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"A REVIEW ON ANTIBIOTIC RESISTANCE & THEIR MECHANISM"

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ABSTRACT

Antibiotic resistance (AR) has escalated into a global health crisis, threatening the very foundations of modern clinical medicine.[1] This review provides an in-depth exploration of how bacterial pathogens have evolved to withstand once-lethal chemical agents. The study begins by tracing the historical timeline from the "Golden Age" of discovery to the current "Post-Antibiotic Era," where common infections once again pose a fatal risk.[2] We examine the classification of antibiotics based on their chemical structure and analyze the intricate molecular mechanisms, such as efflux pumps and enzymatic inactivation, that bacteria employ to survive.[3] Furthermore, the role of horizontal gene transfer via plasmids is highlighted as a primary driver for the rapid dissemination of resistance across diverse bacterial species.[4] The review also addresses the critical impact of socio-economic factors, specifically the irrational use of drugs in healthcare and growth promoters in the livestock industry.[5] Statistical data presented herein underlines the rising mortality rates associated with multi-drug resistant (MDR) organisms like MRSA and Carbapenem-resistant Enterobacteriaceae.[6] Finally, the paper evaluates emerging therapeutic frontiers, including bacteriophage therapy and CRISPRbased antimicrobials, emphasizing that a multidisciplinary "One Health" approach is essential to mitigate this escalating biological threat.[7]

KEYWORDS

- ANTIMICROBIAL RESISTANCE (AMR): Bacteria's ability to survive drugs meant to kill them.

- HORIZONTAL GENE TRANSFER: The movement of genetic material between unicellular and/or multicellular organisms.
- SUPERBUGS: Bacteria strains resistant to most antibiotics used today.
- BETA-LACTAMASE: Enzymes produced by bacteria that provide multiresistance to antibiotics.

INTRODUCTION

ANTIBIOTIC

An antibiotic is a type of antimicrobial substance active against bacteria. They are among our most powerful weapons for fighting life-threatening bacterial infections, though they have no effect against viruses (like the common cold or flu).

Antibiotics generally work in one of two ways:

Bactericidal: They kill the bacteria directly (for example, by destroying the bacterial cell wall).

Bacteriostatic: They stop the bacteria from multiplying, which gives the body's immune system enough time to fight off the remaining infection. Common antibiotics are categorized into "classes" based on their chemical structure and how they attack bacteria. Since different bacteria have different defenses, doctors choose the class that best matches the specific infection.

Here are the most common types used in modern medicine:

1. **Penicillins**

Often the first line of defense for common infections. They work by preventing bacteria from building their cell walls.

Examples: Amoxicillin, Ampicillin, Penicillin V.

Commonly treats: Dental abscesses, ear infections, and skin infections.

2. **Cephalosporins**

These are similar to penicillins but can often treat a broader range of bacteria.

They are categorized into "generations" (1st through 5th).

Examples: Cephalexin (Keflex), Cefuroxime, Ceftriaxone.

Commonly treats: Strep throat, skin infections, and more serious issues like meningitis.

3. Macrolides

These are often prescribed for people who have an allergy to penicillin. Instead of destroying the cell wall, they stop bacteria from producing the proteins they need to grow.

Examples: Azithromycin (Z-Pak), Erythromycin, Clarithromycin.

"A Review on Antibiotic Resistance & their Mechanism"

Commonly treats: Lung and chest infections (pneumonia, bronchitis).

4. Tetracyclines

A broad-spectrum class that is frequently used for skin conditions and certain unusual infections.

Examples: Doxycycline, Tetracycline.

Commonly treats: Acne, Lyme disease, and respiratory tract infections.

5. Fluoroquinolones

These are potent antibiotics usually reserved for more serious or stubborn infections because they can have more significant side effects.

Examples: Ciprofloxacin (Cipro), Levofloxacin.

Commonly treats: Severe urinary tract infections (UTIs) and hospital-acquired pneumonia.

6. Sulfonamides (Sulfa Drugs)

One of the oldest classes of antibiotics, these work by interfering with the bacteria's ability to process folic acid.

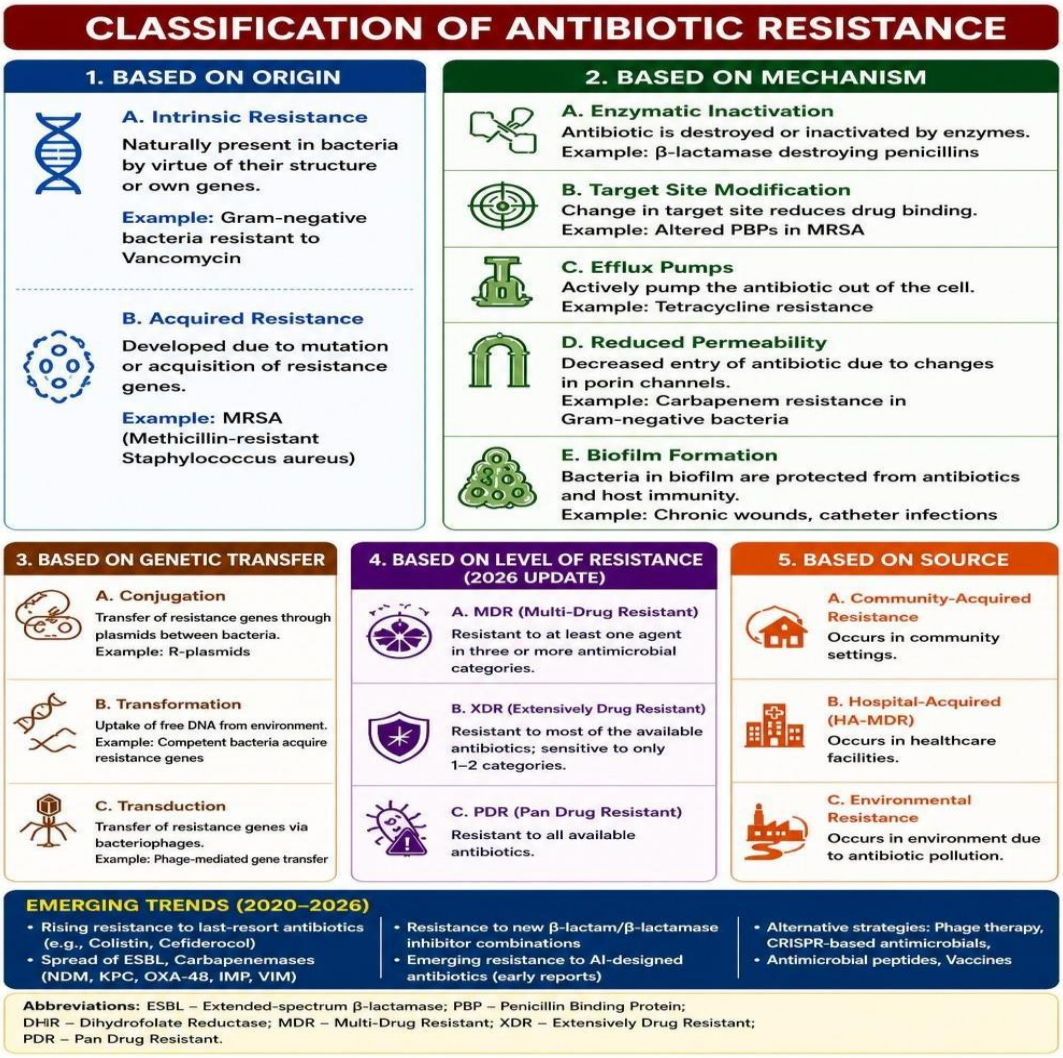
Example: Trimethoprim-sulfamethoxazole (Bactrim).

Commonly treats: UTIs and certain types of ear infections.

ANTIBIOTIC RESISTANCE Antibiotic resistance occurs when bacteria evolve the ability to defeat the drugs designed to kill them. When this happens, the bacteria are not destroyed; instead, they continue to grow and multiply, making infections harder—and sometimes impossible—to treat. It is important to note that it is the bacteria that become resistant, not the person or the animal.

How Resistance Develops Bacteria are constantly mutating. While most mutations are harmless, some can give a bacterium a "survival edge" against a specific drug. Selection Pressure: When you take an antibiotic, it kills most of the sensitive bacteria "A Review on Antibiotic Resistance & their Mechanism" Survival of the Fittest: If a few bacteria have a

mutation that protects them from the drug, they survive.Multiplication: These resistant survivors multiply rapidly, passing on their protective traits to their offspring. Gene Transfer: Bacteria can also "swap" DNA wit

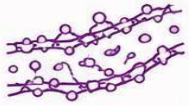
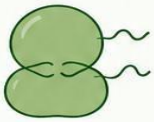
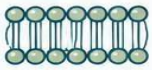


CLASSIFICATION OF ANTIBIOTICS

Antibiotics are diverse chemical compounds that are classified based on their chemical structure, spectrum of activity, and the specific way they target bacterial cells.

Understanding this classification is essential to determining which drug will be effective against a particular pathogen.

CLASSIFICATION OF ANTIBIOTICS

CLASS (BY MECHANISM)	SUBCLASS	EXAMPLES	MECHANISM OF ACTION	SPECTRUM OF ACTIVITY
1. CELL WALL SYNTHESIS INHIBITORS 	β-Lactams (β-Lactam antibiotics)	Penicillins, Cephalosporins, Carbapenems, Monobactams	Inhibit synthesis of peptidoglycan by binding to Penicillin Binding Proteins (PBPs) → weak cell wall → lysis	Broad (Penicillins), Broad to extended (Cephalosporins), Very broad (Carbapenems)
	Glycopeptides	Vancomycin, Teicoplanin	Bind to D-Ala-D-Ala of peptidoglycan precursors → inhibit cell wall synthesis	Gram-positive
	Others	Bacitracin, Fosfomycin	Inhibit early stages of cell wall synthesis	Variable (narrow spectrum)
2. PROTEIN SYNTHESIS INHIBITORS 	30S Subunit Inhibitors	Aminoglycosides (Streptomycin, Gentamicin, Amikacin), Tetracyclines (Tetracycline, Doxycycline)	Bind to 30S ribosomal subunit → Inhibit initiation complex or block tRNA binding	Aminoglycosides – Broad Tetracyclines – Broad
	50S Subunit Inhibitors	Macrolides (Erythromycin, Azithromycin), Lincosamides (Clindamycin), Chloramphenicol, Oxazolidinones (Linezolid)	Bind to 50S ribosomal subunit → Inhibit translocation or prevent peptide bond formation	Macrolides – Moderate to broad Clindamycin – Gram-positive, anaerobes Chloramphenicol – Broad Linezolid – Gram-positive
3. NUCLEIC ACID SYNTHESIS INHIBITORS 	DNA Gyrase Inhibitors	Fluoroquinolones (Ciprofloxacin, Levofloxacin, Moxifloxacin)	Inhibit DNA gyrase (Topoisomerase II) and Topoisomerase IV → inhibit DNA replication	Broad (including Gram-negative)
	RNA Polymerase Inhibitors	Rifamycins (Rifampicin, Rifabutin)	Inhibit DNA-dependent RNA polymerase → inhibit RNA synthesis	Broad (mainly used in combination)
4. METABOLIC PATHWAY INHIBITORS	Folic Acid Synthesis Inhibitors	Sulfonamides (Sulfamethoxazole) DHFR Inhibitors (Trimethoprim)	Inhibit folic acid synthesis → block nucleic acid synthesis	Variable (often in combination)
5. CELL MEMBRANE DISRUPTORS 	Polypeptides	Polymyxins (Colistin, Polymyxin B), Daptomycin	Disrupt cell membrane integrity → leakage of cell contents → cell death	Gram-negative (Polymyxins) Gram-positive (Daptomycin)
	Others	Gramicidin	Form pores in cell membrane	Gram-positive

Origin of Antibiotic Resistance

Antibiotic resistance was reported to occur when a drug loses its ability to inhibit bacterial growth effectively. Bacteria become 'resistant' and continue to multiply in the presence of therapeutic levels of the antibiotics Bacterias, when replicates even in the presence of the antibiotics, are called resistant bacterias.

Antibiotics are usually effective against them, but when the microbes become less sensitive or resistant, it requires a higher than the normal concentration of the same drug to have an effect. The emergence of antimicrobial resistance was observed shortly after the introduction

of new antimicrobial compounds Antibiotic resistance can occur as a natural selection process where nature empowers all bacteria with some degree of low-level resistance. For example, one study confirmed that sulfamethoxazole and trimethoprim (TMP-SMZ), ampicillin and tetracycline that were commonly used in yesteryears, but now have no longer role in treating non-cholera diarrhea disease in Thailand. At the same time, another study conducted in Bangladesh showed the effectiveness of the same drugs in treating them effectively. In fact, resistance was documented even before the beginning of the usage of the antibiotics in fighting the infection. Non-judicial use of antibiotic is responsible for making microbes resistant. Since the introduction of sulfonamides in 1937, the development of specific mechanisms of resistance had provoked their therapeutic use. However, sulfonamide resistance was reported in the 1930s, which reveals the same mechanism of resistance that still operates even now, more than 80 years later.[6] Within six years of the production of the aminoglycosides, aminoglycoside-resistant strains of Staphylococcus aureus was developed.[14] Introduced in 1961, Methicillin was the first of the semisynthetic penicillinase-resistant penicillin to target strains of penicillinase-producing Staphylococcus aureus. However, resistance to methicillin was reported soon after its initiation.[15] Further, although fluoroquinolones were introduced for the treatment of Gram-negative bacterial diseases in the 1980s, fluoroquinolones resistance later revealed that these drugs were also used to treat Gram-positive infections.[16] Quinolone resistance emerged as a stepwise attainment of chromosomal mutations, particularly among the methicillin-resistant strains [Most recently, the clinical isolates of Vancomycinresistant Staphylococcus aureus (VRSA) were found in 2002, after 44 years of Vancomycin introduction to the market

Antibiotics used in agriculture are often the same or similar to antibiotic compounds used clinically his over-usage could also invite drug resistance. The food chain can be considered the main route of transmission of antibiotic-resistant bacteria between animal and human populations In some developed countries, animals receive antibiotics in their food, water, or parenterally which may be responsible for carrying microbe resistance to that specificantibiotic. For example, the use of antibiotics in cattle feed as growth promoters increase antibiotic resistance. Recent evidence suggests that poultry or pork might be a possible source of quinolone resistant-Escherichia coli in the rural villages in Barcelona, where onefourth of children were found to be fecal carriers of these organisms. However, these kids were never exposed to quinolones

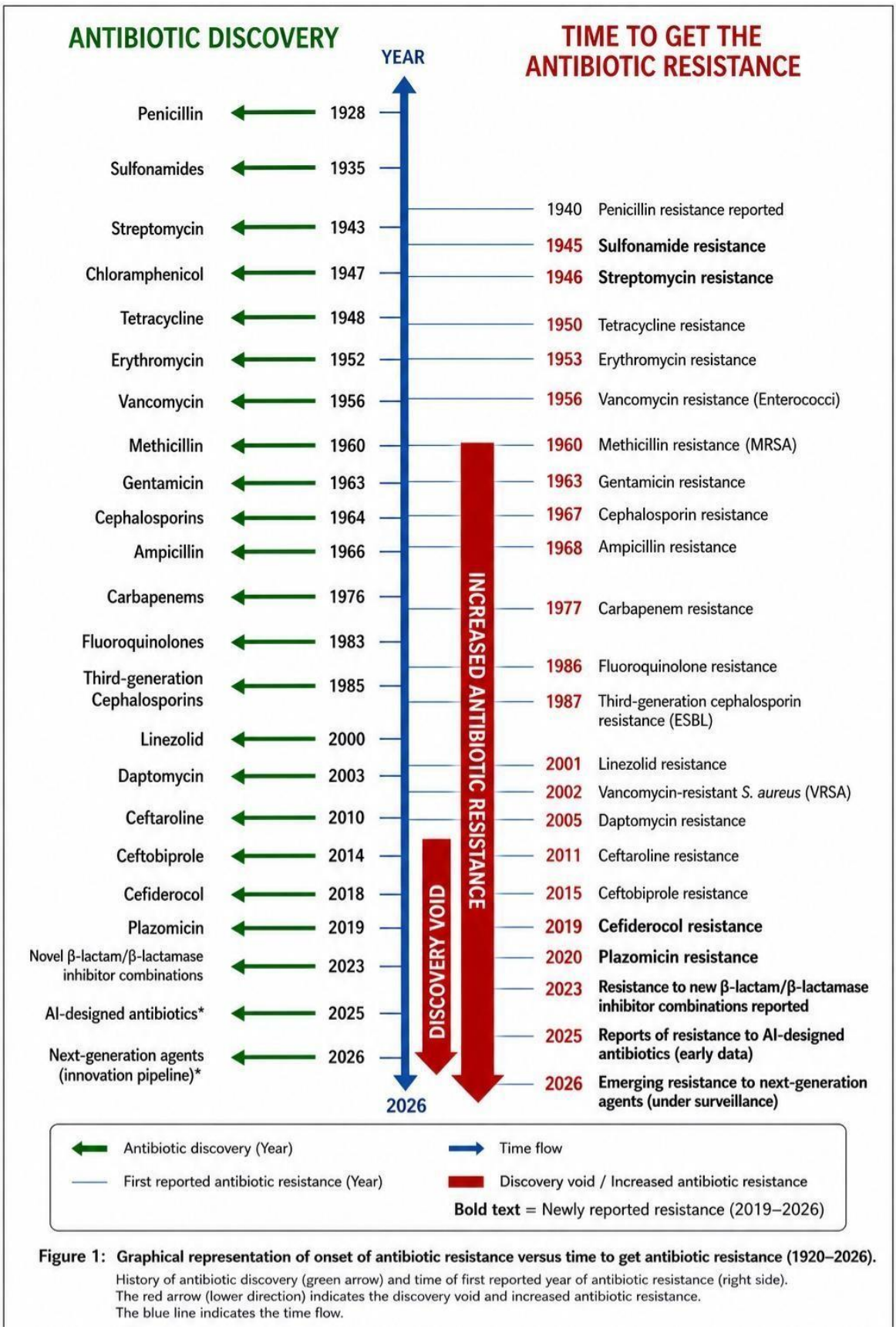


Figure 1: Graphical representation of onset of antibiotic resistance versus time to get antibiotic resistance (1920–2026).

History of antibiotic discovery (green arrow) and time of first reported year of antibiotic resistance (right side).
The red arrow (lower direction) indicates the discovery void and increased antibiotic resistance.
The blue line indicates the time flow.

CONCLUSION

Antimicrobial resistance is no longer a silent threat lurking in the future; it is a clear and present global crisis that challenges the very foundation of modern medicine. The transition from the "Golden Age of Antibiotics" to a potential "Post-Antibiotic Era" has been accelerated by the relentless evolutionary adaptability of bacteria, compounded by decades of human negligence, industrial misuse, and systemic failures in healthcare. As we have seen through the molecular lens, the ability of pathogens to enzymatically deactivate drugs, modify their own cellular targets, and share resistance genes across borders has created a formidable biological enemy.

The socio-economic evidence suggests that the cost of inaction is far too high. If left unaddressed, the world faces a future of staggering mortality rates, a multitrillion-dollar collapse in global wealth, and a dramatic reversal in human life expectancy. However, the crisis also presents an opportunity for a scientific and social renaissance. Through the "One Health" approach—which integrates human, animal, and environmental health—and the development of revolutionary alternatives like Phage therapy and CRISPR-based gene editing, tere is a viable path toward reclaiming our advantage over infectious diseases.

Ultimately, the battle against AMR cannot be won in the laboratory alone. It requires a fundamental shift in how society perceives and utilizes these precious resources. Global cooperation, stringent agricultural regulations, and responsible clinical stewardship are the only defenses that can preserve the efficacy of antibiotics for future generations. We must treat antibiotics not as an infinite commodity, but as a shared global heritage that requires protection, innovation, and respect. The window for intervention is closing, and the actions taken in this decade will determine whether we continue to advance medically or fall back into an age where a simple infection can once again become a death sentence.

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