IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

How Antibiotic Revolutionized Medicine: A Comprehensive Review of their Evolution, Application and Ongoing Challenges

Arefa Sheikh*, Sakshi Nale, Shruti Ramteke, Renuka Balpande
New Montfort Institute of Pharmacy, Ashti, Wardha, Maharashtra, India

Abstract: *This review paper delves into the rich history of antibiotics in subsequent years. Examining their multifaceted uses, we explore the pivotal role antibiotics play in modern medicine, encompassing the treatment of bacterial infections, prophylactic applications, and contributions to various fields, including agriculture. The paper provides an in-depth analysis of the advantages of antibiotics, underscoring their life-saving potential, support for medical procedures, and prevention of severe complications. However, we also address the associated disadvantages, including antibiotic resistance, side effects, and ecological concerns. Current issues, such as the emergence of antibiotic-resistant strains, are discussed alongside ongoing efforts in research and development. This comprehensive exploration aims to provide a nuanced understanding of antibiotics, paving the way for informed decisions in their use and development.*

Keywords: Antibiotic application, antibiotic resistance, global health impact, multi-faceted challenges, evolution of antibiotics.

I. INTRODUCTION

The mid-20th century saw a monumental turning point in the medical world with the arrival of antibiotics. This remarkable breakthrough delivered a powerful weapon against bacterial infections, reshaping the healthcare landscape as we know it. From Sir Alexander Fleming's serendipitous discovery of penicillin to the cutting-edge antibiotics of today, these medications have taken center stage in enhancing patient outcomes and prolonging human life expectancy. In this introduction, we delve into the intricate journey and modern uses of antibiotics, highlighting their remarkable efficacy and the persistent concerns surrounding antibiotic resistance.As we explore the applications of antibiotics in public health, their role in controlling the spread of infectious diseases becomes evident. Swift and targeted antibiotic interventions during outbreaks or epidemics play a crucial role in preventing the escalation of infectious diseases, safeguarding populations, and limiting the impact on healthcare systems. Established surveillance systems and effective antibiotic stewardship programs are essential components of responsible antibiotic use to mitigate the emergence of resistance, as advocated by leading global health entities (1).

In this article, we will explore the multifaceted uses of antibiotics, from their role in individual patient treatment to their impact on broader public health efforts. At the same time, we will delve into the persistent obstacles caused by the emergence of antibiotic-resistant strains. By examining the historical background and current challenges surrounding antibiotics through evidence-based research, we aim to offer a thorough insight into their influence on global health.

Historical Perspective

The origin of the term ‘antibiotic’ can be traced back to the word ‘antibiose’ first used as an antonym to symbiosis by Paul Vuillemin in his 1890 publication to describe the antagonistic action between different microorganisms (for example, fungi vs bacteria; bacteria vs protozoa). Later, the word antibiotic was used to describe naturally occurring secondary metabolites produced by bacteria and fungi possessing either growth inhibitory (bacteriostatic) or killing (bactericidal) activities against bacteria or fungi. Today the term has a broader meaning, in one sense to include designed molecules and a narrower definition, in another and with the terms antibacterial or antifungal, to designate their specific actions against bacteria and fungi, respectively, but not viruses. The term antiviral is reserved for the latter. In the Middle Ages, the miasma (or miasmatic, from the Greek μίασμα, meaning pollution, fowl air, or

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

contaminated vapors) theory was used to explain the causes of various diseases. In 1546 the Italian scholar Girolamo Fracastoro (Hieronymus Fracastorius) proposed transmittable, imperceptible seed-like particles (seminariamorbi) as causative agents for the outbreak of certain diseases. It took several centuries to prove that bacteria are one example of such particles. In the meantime, the Hungarian physician Ignaz Semmelweis, also known as the 'savior of mothers', recognizing the importance of hygiene in hospitals suggested and enforced hand washing with chlorinated lime solutions before patient examinations, while the Scottish surgeon Sir Joseph Lister treated surgery wounds with phenol (carbolic acid) solutions to avoid infections. In the 1860s the French physician Casimir Davaine demonstrated that blood injections from animals infected with anthrax to healthy animals caused infection, providing further clues for the cause of disease. It was also in the second half of the nineteenth century that the French chemist and bacteriologist Louis Pasteur contributed decisively to our understanding of the underlying causes of infectious diseases through his experimental studies with bacteria that culminated in his germ theory of disease. The subsequent contributions of the German physician Robert Koch also proved transformative. His discoveries, including the so-called four 'Koch postulates' establishing a causative relationship between microbes and disease (predicated on the work of Jakob Henle, and together with Friedrich Loeffler), propelled bacteriology toward its modern era. In 1882 Koch, together with Bernhard Fischer and Georg Gaffky, isolated the Mycobacterium tuberculosis, and in 1884 the Vibrio cholerae (a species first described in 1854 by Italian anatomist and pathologist Filippo Pacini), the causative strains that lead to the corresponding diseases. These milestone discoveries earned Koch one of the first Nobel Prizes in Physiology or Medicine (1905).

The first antibiotic to be discovered in nature was mycophenolic acid. As reported by the physician and microbiologist Bartolomeo Gosio in 1893, this antibiotic was isolated from Penicillium glaucum (P. brevicompactum) as a crystalline solid while he was studying pellagra.10, 11 At that time it was shown that mycophenolic acid inhibits the growth of Bacillus anthracis, and later that it also possesses antiviral, antifungal, antitumor and anti-psoriasis properties. This seminal discovery remained unnoticed (probably due to its publication in Italian) until mycophenolic acid was rediscovered in 1913 in the United States. Its structure, however, remained unknown until 1952,while its total synthesis was achieved in 1969.15, 16 It was not until 1995 that the 2-(morpholin-4-yl)ethyl ester of mycophenolic acid was approved by the US Food and Drug Administration, although not as an antibacterial drug but rather as an immunosuppressant to prevent transplant rejection (through a mechanism involving the inhibition of DNA biosynthesis). Events in the Age of Antibiotics is shown in Fig. 1.

Evolution of Antibiotic Resistance

Many of the bacterial pathogens associated with epidemics of human disease have evolved into multidrug-resistant (MDR) forms after antibiotic use. For example, MDR *M. 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 *Acinetobacter Baumannii, Burkholderia cepacian, Campylobacter jenuni, Citrobacter freundii, Clostridium difficile, Enterobacter spp., Enterococcus faecium, Enterococus faecalis, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, 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 molecular mechanisms of resistance to antibiotics have been studied extensively (Following Table, Table 1) and have involved investigations of the genetics and biochemistry of many different facets of bacterial cell function (3, 4, 5). 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 (6) and pathogens; most can be disseminated by one or more distinct gene transfer mechanisms. A few of the resistance types that illustrate the difficulties in maintaining effective antibiotic

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

activity in the face of the genetic and biochemical flexibility of bacteria deserve special mention.Modes of action and resistance mechanisms of commonly used antibiotics are listed in the Table 1.

Ecological Roles of Antibiotics and Antibiotic Resistance

Putative antibiotic r genes are omnipresent in natural environments. This raises the question of their natural functions, a topic that has been the subject of several thought-provoking reviews (8, 9, 10). Do bacteria develop antibiotic resistance traits in their natural surroundings? Do these genetic factors exist solely for resistance purposes, or do they also serve other genetic or biochemical functions? It is reasonable to assume that bacteria are regularly exposed to a diverse range of toxins or other inhibitory substances in their environment. What roles do naturally occurring low-molecular-weight products, known to possess antibiotic properties in lab settings, play in ecological systems? These products have a variety of sources, including breakdown products from natural polymers during nutrient processing, plant-derived compounds, antibiotic substances from insects and fungi, and general organic decomposition. It is worth noting that plants themselves produce numerous compounds that can impede bacterial growth in the rhizosphere.

The major bacterial solution to toxic challenges takes the form of multivalent pumping systems that prevent intracellular accumulation of structurally diverse bactericidal and bacteriostatic substances (11, 12). Actinomycetes and other microbes producing antibiotics and bioactive small molecules invariably possess multiple efflux systems (13), as demonstrated for the tetracycline-producing organism *Streptomyces rimosus* (14). The coexistence of production and resistance functions has been confirmed extensively in recent studies of antibiotic biosynthetic gene clusters and examinations of the genome sequences from producing strains (15, 16).

With the exception of nonspecific efflux systems, the potential antibiotic resistance determinants found in antibiotic-producing strains are generally associated with structural types or modes of action. It has been suggested that these resistance mechanisms are for “self-protection” of the host, on the assumption that the producer would self-destruct if it started to make its antibiotic product (17). However, this notion has not been proven.

Changes in ribosomal protein genes can result in antibiotic resistance and also cause other effects outside of ribosomal function such as mistranslation, temperature sensitivity, and even phage propagation. These effects can greatly impact the overall function of the cell. Depending on the specific pressures present, different mutations may occur that coincidentally increase antibiotic resistance. Furthermore, the development of an antibiotic resistance phenotype is not exclusively triggered by exposure to antibiotics.

Recent studies of microbes in natural settings have challenged our previous understanding of how bacteria live and function. For example, we now know that in the wild, bacteria do not grow in isolated, single colonies. This has caused researchers to question the potential roles of the countless bioactive compounds produced by these microbes. While the traditional practice of isolating single bacterial colonies on agar was once crucial for identifying bacteria and studying their pathogenicity, it has actually hindered the progress of microbial ecology. Today, there is a growing focus on investigating the dynamics within complex bacterial communities, known as microbiomes, in various environments. This is particularly important as many diseases are caused by multiple species of bacteria working together.

Applications and Impact on Global Health

Ever since antibiotics were first discovered, they have been a game-changer in the medical field. They have transformed the way we treat bacterial infections and have played a crucial role in improving patient outcomes and extending life expectancy. This section explores the wide range of uses for antibiotics, showcasing their immense therapeutic potential and their significant contribution to health worldwide. The primary application of antibiotics lies in clinical settings where these medications play a crucial role in treating bacterial infections. From common respiratory tract infections to severe cases of sepsis, antibiotics target and eliminate pathogenic bacteria, enabling the body's natural defense mechanisms to restore health. The extensive array of antibiotics available, including penicillins, cephalosporins, macrolides, and fluoroquinolones, allows healthcare professionals to tailor treatments to the specific characteristics of bacterial pathogens (18).

Antibiotics have become an integral component of surgical procedures, where preventing postoperative infections is paramount. Prophylactic antibiotic administration before surgery reduces the risk of surgical site infections, minimizing complications and promoting faster recovery. Guidelines from health organizations, such as the World Health

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

Organization (WHO) and the Centers for Disease Control and Prevention (CDC), underscore the importance of judicious antibiotic use in surgical settings to optimize efficacy and mitigate the development of antibiotic resistance (19). Beyond human medicine, antibiotics play a significant role in agricultural practices. They are employed in animal husbandry to promote animal health and prevent the spread of infectious diseases within livestock populations. However, the overuse and misuse of antibiotics in agriculture have raised concerns about the development of antibiotic-resistant strains of bacteria, emphasizing the need for responsible and sustainable practices in food production (20).

Antibiotics contribute to public health initiatives by controlling the spread of infectious diseases. In the context of outbreaks or epidemics, swift and targeted antibiotic interventions can prevent the escalation of infectious diseases, safeguarding populations and limiting the impact on healthcare systems. Well-established surveillance systems, combined with effective antibiotic stewardship programs, are essential to ensuring the responsible use of antibiotics and mitigating the emergence of resistance (21).

Antibiotics play a crucial role in numerous areas, from treating individual patients to safeguarding public health initiatives. As we confront the ever-changing realm of infectious diseases, it is crucial that we carefully manage the use of antibiotics to protect their potency. By delving into the historical and modern obstacles surrounding antibiotics, we can work towards securing their lasting effectiveness for the well-being of present and future populations.

Ongoing Challenges in Antibiotics: Navigating the Threat of Resistance

The use of antibiotics has been crucial in combatting bacterial infections, but our ability to rely on them is under threat. The rise of antibiotic resistance poses a major challenge to their effectiveness. In this section, we delve into the persistent obstacles caused by the excessive and improper use of antibiotics, shedding light on the emergence of resistant bacteria and emphasizing the pressing need for a comprehensive, worldwide approach to confront this pressing issue.One of the primary challenges facing antibiotics is the rise of antibiotic resistance. The overuse and misuse of these medications contribute to the selection of resistant bacterial strains, rendering previously effective treatments ineffective. This phenomenon poses a significant threat to public health, as antibiotic-resistant infections are associated with increased morbidity, mortality, and healthcare costs (22). In clinical settings, the inadequate implementation of antibiotic stewardship programs remains a pressing challenge. Antibiotic stewardship involves optimizing the use of antibiotics to ensure effective treatment while minimizing the development of resistance. Insufficient adherence to stewardship principles, including inappropriate prescribing practices and unnecessary antibiotic use, contributes to the acceleration of antibiotic resistance (23).

The pipeline for new antibiotic development has remained notably dry in recent decades. Pharmaceutical companies face economic challenges and reduced incentives to invest in the research and development of new antibiotics. Consequently, the lack of novel therapeutic options diminishes the medical community's ability to address emerging resistant strains, exacerbating the global threat of antibiotic resistance (24). The interconnectedness of our globalized world facilitates the rapid spread of antibiotic-resistant strains across borders. Resistant bacteria can emerge in one region and swiftly disseminate to other parts of the world through travel, trade, and migration. International collaboration and coordinated efforts are essential to mitigate the global impact of antibiotic resistance and prevent the spread of resistant strains (25).The environmental dimension of antibiotic resistance adds complexity to the challenge. The discharge of antibiotics into water systems, whether through pharmaceutical manufacturing or agricultural runoff, contributes to the development of antibiotic-resistant bacteria in the environment. This environmental reservoir of resistance genes poses a potential threat to human health and demands a comprehensive approach to address the environmental factors driving antibiotic resistance (26).

The pressing issues surrounding antibiotics, such as the alarming increase in antibiotic resistance, demand immediate action and unified efforts on a global scale. Confronting these issues requires a multifaceted strategy that includes promoting responsible antibiotic usage, investing in the development of new antibiotics, and working together internationally to contain the spread of resistant bacteria. In the midst of these challenges, it is crucial to prioritize the preservation of antibiotic effectiveness in order to protect the well-being of people worldwide.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

II. CONCLUSION

The development of antibiotics marks a momentous milestone in the field of medicine, completely transforming our ability to fight against bacterial infections and ultimately, saving numerous lives. From Sir Alexander Fleming's groundbreaking discovery of penicillin to modern times, antibiotics have been at the forefront of revolutionizing healthcare and extending human longevity. While we praise these extraordinary achievements, it is crucial to recognize the continued obstacles and to unite globally in order to preserve the effectiveness of antibiotics.

To sum up, the advancement of antibiotics holds immense significance in the field of modern medicine, equipping us with powerful measures to combat bacterial infections and enhance the well-being of patients. However, navigating the present scenario calls for a united front, as we face the daunting task of tackling antibiotic resistance. This calls for vigorous antibiotic stewardship initiatives, greater funding towards innovative research for new antibiotics, and a collaborative approach on a global scale to minimize the effects of resistant strains.

In our journey through the intricacies of antibiotic resistance, it is vital that we pause and reflect on the valuable lessons gained from the era of antibiotics. It is imperative to implement evidence-backed tactics in order to guarantee the ongoing efficacy of these vital medications. In doing so, we can uphold the enduring legacy of antibiotics as a fundamental pillar of medical advancement and safeguard their ability to protect the health of our global community.

ACKNOWLEDGEMENT

We owe a great deal of gratitude to the dedicated researchers and healthcare professionals whose groundbreaking efforts have greatly enhanced our knowledge of antibiotics and their pivotal role in the medical field. I am grateful towards each faculty of New Montfort Institute of Pharmacy, Ashti for providing me professional guidance and taught me a great deal about pharmacy, medicine, research and life in general.

I would like to thank my dearest father, Faiz Sheikh and my lovely mother whose love and guidance are with me in whatever I pursue. And lastly, I express my gratitude towards my friends who supported me throughout the research and have given the most important inputs. Immense respect for all of you.

REFERENCES

[1]. World Health Organization. (2015). Global Action Plan on Antimicrobial Resistance.

[2]. Abraham, E. P., and E. Chain. 1940. An enzyme from bacteria able to destroy penicillin. *Rev. Infect. Dis.*10**:**677-678.

[3]. Gale, E. F., E. Cundliffe, P. E. Reynolds, M. H. Richmond, and M. J. Waring (ed.). 1981. *The molecular basis of antibiotic action, 2nd ed.* John Wiley, Chichester, United Kingdom.

[4]. Walsh, C. 2003. *Antibiotics: actions, origins, resistance.* ASM Press, Washington, DC.

[5]. Marshall, B. M., D. J. Ochieng, and S. B. Levy. 2009. Commensals: unappreciated reservoir of antibiotic resistance. *Microbe*4**:**231-238.

[6]. Wright, G. D., and M. Morar**.** The genomic enzymology of antibiotic resistance. *Annu. Rev. Genet.*, in press.

[7]. Allen, H. K., J. Donato, H. H. Wang, K. A. Cloud-Hansen, J. E. Davies, and J. Handelsman. 2010. Call of the wild: antibiotic resistance genes in natural environments. *Nat. Rev. Microbiol.*8:251-259.

[8]. Aminov, R. I., and R. I. Mackie. 2007. Evolution and ecology of antibiotic resistance genes. *FEMS Microbiol. Lett.*271:147-161.

[9]. Martinez, J. L. 2009. The role of natural environments in the evolution of resistance traits in pathogenic bacteria. *Proc. Biol. Sci.*276:2521-2530.

[10]. Piddock, L. J. 2006. Multidrug-resistance efflux pumps—not just for resistance. *Nat. Rev. Microbiol.*4:629-636.

[11]. Poole, K. 2005. Efflux-mediated antimicrobial resistance. *J. Antimicrob. Chemother.*56:20-51.

[12]. Mendez, C., and J. Salas. 2001. The role of ABC transporters in antibiotic-producing organisms: drug secretion and resistance mechanisms. *Res. Microbiol.*152:341-350.

[13]. Petkovic, H., J. Cullum, D. Hranueli, I. S. Hunter, N. Peric-Concha, J. Pigac, A. Thamchaipenet, D. Vujaklija, and P. F. Long. 2006. Genetics of *Streptomyces rimosus*, the oxytetracycline producer. *Microbiol. Mol. Biol. Rev.*70:704-728.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

[14]. Chater, K. F., and C. Bruton. 1985. Resistance, regulatory and production genes for the antibiotic methylenomycin are clustered. *EMBO J.*4:229-241.
[15]. D'Costa, V. M., E. Griffiths, and G. D. Wright. 2007. Expanding the soil antibiotic resistome: exploring environmental diversity. *Curr. Opin. Microbiol.*10:481-489.
[16]. Hopwood, D. A. 2007. How do antibiotic-producing bacteria ensure their self-resistance before antibiotic biosynthesis incapacitates them? *Mol. Microbiol.*63:937-940.
[17]. World Health Organization. (2019). Global Antimicrobial Resistance Surveillance System (GLASS) Report.
[18]. Centers for Disease Control and Prevention. (2020). Antibiotic Use in the United States, 2018 Update: Progress and Opportunities.
[19]. Spellberg, B., Bartlett, J. G., & Gilbert, D. N. (2013). The future of antibiotics and resistance: a tribute to a career of leadership by John Bartlett. Clinical Infectious Diseases, 56(9), 1287–1292. doi: 10.1093/cid/cit020.
[20]. World Health Organization. (2022).
[21]. Centers for Disease Control and Prevention. (2019). Antibiotic Resistance Threats in the United States.
[22]. World Health Organization. (2019). Antimicrobial Stewardship Programs in Health-Care Facilities.
[23]. Tacconelli, E., Carrara, E., Savoldi, A., Harbarth, S., Mendelson, M., Monnet, D. L., ... & Olesen, S. W. (2018). Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. The Lancet Infectious Diseases, 18(3), 318-327.
[24]. Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A. K., Wertheim, H. F., Sumpradit& Greko, C. (2013). Antibiotic resistance—the need for global solutions. The Lancet Infectious Diseases, 13(12), 1057-1098.
[25]. Pruden, A., Larsson, D. G., Amézquita, A., Collignon, P., Brandt, K. K., Graham& Snape, J. R. (2013). Management options for reducing the release of antibiotics and antibiotic resistance genes to the environment. Environmental Health Perspectives, 121(8), 878-885.

Table1: Modes of action and resistance mechanisms of commonly used antibiotics (7).

Modes of action and resistance mechanisms of commonly used antibiotics			
Antibiotic class	**Example(s)**	**Target**	**Mode(s) of resistance**
β-Lactams	Penicillins (ampicillin), cephalosporins (cephamycin), penems (meropenem), monobactams (aztreonam)	Peptidoglycan biosynthesis	Hydrolysis, efflux, altered target
Aminoglycosides	Gentamicin, streptomycin, spectinomycin	Translation	Phosphorylation, acetylation, nucleotidylation, efflux, altered target
Glycopeptides	Vancomycin, teicoplanin	Peptidoglycan biosynthesis	Reprogramming peptidoglycan biosynthesis
Tetracyclines	Minocycline, tigecycline	Translation	Monooxygenation, efflux, altered target
Macrolides	Erythromycin, azithromicin	Translation	Hydrolysis, glycosylation, phosphorylation, efflux, altered target
Lincosamides	Clindamycin	Translation	Nucleotidylation, efflux, altered target
Streptogramins	Synercid	Translation	C-O lyase (type B streptogramins), acetylation (type A streptogramins), efflux, altered target
Oxazolidinones	Linezolid	Translation	Efflux, altered target
Phenicols	Chloramphenicol	Translation	Acetylation, efflux, altered target
Quinolones	Ciprofloxacin	DNA	Acetylation, efflux, altered target

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

		replication	
Pyrimidines	Trimethoprim	C_1 metabolism	Efflux, altered target
Sulfonamides	Sulfamethoxazole	C_1 metabolism	Efflux, altered target
Rifamycins	Rifampin	Transcription	ADP-ribosylation, efflux, altered target
Lipopeptides	Daptomycin	Cell membrane	Altered target
Cationic peptides	Colistin	Cell membrane	Altered target, efflux

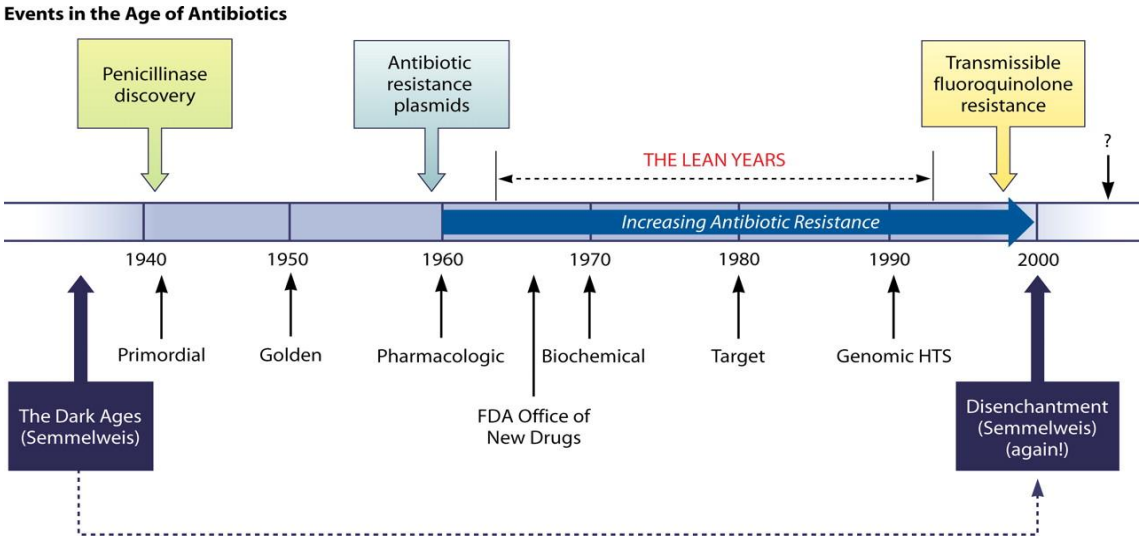

Fig. 1: History of antibiotic discovery and concomitant development of antibiotic resistance. The dark ages, the preantibiotic era; primordial, the advent of chemotherapy, via the sulfonamides; golden, the halcyon years when most of the antibiotics used today were discovered; the lean years, the low point of new antibiotic discovery and development; pharmacologic, attempts were made to understand and improve the use of antibiotics by dosing, administration, etc.; biochemical, knowledge of the biochemical actions of antibiotics and resistance mechanisms led to chemical modification studies to avoid resistance; target, mode-of-action and genetic studies led to efforts to design new compounds; genomic/HTS, genome sequencing methodology was used to predict essential targets for incorporation into high-throughput screening assays; disenchantment, with the failure of the enormous investment in genome-based methods, many companies discontinued their discovery programs. Other milestones in this history include the creation of the FDA Office of New Drugs after the thalidomide disaster led to stricter requirements for drug safety, including the use of antibiotics. This slowed the registration of novel compounds. Before antibiotics were discovered, Semmelweis advocated hand washing as a way of avoiding infection; this practice is now strongly recommended as a method to prevent transmission.