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A Review of Antibiotic Resistance

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Abstract:

Antibiotics are 'wonderful drugs' that fight germs. Antibiotic resistance is projected to be one of the greatest healthcare challenges of the 21st century Infection is a major cause of death in the developing world. This is mainly due to the emergence of new infectious viruses and mainly due to the emergence of antimicrobial resistance. Over time, with the bacteria becoming clearer and more consistent, the careless use of antibiotics in clinical practice has led to bacterial resistance to antimicrobial agents. Antimicrobial resistance is known to be a major problem in the treatment of infectious diseases. Antibiotic resistance mechanisms include the following: antibiotic inactivation, target modification, permeability, and "bypass" of the metabolic pathway. Determination of antibiotics of all classes (phenotypes) and antibodies responsible for antimicrobials (genetic analysis) is helpful This review article also uses the effective use of antibiotics in human and animal health to reduce resistance to germs. Evidence from the literature shows that information about antibiotic resistance in humans is still available. Therefore, the need to educate patients and the community is important in the fight against the virus.

Keywords: antibiotic resistance, antibiotic, bacterial infection

Introduction:

Antibiotic resistance is a direct result of the use of antibiotics. Antibiotics, either cytotox or cytostatic in microorganisms, allow the body's natural defenses, such as the immune system, to destroy them. They usually do so by blocking cell adhesion, protein synthesis, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), by membrane separation agents, or other specific actions. Antibiotics can enter the bacterial cell wall by attaching them to it, using energyefficient pathways in the ribosomal areas, leading to the inhibition of protein synthesis. Ehrlich Antibiotics were considered a magic bullet that selectively targeted microbes that were responsible for disease to cause, but at the same time would not affect the manager. Fleming was the first to warn against penicillin if too little or too short a doswwas used. It is clear that while antibioticresistant antibodies are much older than modern chemotherapy, their storage and distribution in our health care facilities depends on widespread prevalence of antimicrobials.

Antibiotic: An antiseptic (beta lactam)

- Bacteriostatic Drug: something that reduces the growth of bacteria or stops the production of bacteria.

How big is the problem?

It is hard to say for sure, but the US Centers for Disease Control and Prevention (CDC) estimates that in the US alone there are about 23,000 people who die every year from antibiotic-resistant infections. For example, they estimate that resistance to antibiotics that treat Clostridium difficile (C. difficile) causes almost 500,000 infections in the US every year, which lead to about 15,000 deaths. (But Amanda Jezek, a spokesperson specializing in policy and government relations at the Infectious Diseases Society of America, a group that represents many of the country's infectious disease doctors and scientists, says the overall number of deaths is a conservative estimate and likely higher

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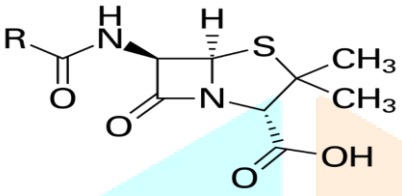
Meanwhile, **a 2015 study published in Nature** found that global antibiotic consumption went up 30% between 2000 and 2010

1]Penicillin and other antibiotics:



Penicillin was discovered in 1928 by Scottish scientist Alexander Fleming as a crude ingredient in P. Ruben's. Fleming student Cecil George Paine was the first to successfully use penicillin to treat ophthalmia neonatorum. Penicillin is a group of antibiotics originally found in Penicillium fungi, especially P. Chrysogenum and P. Ruben's. Most clinically used penicillin is chemically derived from naturally occurring penicillin. There are many natural penicillin's available but only two diluted compounds used in the clinic such as penicillin G (intravenous use) and penicillin V (oral or oral) are used. Penicillin was one of the first drugs to be used in the fight against staphylococci and streptococci in the 1930's.

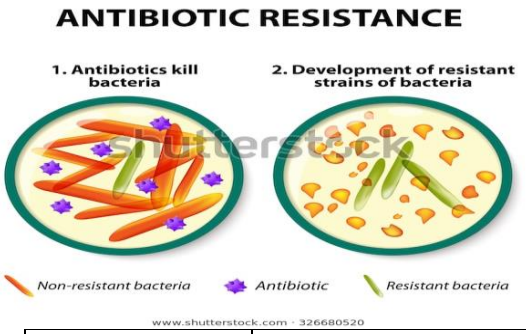
The first known expert work is to analyze the potential therapeutic effects of their antimicrobial activity. In his opinion, Duchesne suggested that bacteria and fungi take part in the endless battle of life. Duchesne noted that E. Coli was removed by Penicilliu m glaucum when they were both it has grown in the same culture. He also noticed that when he injected laboratory animals with deadly doses of bacilli typhoid and Penicillium glaucum, animals did not get typhoid. Unfortunately, Duchesne's military career after graduation prevented him from doing further research. Duchesne died of tuberculosis, a disease that has now been treated with antibiotics. In 1928, Sir Alexander Fleming described the presence of penicillin, a molecule produced by fungi that kill or inhibit the growth of certain bacteria. Fleming was working on a culture of pathogens when he noticed the seeds of the green fungus, Penicillium Chrysogenum, in one of his cultures. plates. Be aware that the presence of mold kills or inhibits the growth of bacteria. Fleming wrote that the fungus must release an antibacterial agent, which he named penicillin in 1928. Fleming believed that its antibacterial properties could be used in chemotherapy. He first showed some of the living things and tried to use the wrong preparations to treat other diseases, but he could not move forward without help. of trained chemists. Later, Norman Healthy developed a back-to-back procedure to thoroughly purify penicillin in bulk. The chemical structure of penicillin was first proposed by Abraham. Purified penicillin shows strong antibacterial activity against a variety of bacteria and he had low toxicity to humans. In addition, its activity was not inhibited by biological elements such as red, in contrast to synthetic sulfonamides. The development of penicillin has led to a resurgence of interest in the search for effective antibiotic compounds with similar safety precautions. With their successful developmentof penicillin, Fleming received it by mistake but could not grow it, as a therapeutic drug, Chain and Florey shared Fleming's 1945 Nobel in Medicine. World War II. Gramicidin, however, could not be used systematically due to its toxicity. Tyrocidine has also been shown to be highly toxic to systemic use. The research results obtained at that time were not dividedbetween Axis and Allied forces during World War II and limited access during the Cold War.

Evolution and spread of resistance

Since antibiotic resistance is the result of n atural selection for resistance-conferring mutations, it is important to und erstand the evolutionary processes underlying this selection. One interesting element to t his puzzle is that bacteria acquire resistance to different antibiotics at different rates. In a *PLOS Biology* article, the authors sought to understand the properties that determine how quickly resistance will evolve .They i dentified two properties, resistance variability and dose sensitivity, that could predict the rate of evolution in seven of eight of the drugs. Methicillin-resistant *Staphylococcus aureus* (MRSA) is t he most common antibiotic resistant infectio n in humans, and the most frequent mecha nism of resistance in MRSA is via the acq uisition of *mecA* .mecA is a member of th e penicillin-binding protein family that doesn't bind β-lactams (like penicillin) effectively and is th us immune to its effects. In a *PLOS Genet ics* article, the scientists map the evolution of *mecA* from its original role cell wall bi osynthesis .They identify four mechanisms t hat have led to its new role in resistance, and most importantly, show that it was the use of antibiotics in medicine and in lives tock feed that drove this evolution and spre ad of antibiotic.

Table representing the mechanism of drug resistance of common antibiotics

• Antibiotic class	• Example(s)	Mode(s) of resistance
• P-Lactams	• penicillin, Cephalosporins, Monobactams	• Hydrolysis, efflux, altered target
• Aminoglycosides	• Gentamicin, Streptomycin, Spectinomycin	• Phosphorylation, acetylation, nucleotidylation, efflux, altered target
• Glycopeptides	• Vancomycin, Teicoplanin	• Reprogramming peptidoglycan biosynthesis
• Tetracyclines	• Minocycline, Tigecycline	• Monooxygenation, efflux, altered target
• Macrolides	• Erythromycin, azithromycin	• Hydrolysis, glycosylation, phosphorylation, efflux, altered target
• Lincosamides	• Clindamycin	• Nucleotidylation, efflux, altered target
• Streptogramins	• Synergic	• Carbon-Oxygen lyase, acetylation, efflux, altered target
• Oxazolidinones	• Linezolid	• Efflux, altered target
• Phenicol's	• Chloramphenicol	• Acetylation, efflux, altered target
Quinolones	floxacin	Acetylation, efflux, altered target



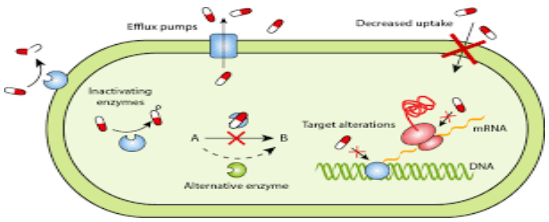
• Pyrimidines	• Trimethoprim	• Efflux, altered target
• Sulfonamides	• Sulfamethoxazole	• Efflux, altered target
• Rifamycin	• Rifampin	• ADP-ribosylation, efflux, altered target
• Lipopeptides	• Daptomycin	• Altered target
• Cationic peptides	• Colistin	• Altered target, efflux

The origin of antibiotic resistance:

Antimicrobial resistance has been reported to occur when the drug loses its ability to effectively inhibit bacterial growth. Bacteria begin to 'resist' and continue to multiply before the levels of antibiotic treatment Bacteria, when replicated even before antibiotics, are called antibodies. Antibiotics are usually effective against them, but when microbes are highly resistant or resistant, they need to have a greater impact than conventional screening of the same drug. The emergence of antimicrobial resistance was seen shortly after the introduction of new antimicrobial chemicals. Antibiotic resistance can occur as a natural a selective process in which the environment empowers all bacteria with a certain level of low resistance. For example, some studies have confirmed that sulfamethoxazole and trimethoprim (TMP-SMZ), ampicillin and tetracycline were widely used in previous years, but now no longer play a role in the treatment of non-cholera diarrhea in Thailand. At the same time, another study conducted in Bangladesh shows the effectiveness of similar drugs in effective treatment. In fact, drug resistance was documented even before the advent of antibiotics in the fight against infection [. Non-judgmental use of antibiotics is aimed at making the drug resistant to bacteria. Since the introduction of sulfonamides in 1937, advances in certain resistance systems have fueled their use in medicine. However, sulfonamide resistance was reported in the 1930's, revealing a similar resistance method that still works, more than 80 years later]. Less than six years after the aminoglycosides were produced, the aminoglycoside species of Staphylococcus aureus launched in 1961, Methicillin became the first penicillin-resistant penicillinase to identify the penicillinase species that produce Staphylococcus aureus. However, methicillin resistance was reported shortly after its launch. In addition, although fluoroquinolones were included in the treatment of Gram-negative infections in the 1980's, fluoroquinolones resistance later revealed that these drugs were used to treat Gram-positive Antimicrobial resistance in bacterial pathogens is a challenge that is associated with high morbidity and death. Multi-drug resistance patterns in Gram-positive and -negative bacteria are difficult to treat and may not be treated with standard antimicrobials. Currently there is a shortage of effective drugs, a lack of effective preventive measures, and only a few new antibiotics, which require the development of new therapies and other antimicrobial therapies. Biofilms

are involved in many drug resistances and can present infection control challenges. Antibodies are known as superbugs. This is not only a laboratory concern but also a global threat to high mortality rates and life-threatening diseases. The effects of these infections are greatly exacerbated by changing circumstances such as civil unrest, violence, famine and natural disasters. The World Health Organization (WHO) has warned that the post-antibiotic period that will lead to frequent infections and minor injuries may result in death if we fail to act in accordance with antimicrobials. Many drug-resistant germs cause many deaths worldwide. More than 63,000 patients from the The United States of America (USA) dies every year from hospital-acquired infections. Every year, an estimated 25,000 patients die from infections in Europe. Many countries face the burden of infection with nosocomial Staphylococcus aureus (S. Aureus) as clonal distribution waves. Methicillin-resistant strains Staphylococcus aureus (MRSA) are spreading rapidly around the world. Estimated costs due to multiple drug-resistant viruses may include additional health care costs and product losses. It has become common practice in many pharmaceutical companies to distribute antibiotics that have become obsolete or have lost their regulatory license. Evidence suggests that increased use of antibiotics can lead to better interactions and higher levels of resistant strains of bacteria, while reduced use of antibiotics indicates lower levels of resistance. There is clear evidence that patients historically treated with antibiotics are there is a good chance of developing an antibiotic. In addition, the recurrence of antibiotics from the first cycle accelerates the resistance mechanisms. Antibiotics promote selective stress for bacterial mutations when administered frequently or unconsciously. Individuals and provinces play a role in evolution of antibiotic resistance .For example, Clarithromycin consumption and its resistance similarly increased fourfold in Japan between 1993 and 2000 in comparison to other countries.

Mechanisms of resistance to antimicrobial agents in different bacteria:



Since the discovery and subsequent widespread use of antibiotics, a variety of Gram positive and Gram-negative bacteria of human and animal origin have developed numerous mechanisms of antibiotic resistance .In this review we are demonstrated some of bacteria. Staphylococci, together with pneumococci and streptococci, are members of a group of invasive Gram-positive pathogens, known as the pyogenic cocci, which cause various suppurative or pus-forming diseases in humans and animals. When antibiotic resistance was first encountered among bacteria, including Staphylococcus aureus, it was believed to arise solely by mutation and selection. Spontaneous bacterial mutants resistant to certain antibiotics can be generated at frequencies of 10- to 10 per cell in the laboratory, and it was assumed that analogous events had occurred in natural populations to produce resistant organisms. Indeed, resistance within the staphylococci to several therapeutically useful antibiotics, including streptomycin, rifampin, fusidic acid, and novobiocin, is thought to be derived by chromosomal mutation. A few resistance determinants have been mapped on the S. aureus chromosome. In some cases, however, chromosomal point mutations, which lead to antibiotic resistance, can be deleterious to the organism, resulting in the creation of less virulent forms. The acquisition of new characters, without affecting the fitness of the bacteria to survive in their natural environment, would therefore be expected to occur over a substantial time span. In an evolutionary sense, then, the accumulation of chromosomal mutations would seem to be unsatisfactory as the sole explanation for the rapid emergence of multidrug resistance bacteria. The relatively minor role played by spontaneous mutation in the stridden appearance of antibiotic-resistant microorganisms was confirmed by the discovery of gene transfer and the demonstration that bacteria can acquire additional genetic material in the form of extrachromosomal or plasmid DNA. The existence of plasmid DNA molecules was suggested by the transfer of discrete genetic units of resistance between bacterial strains and the irreversible loss of such units from cells at relatively high frequencies

A common mechanism used by bacteria to minimize the effects of antibiotics is to acquire or increase the expression of drug efflux pumps. As the name implies, these pumps expel drugs from the cytoplasm, limiting their ability to access their target. In a *PLOS Pathogens* article, researchers investigated how efflux pump expression is regulated in the human pathogen *Pseudomonas aeruginosa* They found that the multifaceted transcription regulator CpxR regulates the expression of the major efflux pump in *P. aeruginosa* and is involved in modulating resistance in clinical isolates.

Antibiotic inactivation: Sometimes a cell can get resistant to viruses by doing an enzyme that makes the drug ineffective, or that reduces the effectiveness of antibiotics. An excellent example is beta lactamases that can break the beta-lactam rings of beta lactam antibiotics like penicillin. Thus, the breakdown of the beta-lactam ring stops the antibiotic from being able to adhere to peptidoglycan precursors. But it is unlikely that penicillin or other similar drugs will be able to break the integrity of the cell wall, as long as the body produces beta lactamases]. This resistance can be transferred from one bacterium to another through the production of R-plasmids, and is common in methicillin resistance to Staphylococcus aureus (MRSA)

Reduced membrane permeability: Another common way to interrupt antibiotics by preventing drug entry into the cell. Gram negative bacteria also have an outer cell membrane, and the drug must pass through the pores of the cell, which are channels that open the outer membrane and allow the entry and exit of substances inside and outside the cell. To enter the cell or interact with the cell wall, the drug must be able to pass through the pores . Genetic mutations can lead to pores, often by altering the electrical charge or body composition that may make it more difficult for antibiotics to enter the cell. The antibiotic is still effective, but will fail to reach its target. The microorganism can grow to withstand multiple stages of treatment simultaneously in this way. But some gram-negative bacteria are resistant to the environment and larger drugs such as vancomycin, which are much larger than they can pass through. even before the advent of reform.

Modification of target site: Many antibiotics act responsibly in the target cell membrane. A microorganism can reduce a drug's effectiveness if the target molecule changes slightly in its structure so that the antibiotic can no longer interact with the target molecule. For example, tetracyclines block the RNA entry site by binding. Minor changes at the entry site can lead to viral resistance in tetracyclines . Efflux or antibiotic transport: One-way germs can fight off germs is by using an efflux pump. An efflux pump is a biological pump that can force an antibiotic out of the cell, so that it cannot reach or remain in contact with its target. This antibiotic resistance may cause resistance to more than one class of antibiotics, especially macrolides, tetracyclines, and fluoroquinolones because these antibiotics inhibit various protein and DNA biosynthesis and therefore must be intracellular in order to act. the result is resistance to antibiotics in one or more of the four systems methods, as shown in targeted molecules that are modified by their structure to prevent antibiotics binding: reducing gastric obstruction (antibiotics are released from cell implants); antibiotics are ineffective due to enzymatic depletion; or released from the cell by efflux pump.

THE FUTURE OF ANTIBIOTIC RESISTANCE

Stop Abusing Antibiotics in Agriculture

Stop abusing antibiotic in humans

Ramp Up Infection Prevention

Determinants:

antimicrobial resistance is a multifaceted problem, it is related to existing health care delivery system of the country. In India, around 5% of GDP is spent on health out of which public health sector contributes to 0.9% and a major portion of the remaining is by the private health sector. Again around 80% share of private health sector contribution comes from out-of-pocket expenditure mostly for medicines AMR results in many consequences. The patient remains sick for a longer period thus requiring prolonged treatment usually with expensive and at times toxic drugs which results in increased morbidity and mortality. The burden on health system also increases.[15] Hospital acquired infection in vulnerable patients with resistant strains is another major threat in the Indian context. The success of treatments such as organ transplantation, cancer chemotherapy and major surgery would be compromised without effective

.

Spotting resistance:

Scientist in each looking at the microbiome in the gut and mouth. The microbiome is crucial in understanding antibiotic resistance, as it is the sum total of all microbes (including bacteria, fungi, and viruses) found in a particular part of the body. But only some of the bacteria microbiome may carry antibiotic-resistant genes.

We compared DNA sequences from different mouth and stool microbiomes collected from people living in China, Fiji, France, Germany, the Philippines, and the US. This allowed us to create an overview of all genetic material in these samples, which we then compared with a database of thousands of genes known to cause antibiotic resistance. An algorithm then helped us reconstruct the genes and remove DNA sequences not responsible for antibiotic resistance We compared these remaining sequences with a database to see which genes cause antibiotic resistance. This showed us the number of resistance genes (in both individual bacteria species and bacterial communities) in a person's mouth and stomach

An antibiotic resistance is global problem, we also wanted to know how resistance differed between people from different countries. While we did find that people from Asia carried more bacteria with antibiotic resistance genes in their gut (likely because of how frequently antibiotics are prescribed or are taken), we were surprised to find that the numbers and species of antibiotic-resistant bacteria did not vary that significantly from country to country. Rather, there are greater differences in antibiotic-resistant bacterial species between your own gut and mouth than if you compared the bacteria in your mouth with someone from Fiji.

Medicinal Use o antibiotics:

Antibiotics are used to treat or prevent bacterial infections, and sometimes protozoan infections. When the infection was suspected to be the cause of the disease, but the unanswered pathogen had not yet been identified, aggressive treatment was accepted. This includes a wide range of antibiotic-based treatment based on the symptoms and signs presented and initiates the results in a waiting laboratory that may take a few days. When a pathogenic microorganism is already known or detected, specific treatment can be initiated. This often involves the use of antibiotics. The choice of antimicrobials will also be based on their cost. Diagnosis is very important as it can reduce the cost and toxicity of antimicrobials and reduce the likelihood of developing antimicrobial resistance. To avoid surgery, antibiotics can be given for mild appendicitis. Antibiotics can be given as a prophylactic method and this is often limited to people at risk such as those with weakened immune systems (especially in cases of HIV to prevent pneumonia), those taking antiretroviral drugs, cancer patients and those who are being offered . They play an important role in dental antibiotic prophylaxis where its use can prevent bacteremia and subsequent endocarditis infection. Antibiotics are used to prevent infection in cases of neutropenia especially cancer-
related. There are many management options for antibiotic treatment. Antibiotics are usually taken orally. In more severe cases, especially serious chronic diseases, antibiotics can be given intravenously or by injection. The use of topical ingredients is also one of the treatments for certain skin conditions including acne and cellulitis. The benefits of using the articles include achieving a high and continuous diagnosis of antibiotics in the area of
infection; reducing systemic and toxic absorption capacity, and the total number of required antibiotics is reduced, thereby reducing the risk of antibiotic abuse. Topical antibiotics used for certain types of surgical wounds have been reported to reduce the risk of infection at the surgical site. However, there are some common causes for concern over the control of chemicals by antibiotics. Some systemic antibiotic interventions are possible; the amount of antibiotics used is difficult to determine with precision, and there is also the possibility of a local hypersensitivity reaction or contact with dermatitis.

Side-effects of antibiotic:

Antibiotics have been tested for any adverse effects before being approved for clinical use and are generally considered safe and well tolerated. Some antibiotics are associated with a wide range of side effects ranging from mild to severe depending on the type of antibiotic used, the targeted microbes, and each patient. Side effects may indicate drug overdose or antibiotic resistance or may include allergies or allergies. The new drug safety profiles are often not established as those with a long history of use. Common side effects include diarrhea, which results from disruption of plant species in th

e intestinal tract, leading to, for example, a n increase in pathogenic bacteria, such as Clostridium kengoku. 24 Bacteria can also affect the vaginal flora and may lead to ov ergrowth of yeast species of the genus.

Conclusion:

Antibiotic resistance is at all-time high in all the parts of the world. De spite measures taken by some member state s of WHO, antibiotic use in humans, anima ls, and agriculture is increasing. The high e conomic burden in the healthcare sector has become a burning issue, due to extended hospital stays, isolation wards, stringent infe ction control measures and treatment failures . The public health leaders should establish a pan surveillance system coordinated at n ational and international levels, ongoing anal ysis, and a mandatory reporting system for antibiotic resistance. Both domestic and gl obal policies need to be conventional and a dhered-to to stop the overuse and misuse of antibi otic.

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