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The Misuse of Antibiotics and the Rise of Bacterial Resistance: A Global Concern

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Abstract

Antibiotics are one of the basic drugs prescribed for hospitalized patients. Irrational prescription of antibiotics not only increases adverse drug reactions, but also helps for the development of resistance in bacteria. The rational prescription of antibiotics is necessary to control bacterial resistance that is developing throughout the world. Rationality means prescribing the clinically approved drug in a correct dose with exact knowledge of the drug and the disease, taking into account economic factors. In some conditions such as severe infections, we can see combination therapy with antibiotics, but this should be done according to the guidelines and we should also consider the characteristics and spectrum for prescribing combinational therapy with antibiotics. They are not recommended for minor infections. Bacteria use beta-lactamase enzyme to hydrolyze the beta-lactam ring, which is a type of resistance mechanism developed by bacteria against antibiotics that led to the development of antibiotics with new combinations. Self-medication of antibiotics and less compliance are one of the major reasons for the development of resistance along with irrational prescribing patterns. We must make sure that patients are always given evidence-based medicine. Physicians should be cautious about the consequences of the irrational antibiotic prescriptions before prescribing them to patients. The public should be more aware of the importance of antibiotics and their adherence.

Keywords

Antibiotics, Rationality, Self-Medication, Resistance, Awareness

1. Introduction

Antibiotics, first discovered by Alexander Fleming in 1928, have revolutionized healthcare by dramatically reducing morbidity and mortality associated with

infectious diseases. These invaluable agents combat bacterial infections, particularly in resource-limited settings. However, this widespread use has led to antibiotics becoming one of the most commonly prescribed drugs globally [1], even for minor infections. While antibiotics have significantly decreased the burden of foodborne and other infectious diseases, especially in developing countries, their overuse raises concerns [2].

Rational antibiotic prescribing, considering factors like appropriate dosage, disease knowledge, and cost-effectiveness, is crucial. Unfortunately, the influence of pharmaceutical companies often leads to irrational prescriptions, increasing costs and the risk of adverse drug reactions for patients [3]. Moreover, this practice fuels the growing global threat of antibiotic resistance [4]. Therefore, promoting the judicious use of antibiotics is essential to preserve their effectiveness and combat the rise of resistant bacteria.

One of the main drivers of antibiotic resistance is the overuse and misuse of these medications. Despite the known risks, an estimated 10 million tons of antibiotics are used worldwide every ten minutes, much of which is not for justified medical purposes [5]. This overuse puts pressure on bacteria, forcing them to mutate and develop resistance mechanisms. Furthermore, the dependence on antibiotics for disease treatment and prevention contributes to the problem [6].

The economic burden of AMR is also substantial. Prolonged hospitalizations, expensive treatments, and the need for additional healthcare resources contribute to significant financial strain on healthcare systems. It is projected that AMR could result in US$1 trillion in additional healthcare costs by 2050 and US$1 trillion to US$3.4 trillion in GDP losses per year by 2030 [3].

2. Rational Prescribing: A Cornerstone of Antibiotic Stewardship

To preserve the efficacy of antibiotics and mitigate the rise of resistant strains, rational prescribing is paramount. This involves selecting the appropriate antibiotic, considering factors such as the infection type, patient characteristics, and local resistance patterns, and administering it at the correct dose and duration. Antibiotic stewardship programs are essential in promoting responsible prescribing practices through education, guidelines, and targeted interventions.

3. Mechanisms of Antibiotic Resistance

Bacteria have evolved a variety of mechanisms to counteract the effects of antibiotics. One crucial strategy is the utilization of efflux pumps, which are protein structures embedded in the bacterial cell membrane [4] [5]. These pumps act as gatekeepers, actively expelling antibiotics from the bacterial cell, preventing them from reaching their targets and rendering them ineffective. Another key mechanism is target modification. Bacteria can alter the antibiotic's target site, hindering the drug's ability to bind and exert its action [6]. This can occur through mutations in the genes encoding target proteins or enzymatic modifications of the

targets themselves. These mechanisms, along with others, contribute to the growing challenge of antibiotic resistance.

4. Global Impact of Antibiotic Resistance

The rise of antimicrobial resistance (AMR) poses a serious threat to public health in the United States and an even more alarming threat globally [7]. The rise of antibiotic resistance is a global health crisis, recognized by the United Nations General Assembly as a major threat requiring urgent action. The World Health Organization (WHO) estimates that antimicrobial resistance (AMR) was directly responsible for 1.27 million deaths globally in 2019 and contributed to 4.95 million deaths [8]. In the U.S., the Centers for Disease Control and Prevention (CDC) reports that over 2.8 million antimicrobial-resistant infections occur each year, resulting in over 35,000 deaths [9]. These figures underscore the urgent need for action.

The issue of bacterial resistance across the globe was discussed in the 71st United Nations General Assembly, making it the fourth health issue to be discussed in the organization's history [9]. Antibiotic therapy to a patient generally depends on the sensitivity of microbes, especially when there is no effect of treatment on the microbes. First-line agents are selected based on the type of bacteria and the location of the infection; alternative therapy is recommended only if the first-line agents are proved to be ineffective or the patient has an allergy to the prescribed drug [10].

Antibiotics are given as prophylaxis to any type of infection, but after determining the causative bacteria, therapy should be according to the guidelines, and an antibiotic suitable for treating the infection should be prescribed. In some conditions, such as severe infections, combination therapy with antibiotics can be seen, but this should be done according to the guidelines, considering the characteristics and spectrum for prescribing combinational therapy with antibiotics. They are not recommended for minor infections. In China, resistance to third-generation cephalosporins by E. coli is 59%, according to the National Resistance Monitoring Network (CARSS) in 2015 [11].

Alarmingly, studies reveal a lack of awareness and responsible use of antibiotics among the public. Research in Saudi Arabia found that 43% of subjects take antibiotics without a prescription, and 42% stop using them prematurely [12]. This highlights the need for public education and awareness campaigns to promote responsible antibiotic use and combat the growing threat of resistance.

High rates of self-medication and irrational prescribing have been reported in various regions, including Europe, Asia, Africa, and the Americas. For example, studies have shown that in Saudi Arabia, 78.7% of patients consume antibiotics without a prescription [13], and in the Republic of Srpska, 58% of pharmacies sell antibiotics without a prescription [14].

Addressing this global health crisis requires a multifaceted approach. Key strategies include promoting rational antibiotic prescribing, implementing infection

prevention measures, investing in the development of new antibiotics, and educating the public about the responsible use of these vital medications.

Antibiotic self-medication is ubiquitous in eastern and southern Europe due to the availability of antibiotics for diseases such as URTI and cold. According to a study conducted in the Republic of Srpska on antibiotic sales in pharmacies, 58% of pharmacies sold antibiotics without any therapeutic prescription of antibiotics [14].

The study by Erick Mboya *et al.* in Moshi municipality of Northern Tanzania revealed that 88.8% of the antibiotics used are irrational, of which 76.3% of them are dispensed without appropriate prescription. The prevalence of antibiotic use irrationally is around 30% and 19% in Southern and Eastern Europe, respectively [15].

Around 33,000 deaths per year occur due to antimicrobial resistance which also causes 1.5 billion euros annually for health care cost and also a deficit in productivity. Irrational prescribing of antibiotics can be seen in all countries, but in developing countries, it is observed prominently due to the fragile health care system. Insufficient knowledge about drugs for the physician or the patient, easy availability of antimicrobial agents without any prescription, patient pressure on prescriber for the requirement of antibiotics, improper testing of microbes, and lack of proper communication between health care professionals are the major causes for the increased irrationality in antibiotic use. The "Post-antibiotic era" is the term given by the World Health Organization in 2014 where minor infections can become fatal as antibiotics would be ineffective [16].

In 2014, the estimated number of deaths due to antimicrobial resistance (AMR) was approximately 700,000 and without proper intervention the annual death rate due to AMR would be ten million by 2050. According to the study done by Shapiro *et al.*, in the US 50% of the antibiotics prescribed are inappropriate and 30% are unnecessary. The results of the study conducted in 28 European countries revealed that broad-spectrum antibiotics constitute 80% of antibiotics prescribed in 22 countries [17].

Beta-lactam antibiotics are the most widely used antibiotics in the world, whose mechanism of action is by inhibiting cell wall synthesis in bacteria. However, bacteria had developed a resistance mechanism for beta lactam antibiotics through the production of beta lactamase enzyme, which became a major threat to the health of the global population. In the last 30 years, a lot of work has been done to develop compounds that can inhibit the activity of beta lactamase. Beta lactamase inhibitors are developed successfully for combination therapy, but the high amount of beta lactamases synthesized by resistant bacteria and the inconsistent compatibility with various beta lactamases by the inhibitors are the challenges for their therapeutic efficacy. Lytic transglycosylase is an important factor required for the induction of beta lactamase. Targeting this lytic transglycosylase can prevent beta lactamase induction. Aminoglycosides are another class of antibiotics that are widely used across the world. Microbes also developed resistance for this

class of drugs, by the synthesis of enzymes that modify the structure of aminoglycoside antibiotics [18].

According to a study conducted by Zahra sheriff *et al.*, in Iran, it was found that despite regulations and the guidelines or establishing the National Committee for the rational use of drugs (NCRUD) whose main purpose was to educate people about the rational use and implement new protocols for the therapy with expensive antibiotics in hospitals, the number of antibiotics prescribed still higher than the national and international standards. In addition to this, the irrationality in the prescription of antibiotics by physicians is high, and antibiotics are available in pharmacies without prescription although they are not considered as over-the-counter medication. The lack of adequate knowledge among the Iranian public about the antibiotic rationality and the lower compliance to treatment with antibiotics are the reasons for the increase in antimicrobial resistance [19].

According to a study conducted in China, the rate at which antibiotics were prescribed to outpatients from primary care hospitals was 52.9% between 2009 and 2011 and in those prescriptions, 60.6% of the antibiotics prescribed were considered inappropriate, but these numbers changed gradually due to increased health care management. However, in secondary health care systems, the rate of antibiotic prescription for outpatients decreased from 16.2% to 7.7% from 2011 to 2017. In developing countries such as India, Malaysia, South Korea, the prescription of antimicrobial agents in primary health care hospitals, particularly in rural areas is high, which about 50%. These numbers are relatively lower in developed countries. The rate at which antibiotics were prescribed for different diseases also varies for different countries. For acute respiratory tract infections, it was approximately 14.7% in the United States whereas, the number was approximately 33% in the United Kingdom. Studies have revealed that in many countries, one of the main reasons for antibiotic irrationality is the lack of the knowledge and expertise [20].

Findings by McCullough *et al.* revealed that most of the people believe that unnecessary or excessive use of antibiotics and not adhering to antibiotic therapy were the factors responsible for the increased resistance against antibiotics in bacteria, and when asked about minimizing strategies 84% of the patients preferred to contact clinicians and 75% think that it is better to minimize the use of antibiotics. Data also reveal that people have partial knowledge and a high misconception about antibiotic resistance [21].

After exposure to antibiotics, many bacterial species have evolved into multiple drug resistant forms (MDR). Bacteria that have amplified morbidity and mortality rate are called "superbugs" and undergo various mutations that help them to be resistant against the antibiotics that are used as therapy against these organisms. Due to this reason, the treatment options for these superbugs are reduced and limited, eventually increase the cost of therapy and length of hospital stay [21].

In the African country of Cameroon, resistance to antibiotics is commonly seen and reported. According to the data, the prescription and therapy with antibiotics

is suboptimal in the resistance country and the rate is 55% to amoxicillin, whereas for Cotrimaxazole it is more than 65%. Studies in the country also revealed that 87% of the population do not know that antibiotics are ineffective against all microbes and 43.7% of the participants think that bacteria can be killed by antibiotics. Furthermore, 11.8% of them believe that antibiotics can be effective against viruses infections. It was also revealed that people believe that antibiotics can potentially be used as therapy in the place of antipyretics, antitussives, and painkillers [22]. Lack of proper knowledge about antibiotic use is the only possible explanation for the irrationality in antibiotic use and the reason for the appearance of serious adverse reactions due to their abuse. People believe that self-medication can reduce the cost of therapy for minor ailments and also reduce the pressure on healthcare providers. But open access to drugs such as antibiotics can make the patient believe that every disease has a potential pharmacological therapy that can lead to drug abuse, and increased adverse drug events that eventually lead to the development of resistance against antibiotics all over the world [23].

5. Self-Medication: A Multifaceted Challenge

Self-medication of antibiotics is widely practiced in both developed and developing countries and it is seen mainly where they can be easily accessed without prescription [24]. Most of the patients, regardless of their diseases will be expecting antibiotics in their prescription. They always think that antibiotics are required to treat any type of infection and demand antibiotics in their drug regimen. Indiscriminate self-medication may also be a factor for bacterial resistance [25]. The use of broad-spectrum antibiotics to minute bacterial infections and for viral infections can enhance the chance for resistance in bacteria. Antibiotic therapy to a patient generally depends on the sensitivity of the microbes, especially when there is no effect of treatment on the microbes. Antibiotics are given as prophylaxis to any type of infection, but after determining the causative bacteria, therapy should be according to the guidelines and an antibiotic that is suitable for treating the infection should be prescribed. In some conditions such as severe infections, we can see combination therapy with antibiotics, but this should be done according to the guidelines and also we should consider antibiotic characteristics and spectrum for prescribing combinational therapy of antibiotics [26].

5.1. The Drivers of Self-Medication

One driver of self-medication is patient demand [27]. Many patients expect and even demand antibiotics as part of their treatment, regardless of whether they are necessary for their condition. This expectation stems from a common misconception that antibiotics are required to treat any type of infection, even minor ones or those caused by viruses.

Pharmaceutical marketing activities also contribute to the problem. With antibiotics being one of the most commonly prescribed drugs, pharmaceutical companies actively promote their use, sometimes even encouraging physicians to

prescribe them for conditions where they are not necessary. They may also use community pharmacists to promote their products, further increasing the self-medication of antibiotics by patients.

Hospital settings can also be a driver of antibiotic self-medication. In some cases, doctors may prescribe antibiotics based on hospital inventory or due to a fear of losing patients if they don't provide them. Additionally, some hospitals have guidelines that promote antibiotic use regardless of whether they are clinically necessary [28].

The easy availability of antibiotics in many countries without a prescription further facilitates self-medication. This, coupled with misconceptions about the need for antibiotics and cultural norms that view them as a cure-all, leads to their pervasive and often inappropriate use.

5.2. Consequences of Irrational Antibiotic Use

Irrational prescription may be due to several factors such as the use of drugs which are not related to diseases, inappropriate dose, and inappropriate direction of use. Purchase of antibiotics from the pharmacy without prescription can also be a reason for antibiotic resistance. The study by Shiva Hashemi *et al.* reveals that, in Iran prescription of antibiotics was not justified in 49.7% of the cases and this country is one of the highest consumers of antibiotics in the world [29].

The prescription of antibiotics, even for minor infections, can lead to the development of resistance in bacteria. For instance, beta-lactam antibiotics like penicillin are the oldest antibiotics known and because of their overuse and abuse, became ineffective due to the development of resistance against them. Microbes adapt several mechanisms to develop resistance to antimicrobial agents, such as causing beta-lactam ring hydrolysis using the beta-lactamase enzyme. Antibiotic-resistant bacterial infection can increase mortality and also hospital stay. It also causes failure of therapy in half of the patient population, leading to the development of antibiotics with new combinations and doses which is not good for the patient population [30].

Today, people seek antibiotics as a therapy for the majority of diseases and expect them on prescription even for minor ailments. Some do not even consult with the physician before using antimicrobial agents. After symptoms disappear, many people stop taking medications. Some of them do not have compliance to therapy and some others do not have any idea for what purpose antibiotics were prescribed, but they use them anyway. Most people adhere to the therapy suggested by the physician, but few others take antibiotics without guidance, which is the major cause of resistance development. Irony is that some people are well aware of antibiotic resistance and still do not adhere to prescription and use antibiotics on their own, increasing the chance for antibiotic resistance [31].

"Antibiotic golden age" is the period when antibiotics were identified and all bacteria infections were curable by antibiotics. It was started in 1941 by the discovery of penicillin to the Nalidixic acid in 1962. After this period, only a few

antibiotics were developed in clinical practice. As a result of resistance before the recovery of the cost of new drug development, pharmaceutical companies decreased their investment in the development of new antibiotics. The use irrationally caused the global spread of a resistant bacterial population [32].

Infectious diseases that were easily curable in the past (such as malaria, TB, pneumonia, and gonorrhea) became fatal, risking the life of millions due to the increased antimicrobial resistance. A cautionary letter written by W.H.O. in 2014 indicated that the entire world was entering a post-antibiotic era, in which easily curable minor infections can once again becomes fatal [33]. Across the globe, deaths from MRSA (Methicillin-Resistant Staphylococcus aureus) are higher than many other diseases. MRSA is becoming Multidrug Resistant (MDR) in many Asian countries. In the USA before the discovery of penicillin, 30% of the deaths are due to pneumonia, tuberculosis, and gastroenteritis and due to the development of antimicrobial resistance these diseases are reemerging with serious outcomes [33]. Studies in Pakistan revealed that antimicrobial self-treatment was primarily taken for cold, cough, diarrhea, fever, and sore throats. In a country like Malaysia, urinary tract infections caused by E. coli were treated with ampicillin. Erythromycin was used to treat pneumonia induced by Streptococcus pneumoniae. However, it was revealed that these drugs are ineffective against half of Escherichia Coli-caused infections and 25% of the Streptococcus infections.

This number increased to 35.7% for erythromycin resistant streptococcus pneumoniae and for Vancomycin resistant Enterococcus faecium, it is up to 9.3%. The main reason for the increase in antibiotic resistance is the irrationality in the pattern of antibiotics which made common infections much more difficult to treat and also increased the cost of antibiotic therapy [34]. For patients who were infected with antibiotic resistant bacteria, the cost of therapy ranges from 6000 - 30,000 USD, which is higher than the therapy for antibiotic-susceptible organisms. Based on the study from the United States, 2,000,000 patients were infected with resistant microbes, leading to 23,000 deaths, and an increased cost of therapy up to USD 55 - 70 billion per year. In Saudi Arabia, 78.7% of patients consume antibiotics without prescription from the physician [13]. Antibiotics that are effective against Gram negative bacteria are less because they develop resistance rapidly compared to gram positive bacteria, and in the last 20 years, the therapeutic cover given by drug development programs was inadequate [35].

5.3. Prevalence of Irrational Prescribing in Children

The World Health Organization revealed that more than three million neonatal deaths occur annually across the globe in the early neonatal period. In a study conducted for the prescribing practice among children in Pakistan, among antibiotics prescribed in public hospitals, 64.7% to neonates, 64.4% to infants, and 60.2% for children in the PICU/NCU were irrational. In private hospitals, the numbers were 44.1% to children, 42.7% to newborns, and 38% to infants. The therapeutic indication for antibiotic prescription was also not appropriate. In

public hospitals, 63% of the children admitted in the ICU received unnecessary antibiotic therapy, whereas in private hospitals 40% of the children received inappropriate antibiotic therapy.

From these data, it is evident that irrational antibiotic prescription is more prevalent in public hospitals than in private hospitals across the country [36]. Annually, more than nine million children under five years of age are dying due to common diseases like pneumonia, diarrhea, and so on. Most of them can be effectively cured with the help of antimicrobial agents. However, irrationality in antibiotic use can lead to resistance development and the drugs can become ineffective against these common pathogens [37].

Overuse or incorrect usage of Antibiotics can increase the chances for microbes to acquire resistance, and gradually the drug become ineffective. Therefore, they should be used rationally. Irrational antibiotic use is particularly concerning in pediatric populations, where it can lead to the development of resistance early in life. Studies have shown high rates of inappropriate antibiotic prescriptions in children hospitalized for common infections [38]. In many countries, pediatrics constitutes the majority of the population. In these populations, the respiratory tract and gastrointestinal tract are more susceptible to repeated infections.

In children less than five years of age, the main causes of death are lower respiratory tract infections. If an antibiotic is found to be effective in one patient, then the patient believes that it might be effective against the same disease condition in another patient without proper prescription from the physician, which is a myth. All these factors can lead to the development of resistance in bacteria [39]. Antibiotics were prescribed in children who were hospitalized for normal infections such as sore throat and common flu which were caused by the virus, and they have no therapeutic effect on the virus, but may assist in the development of bacterial resistance. Refilling and sharing of drugs without proper guidelines is also common in developing countries [40].

5.4. Why the Challenge Exists

More than 2.8 million infections that are resistant to antibiotics were reported annually in the United States, according to reports from "Center for Disease Control and Prevention". More than 33,000 deaths per year in Europe and 35,000 deaths in the US are occurring due to these antibiotic resistant infections. By 2050 the annual death rate is 10 million globally out of which more than four million occur in the African continent. The development of antibiotic resistance is a common event that occurs due to the pressure caused by the antibiotic that leads to the development of bacterial strains that can be able to resist the antibiotic action, but increased irrationality in antibiotic usage enhanced the resistance process. According to reports from the World Health Organization, the pharmaceutical industries influence physicians regarding the prescription information and do not educate patients regarding the antibiotic activity [21].

Concentrations of antibiotics in the sub inhibitory and subtherapeutic range

initiates development of resistance in bacteria against antibiotics by alterations in genes such as changes in gene expression, mutagenesis, and HGT. Increased mutagenesis and HGT can promote alteration in antibiotic resistance and its spread. In 30% to 50% of cases, the antibiotics used, therapy indication and treatment duration of antibiotic therapy treatment are inappropriate. Sub-inhibitory concentrations of Piperacillin and/or Tazobactam can induce broad proteomic changes in Bacteroides fragilis [41].

The incorrect prescribing of antibiotics can cause patients to be exposed to antibiotic therapy. Penicillin was the first antibiotic and it was successful in treating severe infections in the 1940s and also in reducing bacterial infections within soldiers of World War II. Due to the development of resistance, various beta-lactam antibiotics were discovered in the 1950s. Regrettably, bacteria had developed resistance to most antibiotics discovered so far over the course of time. **Table 1** shows the timeline of antibiotic development over the years and the year in which resistance was developed against the antibiotic by the microbe [42].

Table 1. Timeline of antibiotic development.

Year of Antibiotic Discovery	Year of Resistance Identified
1943 Penicillin	1940 Penicillin-R Staphylococcus
1950 Tetracycline	1959 Tetracycline-R Shigella
1953 Erythromycin	1962 Methicillin-R Staphylococcus
1960 Methicillin	1965 Penicillin-R pneumococcus
1967 Gentamycin	1968 Erythromycin-R Streptococcus
1972 Vancomycin	1979 Gentamicin-R Enterococcus
1985 Imepenam and Ceftazidime	1987 Ceftazidime-R Enterobacteriaceae
1996 Levofloxacin	1988 Vancomycin-R Enterococcus
2000 Linezolid	1996 Levofloxacin-R pneumococcus
2003 Daptomycin	1998 Imipenem-R Enterobacteriaceae
2010 Ceftaroline	2000 XDR tuberculosis
	2001 Linezolid-R Staphylococcus
	2002 Vancomycin-R Staphylococcus
	2009 PDR- Enterobacteriaceae
	2011 Ceftaroline-R Staphylococcus

R—Resistant; **XDR**—Extensively drug resistant; **PDR**—Pan drug resistant; Adapted from the Centers for Disease Control and Prevention.

Bacteria possess an arsenal of strategies to combat antibiotics, and a deeper dive into these mechanisms can shed light on the complexities of resistance. One critical mechanism is the employment of efflux pumps, which are protein structures embedded in the bacterial cell membrane. These pumps act as molecular gatekeepers, actively expelling antibiotics from the bacterial cell, preventing them from reaching their intended targets and rendering them ineffective. Another key

tactic is target modification. Bacteria can alter the target site of the antibiotic, making it difficult for the drug to bind and exert its action. This can involve mutations in the genes encoding the target proteins or enzymatic modifications of the targets themselves. These mechanisms, along with others, contribute to the growing challenge of antibiotic resistance.

Six organisms called ESKAPE (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aureginosa, and Enterobacter species) are identified as the supreme challenge by the Infectious Disease Society of America. The prescription of high-potent antibiotics for the patient with minor infections is also one of the reasons for developing antibiotic resistance. New and more potent antimicrobials are usually kept as a reserve for diseased patients who do not have a proper response to the basic conventional antibiotics.

Bacteria possess an arsenal of strategies to combat antibiotics, and a deeper dive into these mechanisms can shed light on the complexities of resistance. One critical mechanism is the employment of efflux pumps, which are protein structures embedded in the bacterial cell membrane. These pumps act as molecular gatekeepers, actively expelling antibiotics from the bacterial cell, preventing them from reaching their intended targets and rendering them ineffective. Another key tactic is target modification. Bacteria can alter the target site of the antibiotic, making it difficult for the drug to bind and exert its action. This can involve mutations in the genes encoding the target proteins or enzymatic modifications of the targets themselves. These mechanisms, along with others, contribute to the growing challenge of antibiotic resistance.

5.5. Addressing the Challenge

According to the CDC, 30% of antibiotics prescribed in outpatient settings in the US are unnecessary [43]. To combat the growing threat of antibiotic resistance, a multifaceted approach is needed to address self-medication and promote responsible antibiotic use. This includes:

- Raising awareness about the risks of antibiotic misuse, the importance of completing prescribed courses, and when antibiotics are not necessary.
- Strengthening regulations to restrict over-the-counter access to antibiotics and enforcing prescription requirements.
- Educating healthcare providers about rational prescribing practices and providing them with the tools and resources to promote responsible antibiotic use.
- Empowering pharmacists to provide guidance on antibiotic use, enforce prescription requirements, and educate patients about responsible use.

The CDC launched a program called "Get Smart; know when antibiotics work" in 2003 to minimize the improper use of antibiotics [44]. The World Health Organization also implemented a 5-year strategic framework in 2015 for its worldwide efforts against antimicrobial resistance [45].

6. Collaborative Approach to Antibiotic Stewardship

Combating antibiotic misuse and promoting rational use requires a collaborative approach involving various healthcare professionals. Pharmacists play a critical role in educating patients about antibiotics, ensuring proper dispensing, and monitoring for potential adverse drug reactions. Nurses contribute by educating patients about their treatment, monitoring for signs and symptoms of infection, and practicing infection control measures. A multidisciplinary approach to antibiotic stewardship can optimize patient outcomes and minimize the emergence of antibiotic resistance.

7. Global Strategies to Combat Antibiotic Resistance

Antibiotic resistance is a global challenge that requires a multifaceted approach. Different countries and regions are implementing various strategies to address this issue. Surveillance programs track resistance patterns, providing valuable data for guiding treatment decisions and public health interventions. Regulatory changes, such as restricting the over-the-counter sale of antibiotics, aim to curb antibiotic misuse. Public education campaigns raise awareness about the importance of responsible antibiotic use. International collaboration is crucial for sharing best practices and coordinating efforts to combat antibiotic resistance.

To combat antibiotic resistance, a multifaceted approach is required. Responsible antibiotic use is essential, prescribing antibiotics only when necessary and following guidelines. Infection prevention measures, such as implementing hygiene practices and vaccination programs, are also important. The development of new antibiotics and alternative treatments is crucial. Public education about the proper use of antibiotics and the dangers of misuse is also needed. Finally, regulatory measures must be enforced to control the sale of antibiotics and prevent over-the-counter availability without a prescription.

8. Future Directions: Antibiotic Development and Innovation

The development of new antibiotics is essential for combating the growing threat of antibiotic resistance. However, bringing new antibiotics to market is challenging and costly. Innovative approaches to overcoming resistance are being explored, such as bacteriophage therapy, which utilizes viruses to target bacteria, and antimicrobial peptides, which offer a novel mechanism of action. Continued investment in research and development is crucial for ensuring the availability of effective antibiotics for future generations.

9. Conclusion

The misuse of antibiotics and their self-medication can lead to increased resistance, which is a growing concern worldwide. It is mainly due to irrational prescribing habits of physicians and the lack of knowledge about antibiotics among the public, leading to increased morbidity, mortality, and treatment costs. We must always ensure that patients are given evidence-based medicine. Assessing

public knowledge and approach to antibiotics is essential and educating them about the proper use of antibiotics is necessary. The public should be informed about the importance of antibiotics. Physicians should be mindful of the consequences of irrational prescriptions before prescribing antibiotics to patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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