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A REVIEW ON MECHANISM OF ANTIBIOTIC RESISTANCE

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ABSTRACT :

Antibiotic resistance is a growing public health concern, with the emergence of resistant E. coli strains posing a significant threat. This review explores the mechanisms of antibiotic resistance, including reduced permeability, increased efflux, and target modification. The genetic basis of resistance, including mutational resistance and horizontal gene transfer, is also discussed. Understanding these mechanisms is crucial for developing effective interventions and treatments.

KEY WORDS: Antibiotic Resistance, E. coli, Mechanisms, Public Health, Therapeutic Strategies

Introduction :

Modern medicine was transformed and the therapeutic paradigm was altered by the discovery, commercialization, and widespread use of antimicrobial agents to treat infections. Antibiotics are, in fact, now among the most crucial medical interventions required for the advancement of sophisticated medical techniques, including solid organ transplantation, advanced surgical techniques, and the treatment of cancer patients, among others. According to some research on bacterial resistance, there is a vast variety of resistance mechanisms, most of which have complicated and unknown distributions and interactions. Nonetheless, a number of physiological and biochemical processes contribute to the emergence of antibiotic resistance. Antibiotic-resistant illnesses are becoming more and more common, which makes it difficult to treat humans and animals effectively.

Prevention of access to target :

Reduced permeability.

Gram-negative bacteria's outer membrane creates a permeability barrier, making them inherently less susceptible to many drugs than Gram-positive species18,19. Antibiotics that are hydrophilic diffuse through the porin proteins of the outer membrane. The outer-membrane proteins OmpF and OmpC of E. coli are examples of large porins in the majority of Enterobacteriaceae that are believed to act as non-specific channels; prior studies that suggested drug-binding sites were present inside these channels appears to be false. The quick accumulation of mutations in these genes in E. coli and Enterobacter species following carbapenem exposure demonstrates the selection pressure that carbapenems impose to favor the appearance of mutations in porin genes as well as genes that regulate porin production.

Increased efflux.

The intrinsic resistance of Gram-negative bacteria to many of the medications that can be used to treat Gram-positive bacterial infections is mostly due to bacterial efflux pumps, which actively move a large number of antibiotics out of the cell. Efflux pumps can potentially confer large degrees of resistance to drugs that were once clinically helpful when they are overexpressed. While certain efflux pumps, as Tet pumps, have limited substrate specificity, many are referred to as multidrug resistance (MDR) efflux pumps because they may transport a variety of structurally different substrates. Induction in response to environmental cues and under circumstances where their function is necessary can also result in increased expression of efflux pumps. For instance, Salmonella species and E. coli's acrAB genes are triggered by little

Changes in antibiotic targets by mutation :

The majority of antibiotics have a high affinity for their targets and attach to them selectively, stopping the target's usual activities. Resistance may be conferred by structural alterations to the target that hinder effective antibiotic binding while allowing the target to perform its typical function (FIG. 3). Large and varied populations of pathogens frequently exist throughout infection, and strains with a single point mutation in the gene encoding an antibiotic target can multiply if the change confers antibiotic resistance.

GENETIC BASIS OF ANTIMICROBIAL RESISTANCE

Because of their exceptional genetic flexibility, bacteria can adapt to a variety of environmental dangers, such as the presence of antibiotic compounds that could endanger their life. Because of their innate resistance, bacteria that inhabit the same biological niche as species that produce antibiotics have developed long-standing defenses against the damaging effects of the antibiotic molecule, allowing them to flourish there. According to evolutionary theory, bacteria employ two main genetic strategies to counteract the antibiotic "attack": (i) mutations in the gene or genes frequently linked to the compound's mechanism of action, and (ii) horizontal gene transfer (HGT) to acquire foreign DNA coding for resistance determinants.

Mutational Resistance

In this case, a fraction of bacterial cells from a vulnerable population undergoes gene alterations that impact the drug's activity, preserving cell survival when the antimicrobial molecule is present. The antibiotic destroys the susceptible population once a resistant mutation appears, and the resistant germs take over. Resistance-causing mutational alterations are frequently expensive to cell homeostasis (i.e., reduced fitness) and are only sustained when the antibiotic is present.

HGT

One of the most significant forces behind bacterial evolution is the acquisition of foreign DNA material by horizontal gene transfer (HGT), which is also commonly the cause of the emergence of antibiotic resistance. The majority of antimicrobial agents utilized in clinical settings are either naturally occurring products of the environment, primarily soil, or are derived from them. Intrinsic genetic markers of resistance are present in bacteria that share their surroundings with these compounds, and there is strong evidence that this type of "environmental resistome" is a major source of antibiotic resistance genes in clinically important bacteria. Additionally, the spread of resistance to numerous commonly used antibiotics has been linked to this genetic exchange.

Antibiotic Resistance

The ability of bacteria or other microorganisms to endure and proliferate when exposed to antibiotic dosages that were once believed to be effective against them is known as antibiotic resistance. Although the source of antibiotic resistance genes is unknown, research employing clinical isolates obtained prior to the advent of antibiotics showed susceptibility despite the presence of conjugative plasmids. In a naive, susceptible bacterial population that might produce an infection, the majority of cells are often susceptible to a certain antibiotic upon exposure. Nonetheless, a tiny subset of resistant bacterial cells will always be able to proliferate at higher concentrations when there is not enough antibiotic present, killing the subpopulation and allowing the microorganisms to continue existing in the environment. Reduced bacterial fitness is frequently linked to resistance, and it has shown.

MECHANISTIC BASIS OF ANTIMICROBIAL RESISTANCE

It should come as no surprise that bacteria have developed complex drug resistance mechanisms to evade being killed by antimicrobial compounds. This process most likely took place over millions of years of development. Notably, a single bacterial cell may be able to use a variety of resistance mechanisms to withstand the effects of an antibiotic, and resistance to a single class of antibiotic can typically be attained by a number of biochemical pathways. For instance, fluoroquinolone resistance can arise through three different biochemical pathways, all of which can coexist in the same bacteria at the same time, resulting in an additive effect that frequently raises resistance levels: mutations in DNA gyrase and topoisomerase IV genes, which encode the fluoroquinolone target site. Especially if the mechanisms of action are similar, an organism may develop resistance to numerous antibiotic classes through a single mechanism. Through the creation of "resistance plasmids," which are DNA fragments that can be moved from one cell to another, bacteria can occasionally exchange resistance.

1. **Porin Mutations**

Antibiotic entry into bacterial cells may be restricted by modifications in porin proteins, and bacterial survival in the presence of antibiotics may be possible due to changes in porin genes that result in reduced permeability.

2. **Biofilm Formation**

Biofilms, which are communities of bacteria that stick to surfaces and are covered in a protective matrix, are formed by E. coli and operate as a physical barrier that inhibits the immune system and antibiotics, making illnesses more difficult to cure.

3. **Persister Cells**

Persister cells, which are highly resistant to antibiotics, are a dormant state that some E. coli can go into. These cells can withstand antibiotic treatment and repopulate once the therapy is stopped.

4. **Adaptive Stress Responses**

In order to withstand the effects of antibiotic pressure, E. Coli can trigger stress response systems, which may involve modifications to metabolism and gene expression that improve survival.

5. **Regulatory Systems**

The development of resistance mechanisms is coordinated by intricate regulatory networks in bacteria, and knowledge of these systems might help identify possible treatment targets to address resistance.

Implications for Public Health :

- The public health is seriously threatened by the emergence of E. Coli strains that are resistant to antibiotics, which calls for immediate action.
- To address this escalating epidemic, tactics like creative therapy approaches, the creation of novel antibiotics, and careful antibiotic stewardship are crucial.
- The development of successful interventions and treatments will be aided by ongoing study into the mechanisms of resistance.

Conclusion :

The rise of antibiotic-resistant E. coli strains is a pressing public health concern that requires immediate attention and action. A comprehensive approach, including innovative therapeutic strategies, development of novel antibiotics, and responsible antibiotic stewardship, is essential to combat this growing epidemic. Ongoing research into the mechanisms of resistance is critical for informing effective interventions and treatments, and ultimately, for protecting public health.

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