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A REVIEW OF RESISTANCE MECHANISMS OF BACTERIA, EVOLUTION OF RESISTANCE STRATEGIES

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ABSTRACT

Although some may believe that using antibiotics is the best way to eradicate illnesses, did you know that overuse of antibiotics is the main cause of antibiotic resistance and, in certain situations, treatment failure? A thorough overview of this kind of medication, including its types, effects, usage instructions, significance, and a correction of widely held misconceptions, may be found below. These drugs cure bacterial infections in both humans and animals by either killing or inhibiting the growth of germs. It is important to note that viral illnesses like colds, influenza, and even COVID-19 cannot be treated with antibiotics. To make sure that bacteria are eliminated and unable to proliferate and spread to other areas of the body, doctors advise only using antibiotics when absolutely necessary. Antibiotics abuse can be occasional results from prescription of a incorrect drugs or dosages. Antibiotic resistance is currently regarded as one of the largest public health issues since misuse can also happen when people do not take the antibiotic as directed by their doctor. Antibiotic-induced allergic reactions can be either immediate or delayed, which means that a patient may be negatively impacted by the medication within hours or weeks. As a result, anyone experiencing an allergic reaction to an antibiotic ought to notify their physician. Rarely, people experience anaphylactic reactions, which are severe and deadly reactions. It's also important to remember that the greatest method to lower hazards is to use less unnecessary antibiotics.

KEYWORDS: Antibiotics abuse can be occasional results from prescription of a incorrect drugs or dosages.

INTRODUCTION

antibiotics are organic materials or compounds that either kill or stop the growth of bacteria. Waxman used the term "antibiotics" in 1942 to refer to any material made by microbes that prevents the growth of other germs in a very diluted medium. The Scottish chemist Alexander Fleming discovered penicillin, the first antibiotic, in 1929. It is a beta-lactam antibiotic. At this point, he became aware of Penicillium notatum, one of the fungal colonies, having the capacity to stop Staphylococci colonies from growing. Although they were derived from a variety of sources, beta-lactam antibiotics were primarily found in bacteria and fungi (Ibezim, 2005).

According to Talaro and Chess (2014), early human civilizations employed a variety of crude treatment techniques, such as the use of plant, animal, or mineral materials that were discovered by accident or experience. For example, the Greeks used plant resins and diverse mineral salts to treat illnesses. One of the earliest indications to modern science that bacteria prevent the formation (cultivation) of pure anthrax was Louis Pasteur's studies in 1877. As science advanced, a definition of the compounds used to cure illnesses was established. Vuilleman (1889) first used the term "antibiosis" to describe the trait of animosity between organisms in general (2011 and Sue Vander, 2008; From their discovery in the 1940s till now, beta-lactam antibiotics are regarded as some of the most often utilized compounds. This is because the majority of the so-called broad-spectrum antibiotics in this group is effectives against microorganisms that are both gram-positive and gram-negative.

When researchers Chain, Florey, and their associates succeeded in producing penicillin for commercial use in

1941, the string of discoveries resumed after a lull. Then, in 1948, the scientist Giuseppe Brotza made the discovery of cephalosporins (Mandell et al., 1995; Murray et al., 1999). Penicillins, cephalosporins, carbapenems, and monobactams are the four primary categories of antibiotics that are categorized as beta-lactams. They all share the B-lactam ring. The type of extra ring that is joined to the beta-lactam ring distinguishes these antibiotics from one another (Samaha-Kfoury Araj, 2003). Beta-lactam antibiotics were the most significant and often used class of antibiotics for a long time. In Norway, for instance, beta-lactam antibiotics accounted for 46% of the systematic infections (Norm-Vet, 2010).

Fleming Alexander Duchesne, a chemist, made the initial discovery of penicillin, the most significant and first antibiotic, in 2013. The narrow-spectrum nature of penicillins is one of its characteristics. Both certain Gram-negative and Gram-positive bacteria can be effectively combatted by them. Two significant and excellent examples of limited-spectrum antibiotics are Penicillin G and V (Kiffer et al., 2005).

Antibiotics Resistance

Our bodies naturally contain bacteria, which are an essential component of our ecosystem. They may, nevertheless, be the underlying cause of severe health issues. Treatment techniques have depended on antibiotics to eradicate dangerous bacteria since their discovery in the 1920s and their introduction into mainstream medicine during World War II. Antibiotic resistance is still increasing, though. Center of Diseases Controls and Prevention (CDC).A United States experients at least 2,049,442 diseases annually as a result of drug resistance to treatments for bacterial or fungal infections. Additionally, when these drugs don't work as intended, roughly 23,000 people pass away each year.

One for a biggest risks into global In the twenty-first century, antimicrobial resistance (AMR) is a public health concern (Ferdinand et al., 2024). AMR happens when microorganisms—such as viruses, bacteria, fungi, and parasites—develop resistance to antimicrobial medications, including antibiotics, which are frequently used to treat these diseases (Ruckert et al., 2014). The widespread problem is mostly ascribed to the consequences of excessive or careless use of antibiotics in a variety of settings, primarily in clinical care, farming, veterinary medicine, emergencies, and the food chain (Hussein et al., 2014). AMR is sometimes referred to as the "Silent Pandemic" and requires prompt and effective action rather than being put off until later (Founou et al., 2021). Without preventative actions, estimates suggest that by 2050, AMR might possibly.

Antibiotics resistance are cause by a variety for factors, that such as natural selection, the overuse and abuse of antibiotics, the lack of access to sanitary facilities and clean water, and the use of subpar and counterfeit drugs (Endale et al., 2023). A few instances of antibiotic abuse and misuse include self-medication, improper prescriptions, and inadequate therapies. Bacteria that survive a partial course of antibiotics may develop resistance. Additionally, self-prescribing, utilizing leftover antibiotics without a doctor's supervision, and prescribing drugs for viral diseases can all lead to AMR.

The spread of infectious diseases is exacerbated by inadequate sanitation and inadequate hygiene habits.

These defense mechanisms allow microbes to withstand the effects of antibiotics and other antimicrobial substances, which frequently prevent or kill them. Through structural changes and the use of clever metabolic pathways, bacteria and other parasites exhibit amazing adaptation mechanisms that allow them to ignore or neutralize dangerous antimicrobial agents (Chiș et al., 2022).

Resistance mechanisms into antibiotics

Over the past few decades, antibiotics resistances has been produced by a number of microbes via various mechanisms. resistant to methicillin Because of horizontal gene transfer and changes in the mecA and mecC genes, Staphylococcus aureus is resistant to many drugs, including methicillin (Peacock and Paterson , 2015). resistant to carbapenem By obtaining carbapenemase genes, Enterobacteriaceae, including Escherichia coli and Klebsiella pneumoniae, have developed resistance to carbapenem medications (Baroud et al., 2013). Plasmids are frequently used to carry these genes, which makes it easier for bacteria to spread them. By acquiring ESBL genes, usually via plasmids, the antibiotics and ESBL-produce from E. coli becomes resistants into a wide range for medicines, including cephalosporins and penicillins. MDR Mycobacterium tuberculosis is resistant to numerous anti-tuberculosis drugs due to mutations in its DNA (Mishra Et al., 2015). As part of their natural development, bacteria undergo frequent DNA mutations, which enables them to continuously modify their genetic composition. When a germ develops a natural resistance to an antibiotic, it continues to live even after being treated with antibiotics. Another characteristic of germs is their capacity for horizontal gene transfer, or the transfer of genes from one germ to another.

a- **Changes at a antibiotic's chemical compositions**

One well-known methods for acquire antibiotics resistance at both Both Gram-positive and Gram-negative bacteria are products of all enzymes that have the ability to chemically change the antibiotic molecule. Notably, most antibiotics affected by these enzymatic alterations function by blocking the production of proteins at the ribosome level (Wilson, 2014). Acetylation (aminoglycosides, chloramphenicols, streptogramins), phosphorylation (aminoglycosides, chloramphenicol), and adenylation (aminoglycosides, lincosamides) are the most frequent biochemical

processes that enzymes can catalyze. Many varieties of modifying enzymes have been identified. Whatever the biochemical process, the end outcome is frequently associated with steric hindrance, that lowers a drug's avidity of its target and raises the bacterial minimum inhibitory concentration (MIC).

b- The antibiotic molecule is destroyed

The primary mechanisms for β-lactam resistances its depends on β-lactamase break down these substances. And These enzymes makes a antibiotics ineffective by breaking the β-lactam ring's amide bond. Although there is evidence that β-lactamases have existed for millions of years, they were initially described at a early 1940s, oneyear before penicillins was put on a market (**D'Costa et al., 2011**). Following the widespread availability of penicillin and the discovery that a mechanism for resistances was a encoded by plasmid penicillinase that were easily transferred between strains of S. aureus, leading to the rapid dissemination of the resistance trait, infections cause by penicillin-resistant S. aureus became clinically relevants (bush, 2013). In order to address this issue, novel β-lactam molecules having a greater range of activity and less.

c- Reduced permeability

The bacterial target for most for antibiotics it used at clinical practice that are found inside cells, or at a membrane of cytoplasme (inner membrane) in a case of Gram-negative bacteria. of a chemical into has an antibacterial actions, it must therefore pass through the cytoplasmic and/or outer membrane. By reducing the antimicrobial molecule's absorption, bacteria have evolved defenses against antibiotics that stop them from reaching their intracellular or periplasmic target. This mechanisms, that restricts a inflow for chemicals from an external environments, itis especially significant at Gram-negative bacterial cells (for the reasons mentioned above). At Actually, the outer membranes serves as a body's initial lines for defense against a entry for various more harmful substances, such aantibacterial agentes. Tetracyclines and β-lactams are examples of hydrophilic compounds (Jose and Arias, 2016).

d- Efflux pumps

The development of intricate bacterial machinery that may extrude a poisonous substance from a cell can be also leads into antimicrobial resistance. An efflux mechanism that could pumps tetracycline out a cytoplasme for E. coli were one of a first to be reporte at an early 1980s (**McMurry et al., 1980**). Numerous efflux pump classes have since been identified in both Gram-positive and Gram-negative bacteria. Tet determinant of tetracyclines and mef gene of macrolides in pneumococci is example of substrate-specifics systems. These systems can also possess extensive substrate selectivity, a trait commonly observed in MDR microorganisms. (poole, 2005).

e- Targets site mutations

The emergences for rifampin resistances is one for a classic instances of mutational resistance. By blocking a DNA-dependents RNA polymerase, the complex enzymes with a $\alpha 2\beta\beta'\sigma$ subunit structure, rifampin, a rifamycin, prevents bacterial transcription. The highly conserved rifampin binding site is found in the β component of the RNA polymerase (encoded by rpoB). Once the antibiotic molecule binds, it stops transcription by directly obstructing the nascent RNA's route (Campbell et al., 2001). Numerous genetic alterations have been documented, and single-step point mutations that result in amino acid substitutions at rpoB genes has been demonstrate into cause higher-level rifampin resistances. Notably, although this alterations cause a drug affinity of it a target into decrease,

CONCLUSION

Although antibiotics are among the best discoveries ever made and have helped humans treat a wide range of illnesses, their frequent usage leads to resistance and adaptability in microbes, meaning that therapy has little effect on certain species. Consequently, novel approaches to treating and preventing this resistance—which could be brought about by mutations that microbes have acquired—must be developed.

One of the most effective developments in modern medicine has been the application of antimicrobial therapy in clinical settings. This has opened the door for intricate and extremely sophisticated medical procedures that have greatly increased the average lifespan of people worldwide. Bacteria have evolved sophisticated and inventive ways to evade the antibiotic onslaught in order to survive, a process that is probably influenced by a growing use for antimicrobials at clinical practices. For one a bigger concerns into publics health at twenty-first century its antibiotic resistances, which has developed quickly over the last few decades.

REFERENCES

1. Ferdinand., C. McEwan, C. Lin, K. Betham, K. Kan dan, G. Tamolsaian, B. Pugeva, J. McKenzie, G. Bro wning, J.Gilkerson Development of a cross-sectoral antimicrobial resistance capability assessment framework BMJ Glob, Heal, 2024; 9: Article e013280.
2. Ruckert A., S. Lake, S.R. Van Katwyk Developing a protocol on antimicrobial resistance through WHO's pandemic treaty will protect lives in future pandemics Glob. Health, 2024; 20.
3. Hussein S., S.K. Ahmed, K. Qurbani, A. Fareeq, R.A. Essa Infectious diseases threat amidst the war in Gaza J. Med. Surgery, Public Heal, 2024; 2.
4. Founou.R.C., A.J. Blocker, M. Noubom, C. Tsayem, S.P. Choukem, M.Van Dongen, L.L. Founou The COVID-19 pandemic: A threat to antimicrobial resistance containment Futur Sci. OA, 2021; 7, Article FSO736

5. Endale H., M. Mathewos, D. Abdeta Potential Causes of Spread of Antimicrobial Resistance and Preventive Measures in One Health Perspective-A Review Infect. Drug Resist, 2023; 16: 7515-7545,
6. Chiș A.A., L.L. Rus, C. Morgovan, A.M. Arseniu, A. Frum, A.L. Vonica-țincu, F.G. Gligor, M.L. Mureșan, C.M. Dobrea Microbial Resistance to Antibiotics and Effective Antibiotherapy Biomedicines, 2022; 10: 1121.
7. Peacock, G.K. Paterson S.J. Mechanisms of methicillin resistance in Staphylococcus aureus Annu. Rev. Biochem., 2015; 84: 577-601.
8. Mishra R., P. Shukla, W. Huang, N. Hu Gene mutations in Mycobacterium tuberculosis: Multidrug-resistant TB as an emerging global public health crisis Tuberculosis, 2015; 95: 1-5.
9. M., I. Dandache, G.F. Araj, R. Wakim, S. Kanj, Z. K anafani, M. Khairallah, A. Sabra, M. Shehab, G. Db aibo, G.M. Matar Underlying mechanisms of carbapenem resistance in extended-spectrum β-lactamase-producing Klebsiella pneumoniae and Escherichia coli isolates at a tertiary care centre in Lebanon: Role of OXA-48 and NDM-1 carbapenemases Int. J. Antimicrob Agents, 2013; 41: 75-79.
10. D'Costa VM, King CE, Kalan L, Morar M, Sung WW, Schwarz C, Froese D, Zazula G, Calmels F, Debruyne R, Golding GB, Poinar HN, Wright GD. 2011. Antibiotic resistance is ancient. Nature, 477: 457–461.
11. Bush K. 2013. Proliferation and significance of clinically relevant β-lactamases. Ann N Y Acad Sci, 1277: 84–90.
12. Wilson DN. 2014. Ribosome-targeting antibiotics and mechanisms of bacterial resistance. Nat Rev Microbiol, 12: 35–48.
13. Jose M. Munita, Cesar A. Arias.2016. Mechanisms of Antibiotic Resistance. ASM Journals Microbiology Spectrum, 4(2).
14. McMurry LM, Petrucci RE, Jr, Levy SB. 1980. Active efflux of tetracycline encoded by four genetically different tetracycline resistance determinants in Escherichia coli. Proc Natl Acad Sci USA, 77: 3974–3977.
15. Poole K. 2005. Efflux-mediated antimicrobial resistance. J Antimicrob Chemother, 56: 20–51.
16. Campbell EA, Korzheva N, Mustaev A, Murakami K, Nair S, Goldfarb A, Darst SA. 2001. Structural mechanism for rifampicin inhibition of bacterial RNA polymerase. Cell, 104: 901–912.
17. Kadhim, M.I., Jabbar, A.H. Synthesis of nucleotide - Amino acids via new branched chain sugar, Systematic Reviews in Pharmacy, 2020; 11(6): 404–408.
18. Luaibi, H.M., Alfarhani, B.F., Kadhim, M.I. Detection of Fe(III) levels via. Two different spectrophotometric methods in Diwaniah City/Iraq Journal of Engineering and Applied Sciences, 2018; 13(24): 10380–10383.
19. Hassan, M.F., Kadhim, M.I. Preparation, the spectroscopic and biological study of some derivatives of (β-lactam, oxazepine, and imidazole) linked to a heterocyclic nucleus, AIP Conference Proceedings, 2023; 2834(1): 030006.
20. Thabit, J.A., Almzaiel, A.J., Kadhim, M.I., Alrufaie, M.M., The impact of reproductive hormone changes on the immune response of patients with leukemiaAnaesthesia, Pain and Intensive CareThis link is disabled., 2023; 27(5): 585–591.
21. M.Irhaeem, Janan A.Thabit, Anwar J.Almzaiel, Methylenetetrahydrofolate reductase levels and gene expression in leukemia Current Issues in Pharmacy and Medical Sciences, 2024; 37(1): 7-12.
22. A.H., Jabbar, Abeer Hamoodi, I.H., Al-Azawi, Ibtisam Habeeb. 2020. The Detection and Investigation of Tetracycline Resistance Associated Genes among Shigella Isolates Using Polymerase Chain Reaction and Phylogenetic Analysis Methods in Al-Diwaniyah province, Iraq. Conference Paper • *Open access.*