International Journal of Research in Engineering and Science (IJRES)
ISSN (Online): 2320-9364, ISSN (Print): 2320-9356
www.ijres.org Volume 10 Issue 6 ǁ 2022 ǁ PP. 419-426

A Comprehensive Review on Microbial Resistance of Various Antibiotics

Anushka Vijay Thube , Kanchan Khedkar[1]
Student, Department pharmaceutical chemistry, S.M.B.T.College of Pharmacy, Nashik, India

ABSTRACT
Antibiotics are "magic drugs" for fighting microbes. For decades, different types of antibiotics have been used not only for therapeutic purposes but also for prevention in other industries such as agriculture and animal husbandry. Uncertainty arose when the microbes became resistant to common antibiotics while the host was unaware of the emergence of antibiotic resistance. The aim of this study is to examine the origin, development and current status of antibiotic resistance, its regulation and challenges by reviewing the existing literature. We found that antibiotic resistance was increasing at an alarming rate. A growing number of infections such as pneumonia, tuberculosis, and gonorrhoea are becoming increasingly difficult and sometimes impossible to treat, while antibiotics are less effective. Antibiotic-resistant infections are related to the amount of antibiotic use. The illegal use of antibiotics is often responsible for antibiotic resistance. The range of antibiotic treatments for bacterial infections that are resistant to various common or new drugs is limited, resulting in high morbidity and mortality. This article provides an overviewof the optimal use of antibiotics for human and animal health to reduce antibiotic resistance. Evidence from the literature suggests that knowledge about antibiotic resistance is still scarce in the population. Therefore, educating patients and the public is essential to combat antimicrobial resistance.

KEYWORDS: *ANTIBIOTIC RESISTANCE, KNOWLEDGE, RATIONAL USE, MICROBES.*

Date of Submission: 26-05-2022 Date of acceptance: 08-06-2022

I. INTRODUCTION

Antibiotics are cytotoxic or cytostatic to microorganisms and enable the body's natural defenses, such as the immune system, to deactivate them. They often work by inhibiting bacterial cell synthesis, protein synthesis, deoxyribonucleic acid (DNA), RNA or by a membrane-dissolving agent or other specific measures [1]. Antibiotics can also penetrate the bacterial cell wall by binding to it, using energy-dependent transport mechanisms at ribosomal sites and then inhibiting protein synthesis [2]. To fight infections or germs, antibiotics are undoubtedly a gift to human civilization that has saved millions [3]. Various types of antibiotics have been used for therapeutic purposes over time. Antibiotics were known as "amazing medicine" in the middle of the 20th century. At the time, there was optimism that infectious diseases were on the verge of fading away. The beginning of the modern "age of antibiotics" is associated with the names Alexander Fleming and Paul Ehrlich. Antibiotics were thought to be drugs that selectively targeted the microbes responsible for the disease, but at the same time did not affect the host. Fleming was the first to warn of possible penicillin resistance if the duration of treatment was too short [4]. The period from the 1950s to the 1970s was seen as the golden age for the discovery of new classes of antibiotics [5]. Millions of new classes of antibiotics have been manufactured in the past 60 years since their introduction. The increasing demand for antibiotics in many sectors has enabled cheaper drugs to be used illegally. On the other hand, due to the widespread and irresponsible use of antibiotics, it has contributed significantly to the development of resistant strains [6]. In the past, the production of new antibiotics was directly related to the development of resistant strains. However, the prevailing approach to disease control is currently focused on adapting existing antibiotics to combat resistance to pathogens emerging and re-emerging around the world [5]. Antibiotic resistance develops very quickly and is therefore a major problem [7]. As technology advances, more people are now aware of the negative effects of resistance to existing drugs, but few take preventive measures to reduce resistance by not using too many antibiotics [8]. In developing countries, almost all antibiotics are available over-the-counter are a major cause of resistance. Therefore, if antibiotic resistance needs to be reduced, the only way forward is to educate patients and the general public. The current assessment is a way to educate people by showing the acceptable evolution and future of antibiotic resistance and current regulations to reduce the antibiotic resistance crisis.

II. ORIGIN OF ANTIBIOTIC RESISTANCE

Antibiotic resistance has been reported when a drug loses its ability to effectively inhibit bacterial growth. In the presence of therapeutic antibiotic concentrations, bacteria become "resistant" and continue to multiply [9]. If bacteria multiply in the presence of antibiotics, the bacteria are said to be resistant. Antibiotics are usually effective against them, but as the germs become less sensitive or resistant, they need a higher than usual concentration of the same drug to work. The emergence of antibiotic resistance was observed shortly after the introduction of new antimicrobial compounds [10]. Antibiotic resistance can occur as natural selection process in which nature ensures that all bacteria have a low level of resistance

One study confirmed that sulfamethoxazole, trimethoprim (TMP-SMZ), ampicillin and tetracycline, which were common yesterday, no longer play a role in the treatment of non- cholera diarrhoea in Thailand . At the same time, another study in Bangladesh showed the effectiveness of the same drugs in their effective treatment . In the fight against infections, resistances were recorded even before antibiotics were used [13]
. The illegal use of antibiotics leads to resistance to germs. Since the introduction of sulfonamides in 1937, the development of specific mechanisms of resistance has led to their therapeutic application.

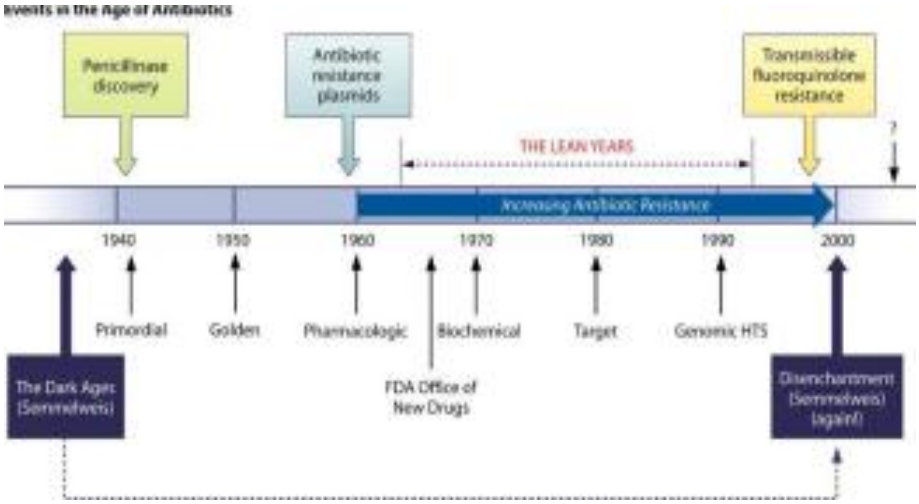

Fig 1: Origin of Antibiotic resistance

In the 1930s, however, resistance to sulfonamides was reported that showed a similar resistance mechanism that is still active more than 80 years later [6]. During six years of aminoglycoside production, aminoglycoside-resistant strains of Staphylococcus aureus were developed [14]. Methicillin was introduced in 1961 and was the first type of penicillinase-resistant semi-synthetic penicillin that was directed against Staphylococcus aureus-producing penicillinase strains. However, resistance to methicillin was reported shortly after onset [15]. Although fluoroquinolones were introduced in the 1980s to treat gram-negative bacterial diseases, it was later shown that these drugs were also used to treat gram-positive infections [16]. Clinical isolates of vancomycin-resistant Staphylococcus aureus (VRSA) were last discovered in 2002, 44 years after the introduction of vancomycin [17]. Antibiotics used inagriculture are often similar or similar to clinically used antibiotics [18], and this overuse can also lead to drug resistance. The food chain can be seen as the main route of transmission of antibiotic-resistant bacteria between animals and humans [19]. In some industrialized countries, animals are given antibiotics with food or water, or through injections, which may be responsible for the development of antimicrobial resistance to this particular antibiotic [18].

For example, the use of antibiotics in animal feed as growth stimulants increases antibiotic resistance [20]. Recent evidence suggests that poultry or pigs could be a potential source of quinolone resistance to E. coli in rural Barcelona, where four children have been identified as carriers of the organism. However, these children were never exposed to quinolones. [21]

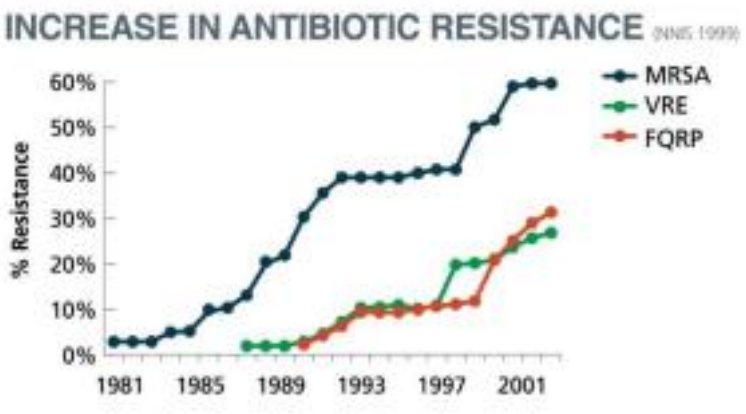

Fig 2 : Dramatic increase of antibiotic resistance between 1981 and 2001

2.2 Intrinsic Resistance

Internal resistance refers to the presence of genes in the bacterial genome that can produce a resistance phenotype, i.e. H. a primary or semi-resistant resistance. Different genera, species, strains, etc. display a wide range of phenotypes of the antibiotic response. Since the turn of the millennium, the availability of genome-level mutagenesis techniques and the rapid sequencing of the bacterial genome have uncovered several potential / inherent genetic functions in bacteria that can lead to drug-resistant phenotypes in the clinical setting. For example, a common genetic approach to improving antibiotic resistance is gene amplification, particularly for resistance to sulfonamides and trimethoprim. These studies provide good evidence of what can happen in the future. The phenotypic analysis of partially or "completely" missing gene libraries by saturated mutations enables bacterial genomes to identify specific mutations that cause hypersensitivity reactions to antibiotics. It is believed that overexpression of the relevant wild-type gene could develop a resistance phenotype. Such predictive studies have been carried out on a range of organisms and have led to the prediction of new classes of resistance. This type of analysis was first performed using a partial mutant library of Acinetobacter baylyi. A more comprehensive review of QE disease. The gene library of the Gypsy mutants identified a total of 140 different isolates that were highly sensitive to a large number of different classes of antibiotics. Studies have been carried out on Pseudomonas aeruginosa. Many of the possible identified "sensitivity genes", such as genetically recessive genes, may not lead to the resistance phenotype. However, these methods identify potential r genes and provide information about the biology of resistance systems. An RNA microarray analysis of the effects of antibiotics provided similar prognostic information. Put simply, an increase in the copy number of antibiotic target genes by titration can lead to a decrease in the intracellular concentration of the inhibitor. Yassin and Mankin used a mutant method to identify potential target sites for ribosomal function inhibitors. RRNA studies have identified a number of RNA fragments tha could be new targets for small-molecule translation inhibitors. Such innovative analyzes show that many potential drug targets have not yet been used for antimicrobial discoveries despite suggestions to the contrary. Reliable predictions of resistance - and appropriate action - will be a valuable approach to extending the life of antibiotics

2.3 The Resistome

It has long been known that antibiotic-resistant bacterial strains can be isolated by covering environmental bacteria in the laboratory on media containing antibiotics. This is not surprising to antibiotic-producing actinomycetes, since most of them have genes that encode resistance to the compounds they produce. In many cases, resistance mechanisms have been identified and demonstrated as specific enzymatic changes in antibiotics. Streptococcal fungi have long been known to produce a variety of beta-lactamases, which may be the source of some clinical forms of beta-lactam resistance [17, 12]. As mentioned earlier, the ecological species Kluyvera was the source of the CTX-M genes. In other cases, the resistance of organisms that produce their products based on flow regimes has been determined. Several mechanisms of resistance, such as those found in the tetracycline product Streptomyces rimosus, are replicated in the production of bacteria. Based on biochemical and genetic similarities, these resistance mechanisms predict mechanisms that would later be found in antibiotic-resistant pathogens. In a new and comprehensive approach to quantifying peripheral phenotype r / density genes, Wright et al. a group of spore-forming actinomycetes (consisting of several known antibiotic-producing strains) for resistance to 21 different antibiotics. Many strains were resistant to an average of 7 or 8 antibiotics. He was a bit resilient by nature. The enumeration of R genes in nature is called resistant environmental antibiotics [17, 15]. Obviously, different environments are expected in terms of the number and type of resistance. The group identified new mechanisms of resistance as well as several mechanisms that are

related to those in pathogens. This is the best evidence of the existence of a wide range of genes in the environment that have the potential to capture and express them as determinants of resistance to overused inhibitors. However, more studies are needed to establish a strong link between the environment and the clinic [30]. Similar studies on other antibiotic-producing bacteria such as Bacillus, Pseudomonas, cyanobacteria, and the extended family of actinomycetes, a genetic group that produce many small molecules, will be of great value to our understanding of nature. From r genes that occur in nature.

2.4 The Subsistome

By screening soil bacteria for biochemical processes that destroy or inactivate antibiotics, Dantas et al. an approach that supplemented the approach of DCosta *et al* [36]. Hundreds of strains were randomly isolated from 11 different urban and rural soils and tested for their ability to live or grow with one or more 18 different antibiotics as the sole source of carbon and nitrogen. Perhaps surprisingly, several strains were isolated that grew effectively on popular antimicrobial agents including aminoglycosides, fluoroquinolones, and other classes. Most of the strains identified in this study were proteobacterial and more than 40% of the strains were Burkholderia spp. Pseudomonas is also shown well. It is clear that the breakdown pathways responsible for the digestion of antibiotics in nature are a rich source of potential resistance factors. Additional studies should reveal new mechanisms of resistance to most classes of antibiotics. Work on antibiotic degrading bacteria was reported in the 1970s, but Dantas et al. was examined.

Metagenomic Analyses of Environmental Samples

Simulation, PCR, and gene expression techniques have been used to identify natural genes in randomly recombinant clones derived from soil and sediment bacterial DNA libraries [3, 29]. One potential problem is that the determination of functional resistance requires epigenetic expression (transcription and translation) of genes that have been cloned into a heterogeneous host. So far only E. coli has been used. Some r genes have been identified, but we are surprised that several genes can be found using a wide range of expression and host systems. The next global sequencing approach by DCosta et al. and Dantas et al. [36] suggests that this number could have been large.

Taken together, these studies confirm the existence of multiple antibiotic genes and potential mechanisms in nature. Many questions remain. The role of these environmental reservoirs in the development of hypothetical clinical resistance and the primary metabolic functions of proto R genes in microbial assemblies are still unknown.

2.5 Metagenomic Analyses of Environmental Samples

Simulation, PCR, and gene expression techniques have been used to identify natural genes in randomly recombinant clones derived from soil and sediment bacterial DNA libraries [3, 29]. One potential problem is that the determination of functional resistance requires epigenetic expression (transcription and translation) of genes that have been cloned into a heterogeneous host. So far only E. coli has been used. Some r genes have been identified, but we are surprised that several genes can be found using a wide range of expression and host systems. The next global sequencing approach by DCosta et al. and Dantas et al. [36] suggests that this number could have been large.

Taken together, these studies confirm the existence of multiple antibiotic genes and potential mechanisms in nature. Many questions remain. The role of these environmental reservoirs in the development of hypothetical clinical resistance and the primary metabolic functions of proto R genes in microbial assemblies are still unknown. We have little or no evidence that any of the potential genes identified in these environmental studies have been mobilized in pathogenic bacteria and expressed as resistant phenotypes. When the concentration of antibiotic compounds in natural environments is essentially undetectable.

III. Resistance Due to Anthropogenic Activities

The dominant role of human activity, unlike the generation of environmental reservoirs, is not antibiotic resistance. Since 1940, an increase in dynamic and clinical antibiotics has been used in the environment and are widely distributed and guaranteed constant pressures and maintain pressure populations in all environments. It is difficult to make detailed statistics on the antimicrobial values produced by the pharmaceutical industry (not in favor of pharmaceutical companies to provide this information), but it can be estimated that many of the millions of antibiotics in the past half are spent on the biosphere have a century since only available data appears that antibiotics produce antibiotics that naturally occur in its main environment. We must assume that commercial production ensures the vast majority of antibiotics in the vital ocean. The numbers of replacement applications of anti-microbial agents are:

(1) Increase in growth / preventive use of animals

(2) The use of human therapy / preventive

(3) Therapeutic / preventive use of water culture
(4) Therapeutic / preventive use of pets
(5) Insect control / reproduction of plants and agriculture
(6) Use dynamic transportation shower delivery and hand care products of household cleaning
(7) Cultural infertility, reproduction and selection in research and industry. It should be noted that the use of human therapy shows less than half of the generated commercial antibiotics.

Due to the wide extensive removal of toxic, minerals, disinfectants, printing processes and vital production, the values of harmful anti-essential criminals cannot be made. The fact is that many chemicals are removed to re-repeat to analyse vehicles. Ciprofloxacin in rivers at more than 50 kg per day by drug manufacturers in Hyderabad, in the centre of India [34], the most terrible stories of the horror due to removal of irresponsible; However, comparable levels of pollution may occur (non-) somewhere elsewhere in the world. Apart from providing a wide range of resistance species in all bacterial generations (this information has not yet been published), physiological damage cannot be overcome by local residents, birds, animals and animals [28.31]. Many types of human activities, including the use of antibiotics in agriculture and aquaculture, non-water antibiotics programs, waste disposal, large environmental reserves, probably full, vacuum genes and objects that other examples And follow genetic studies, genetic studies of sewage treatment plants are shown, they are rich tanks of R genes and resistance objects; Genes are often expanded as jenum islands in plasmids and provide ready resources for resistance collections. Such treated plants, which were created for common welfare, was just bad. The steps to ensure better control over the launch of antibiotics and all users should be immediate and compulsory. Erotic puzzles are found in relation between antibiotics and antibiotics development. Recent studies have shown that the presence of antibiotics and even the integration of resistance coding in Flora, people who are isolated in areas are not provided by modern and non-exhibitions [18, 25.32].

IV. Development of antibiotic resistance

Antibiotics fights bacteria tend to have a natural process that increases resistance. The resistance process occurs through mutations at the gene level. [22]. Antibiotics cause selection pressure and genes interact with selection pressure [20]. Bacteria have the ability to transmit genetic material directly between themselves by transferring plasmids, suggesting that natural selection is not the only mechanism that creates resistance. Broad spectrum antibiotics are prescribed in hospitals as a solution to nosocomial infections. However, it increases resistance [16]. Antibiotics can generally kill most of the bacteria in a colony. However, there may be several colonies of genetically modified bacteria that can lead to resistance [23]. It was found that the rate of antibiotic-resistant infections is closely related to the rate of antibiotic use [24]. Resistance can also arise if consumers do not take all of the prescribed antibiotics. After that, the bacteria remain stable and become stronger against antibiotics [20]. Bacteria can accumulate multiple resistance traits over time and can become resistant to multiple classes of antibiotics [25]. For example, resistance to staphylococci to chromosome mutations, ineffective transfer of aminoglycosides to bacteria and enzyme modifications have been observed [16]. An antibiotic alone cannot resist a particular drug. Resistance can be generated with other structurally related compounds of the same class. For example, tetracycline resistance can develop resistance to oxytetracycline, chlortetracycline, doxycycline, and minocycline [26]. Antibiotics have resistance genes that protect their antimicrobial products, and these genes developed resistance to antibiotics long before antibiotics were used [27]. The various mechanisms of resistance to common drugs are shown in Table 1.

Table 1: Table representing the mechanism of drug resistance of common antibiotics

Antibiotic class	**Example(s)**	**Mode of resistance**
Aminoglycosides	Gentamicin, Streptomycin, Spectinomycin	Phosphorylation, acetylation, nucleotidylation, efflux, altered target
P-Lactams	Penicillins, Cephalosporins, Penems, Monobactams	Hydrolysis, efflux, altered target
Glycopeptides	Vancomycin, Teicoplanin	Reprogramming peptidoglycan biosynthesis
Tetracyclines	Minocycline, Tigecycline	Monooxygenation, efflux, altered target
Macrolides	Erythromycin, azithromycin	Hydrolysis, glycosylation, phosphorylation, efflux, altered target
Lincosamides	Clindamycin	Nucleotidylation, efflux, altered target

Streptogramins	Synercid	Carbon-Oxygen lyase, acetylation, efflux, altered target
Phenicols	Chloramphenicol	Acetylation, efflux, altered target
Sulfonamides	Sulfamethoxazole	Efflux, altered target
Lipopeptides	Daptomycin	Altered target

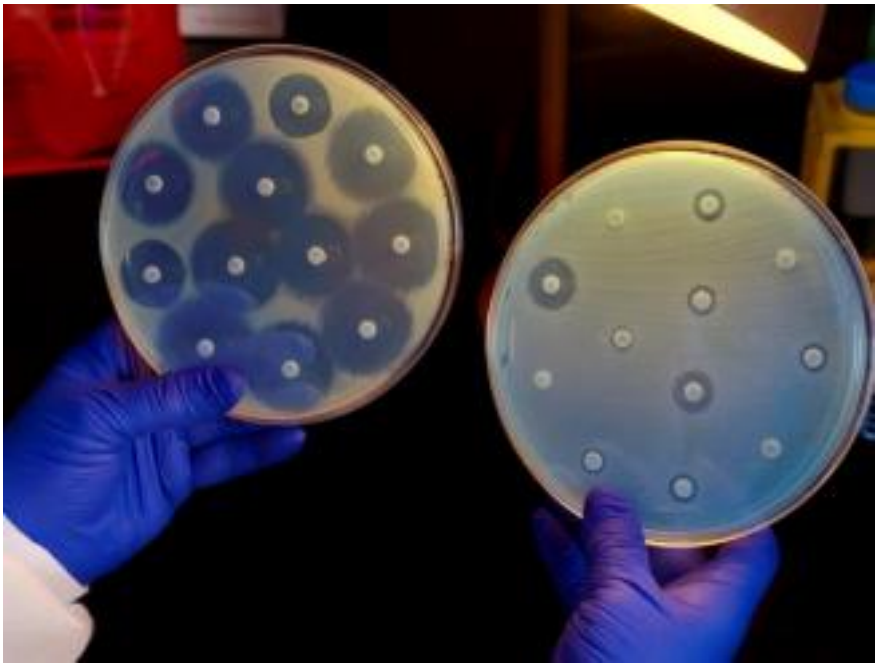

Fig 2: Development of Antibiotic resistance in *E. coli*

V. Consequence of antibiotic resistance

Organisms resistant to antibiotics are known as superbugs. This is not only a problem for laboratories, but it has become a global threat, responsible for the rising number of deaths and life-threatening infections [28]. The effects of this infection intensify in unstable situations such as civil unrest, violence, famine, and natural disasters [29]. The World Health Organization (WHO) [29] warns that the post-antibiotic age is leading to recurrent infections and that minor infections can lead to death if we are not careful about antibiotic resistance. Multi-resistant bacteria cause more deaths worldwide. More than 63,000 patients in the United States die each year from hospital-acquired bacterial infections. An estimated 25,000 patients die each year in Europe from multi-drug resistant bacterial infections (MDR) [31]. Many countries are exposed to Staphylococcus aureus infection in hospitals due to the spread of clonal waves. MRSA is spreading rapidly around the world [16]. The estimated costs of multidrug-resistant bacterial infections can lead to additional healthcare costs and decreased productivity [31]. It is common for most pharmaceutical companies to sell antibiotics that may not be effective or have no regulatory approvals [1]. There are indications that an increased use of antibiotics could lead to a positive correlation with an increased prevalence of resistant microorganisms, while a decrease in the use of antibiotics shows less resistance. There is clear evidence that patients who have been treated with antibiotics in the past are more likely to develop antibiotic resistance [22]. In addition, the repeated administration of antibiotics from the early phase accelerates the resistance mechanisms [32]. Antibiotics stimulate selection pressure for bacterial growth when consumed excessively or irrationally. Individuals and countries are involved in the development of antibiotic resistance [22]. For example, clarithromycin consumption and resistance in Japan quadrupled between 1993 and 2000 compared to other countries [33].

VI. Regulatory issues related to antibiotic resistance

The same international management guidelines for daily antibiotic activity are not yet available. Therefore, the legal guidelines vary from country to country. Some countries have acted quickly to provide guidance, such as the UK, while others have not yet intervened. As with children in developing countries, the World Health Organization recommends the use of antibiotics only for the treatment of acute dysentery and

cholera [34-35]. Since the beginning of the Industrial Revolution, we have dumped more and more organic and mineral toxins into rivers, streams, oceans, land and air. There are insufficient guidelines in the personal care industry to monitor home health products that are likely to be at higher risk of resistance because these products contain high levels of antibacterial agents [22]. Despite the abundance of evidence, there is no room to ignore global antibiotic resistance. Antibiotic resistance can become more common with more antibiotics. The lack of regulation and monitoring of antibiotic use is significant and should be addressed worldwide. Developing countries are more at risk. Developing countries are increasingly burdened by low prices, availability and unnecessary use of antibiotics [1]. The use of antibiotics in countries where there is no public health insurance for their citizens is considered to be relatively uncontrollable [36]. Hence, the irrational use of drugs has become a major problem. According to a survey in the UK, 11.3% of respondents said they did not complete their last antibiotic course as prescribed. When asked why this cycle was not followed, 65% of those questioned said that they felt better or had forgotten an antibiotic in time [37]. We are all affected by this complex public health problem. A cross-sectoral problem that affects not only clinical staff and microbiologists, but service staff, industrial actors, professionals and the general public as well. We need to take action to meet this complex challenge. Social awareness, motivation and commitment in the responsible areas as well as strict rules and regulations should be in the foreground. In addition, in all sectors, we need to take dual action on the proper use of antibiotics, best management practices and behavioral changes to address this public health burden. The use of modern technology can help the patient with the timely use of antibiotics [38]. Currently, the best-known staphylococcus from Staphylococcus aureus is gram-positive [16]. This pathogen causes fear because the antibiotic resistance is greatly increased. Staphylococcus aureus has been associated with humans in the recent past and is sometimes misunderstood [16]. These tendencies lead to high levels of resistance, which leads to immediate risks to human health. In particular, the irrationality observed in the use of antibiotics in cattle. Animals are given antibiotics to help them grow faster and prevent disease. In agriculture, strict regulations are required to limit adverse effects. The treatment of bacterial infections becomes more intense every day. The infection continues with antibiotic resistance. Treatment failure is often due to antibiotic resistance and multiple resistances, such as tuberculosis. Modern and effective antibiotics with no known resistance to bacteria are in great demand. Alternative therapies to combat bacterial infections are being explored. Passive immunization or the administration of non-immunized antibodies has been shown to be effective in preventing bacterial infections [39]. Another effective intervention is phage therapy, while phage's are used to treat pathogenic bacterial infections [40]. There are several new classes of antibiotics for combating antibiotic resistance in the pipeline for clinical trials [41]. Intervention strategies focus not only on goals, but also on biological networks that can help develop new antibacterial therapies [42]. Combination therapies that combine antibiotics with antibiotic-enhancing phage have shown the potential for a promising antimicrobial intervention [4].

VII. CONCLUSIONS

Antibiotic resistance is always high around the world. Despite measures taken by some W.T.O.(World Trade Organization) member states, the use of antibiotics in humans, animals and agriculture is increasing. The high economic burden on the health system has become an immediate problem due to long hospital stays, isolated wards, strict infection control measures and treatment failures. Public health executives must put in place a comprehensive, coordinated national and international monitoring system, continuous analysis and mandatory reporting system for antibiotic resistance. Both local and global guidelines must be traditional and must be followed to prevent excessive and improper use of antibiotics.

REFERENCES

[1]. Levy SB, Marshall B: Antibacterial resistance worldwide: causes, challenges and responses. Nat Med. 2004, 10:122–129. 10.1038/nm1145

[2]. Maranan MC, Moreira B, Boyle-Vavra S, et al.: Antimicrobial resistance in staphylococci: Epidemiology, molecular mechanisms, and clinical relevance. Infect Dis Clin North Am. 1997, 11:813–849. 10.1016/S0891-5520(05)70392-5

[3]. Levy SB: From tragedy the antibiotic age is born . The Antibiotic Paradox. Springer; 1992. 1– 12.

[4]. Aminov RI: A brief history of the antibiotic era: lessons learned and challenges for the future . Front Microbiol. 2010, 1:134. 10.3389/fmicb.2010.00134

[5]. Davies J, Davies D: Origins and evolution of antibiotic resistance. Microbiol Mol Biol Rev. 2010, 74:417–433. 10.1128/MMBR.00016-10

[6]. Chopra R, Alderborn G, Podczeck F, et al.: The influence of pellet shape and surface properties on the drug release from uncoated and coated pellets. Int J Pharm. 2002, 239:171– 178. 10.1016/S0378-5173(02)00104-7

[7]. Levy SB: The challenge of antibiotic resistance. Scientific American. 1998, 278:32–39. 8. Grigoryan L, Burgerhof JG, Haaijer-Ruskamp FM, et al.: Is self-medication with antibiotics in Europe driven by prescribed use?. J Antimicrob Chemother. 2007, 59:152– 156. 10.1093/jac/dkl457

[8]. Overview of Bacteria. (2017). Accessed: June 19: http://www.merckmanuals.com/home/infections/bacterial-infections/overview-of bacteria.

[9]. Levy SB: Antibiotic Resistance: An Ecological Imbalance, in Ciba Foundation Symposium 207 - Antibiotic Resistance: Origins, Evolution, Selection and Spread. Chadwick DJ, Goode J. John Wiley & Sons, Ltd. (ed): Chichester, UK, 2007; 2007. 1:1- 14. 10.1002/9780470515358.ch1

[10]. Hoge CW, Gambel JM, Srijan A, et al.: Trends in antibiotic resistance among diarrheal pathogens isolated in Thailand over 15 years. Clin Infect Dis. 1998, 26:341–345. 10.1086/516303

[11]. Rahman AE, Iqbal A, Hoque DE, et al.: Managing neonatal and early childhood syndromic sepsis in sub-district hospitals in resource poor settings: improvement in quality of care through introduction of a package of interventions in rural Bangladesh. PloS one. 2017, 12:10.1371/journal.pone.0170267

[12]. Abraham EP, Chain E: An enzyme from bacteria able to destroy penicillin. Nature. 1940, 146:837. 10.1038/146837a0

[13]. Gootz TD: Discovery and development of new antimicrobial agents . Clin Microbiol Rev. 1990, 3:13–31. 10.1128/CMR.3.1.13

[14]. Jevons MP: ―Celbenin‖-resistant staphylococci. Br Med J. 1961, 1:124–125. 16. Lowy FD: Antimicrobial resistance: the example of Staphylococcus aureus . J Clin Invest. 2003, 111:1265–1273. 10.1172/JCI18535

[15]. Appelbaum P: The emergence of vancomycin- intermediate and vancomycin- resistant Staphylococcus aureus. Clin Microbiol Infect. 2006, 12:16–23. 10.1111/j.1469- 0691.2006.01344.x

[16]. McEwen SA, Fedorka-Cray PJ: Antimicrobial use and resistance in animals . Clin Infect Dis. 2002, 34:93–106. 10.1086/340246

[17]. Witte W: Medical consequences of antibiotic use in agriculture . Science. 1998, 279:996– 997. 10.1126/science.279.5353.996

[18]. Levy SB: The antimicrobial paradox. How miracle drugs are destroying the miracle . N Engl J Med. York, Plenum Press; 1993. 328:1792. 10.1056/NEJM199306173282418 21. Garau J, Xercavins M, Rodríguez-Carballeira M, et al.: Emergence and dissemination of quinolone-resistant Escherichia coli in the community. Antimicrob Agents Chemother. 1999, 43:2736–2741.

[19]. Laxminarayan R, Brown GM: Economics of antibiotic resistance: A theory of optimal use . J Environ Econ Manage. 2001, 42:183–206. 10.1006/jeem.2000.1156 23. Alanis AJ: Resistance to antibiotics: Are we in the post-antibiotic era? . Arch Med Res. 2005, 36:697–705. 10.1016/j.arcmed.2005.06.009

[20]. Goossens H, Ferech M, Vander Stichele R, et al.: Outpatient antibiotic use in Europe and association with resistance: A cross-national database study. The Lancet. 2005, 365:579– 587.

[21]. Avorn J, Barrett JF, Davey PG, et al.: Antibiotic resistance: Synthesis of recommendations by expert policy. 2001,

[22]. Chopra I, Roberts M: Tetracycline antibiotics: mode of action, applications, molecular biology, and epidemiology of bacterial resistance. Microbiol Mol Biol Rev. 2001, 65:232–260. 10.1128/MMBR.65.2.232-260.2001

[23]. Chadwick D, Goode J: Antibiotic resistance: origins, evolution, selection and spread. John Wiley, Sons; 1997.

[24]. 28. Lipp EK, Huq A, Colwell RR: Effects of global climate on infectious disease: The cholera model . Clin Microbiol Rev . 2002, 15:757–770. 10.1128/CMR.15.4.757- 770.2002

[25]. Fact sheet 2016- Antibiotic resistance. (2017). Accessed: 16 June: http://www.who.int/mediacentre/factsheets/antibiotic-resistance/en/..

[26]. 30. Aminov RI, Mackie RI: Evolution and ecology of antibiotic resistance genes. FEMS Microbiol Lett. 2007, 271:147-161. 10.1111/j.1574-6968.2007.00757.x 31. Freire-Moran L, Aronsson B, Manz C, et al.: Critical shortage of new antibiotics in development against multidrug-resistant bacteria—Time to react is now. Drug Resist Updat. 2011, 14:118–124. 10.1016/j.drup.2011.02.003

[27]. Freire-Moran L, Aronsson B, Manz C, et al.: Critical shortage of new antibiotics in development against multidrug-resistant bacteria—Time to react is now. Drug Resist Updat. 2011, 14:118–124. 10.1016/j.drup.2011.02.003

[28]. Anderson RM, May R: Infectious diseases of humans. Oxford. Publication Google, 1991.

[29]. Perez Aldana L, Kato M, Nakagawa S, et al.: The relationship between consumption of antimicrobial agents and the prevalence of primary Helicobacter pylori resistance. Helicobacter. 2002, 7:306–309. 10.1046/j.1523-5378.2002.00096.x

[30]. WHO: The treatment of diarrhea: a manual for physicians and other senior health workers. . CAH. Geneva; 1995.

[31]. Zaman SB, Hossain N, Yasir Arafat SM, et al.: Management of newborn infection: Knowledge and attitude among health care providers of selected sub-district hospitals in Bangladesh. IJPPH. 2017, 1:127–132.

[32]. Zaman SB, Hossain N: Universal Health Coverage: A burning need for developing countries . J Med Res and Innov. 2017, 1:18–20. 10.5281/zenodo.546770

[33]. Woodhead M, Finch R: Public education—a progress report . J Antimicrob Chemother. 2007, 60:53–55. 10.1093/jac/dkm158

[34]. Zaman SB, Hossain N, Ahammed S, et al.: Contexts and opportunities of e-health technology in medical care. J Med Res and Innov. 2017, 1:1–4. 10.5281/zenodo.570870 39. Keller MA, Stiehm ER: Passive immunity in prevention and treatment of infectious . Clin Microbiol Rev. 2000, 13:602–614. 10.1128/CMR.13.4.602-614.2000

[35]. Monk BJ, Herzog TJ, Kaye SB, et al.: Trabectedin plus pegylated liposomal doxorubicin in recurrent ovarian cancer. J Clin Oncol. 2010, 28:3107–3114. 10.1200/JCO.2009.25.4037

[36]. Devasahayam G, Scheld WM, Hoffman PS: Newer antibacterial drugs for a new century. . Expert Opin Investig Drugs. 2010, 19:215–234. 10.1517/13543780903505092

[37]. Kohanski MA, Dwyer DJ, Collins JJ: How antibiotics kill bacteria: from targets to networks . Nat Rev Microbiol. 2010, 8:423–435. 10.1038/nrmicro2333