Review

RESISTANCE OF ANTIBIOTICS: END OF THE ROAD? INDISCRIMINATE AND IRRATIONAL USE OF ANTIBIOTICS - A MAJOR RISKS TOOLS FOR HOST HUMAN

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ABSTRACT

Antibiotics have always been considered one of the wonder discoveries of the 20th century. This is true, but the real wonder is the rise of antibiotic resistance in hospitals, communities, and the environment concomitant with their use. Antibiotic resistance is one of today's most urgent public health problems, threatening to undermine the effectiveness of infectious disease treatment in every country of the world. Major drawback to this practice is development of antibiotic resistance, which has become a major concern and has resulted in a much more restricted use of antibiotics by physicians and hospitals.Specific individual behaviors such as not taking the entire antibiotic regimen and skipping doses contribute to resistance development as does the taking of antibiotics for colds and other illnesses that antibiotics cannot treat.For patient safety, it is also important that not take antibiotics directly from a chemist shop without a proper prescription from doctor and to use all of the antibiotics that are prescribed. If one does not, it is likely that not all bacteria in system will be killed. With more discriminate use of antibiotics, we can keep the numbers of resistant bacteria under control and make sure that antibiotics are an effective tool for generations to come. This review presents the salient aspects too aware the physicians' knowledge and attitudes regarding antibiotic resistance and prescribing practices regarding antibiotic treatment. There is urgent need to develop and strengthen antimicrobial policy, standard treatment guidelines and plan for containment of antimicrobial resistance at community and hospital.

KEY WORDS: Antibiotic resistance, Public health, Patient safety, Antimicrobial policy, Standard treatment guidelines

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1. INTRODUCTION

The sale of antimicrobial drug is a big business. In the United States millions of pounds of antibiotics valued at billions of dollars are produce annually. Approximately 40 to 50% of these antibiotics are livestock feed. When an antibiotic were first identified, they were called wonder drugs, and doctors and patient alike consider them appropriate for just about everything. Antibiotics have always been considered one of the wonder discoveries of the 20th century. This is true, but the real wonder is the rise of antibiotic resistance in hospitals, communities, and the environment concomitant with their use [1]. There were few antibiotic resistant bacteria before antibiotics existed and widespread and unnecessary use of antibiotics has caused more bacteria to become resistant, a process called evolutionary pressure [2].Antibiotic resistance is one of today's most urgent public health problems, threatening to undermine the effectiveness of infectious disease treatment in every country of the world [3, 4]. Although combating antibiotic resistance is a war that must be waged on one front by biological scientists, social scientists also have a key role to play because of the behavioral aspects of the problem (e.g. not taking an entire prescribed regimen, skipping doses and taking antibiotics for viral illnesses).

The emergence of antibiotic resistance as a global problem underscores the need for physicians to be aware of its existence and the factors that drive its development. Relative resistance refers to the gradual increase in the minimal inhibitory concentration (MIC90) occurring in susceptible organisms [5]. Absolute resistance occurs when a previously sensitive organism no longer responds to an antibiotic, independent of dose. Acquired absolute resistance to antibiotics is the most common and serious resistance problem seen clinically [6]. Resistance develops through multiple mechanisms. Bacteria can undergo genetic changes, resulting in the production of enzymes that inactivate or destroy the antibiotic, alteration of the antibiotic target site, or prevention of antibiotic access to the target site [7, 8]. Development of resistance may also be influenced by antibiotic usage which selects for resistant sub populations. In some cases, antibiotics actually induce the production of enzymes that cause resistance [9].

The misuse of antibiotics fosters the increase and spread of antibiotic resistance, and may lead to super infections [10]. The spread of drug-resistant pathogens is one of the most serious threats to the successful treatment of microbial disease. Resistance may be due to a pre-existing factor in the microorganism, or it may be due to some acquired factors [11].Because of the massive quantities of antibiotics being prepared and used, an increasing number of disease are resisting treatment due to the spread of drug resistance.

A good example is *Neisseria gonorrhoeae*, the causative agent of gonorrhoeae. Gonorrhoeae was first treated successfully with sulphonamides in 1936, but by 1942 most strains were resistance and physicians turned to penicillin [10]. Within a 16 years Penicillin resistance, for example may result from the production of penicillinase by resistance organism, which convert penicillin in to inactive penicilloic acid.

Haemophilus influenza type b is responsible for many cases of childhood pneumonia and middle ear infections, as well as respiratory infections and meningitis. It is now becoming increasingly resistant to tetracyclines, ampicillin and chloramphenicol. The same condition is occurring for *Streptococcus pneumonia*.

In 1946 almost all strains of *Staphylococcus* were penicillin sensitive. Today most hospital strains are resistance to penicillin G, and some are now resistance to methicillin and or gentamicin and only can be treated with vancomycin. Methicillin-resistant *Staphylococcus aureus* (MRSA) was first detected in Britain in 1961and now is quite common in hospitals. Increased rates of MRSA infections are seen when using glycopeptides, cephalosporins, and quinolones [12, 13].Half of all *S. aureus* infections in the US are resistant to penicillin, methicillin, tetracycline and erythromycin.

Recently a few cases of vancomycin-resistant *Staphylococcus aureus* have been reported in the Japan in 1996. The first documented strain with complete resistance to vancomycin, termed vancomycin-resistant *Staphylococcus aureus* (VRSA) appeared in the United States in 2002 [14]. However in 2011, a variant of vancomycin has been tested that binds to the lactate variation and also binds well to the original target, thus reinstating potent antimicrobial activity [15].

A new class of antibiotics, oxazolidinones, became available in the 1990s, and the first commercially available oxazolidinone, linezolid, is comparable to vancomycin in effectiveness against MRSA. Linezolid-resistance in *S. aureus* was reported in 2001 [16].Some strains of *Enterococcus* have become resistant to most antibiotics; including vancomycin. At present these strains are only intermediately resistant to vancomycin. If full vancomycin resistant develops and spreads, *S. aureus*may become untreatable.

Geographically dispersed out breaks of *Clostridium difficile* strains resistant to fluoroquinolones antibiotics such as ciprofloxacin and levofloxacin, were also reported in North America in 2005 [17].Cephalosporin, and particularly quinolones and clindamycin are more likely to produce colonisation with *Clostridium difficile* [18].*Clostridium difficile* is a nosocomial pathogen that causes diarrheal disease in hospitals worldwide.

It has been observed that areas within hospitals that have the highest resistance rates also have the high estrates of antibiotic use. Previous studies evaluating physicians have shown both deficient knowledge of the magnitude and causes of resistance, as well as poor correlation between knowledge and practices [19–22]. Increasing bacterial resistance correlates with the volume of antibiotic prescribed, and not lack of compliance with taking antibiotics [23].Inappropriate prescribing of antibiotics has been attributed to a number of causes, including people insisting on antibiotics, physicians prescribing them as they feel they do not have time to explain why they are not necessary, and physicians not knowing when to prescribe antibiotics or being overly cautious for medical and/or legal reasons [24]. For example, a third of people believe that antibiotics are effective for the common cold [25] and the common cold is the most common reason antibiotics are prescribed even though antibiotics are useless against viruses. A single regimen of antibiotics even in compliant individuals leads to a greater risk of resistant organisms to that antibiotic in the person for a month to possibly a year [26].

The objective of this study was too aware the physicians' knowledge and attitudes regarding antibiotic resistance and current antibiotic prescribing practices at the national and international level. The information gained can be used in designing more effective antibiotic control interventions and educational programs.

2. Superbug and Super Resistance

Many of the bacterial pathogens associated with epidemics of human disease have evolved into multidrug-resistant (MDR) forms subsequent to antibiotic use. For example, MDR *Mycobacterium tuberculosis* is a major pathogen found in both developing and industrialized nations and became the 20th-century version of an old pathogen. Other serious infections include nosocomial (hospital-linked) infections with *Acinetobacterbaumannii*, *Burkholderiacepacia*, *Campylobacter jejuni*, *Citrobacterfreundii*, *Clostridium difficile*, *Enterobacter* spp., *Enterococcus faecium*, *Enterococcus faecalis*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiellapneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Salmonella* spp., *Serratia* spp., *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Stenotrophomonas maltophilia*, and *Streptococcus pneumoniae*. The term "superbugs" refers to microbes with enhanced morbidity and mortality due to multiple mutations endowing high levels of resistance to the antibiotic classes specifically recommended for their treatment; the therapeutic options for these microbes are reduced, and periods of hospital care are extended and more costly. In some cases, super resistant strains have also acquired increased virulence and enhanced transmissibility. Realistically, antibiotic resistance can be considered a virulence factor.

The most prevalent Gram-negative pathogens, such as *E. coli*, *S. enterica*, and *K.pneumoniae*, cause a variety of diseases in humans and animals, and a strong correlation between antibiotic use in the treatment of these diseases and antibiotic resistance development has been observed over the past half-century. This is especially apparent with the β-lactam class of antibiotics and their related inactivating enzymes, the β-lactamases. At this time, several groups and classes have been identified, comprising up to 1,000 resistance-related β-lactamases. These include novel classes of genes and their mutant radiations [27].

Currently, the most notorious superbug is the Gram-positive organism *S. aureus*whether it is the most serious superbug can be debated, since one wonders to what extent its bad reputation is due to its extensive press coverage. *S. aureus* has a close association with humankind: it is carried as a nasal

commensal in 30% of the population, and its presence has long been linked to common skin infections such as boils. In recent years, this multidrug-resistant pathogen has emerged as the major nosocomial infection [28]. Following the discovery of penicillin, it seemed that *S. aureus* infections were controllable; however, the respite from resistance was short-lived. The landmark discovery and introduction of methicillin (the first designer antiresistance antibiotic) in 1959 were thought to be a sure defence against the penicillinases, but the appearance of methicillin-resistant *S. aureus* (MRSA) within just 3 years led inexorably to other multi antibiotic-resistant variants, and the acronym now denotes multidrug-resistant *S. aureus*. Recently, MRSA has moved outside the hospital and become a major community-acquired (CA) pathogen, with enhanced virulence and transmission characteristics.

Superbugs are omnipresent in the biosphere; their consequences are aggravated enormously in volatile situations such as civil unrest, violence, famine, and natural disasters and, of course, by poor or nonexistent hospital practices. Superbugs are not the only microbial threats, but they are recognized as the most menacing with respect to morbidity and mortality worldwide. In terms of the number of infections and consequences, *Vibrio cholera* should be at the head of the superbug list [29]. While fortunately it is not common in industrialized nations, *V. cholera* is endemic in Asia and South America.

With respect to the global control of endemic and pandemic infectious diseases, a significant problem is the availability of reliable systems for tracking outbreaks of serious infections. Despite the heroic efforts of the World Health Organization, such reporting is nonexistent in many parts of the world. A lack of information concerning the early stages of an epidemic bacterial infection has retarded appropriate remedial action in many cases.

3. Mechanism of Antibiotic Resistance

Many excellent reviews describing the genetics and biochemistry of the origins, evolution, and mechanisms of antibiotic resistance have appeared over the last 60 years. A compilation of the commonly used antibiotics, their mode of action, and resistance mechanism is shown in Table1 [1].The molecular mechanisms of resistance to antibiotics have been studied extensively and have involved investigations of the genetics and biochemistry of many different facets of bacterial cell function [30]. In fact, the study of antibiotic action and resistance has contributed significantly to our knowledge of cell structure and function. Resistance processes are widely distributed in the microbial kingdom and have been well described for a variety of commensals and pathogens; most can be disseminated by one or more distinct gene transfer mechanisms [31]. The ways in which bacteria resist the antibiotics are:

- Destroying the drug: for example, enzymatic deactivation of *penicillin* G in some penicillin-resistant bacteria through the production of β-lactamases. Most commonly, the protective enzymes produced by the bacterial cell will add an acetyl or phosphate group to a specific site on the antibiotic, which will reduce its ability to bind to the bacterial ribosomes and disrupt protein synthesis [32].
- Development of an alternate metabolic pathway which bypasses some reaction that would normally be inhibited by drug: for example, some sulfonamide - resistant bacteria do not require para-aminobenzoic acid (PABA), an important precursor for the synthesis of folic acid and nucleic acids in bacteria inhibited by sulfonamides, instead, like mammalian cells, they turn to using preformed folic acid.
- Target Sites the antibiotic attaches to be altered and less susceptible to the drug: for example, alteration of PBP—the binding target site of penicillins—in MRSA and other penicillin-resistant bacteria. Another protective mechanism found among bacterial species is ribosomal protection proteins. These proteins protect the bacterial cell from antibiotics that target the cell's ribosomes to inhibit protein synthesis. The mechanism involves the binding of the ribosomal protection proteins to the ribosomes of the bacterial cell, which in turn changes its conformational shape. This allows the ribosomes to continue synthesizing proteins essential to the cell while preventing antibiotics from binding to the ribosome to inhibit protein synthesis.
- Reduced drug accumulation: by decreasing drug permeability or increasing active efflux (pumping out) of the drugs across the cell surface [33]. These specialized pumps can be found within the cellular membrane of certain

bacterial species and are used to pump antibiotics out of the cell before they are able to do any damage. These efflux pumps are often activated by a specific substrate associated with an antibiotic [34].

- Over production of the enzyme which is targeted by the drug; Cellular changes that reduce the cell absorbing the drug

4. Origin and Transmission of Drug Resistance

The genes for drug resistance are present on both the bacterial chromosomes and plasmids, small DNA molecules that can exist separate from the chromosome or be integrated in it. These plasmids are called as resistance plasmid. Plasmid resistant genes often code for enzyme that destroy or modify drug; for example the hydrolysis of penicillin or the acetylation of chloramphenicol and aminoglycoside drugs. When a bacterial cell possesses a resistance plasmid, the plasmid may be transferred to other cell through gene exchange process as conjugation, transduction and transformation.

Extensive drug treatment favours the development and spread of antibiotic-resistant strains because the antibiotic destroys normal susceptible bacteria that would usually compete with drug resistant strains. The result may be the emergence ofdrug resistant pathogens leading to a superinfection. Superinfection is a significant problem because of the existence of multiple drug resistant bacteria that produce drug resistant respiratory and urinary tract infections.

The drug can be given in a high concentration to destroy susceptible bacteria and most spontaneous mutants that might arise during treatment. Spontaneous mutations in the bacterial chromosome, although they do not occur very often, will make bacteria drug resistant. Sometimes two different drugs can be administered simultaneously that each drug will prevent the emergence of resistance to the other.

5. Global Trends on antibiotic resistance reveals serious, worldwide threat to public health by World Health Organization (WHO)

Antibiotic resistance, a global concern, is particularly pressing in developing nations, where the burden of infectious disease is high and healthcare spending is low. WHO first global report on antimicrobial resistance, with a focus on antibiotic resistance stated that this serious threat is no longer a prediction for the future [35]. Antibiotic resistance- when bacteria change and antibiotics fail- is happening right now, across the world. Current status by the WHO report, "Antimicrobial resistance: global report on surveillance 2014", notes that antibiotic resistance is occurring across many different infectious agents but the report focuses on antibiotic resistance in seven different bacteria responsible for common, serious diseases such as bloodstream infections (sepsis), diarrhoea, pneumonia, urinary tract infections and gonorrhea (Table 2) [36]. The results are cause for high concern, documenting resistance to antibiotics, especially "last resort" antibiotics, in all regions of the world.

The report is the most comprehensive picture to date, with data provided by 114 countries. Its first to look at antibiotic resistance, globally–reveals that this serious threat is no longer a prediction for the future, it is happening right now in every region of the world and has the potential to affect anyone, of any age, in any country.

Without urgent, coordinated action by many stakeholders, the world is headed for a post-antibiotic era, in which common infections and minor injuries which have been treatable for decades can once again kill[35].Effective antibiotics have been one of the pillars allowing us to live longer, live healthier, and benefit from modern medicine. Unless we take significant actions to improve efforts to prevent infections and also change how we produce, prescribe and use antibiotics, the world will lose more and more of these global public health goods and the implications will be devastating.

5.1 WHO African Region

The report reveals major gaps in tracking of antibiotic resistance in the WHO African Region, with data gathered in a limited number of countries. Significant resistance is reported for several bacteria that are spread in hospitals and communities. This includes significant *Escherichia coli* resistance to third generation cephalosporins and fluoroquinolones–two important and commonly used types of antibacterial medicine. In some parts of the region, as many as 80% of *Staphylococcus aureus* infections are reported to be resistant to methicillin (MRSA), meaning treatment with standard antibiotics does not work.

5.2 WHO Region of the Americas

The Pan American Health Organization, WHO Regional Office for the Americas, coordinates the collection of data on antibiotic resistance from hospitals and laboratories in 21 countries in the Region. The results show high levels of *E. coli* resistance to third generation cephalosporins and fluoroquinolones–two important and commonly used types of antibacterial medicine–in the Americas. Resistance to third generation cephalosporins in *Klebisellaepneumoniae* is also high and widespread. In some settings, as many as 90% of *Staphylococcus aureus* infections are reported to be methicillin-resistant (MRSA).

5.3 WHO Eastern Mediterranean Region

There are high levels of *E. coli* resistance to third generation cephalosporins and fluoroquinolones–two important and commonly used types of antibacterial medicine. Resistance to third generation cephalosporins in *K. pneumoniae* is also high and widespread. In some parts of the Region, more than half of *Staphylococcus aureus* infections are reported to be methicillin-resistant (MRSA).

5.4 WHO European Region

High levels of resistance found to third generation cephalosporins in *K. pneumoniae* throughout the WHO European Region. In some settings, as many as 60% of *Staphylococcus aureus* infections are reported to be methicillin-resistant (MRSA), meaning that treatment with standard antibiotics does not work. The report finds that although most countries in the

European Regionhas well-established national and international systems for tracking antibiotic resistance, countries in other parts of the Region urgently need to strengthen or establish such systems. WHO Regional Office for Europe and its partners are supporting these countries through the newly-established Central Asian and Eastern European Surveillance of Antimicrobial Resistance network (CAESAR). The aim of CAESAR is to set up a network of national systems to monitor antibiotic resistance in all countries of the WHO European Region for standardized data collection so that information is comparable.

5.5 WHO South-East Asia Region

The available data reveal that antibiotic resistance is a burgeoning problem in WHO South-East Asia Region, which is home to a quarter of the world's population. The report results show high levels of *E. coli* resistance to third generation cephalosporins and fluoroquinolones—two important and commonly used types of antibacterial medicine–in the Region. Resistance to third generation cephalosporins in *K. pneumoniae* is also high and widespread. In some parts of the Region, more than one quarter of *Staphylococcus aureus* infections are reported to be methicillin-resistant (MRSA).

5.6 WHO Western Pacific Region

Collaboration on tracking of antibiotic resistance between countries in the WHO Western Pacific Region was established in the 1980s, but suffered setbacks following a series of emergencies in the early 2000s. Recently, WHO Regional Office for the Western Pacific has taken steps to revive the regional collaboration. The report reveals high levels of *E. coli* resistance to fluoroquinolones–an important and commonly used type of antibacterial medicine–in the Region. Resistance to third generation cephalosporins in *K. pneumoniae* is also widespread. In some parts of the Region, as many as 80% of *Staphylococcus aureus* infections are reported to be methicillin-resistant (MRSA), meaning that treatment with standard antibiotics does not work.

5.7 Current Situation in India

The bacterial disease burden in India is among the highest in the world; consequently, antibiotics will play a critical role in limiting morbidity and mortality in the country [37]. As a marker of disease burden, pneumonia causes an estimated 410,000 deaths in India each year, and it is the number-one killer of children [38]. Many of these deaths occur because patients do not have access to life-saving antibiotics when and where these are needed. Although drug resistance is primarily a medical problem, the factors that influence the spread of resistance are ecological, epidemiological, cultural, social, and economic. Patients, physicians, veterinarians, and healthcare facilities and retailers - from large pharmacies to local drug sellers - have little motivation (economic or otherwise) to acknowledge the consequences of their use of antibiotics on others, especially on future generations.

Table 3 Shows the antibiotic resistance rates of various organisms in India [39, 40]. Multi-resistant enterobacteriaceae due to the production of extended spectrum β-lactamases (ESBL) have

become very common in India [41, 42].The issue came to the fore in India when New Delhi metallo-ß-lactamase-1 (NDM-1), first reported in 2009. Briefly, NDM-1 is an enzyme produced by the gene bla_{NDM-1}; it is named for New Delhi because the Swedish patient in whom it was first identified had undergone surgery in a New Delhi hospital [43].

Overprescribing and overuse are seen in all settings: public and private hospitals, clinics and pharmacies. For example, depending on where they live and the type of practitioner they visit, 45 to 80 per cent of patients with symptoms of acute respiratory infections and diarrhoea are likely to receive an antibiotic, even though it will not be effective if they have a viral illness rather than a bacterial one[44].

Why this overuse persists is not so easily determined. The possible reasons, as in other parts of the world, include the following: (*i*) lack of microbiology facilities or unwillingness of patients to undergo tests; (*ii*) some doctors' practice of prescribing antibiotics to any patient with a fever, taking it as a sign of bacterial infection, especially when they are concerned that the patient will not return for follow up; (*iii*) the patient's expectation of being given an antibiotic over-the-counter or a prescription for one at the doctor's office [40, 45]; (*iv*) incentives for pharmacists to make a profit from drug sales [46]; and (*v*) the public's lack of knowledge about the appropriate use of antibiotics [45, 47](Figures.1, 2). All those possible reasons suggest that much of this use could be curtailed without harming health outcomes; in fact, reductions in use could actually improve people's health.

6. DISCUSSION

Antibiotics are synthetic or natural substances used to destroy or prevent the growth of bacteria. These substances have played a significant role in improving public health by helping to reduce the number of deaths from diseases and infections which were previously incurable or fatal. Over the last 30 years, no major new types of antibiotics have been developed and pipeline for development of new antibioticshas been drying up since the 1980s and resistance to antibiotics by microbes is growing. Figure 3shows the sequence of discovery, resistance development for the major classes of antibiotics andshow that these antibiotics are the end of road in the antibiotic era and what shall be future prediction.

Reasons for the widespread use of antibiotics are manifold and include: their increasing global availability over time since the 1950s; their uncontrolled sale in many low or middle income countries, where they can be obtained over the counter without a prescription, potentially resulting in antibiotics being used when not indicated [48]. This may result in emergence of resistance in any remaining bacteria; and Prescribing or obtaining broad-spectrum antibiotics when not indicated: these are more likely to induce resistance than narrow-spectrum antibiotics.

Resistance to the treatment for life-threatening infections caused by common intestinal bacteria, *Klebsiellapneumoniae*–carbapenem antibiotics–has spread to all regions of the world. *K. pneumonia* is a major cause of hospital-acquired infections such as pneumonia, bloodstream infections, infections in newborns and intensive-care unit patients. In some countries, because of resistance, carbapenem antibiotics would not work in more than half of people treated for *K. pneumoniae* infections.

Resistance to one of the most widely used antibacterial medicines for the treatment of urinary tract infections caused by *E. coli*–fluoroquinolones is very widespread. In the 1980s, when these drugs were first introduced, resistance was virtually zero. Today, there are countries in many parts of the world where this treatment is now ineffective in more than half of patients.

Treatment failure to the last resort of treatment for gonorrhoea–third generation cephalosporin–has been confirmed in Austria, Australia, Canada, France, Japan, Norway, Slovenia, South Africa, Sweden and the United Kingdom. An estimated 106 million people are infected with gonorrhoea every year (2008 estimates).

Antibiotic resistance causes people to be sick for longer and increases the risk of death. For example, people with MRSA (methicillin-resistant *Staphylococcus aureus*) are estimated to be 64% more likely to die than people with a non-resistant form of the infection. Resistance also increases the cost of health care with lengthier stays in hospital and more intensive care required.

A second important tier of recommendations involves reducing antibiotic use

by eliminating irrational or inappropriate use. There is no doubt that people benefit from not being treated for what does not ail them. They do not pay for drugs that are not needed, they avoid potential adverse reactions, and they might then be treated for the illness they do have. It has been estimated that over 50% of the antibiotic prescription in hospitals are given without clear evidence of infection or adequate medical indication. Many physicians have administered antibacterial drugs to patients with colds, influenza, viral pneumonia and other viral disease.

A recent study show that over 50% of the patient diagnosed with colds and upper respiratory infections and 66% of those with chest colds (bronchitis) are given antibiotics, even though over 90% of these cases are caused by viruses. However, it is sometimes not possible to tell whether a child is in the early stages of pneumonia or has a common viral cold without laboratory testing, which assumes the availability of not only an experienced doctor but also a microbiology laboratory.

Moreover, older antibiotics are inexpensive and cause relatively few side effects. However, some measures designed to rationalize antibiotic use may come with unintended consequences. For instance, enforcing prescription-only laws and eliminating over-the-counter antibiotic purchases could cut off antibiotic access for some segments of the population, such as the rural poor. As long as this possibility is factored into decisions, ways to mitigate any negative effects can also be brought to bear. But this has not been considered in most cases, either in Asia, Europe or African or in other countries where over-the-counter sales of antibiotics are common.

7. CONCLUSIONS

The importance and value of antibiotics cannot be overestimated; we are totally dependent on them for the treatment of infectious diseases, and they should never be considered mere commodities. Frequently antibiotics are prescribed without culturing and identifying the pathogen or without determining bacterial sensitivity to the drug. This situation is made become worse if the patient compliance is not there. When antibiotic treatment is ended too early, drug-resistant mutants may survive. Drugs are available to the public in many countries; people may practice self-administration of antibiotics and further increase the prevalence of drug-resistant strains. The overuse of antibiotics encourages the bacterial strains that are resistant and thus it becomes harder to treat patients. Now since, doctors are aware of this only prescribe antibiotics when they are sure that illness is caused by bacteria and can be helped by antibiotics.As a patient, one should not expect antibiotics, on every visit to their Doctor. Antibiotics will not affect viral infections such as colds, flu and most sore throats.

People can help tackle resistance by:hand washing, and avoiding close contact with sick people to prevent transmission of bacterial infections and viral infections such as influenza or rotavirus, and using condoms to prevent the transmission of sexually-transmitted infections; getting vaccinated, and keeping vaccinations up to date;using antimicrobial drugs only when they are prescribed by a certified health professional;completing the full treatment course (which in the case of antiviral drugs may require life-long treatment), even if they feel better; never sharing antimicrobial drugs with others or using leftover prescriptions. If one does not, it is likely that not all bacteria in system will be killed. Unfortunately, this is a rampant practice due to lack of effective supervisory mechanism.

There is an urgent need to develop and strengthen antimicrobial policy, standard treatment guidelines and national plan for containment of antimicrobial resistance. **Health workers and pharmacists** can help tackle resistance by: enhancing infection prevention and control in hospitals and clinics; only prescribing and dispensing antibiotics when they are truly needed; prescribing and dispensing the right antimicrobial drugs to treat the illness. **Policymakers** can help tackle resistance by: improving monitoring around the extent and causes of resistance; strengthening infection control and prevention; regulating and promoting appropriate use of medicines; making information widely available on the impact of antimicrobial resistance and how the public and health professionals can play their part; rewarding innovation and development of new treatment options and other tools. **Policy makers, scientists and industry** can help tackle resistance by: fostering innovation and research and development of new vaccines, diagnostics, infection treatment options and other tools. With more discriminate use of antibiotics, we can keep the numbers of resistant bacteria under

control and make sure that antibiotics are an effective tool for generations to come.

Table1: Mode of action and mechanism of resistance in commonly used antibiotics [1]

Antibiotc Class	Examples	Target	Mode of Resistance
β-Lactams	Penicillin (ampicillin), Cephalosporin (cephamycin), Penems (meropenem), Monobactams (aztreonam)	Peptidoglycan biosynthesis	Hydrolysis, efflux, altered target
Lincosamides	Clindamycin	Translation	Nucleotidylation, efflux, altered target
Glycopeptides	Vancomycin, Teicoplanin	Peptidoglycan biosynthesis	Reprogramming peptidoglycan biosynthesis
Aminoglycosides	Gentamicin, Streptomycin, Spectinomycin	Translation	Phosphorylation, acetylation, nucleotidylation, efflux, altered target
Tetracyclines	Minocycline, Tigecycline	Translation	Monooxygenation, efflux, altered target
Macrolides	Erythromycin, Azithromicin	Translation	Hydrolysis, glycosylation, phosphorylation, efflux, altered target
Phenicols	Chloramphenicol	Translation	Acetylation, efflux, altered target
Oxazolidinones	Linezolid	Translation	Efflux, altered target
Lipopeptides	Daptomycin	Cell membrane	Altered target
Quinolones	Ciprofloxacin	DNA replication	Acetylation, efflux, altered target
Streptogramins	Synercid	Translation	C-O lyase (type B streptogramins), acetylation (type A streptogramins), efflux, altered target
Sulfonamides	Sulfamethoxazole	C_1 metabolism	Efflux, altered target
Rifamycins	Rifampin	Transcription	ADP-ribosylation, efflux, altered target
Pyrimidines	Trimethoprim	C_1 metabolism	Efflux, altered target

Table 2: Selected bacteria and resistance combination [36]

Bacteria	**Resistance/decreased susceptibility to:**
Escherichia coli	3rd generations cephalosporins, Fluroquinolones
Klebsiellapneumoniae	3rd generations cephalosporin, Carbapenems
Streptococcus pneumoniae	Penicillin
Staphylococcus aureus	Methicillin (Beta lactam antibiotics) i.e MRSA
Nontyphoidal Salmonella (NTS)	Fluroquinolones
Neisseria gonorrhoeae	3rd generations cephalosporins
Shigella species	Fluroquinolones

Figure1: Prescribing determinants of antibiotics.

Table3: Antibiotic resistance rates of various organisms in India

Microorganisms	Antibiotic	Resistance rate (%)
Acinetobacter	Cefaperazone/Sulbactam	30
	Ciprofloxacilin	36
	Meropenem	6
	Tigecycline	70
Community-associated methicillin *Staphylococcusaureus* (CA-MRSA) strains	Erythromycin	31.32
	Penicillin	92.8
Enterococcal strains	Aminoglycosides	16.67 to 42.86
Klebsiellapneumoniae	Multiple drug resistant and ESBL producer	93.55
Klebsiella spp.	Ampicillin	98.28
	Cephalosporin	>60
	Monobactem	>60
	Piperacillin	>60
	Ticarcillin	98.28
	Tigecycline	61
Metallo-beta-lactamase (MBL) producing bacteria	Ampicillin, Amoxicillin, Cephalexin, Ciprofloxacin, Cotrimaxazole, Erythromycin, Gentamycin	43.3
Neisseria gonorrhoeae	Ciprofloxacin	78
	Penicillin	47
	Tetracycline	51
Pseudomonas aeruginosa	Carbapenem	42.6
Pseudomonas spp.	Ceftazidime	65
	ciprofloxacin	29
	Colistin	8
	Pipercillin-tazobactam	43
Staphylococcus	Oxacillin	72.34
O1 strain of *Vibrio cholera*	Cotrimoxazole	96
	Furazolldone	96
	Nalidixic Acid	0-45
	Tetracycline	2-17

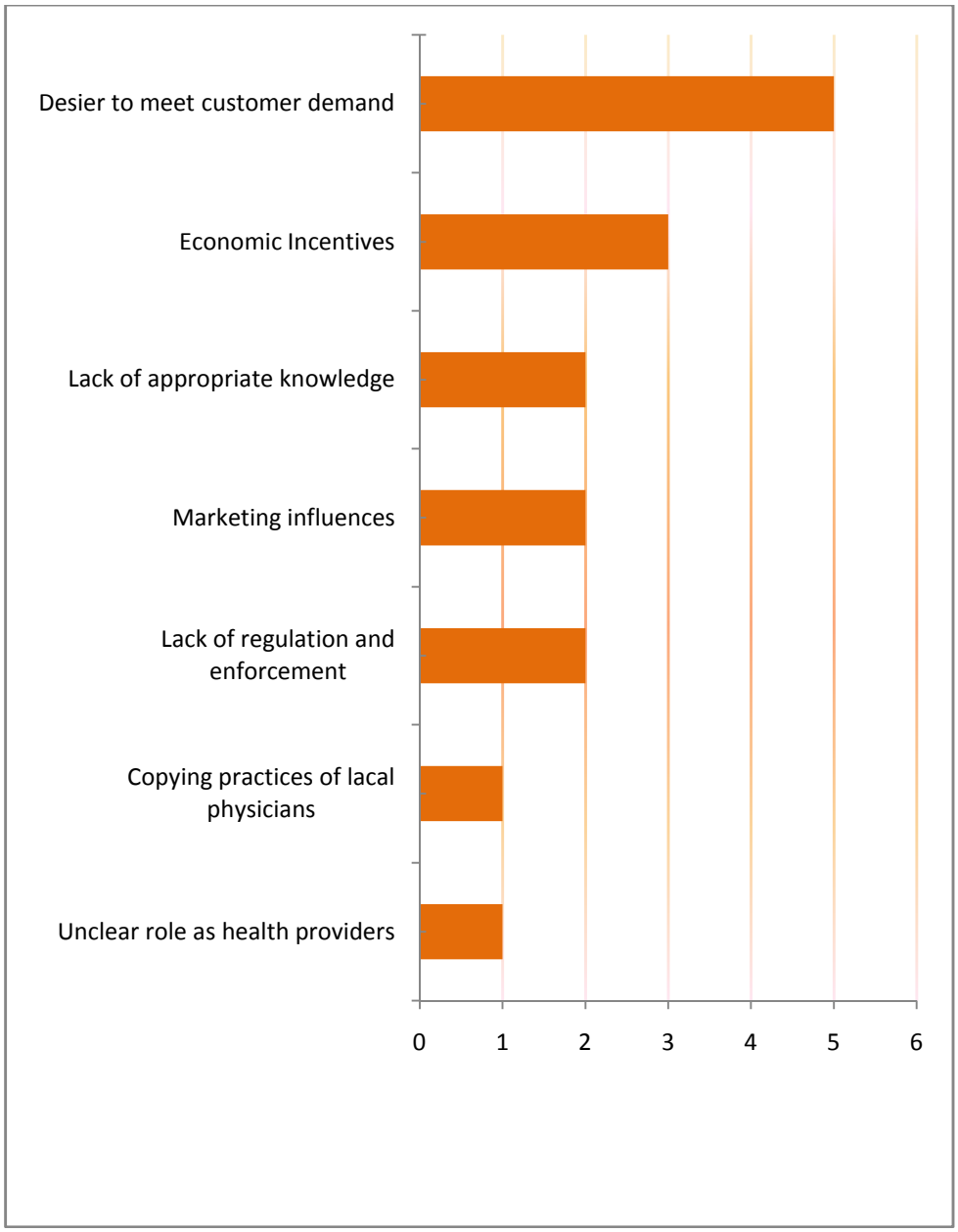

Figure 2: Dispensing determinants of antibiotics.

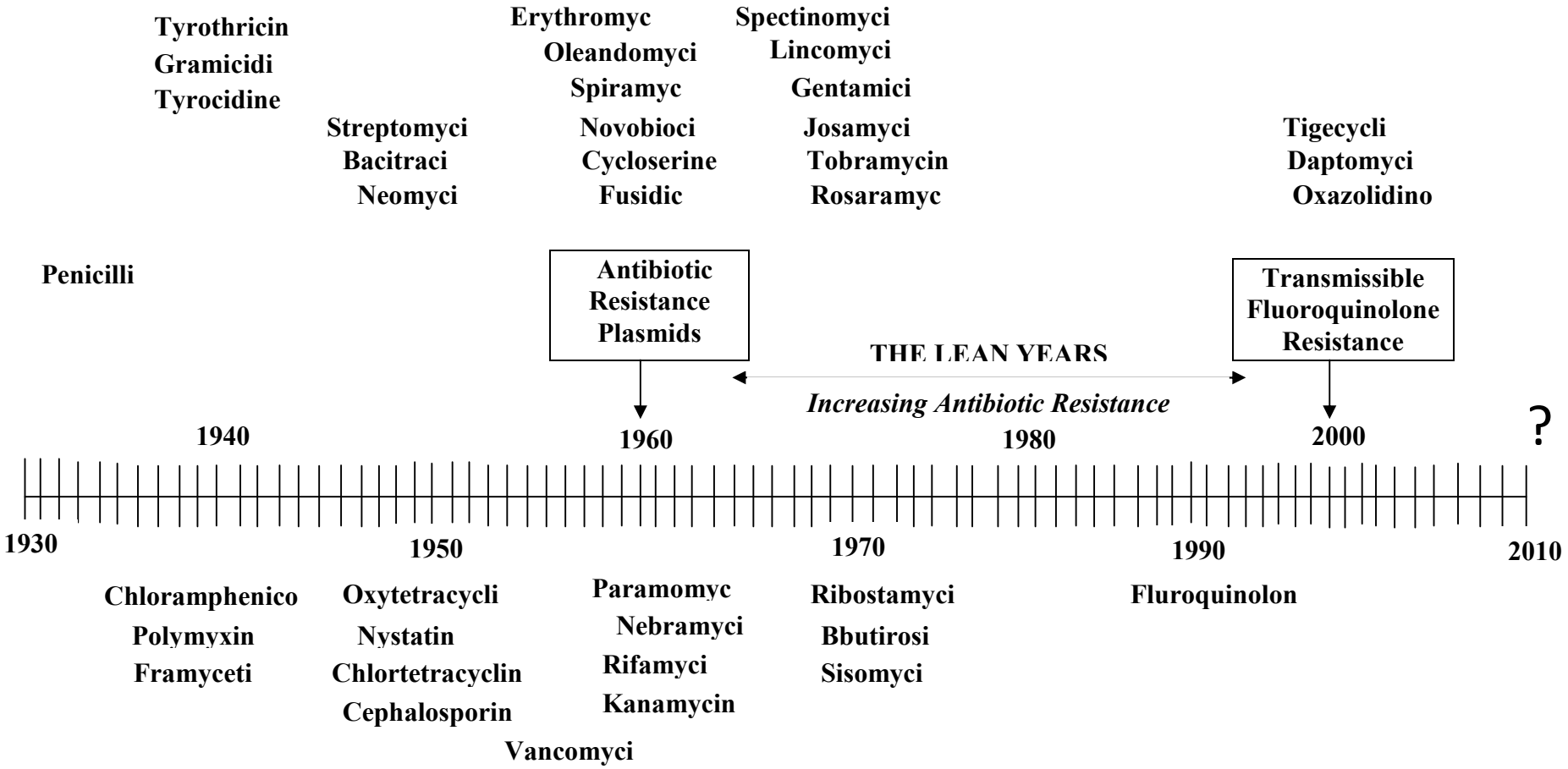

Figure 3: History of antibiotic discovery and development of antibiotic resistance: End of the road?

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