, according to studies examining doctors' prescription habits. This practice of administering antibiotics continues even though these drugs are ineffective against viruses, including the common cold. A large body of research indicates that antibacterial medicines do not reduce the length of sickness in cases of acute bronchitis. [20]

Despite doctors knowing that antibiotics cause germs to become resistant, they nonetheless prescribe them. One research found that almost all doctors (97 percent) think that antibiotic usage is a significant cause of antibiotic resistance. [21] However, these doctors' prescription habits showed they kept giving their patients antibiotics for viral infections. Allergies, side effects, and drug-drug interactions are other possible consequences of antibiotic overprescribing.

4. Antibiotic Use in Agriculture

Intensive farming in developing nations to meet the rising demand for animal protein leads to remnants of antibiotics in animal products, contributing to antibiotic resistance. Antibiotic resistance is a significant public health issue since germs resistant to antibiotics in animals may be harmful to people, readily spread to humans via food chains, and extensively distributed in the environment through animal waste. These may result in intricate, incurable, and protracted infections in people, resulting in increased healthcare expenses and sometimes mortality. Antibiotic resistance in these countries results from various factors such as irrational antibiotic use in clinical and agricultural settings, a low standard of living, poor sanitation, and limited investigation into the resistance of zoonotic bacterial pathogens to commonly used antibiotics. [22]

Antibiotics are often used in animal feed to prevent infections or disorders caused by stress. They may also be used at varying doses, frequently lower, to facilitate accelerated development. For dairy cattle, mastitis may be treated or prevented by administering local intra-locally infusion or systemic injectable antibiotics. Poultry are often administered antibiotics in feed or water due to the impracticality and cost of individual treatment. This approach exposes all birds to antibiotics, but each bird's specific and consistent dosage is still being determined.

Only two antibiotics are authorized in the United States for specific aquaculture purposes, often administered via feed. When fish are bred in warm waters polluted with commensals or human diseases, it increases the chances of antibiotic-resistant bacteria and genes being transferred and spread in both directions. Fish bred in pristine, frigid water have less microbial contamination and are thus less prone to harboring human infections.

In U.S. plant agriculture, antibiotics like streptomycin and oxytetracycline are only used preventively for significant plant diseases like Erwinia. Resistance to streptomycin is common, but resistance to oxytetracycline is rare, leading to an increase in the usage of oxytetracycline. The amount and scope of these uses seem insignificant compared to other agricultural uses of antibiotic substances. [23]

Conclusion

To sum up, antibiotic resistance is an essential issue in world health that needs immediate and thorough intervention. Several factors have contributed to the rapid spread of antibiotic-resistant bacteria, including their abuse and overuse, lax regulation, and a lack of research into new drugs. By raising the likelihood of incurable infections, this phenomenon endangers public health and compromises the efficacy of existing antibiotic therapies.

Promoting responsible antibiotic use in human and animal healthcare, improving monitoring and surveillance systems, investing in developing and researching new antibiotics, and fostering global cooperation are all essential parts of a comprehensive strategy to address antibiotic resistance. Governments, healthcare providers, pharmaceutical companies, and the public must collaborate to establish long-term strategies that protect the effectiveness of current antibiotics and provide room for future innovations.

The possible ramifications of inactivity are dire, including more extraordinary healthcare expenses, longer disease durations, and higher fatality rates. Antimicrobial stewardship, education, and research must be a top priority worldwide as we tackle the problems caused by antibiotic resistance. We might expect to limit the effect of antibiotic resistance and assure a safer future for generations to come by adopting a One Health approach that emphasizes the interconnection of human, animal, and environmental health.

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