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Review article

Antibiotics over usage: a vital contributor of antibiotic resistance

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ABSTRACT

Antimicrobial resistance is a global public health issue resulting from antibiotic misuse. Antimicrobial resistance contributes to serious infections, complications, prolonged hospital stays, and higher mortality rates. Steps must be taken to rectify the damage caused by antibiotic resistance and prevent future resistance development. This article looks into the context and societal situations that allow for antibiotic overuse and misuse in both healthcare professionals and the general public, the biochemical and genetic pathways that enable microbes to evolve drug resistance, the implications that could result if this trend of antibiotic overuse continues, and the different approaches and solutions that have been proposed for preventing and reversing this problem.

Keywords: Antibiotic resistance, Antimicrobial resistance, Overuse of Antibiotics, Evolution.

INTRODUCTION

Antibiotics, which have altered medicine and protected millions of lives, are under threat as resistant bacteria grow rapidly all over the world. The antibiotic resistance dilemma has been blamed on the overuse and misuse of these treatments, as well as a dearth of new drug development by the pharmaceutical sector due to low economic incentives and stringent regulatory constraints [1].

Many doctors alongside other health care providers give antibiotics with little or no caution. Antibiotics are now routinely prescribed for simple and smaller bacterial infections like Streptococcus pyogenes, the bacteria that causes strep throat, which a healthy immune system would usually clear in about ten days. Antibiotic usage causes drug resistance in microorganisms resulting in bacteria that cannot be treated with currently existing antimicrobial treatments [1, 2]

Steps should be undertaken to reverse the existing damage and prevent new resistance development. This work aims to examine the context and social situations that contributed to this acceptance of antibiotic overuse and apparent ignorance toward the issue observed among both healthcare professionals and the public, the biochemical and genetic pathways that enable microbes to develop drug resistance, the different approaches that have been proposed by professionals for avoiding and reversing this issue, and the implications that could follow if the current pattern of antibiotic overuse continues to go on. The article is going to offer a few alternatives to this expanding challenge [3].

A Brief of Antibiotics and Antibiotic Resistance

Penicillin, an original antibiotic produced by Dr. Alexander Fleming by chance in 1928 [4].was regarded as a wonder medicine, saving the lives of numerous soldiers during World War II and improving public health. However, penicillin resistance quickly became a significant clinical problem. In response, novel beta-lactam antibiotics were identified, manufactured, and used. The very first instance of methicillin-resistant Staphylococcus aureus (MRSA) emerged in the United Kingdom in 1962. In 1972, Vancomycin was used to treat methicillin-resistant S. aureus and coagulase-negative staphylococci. Vancomycin resistance in coagulase-

negative staphylococci first became apparent in 1979 and 1983 respectively. Antibiotic discovery continued and expanded during the following decades. There are numerous antibiotics accessible for medical usage: cephalosporin's, tetracycline's, aminoglycosides, monobactam, Carbapenems, macrolides, streptogramins, and dihydrofolate reductase inhibitors have been readily accessible in the early 1990s to treat bacterial infections [5]. Today, there are more than 100 antibiotic classes, with penicillin derivatives accounting for the vast majority.

Medical practitioners frequently prescribe the several antibiotics that are currently available. All are being utilized in an increasingly careless manner, exacerbating while adding to the contemporary times antibiotic dilemma. Many causes contribute to the current situation, including pharmaceutical firms, prescribers, patients, the agricultural sector, and bacteria's genetic potential.

Different Roles Leading to Antibiotic Resistance

Role of Medical Doctors

Physicians' prescription decisions are extremely complex and are influenced by a variety of factors. Clearly, in cases of infectious disease, the decision to treat is based on the presence of a bacterial infection or the likelihood of one. The amount and kind of antibacterial are determined by the most prevalent pathogen and its local in-vitro susceptibility, the extent of the infection, and the patient's state. In most cases, the pathogen and its in-vitro resistance are unknown. Antibiotic use is rapidly growing worldwide, particularly in more developed countries [6].

Antibiotic over prescription is extremely expensive and has been linked to bacterial resistance. Antibiotics are overused and misused, and they are frequently administered for viral infections that cannot be treated with antibiotics. Antibiotics prescribed for self-limiting infections are likely to be the primary cause of antibiotic-resistant bacteria in community settings. It's baffling to ponder why physicians, who are normally quite well educated, choose to prescribe treatments that will ultimately cause greater damage than beneficial to the patient as well as society as a whole over the long term. This worrying trend has several causes. Regardless of their reasoning, the truth is that antibiotic prescriptions are rarely based solely on clinical criteria. It has been argued that antibiotic overuse is linked to the prescriber's personality and environment. Years of practice, medical specialty, anticipated patient expectations, and a desire to please the patient are among the clinician factors associated with needless prescriptions [1]. General practitioners prescribe over 90% of antibiotics prescription in the United States in a given year, with more than half of them recommended for the treatment of respiratory tract infections. Most highly developed European countries also have statistics that are fairly similar to these numbers. Urinary tract infections are the 2nd leading condition for which antibiotics are usually recommended.

It is estimated that more than half of patients who present to a medical center with signs of a urinary tract infection are immediately treated with antibiotics, even though urinary tract infections are extremely self-limiting and offer a very small threat to an individual's overall health and well-being. Addressing urinary tract infections with antibiotics without conducting the requisite test work is not only irresponsible in terms of germ resistance, but it is also very expensive and ineffectual in treating the sickness. The patient may feel more comfortable knowing that one has been prescribed something concrete, but the benefit will end there. Antibiotic prescriptions for urinary tract infections cause significantly more harm than good to the patient. The majority of the blame for inadequate and irresponsible antibiotic prescribing falls on prescribers, whether they are doctors, physician assistants, or other medical professionals [7]. However, the individual receiving medical care also bears some of the guilt and responsibility. Patient expectations and presuppositions indeed cause doctors to feel intimidated or forced into giving antibiotics "just in case" or to placate a difficult patient who will not leave without a prescription.

A study was conducted in Iceland to investigate how frequently and in what situations medical practitioners, primarily family and general practitioners, prescribe antibiotics to patients who appear with no apparent or definite indications of bacterial infection. Arason refers to this approach of prescribing as "non-pharmacological prescriptions of antibiotics" [2]. The study discovered that the key reasons doctors would give antimicrobial medications to a patient with a non-specific bacterial disease are all related to the constantly shifting doctor-patient relationship. The explanation for the volatility in doctor-patient relations in the study region was thought to be a lack of consistency in health services that most patients wanted. Pressure from patients in a demanding society, the physician's heavy workload, the prescriber's attitude, any supplementary prescribing rewards they may be receiving from pharmaceutical companies, and the physician's lack of confidence or ambiguity in their diagnostic abilities

were the primary variables that resulted in a condition where antibiotic prescriptions were typed of coping strategy for an unpleasant situation with a patient. A European study polled 1,000 general practitioners on their prescribing patterns and procedures. 55% of general practitioners reported experiencing tremendous pressure from patients to prescribe antibiotics, even if the practitioner resisted and explained that the drug was unnecessary and ineffective. 44% of general practitioners admitted to administering antibiotics to a difficult patient simply to get them to leave the place [8].

Overprescribing antibiotics is especially common among children. According to a study published in the Scandanavian Journal of Primary Health Care, children under the age of seven ingested approximately 20% of all antibiotics sold in the region investigated, despite accounting for just about 10% of total family care office visits. More than 50% of these patients were administered medicines for ear infections, which are rarely caused by bacterial infections; mostly viral infection. A link was discovered between the quantity of antibiotics consumed by a child and the probability of that patient becoming a carrier of antibiotic-resistant microorganisms, specifically penicillin non-susceptible pneumococci, in a few weeks after medical treatment [2]. Pediatric ear infections are among the most common ailments that doctors may prescribe antibiotics to treat. Infections of the upper respiratory tract are the main source of antibiotic overprescribing in outpatient settings, both in pediatric and adult populations [7]. Another study conducted in Sweden and published in the same journal discovered that after implementing more extensive diagnostic methods, fewer patients were identified as having bacterial upper respiratory infections. Surprisingly, the percentage of patients who were administered an antibiotic did not decline as expected. The percentage of patients prescribed antibiotics increased over time. This study establishes quite conclusively that clinical considerations such as lab workups rank very low on the list of causes why a physician would recommend antibiotics to a patient. Antibiotic overuse has been demonstrated to enhance the probability that patients go back to a specific provider or office. which could be a contributing factor to needless antibiotic prescribing.

Knowing that one can walk into a doctor's office and leave with definitive therapy, regardless of whether or not that therapy is appropriate for one's specific case and condition, increases the likelihood that the individual will return to that provider. Patient loyalty is probably a contributing element to the antibiotic dilemma [8].

Role of the pharmaceutical industry

Pharmaceutical businesses discover, develop, and market novel antibacterial drugs. Pharmaceutical corporations benefit from promoting the widespread use of antibacterial to justify their development and research costs. This fact, combined with certain clinicians' inclination to prescribe the most recent antimicrobial, undoubtedly raised the prevalence of resistance. Antibiotics were abundant and profitable from 1988 to 2000. Animal testing legislation, for example, was much easier to manage [9]. Since 2003, the FDA has approved only one new antibiotic per year for medical treatment, and the largest pharmaceutical companies have either significantly reduced or discontinued antibiotic research. Focusing on antibiotics is simply less profitable than other areas of research. These businesses have moved their development and research efforts toward treatments with larger markets and bigger profit margins. Large pharmaceutical companies are especially interested in drugs used to treat chronic illnesses. Antibiotics are far more complex and expensive to develop than drugs for high cholesterol, diabetes, arthritis, and depression.

Antibiotics are significantly less lucrative than other so-called "maintenance medications". Antibiotics are utilized only briefly and regularly throughout a person's life. It is undoubtedly challenging to generate money developing a medicine that is going to be utilized for about ten days annually, especially given how difficult antibiotics are to locate, develop, and test. To summarize, there is far more money to be gained from so-called "blockbuster" treatments than from antibiotics which patients would only use occasionally and for a limited length of time [20]. Pharmaceutical corporations are heavily invested in antibiotics that are already being created. They want to continue making money from the effort they've already made.

According to research published in the PLoS Medical Journal, pharmaceutical corporations spent approximately 1.6 billion dollars in 1998 promoting antibiotics to consumers, hospitals, doctors' offices, and pharmacies [7]. This money might easily be used on research into novel medicines or on initiatives to promote safe antibiotic use. Unfortunately, it is being utilized solely to market and promote the continued use of already widely recognized antibiotics.

Pharmaceutical companies have limited incentive to research and develop novel antimicrobial drugs. They may generate even more money by creating medications for other disorders, particularly those that are common and chronic, like diabetes or elevated blood pressure.

Role of Patient

Patients have become significantly more critical and privileged in recent decades. They frequently assume that if they exit a doctor's office without receiving a prescription for antibiotics or other physical and definitive therapy, they are being shortchanged or tricked in some way. Patients perceive prescribers as lazy and indifferent when don't prescribe for the individual's condition. Myths and presuppositions abound in the public's understanding of antibiotics. A study conducted in Europe examined public perceptions of antibiotics and their efficacy. The study discovered that around 50% of the patients polled thought antibiotics were completely successful in treating viruses, colds, and flu and they should therefore be prescribed in those instances [10]. Antibiotics will not improve any of these conditions, which is worrisome. Antibiotics are exclusively effective against bacterial illnesses; they do not work against viruses that cause ear infections, lung infections, flu, or the common cold.

Patient characteristics associated with excess and inappropriate antibiotic prescribing include misconceptions about antibiotic efficacy for viral infections, a need for a tangible result from the clinical interaction, age, ethnic and racial recognition, and insurance status [1]. Older patients, those from disadvantaged locations, and minor patients were found the most likely to get unnecessary antibiotics. Ackerman indicates that the aforementioned qualities predispose these individuals to be people with whom it can be challenging to communicate and clarify unpleasant or confusing material. These limits can make provider-patient interactions challenging at times, but to address the antibiotic epidemic, these impediments must be overcome. When considering the issue of antibiotic overuse, the social features of the relationship between physicians and patients mentioned above must be taken into account.

However, the continual cultural transition in the patient's expected role from passive recipient of medical competence to active medical "consumer" must be carefully considered [1]. Consumers expecting to be sold something, and being turned away without treatment makes them feel tricked or shortchanged in some way. The consumer attitude of American culture is a significant contributor to the antibiotic epidemic.

Role of Uncertainty

Overprescribing antibiotics is also influenced by the uncertainty surrounding diagnostic testing, especially in primary care settings. A 2005 study conducted in the Netherlands revealed that doctors' reluctance to diagnose patients based on clinical signs of a bacterial disease was significantly correlated with their usage of antibiotics [14]. Doctors aim to completely rule out the scenario in which they refuse to give a patient antibiotics and later on the patient contracts a dangerous bacterial infection, becomes gravely ill, or even passes away. Doctors who have to make these decisions bear a great deal of responsibility due to the legal and ethical implications. The issue is that there is very little chance of misdiagnosing a potentially fatal bacterial infection for a restricting viral sickness. Antibiotic resistance gets exacerbated when a doctor writes a "blanket coverage" antibiotic prescription only to allay a patient's concerns or avoid consequences for the doctor. Prescription antibiotics "just in case" is not a good practice for the patient or the healthcare professional.

Antibiotic Resistance

All around the world, antibiotic resistance is increasing to dangerously high levels, and microorganisms have become remarkably resistant to antibiotics. Methicillin-resistant Staphylococcus aureus, in particular, has garnered significant notoriety due to its near-impossible treatment [6]. According to Neu, almost every strain of Staphylococcus aureus found worldwide in 1941 could be treated with penicillin. By 1944, S. aureus had developed penicillinases, also known as beta-lactamase, which was capable of breaking down penicillin. By the end of the 1940s, resistance was present in around 50% of S. aureus strains.

Currently, ampicillin, anti-pseudomonal penicillin’s, and penicillin are not effective against more than 95% of S. aureus. Not because of poor hygiene or unclean surroundings, but rather because hospitals foster the growth and reproduction of specific bacterial strains that carry drug resistance genes, making them ideal environments for the creation of multi-drug resistant bacteria. This is why hospitals become breeding bases for bacterial infections. Another excellent illustration of this behavior is Clostridium difficile. Drug-resistant bacteria can proliferate in the stomach when normal bacteria are disturbed and killed by the overuse or indiscriminate use of antibiotics.

The most common of these bacteria is C. difficile, which can occasionally result in a prolonged and crippling illness that is frequently fatal and can cause opportunistic infections in individuals who have had antibiotic treatment [11].

Bacteria are subject to selection pressure when treated with antibiotics. This pressure encourages the formation of microbial strains that can live and proliferate despite being susceptible to the antibiotics present in the environment. Because of their genetic makeup and mutational capabilities, bacteria can withstand antibiotics. Chromosome mutations, induced expression of a formerly latent gene, transformation-induced genetic material exchange, bacteriophage transduction, and plasmid conjugation—Extrachromosomal DNA—are a few examples of this. Antibiotic research currently focuses a great deal of attention on plasmids. Transposons may also be present in bacteria. Transposons are known as "jumping genes" because of their capacity to infiltrate transmissible plasmids or chromosomes, which allows them to spread antibiotic resistance to both distinct species of bacteria and other bacteria of the same species [6]. Although the opposite is rare, Gram-positive species have shown the capacity to transmit resistance to Gram-negative species.

The ability of several types of bacteria to work together is a fantastic illustration of the intelligence and adaptability bestowed onto microscopic life by their Creator. Antibiotics are evaded by bacteria in three main methods. They can either destroy the antibiotic or alter it in a manner that makes it less effective against the microorganism, rendering it inactive. Second, they can avoid the antibiotic or stop it from entering the microbial body. Finally, they can change the antibiotic target location on the surface of their membrane, which stops the antibiotics from binding. As a result, the microorganism will be less affected or not affected at all.

Potential Repercussions

The biggest worry is that bacterial resistance may cause common illnesses like strep throat to become incurable once more. If antibiotic resistance increases any further, WHO has described what can happen. It is referred to as the "post-antibiotic world" by them. This planet appears to be much like the pre-penicillin age, when infectious disease predominated, rather than Pasteur's vision of the abolition of sickness in the future. Antibiotic resistance could make common diseases uncontrollable and possibly even deadly, the WHO has warned.

Possible Remedies

Scientists, doctors, and other professionals have proposed several strategies to stop the development of additional drug resistance. These include stricter guidelines for when antibiotics are acceptable and should be prescribed, raising awareness among the public regarding the proper use of antibiotics and the negative effects of misusing them, and holding doctors and other healthcare providers to a higher standard when it comes to diagnosing and treating bacterial illnesses.

The best ways to combat antibiotic resistance have been demonstrated to be multifaceted approaches that tackle the issue from multiple angles. The implementation of policies that forbid the selling or buying of antibiotics without no a valid prescription via a licensed dispensing pharmacy, the establishment of management programs that educate the public about the importance of using antibiotics appropriately, the enforcement of laboratory testing before the prescription of antibiotics, training doctors on improved patient interaction techniques, and the provision of incentives for doctors who follow these rules and regulations are among the interventions which have yielded the best results in nations throughout the world [8]. These actions, along with others, are most likely required to keep society from regressing to a pre-antibiotic era.

Public Education about Antibiotics

The general public is gravely misinformed regarding the appropriate use of antibiotics. Education in this field is needed.

The public could be greatly educated about the reality of antibiotic use if curriculum designs for public schools included information regarding antibiotics and safe usage. It would be possible to distribute educational leaflets in government offices like the Social Security Office. TV could be especially helpful in this regard. News articles and documentaries have the potential to educate the audience greatly. It's also possible to use social media as a forum to inform people about antibiotic resistance. Public intervention might take the shape of guidelines being published, freely given educational workshops explaining which ailments antibiotics will and won't treat, local pharmacist interviews being published, messages being broadcast on television, radio, and various other popular media platforms, etc. [12]. These public awareness campaigns will undoubtedly help to lessen the antibiotic epidemic, but raising public awareness

won't end the problem. All it is is a baby step toward the correct path.

Physician Programs and Interventions

Before administering antibiotics to a patient, doctors and other healthcare providers should be urged if not mandated to order diagnostic testing because it can be quite difficult to identify bacterial infections from viral infections at times. In addition to eliminating uncertainty and relieving the doctor's mind and conscience, this will also eliminate the need for the ensuing, frequently awkward justification to the patient for not receiving an antibiotic "just in case." A patient may be far less inclined to put demands on a doctor to prescribe antibiotics when it's neither necessary nor appropriate. Most diagnostic tests are rather easy to do. Typically, they include collecting a urine, blood, or swab sample and forwarding it to the lab. The patient may experience some discomfort from diagnostic testing, but if these steps are not followed, the looming antibiotic crisis will be far more serious than the time missed from their day.

The goal is to assist patients realize how antibiotics may and should be administered appropriately for the benefit of both their own and the society's health at large, not to minimize their worries. In certain circumstances, diagnostic testing may not be necessary before prescribing antibiotics to a patient due to their severity. This is a contextual issue for which adjustments would have to be made. Maybe emergency antibiotic prescriptions might be covered by hospital allowances.

Antibiotic education could be a highly beneficial component of a doctor's medical education, especially when it comes to patient communication. A doctor must be able to appropriately demonstrate to a patient who lacks medical training or experience in the proper use of antibiotics, how they may be exacerbating the antibiotic crisis, and that using antibiotics won't shorten the course of viral or self-limiting illnesses. Informational booklets or brochures that the patient may utilize at home could supplement the spoken information provided by the practitioner [1]. It's also critical that medical professionals can help patients have reasonable expectations regarding the length and severity of their illnesses. Ear infections typically last four days, viral acute sore throats last around a week, the common cold lasts a week and a half, sinus infections last two and a half weeks, and severe coughs or bronchitis can last up to three weeks [14]. This is especially crucial because research indicates that a large percentage of patients think that taking antibiotics is not only appropriate but also required if their symptoms persist for more than three days [4].

Regulations

As the hunt for new antibiotics continues, the presently used antibiotics need to be preserved and safeguarded. Only in circumstances where the patient's life is in danger may it be necessary to permit IV antibiotic therapy while they are hospitalized. To guarantee that the medication is taken only when necessary, in the right quantities, and for the right length of time, oral antibiotics might be temporarily discontinued. This would eliminate the need to inform the public and have faith in the average person to use antibiotics responsibly and safely. Reducing the amount of antibiotics prescribed and used is not the only objective of rules governing the appropriate use of antibiotics. The main goals are to guarantee that antibiotics are only provided to individuals who will benefit from the treatment and to promote the sensible use of antibiotics [14]. A program that would accomplish exactly what is being suggested here is already in the works at the Centers for Disease Control (CDC). The goal of this ambitious effort is to minimize the needless and frivolous use of antibiotics so that they continue to be an effective tool for future generations [2].

Congress provided the CDC with around $160 million in funding for several agencies and projects aimed at combating antibiotic resistance during the 2016 fiscal year. With the help of these funds, the CDC launched the Antibiotic Resistance Solutions Initiative, enhancing the country's capacity to identify, address, and eradicate resistant illnesses in both community and clinical settings. There are problems with this plan. It is not directed at medical professionals or family practitioners, but rather at the usage of antibiotics in hospitals. Furthermore, the application of antibiotics in livestock and agriculture is not included in the CDC's recommended approach. The CDC has several objective categories to combat antibiotic resistance. They intend to establish national targets to enhance the use of antibiotics, namely to reduce incorrect prescription practices by 20% in general practitioner and specialty offices and 50% in hospitals. They intend to support efficient public education campaigns and initiatives for antibiotic stewardship, concentrating their efforts on medical practices, institutions, and assisted living facilities. Researchers looking into antimicrobial resistance as well as those looking for novel antimicrobial compounds that

may one day be medically recognized and utilized to treat patients have received money from the CDC. It's interesting to note that they've also started a program to encourage sepsis early detection. These projects all seem admirable and exciting. The CDC hasn't yet, nevertheless, presented a workable strategy for combating antibiotic resistance. They haven't been planning for the present; instead, they have been concentrating on future projects. Sadly, the antibiotic issue is happening right now, not some distant time in the future [13].

It is necessary to remove pharmaceutical companies from their position of power in the development of antibiotics. They ought to be stopped from providing medical professionals with incentives for prescribing; this could involve taking legal action. Perhaps one of the hardest problems to solve is this one. Without giving the government control over pharmaceutical manufacturing, it might be difficult to eliminate pharmaceutical firms from their position of influence and power. Without question, having government control would be a worse option. For the time being, public pressure and incentives may be needed to acknowledge and potentially counteract the role of shady "big pharma."

Only licensed veterinarians may personally administer antibiotics to animals, or they may write prescriptions that can be filled by a pharmacy. As a precautionary measure, antibiotics should never be sprayed on crops or added to animal feed. Health experts, regulatory bodies, and law enforcement organizations need to acknowledge and include the connection between animal health and human health in their strategies.

Look for New Antibiotics

The quest for new antibiotics is currently underway, albeit at an alarmingly slow pace. It is significantly more challenging for researchers to obtain funding from pharmaceutical corporations to discover and create these new medications. Decades pass between the initial discovery of a prospective novel antibacterial agent and its commercial production approval. Many researchers have abandoned the hunt for new antibiotics due to a lack of motivation and funding.

CONCLUSION

Rapidly developing resistant bacteria jeopardize the enormous health benefits acquired by antibiotics. This epidemic is worldwide, reflecting the world's abuse of these treatments and pharmaceutical companies' failure to produce new antibiotic compounds to address the issue. Antibiotic-resistant illnesses have a significant health and economic impact on the healthcare system and community. Coordinated efforts to enact new regulations, restart research initiatives, and explore crisis-management strategies are critical.

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