



From Discovery to Clinical Application: Understanding Antibiotics and Their Role in Special Population

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ABSTRACT :

Antibiotics are powerful antimicrobial agents that either inhibit the growth of microorganisms or destroy them at low concentrations. Naturally derived from bacteria, fungi, and actinomycetes, they play a critical role in combating infectious diseases. Their spectrum of activity ranges from narrow-spectrum drugs like Penicillin G to broad-spectrum agents such as tetracycline and chloramphenicol, with mechanisms that are either bacteriostatic or bactericidal. Historically, infection treatments date back to 2000 BC through herbal and natural remedies, but a turning point came in 1928 with Alexander Fleming's discovery of penicillin. Its mass production during World War II saved thousands of lives and initiated an era of antibiotic innovation, leading to derivatives like amoxicillin and synthetic antibiotics such as quinolones and sulfonamides. However, the overuse and misuse of antibiotics have resulted in bacterial resistance, making it increasingly difficult to treat certain infections and highlighting the need for responsible use. Antibiotics act through various mechanisms: they inhibit cell wall synthesis (e.g., penicillins, vancomycin), disrupt protein synthesis by targeting bacterial ribosomes (e.g., tetracyclines, macrolides), interfere with DNA replication and transcription (e.g., fluoroquinolones, rifampin), block folic acid metabolism (e.g., sulfonamides, trimethoprim), or cause leakage in bacterial cell membranes (e.g., polymyxins, daptomycin). Their use in special populations requires careful consideration. In pregnant women, only safe antibiotics like penicillins and cephalosporins should be used, while others like tetracyclines and aminoglycosides are avoided due to fetal risks. Lactating women can generally use antibiotics safely, but infants must be monitored for side effects. In pediatrics, weight-based dosing is crucial due to immature organ function, and certain antibiotics such as tetracyclines and fluoroquinolones are contraindicated. Careful, evidence-based antibiotic use is essential to protect current and future public health.

Keywords: Antibiotics, Actinomycetes, Penicillin, Special Population

ANTIBIOTICS

Antibiotic are the antimicrobial agents that when used in low concentration inhibit the growth of microorganism or kill them completely [1]. They are obtained by microorganisms such as bacteria, fungi and actinomycetes and used to eliminate the various infection caused by the microorganism itself in the host body [2]. Antibiotic has a good range of activity covering narrow (Penicillin G and Streptomycin) to broad spectrum (tetracycline, chloramphenicol) [3].

Antibiotics mainly shows two types of action: [4, 5]

1. Bacteriostatic – suppress the growth of bacteria (Tetracycline and Chloramphenicol)
2. Bactericidal – kill the bacteria (Penicillin, Cephalosporin)

CLASSIFICATION OF ANTIBIOTICS:

A. ON THE BASIS OF CHEMICAL STRUCTURE

1. **SULFONAMIDE-** Sulfadiazine, Paraaminosalicylic acid
2. **DIAMINOPYRIMIDINE-** Trimethoprim, pyrimethamine
3. **QUINOLONES-** Norfloxacin, Ciprofloxacin
4. **BETA-LACTUM-** Penicillin, Cephalosporin
5. **TETRACYCLINES-** Oxytetracycline, Doxycyclines
6. **NITROBENZENE DERIVATIVE-** Chloramphenicol
7. **AMINOGLYCOSIDE-** Streptomycin, Neomycin
8. **MACROLIDES-** Erythromycin, Azithromycin
9. **LINCOSOMIDE-** Lincomycin, Clindamycin
10. **NITROIMIDAZOLE-** Metronidazole, Tinidazole
11. **NICOTINIC ACID DERIVATIVE-** Isoniazid, Pyrazinamide
12. **AZOLE DERIVATIVE-** Miconazole, Ketoconazole

B. ON THE BASIS OF TYPE OF ORGANISM

1. **ANTIBACTERIAL-** Penicillin, Erythromycin
2. **ANTIFUNGAL-** Ketoconazole, Amphotericin B
3. **ANTIVIRAL-** Acyclovir, Amantadine
4. **ANTIPROTOZOAL-** Chloroquine, Metronidazole
5. **ANTIHELMINTIC-** Mebendazole, Pyrantel

HISTORY OF ANTIBIOTICS

Since ancient times, people have taken out ways to treat infections, as recorded in records since 2000 BC. Back then people relied on using mixtures of herbs, roots and natural substances that had anti-inflammatory and anti-microbial properties [6, 7].

In 1928 penicillin was identified by Alexander as a natural substance produced by fungi that could inhibit the growth of bacteria [8]. Penicillin was produced in large scale in 1941 during world war II, it was used for treating the infection in the battlefield of Europe [9]. After the war, penicillin became a live saving drug and was produced in large scale to save numerous lives.

Continuous research was done to manufacture and develop antibiotics. Thus, this resulted in development of various derivatives of penicillin, such as amoxicillin, it was introduced in 1972, and cefuroxime, introduced in 1979. Since then many antibiotics were discovered and created synthetically such as- quinolones (ciprofloxacin and norfloxacin) and sulphonamides (trimethoprim and sulfamethoxazole) [10].

Antibiotics brought a huge advancement and revolution in medicine and have been enormously used in treating and curing infection, due to its overuse antibiotics resistance has been created. This happens because the bacteria's have become resistant to existing antibiotics, this has created a condition where it is difficult-to-treat strains of bacterial infections. So though having miraculous effects antibiotics should be used appropriately in limited amount. In the second half of the 20th century, many more types of antibiotics were developed and put into clinical practice, helping to fight off the most resistant bacterial infections. Today, research and development of new antibiotics continues to focus on finding drugs that are effective against hard-to-treat infections. With continued research and use, antibiotics have been an integral part of treating infections and providing better healthcare worldwide [11].

MECHANISM OF ACTION

Antibiotic have various mechanism of action depending on the nature the of drug being consumed and type of microorganism causing infection in the host. The following are action of antibiotics in the host body :

1. Inhibition of cell wall formation

Antibiotics that disrupt bacterial cell wall synthesis are powerful tools in combating infections, as they target peptidoglycan—a vital structural polymer unique to bacteria. This layer maintains cell shape and guards against osmotic stress. Beta-lactam antibiotics, including penicillins and cephalosporins, exert their effect by inhibiting transpeptidase enzymes, also known as penicillin-binding proteins. These enzymes are critical for cross-linking peptidoglycan chains; when blocked, the cell wall weakens and ruptures, leading to bacterial death, particularly in hypotonic conditions [12]. Glycopeptides like vancomycin act through a different but equally effective mechanism, binding to the D-Ala-D-Ala termini of peptidoglycan precursors, thereby halting their integration into the growing cell wall. These antibiotics exhibit selective toxicity, attacking bacterial cells without harming human cells, which lack peptidoglycan [13]. However, bacterial resistance—through enzymatic degradation, target modification, or reduced permeability—can diminish their efficacy. Despite this, cell wall synthesis inhibitors remain a cornerstone of antimicrobial therapy due to their precision and potency.

2. Protein synthesis inhibitors

Protein synthesis inhibitor antibiotics are a powerful class of drugs that exploit the structural differences between bacterial and human ribosomes to achieve selective toxicity. Bacterial ribosomes, composed of 30S and 50S subunits forming the 70S complex, are essential for protein production. Aminoglycosides, such as gentamicin, bind irreversibly to the 30S subunit, causing mRNA misreading and the synthesis of faulty, nonfunctional proteins. Tetracyclines also act on the 30S subunit but prevent aminoacyl-tRNA from attaching, effectively halting protein elongation. Macrolides (e.g., erythromycin), lincosamides, and chloramphenicol target the 50S subunit, disrupting peptide bond formation and ribosomal translocation [14]. These mechanisms either suppress bacterial growth (bacteriostatic) or trigger cell death (bactericidal), depending on the pathogen and drug concentration. Although resistance—via ribosomal mutations, efflux mechanisms, or enzymatic degradation—poses ongoing challenges, these antibiotics remain essential for combating a wide range of bacterial infections [15]. Their precision and effectiveness make them indispensable in modern antimicrobial therapy

3. Interfere with DNA function and synthesis

Antibiotics that disrupt DNA function and synthesis exert their bactericidal activity by targeting fundamental processes essential for bacterial survival, including DNA replication, transcription, and repair. Fluoroquinolones—such as ciprofloxacin and levofloxacin—act by inhibiting bacterial topoisomerase II (DNA gyrase) and topoisomerase IV, enzymes indispensable for relieving DNA supercoiling and segregating replicated chromosomes. Their inhibition results in irreversible DNA damage and cessation of replication [16]. Rifamycins, notably rifampin, selectively bind to the β -subunit of

bacterial RNA polymerase, obstructing the initiation phase of transcription and thereby silencing gene expression. Metronidazole functions as a prodrug, activated under anaerobic conditions to generate cytotoxic nitro radicals that induce DNA strand breaks and structural destabilization. These agents demonstrate selective toxicity by exploiting unique bacterial molecular targets not present in eukaryotic cells. Resistance may emerge through point mutations in target enzymes, decreased intracellular accumulation, or enzymatic degradation. Nonetheless, DNA-interfering antibiotics remain indispensable in the treatment of life-threatening and multidrug-resistant infections [17].

4. Interfere with Intermediary metabolism

Antibiotics that disrupt intermediary metabolism exert their effect by targeting bacterial folic acid biosynthesis—an essential pathway for the production of DNA, RNA, and proteins. Unlike humans, who absorb folic acid through diet, bacteria must synthesize it, making this a highly selective and strategic target [18]. Sulfonamides, such as sulfamethoxazole, mimic para-aminobenzoic acid (PABA) and competitively inhibit dihydropteroate synthase, thereby blocking an early and vital step in folate synthesis. Trimethoprim complements this action by inhibiting dihydrofolate reductase, preventing the formation of tetrahydrofolic acid, which is critical for nucleotide synthesis. When combined as co-trimoxazole, these agents create a potent, sequential blockade of folate metabolism, resulting in bacteriostatic or bactericidal effects depending on the organism and concentration. Resistance may develop through overproduction of PABA, enzyme mutations, or reduced drug permeability. Nevertheless, these drugs remain indispensable in the treatment of urinary tract infections, respiratory illnesses, and gastrointestinal diseases due to their targeted action and broad therapeutic relevance [19].

5. Leakage of cell membrane

Antibiotics that induce bacterial cell membrane leakage act by compromising the structural integrity of the membrane, causing the uncontrolled efflux of vital intracellular components and culminating in bacterial cell death. These agents specifically target the lipid bilayer, undermining its selective permeability and barrier functions. Polymyxins, including polymyxin B and colistin, exemplify this class by binding avidly to the negatively charged lipopolysaccharides (LPS) on the outer membrane of Gram-negative bacteria. This interaction displaces essential divalent cations such as calcium and magnesium, destabilizing the membrane architecture and dramatically increasing permeability [20]. Consequently, critical ions, nucleotides, and metabolites escape the cell, triggering rapid lysis. In contrast, daptomycin targets Gram-positive bacteria by inserting into the cytoplasmic membrane in a calcium-dependent manner, leading to membrane depolarization and loss of membrane potential. These bactericidal antibiotics are invaluable against multidrug-resistant pathogens, though their clinical use is carefully balanced against potential nephrotoxicity and neurotoxicity, underscoring their role as last-resort therapies [21].

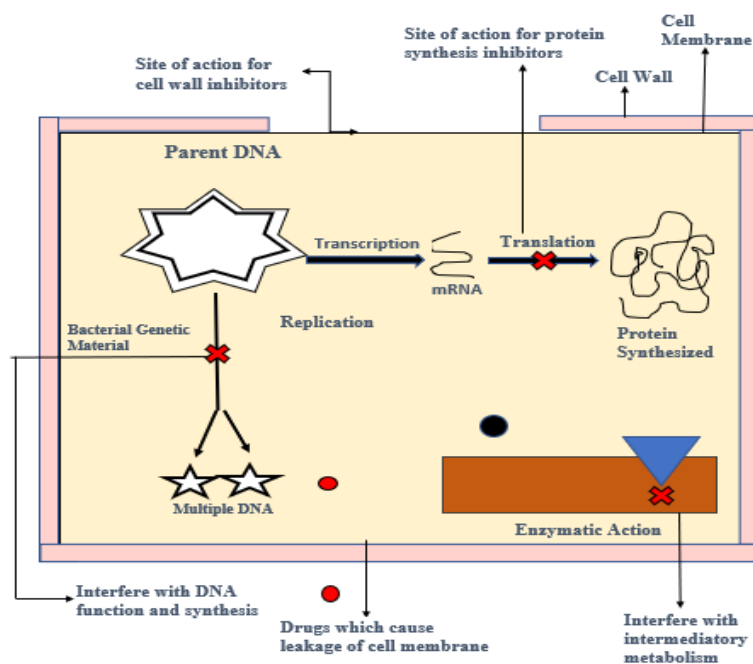


Figure 1 – Mechanism of action of antibiotics

ANTIBIOTICS IN SPECIAL POPULATIONS

The use of antibiotics in special populations demands careful evaluation because of variations in body function, how drugs are processed, and the potential for side effects. These groups—including pregnant women, nursing mothers, infants, the elderly, and individuals with kidney, liver, or immune system impairments—often respond differently to medications compared to the general population. Factors such as altered drug absorption, distribution, metabolism, and elimination can significantly influence how antibiotics work and how safe they are in these individuals [22].

Tailoring antibiotic treatment in these populations involves selecting the safest and most effective agents, adjusting doses appropriately, and closely monitoring for side effects. This patient-specific approach is essential for achieving therapeutic success while minimizing risks. Here's an in-depth look at how antibiotics are used and adjusted in key special populations:

1. Pregnant Women

The administration of antibiotics during pregnancy must be handled with caution due to the potential effects on both the mother and the developing fetus. Pregnancy introduces numerous physiological changes, including increased blood volume, enhanced renal clearance, and altered liver metabolism, all of which can influence how drugs are absorbed, distributed, and eliminated from the body. These changes may necessitate adjustments in antibiotic dosage to maintain effectiveness while avoiding toxicity. The safety of the fetus is a primary concern, particularly in the first trimester when organ development is most critical. Some antibiotics, such as penicillins, cephalosporins, erythromycin (excluding the estolate form), clindamycin, and nitrofurantoin (safe in early pregnancy but avoided near term), are generally considered safe for use during pregnancy. However, others—such as tetracyclines, which can cause tooth discoloration and inhibit bone growth; fluoroquinolones, which may damage developing cartilage; aminoglycosides, which carry a risk of fetal ear toxicity; and trimethoprim, which interferes with folate metabolism—should be avoided or used with extreme caution. Antibiotics are prescribed during pregnancy only when clearly indicated, such as in cases of urinary tract infections, Group B Streptococcus colonization, respiratory infections, sexually transmitted infections, or intra-amniotic and postpartum infections. Throughout treatment, it is essential to monitor both maternal and fetal health to ensure safety and effectiveness. Pregnant women should be educated about completing the full course of antibiotics, recognizing side effects, and seeking medical advice when needed. With careful drug selection, appropriate dosing, and continuous monitoring, infections can be safely and effectively treated during pregnancy [23].

2. Lactating Women

The use of antibiotics in lactating women requires careful consideration, as many antibiotics are excreted into breast milk in varying degrees. While the quantities that pass into breast milk are generally small, even minimal exposure can have effects on a nursing infant, particularly in cases of prolonged use or in newborns with immature organs. Fortunately, many commonly prescribed antibiotics are considered compatible with breastfeeding and are not known to cause harm when used appropriately. Among the antibiotics that are generally regarded as safe during lactation are *penicillins*, *cephalosporins*, and *macrolides* such as *azithromycin*. These medications have been widely used in breastfeeding women and, based on available evidence, pose a low risk of significant adverse effects in infants. Their concentrations in breast milk are typically too low to cause serious problems, making them preferred options when antibiotic therapy is required during the postpartum period. However, not all antibiotics are equally safe. Certain drugs must be used with caution, or avoided altogether if possible. For example, *chloramphenicol*, although rarely prescribed today, is known to pose a risk of *bone marrow suppression* in infants and should be avoided during breastfeeding. Similarly, *tetracyclines* can bind to calcium in developing teeth and bones, potentially causing *tooth discoloration* or affecting bone growth if used over a prolonged period. Although short-term use of tetracyclines is unlikely to cause harm, alternative antibiotics are usually preferred. It is essential for healthcare providers to assess the necessity of antibiotic treatment in lactating women, choosing medications with a well-established safety profile whenever possible. Even when using generally safe antibiotics, it is important to *monitor the infant for potential side effects*. Some of the signs that may indicate a reaction to antibiotic exposure through breast milk include *diarrhea*, *oral thrush* (a fungal infection in the mouth), or *allergic responses* such as rashes or unusual fussiness. If any of these symptoms occur, medical advice should be sought promptly [24].

3. Pediatrics (Infants and Children)

The administration of antibiotics in pediatric patients, particularly infants and young children, demands a highly cautious and calculated approach due to their unique physiological characteristics. In this population, the *immaturity of liver and kidney function* significantly influences how drugs are processed and cleared from the body. These underdeveloped organs can lead to slower metabolism and elimination of medications, increasing the risk of drug accumulation and potential toxicity. Therefore, antibiotic therapy in children must be tailored with precision to balance effectiveness and safety. One of the most critical aspects of pediatric antibiotic administration is *accurate dosing based on body weight*. Unlike adults, children require weight-based calculations (typically expressed in mg/kg) to ensure that the dosage is both safe and therapeutically effective. Administering too low a dose may lead to treatment failure, while excessive doses can cause harmful side effects. This underscores the importance of regular weight monitoring and individualized prescription practices in pediatric care. Several antibiotics are widely accepted as safe and effective in children and are frequently used to treat common bacterial infections. *Amoxicillin*, a penicillin derivative, is often the first-line choice for respiratory and ear infections. *Cefdinir*, a third-generation cephalosporin, and *azithromycin*, a macrolide antibiotic, are also commonly prescribed due to their favorable safety profiles and good palatability, making them suitable for young patients. However, not all antibiotics are appropriate for pediatric use. Certain classes of antibiotics are known to carry serious risks in children and should be avoided unless absolutely necessary. *Tetracycline's*, for example, are contraindicated in children under the age of eight due to their tendency to bind to calcium in developing teeth and bones, resulting in *permanent tooth discoloration* and potential interference with bone growth. *Fluoroquinolones* are another group to avoid, as they have been associated with *joint and cartilage damage*, particularly in growing children. *Chloramphenicol*, once commonly used, is now largely avoided in neonates due to the risk of "*gray baby syndrome*," a potentially fatal condition caused by the infant's inability to properly metabolize the drug [25].

4. Geriatric Patients

Antibiotic administration in geriatric patients requires a highly attentive and individualized approach due to the profound physiological changes that accompany aging. As people age, there is a natural decline in *renal and hepatic function*, which significantly affects the body's ability to metabolize and eliminate medications, including antibiotics. These changes can result in prolonged drug half-life, higher plasma concentrations, and an increased risk of drug accumulation, potentially leading to serious *adverse effects* if not properly managed. One of the most critical concerns in elderly patients is their *heightened vulnerability to drug-related toxicity*. For instance, antibiotics like *aminoglycosides*, which are primarily eliminated through the kidneys, can cause *nephrotoxicity* or even damage the auditory system if dosed inappropriately. This risk is compounded by the reduced glomerular filtration rate (GFR) that often accompanies aging, making it imperative to carefully calculate dosages based on *renal function*. Routine monitoring of kidney performance—especially through measurements like estimated glomerular filtration rate (eGFR)—is essential to ensure medications are both safe and effective. Another major challenge in the geriatric population is *polypharmacy*, the concurrent use of multiple medications, which is highly prevalent due to the presence of chronic conditions such as hypertension, diabetes, heart disease, and arthritis. This polypharmacy dramatically increases the likelihood

of *drug-drug interactions*, some of which can diminish the efficacy of antibiotics or exacerbate their side effects. For example, combining certain antibiotics with anticoagulants or diuretics can lead to dangerous outcomes like bleeding complications or renal overload. Therefore, it is crucial to assess a patient's full medication profile before initiating antibiotic therapy and to be vigilant about potential interaction. In addition to physiological and pharmacological considerations, the *presentation of infection in older adults is often atypical*—for example, fever may be absent, or symptoms may be masked by cognitive impairments such as dementia. This makes early diagnosis and prompt treatment more difficult, further emphasizing the need for clinical vigilance and judicious antibiotic use [26].

5. Patients with Renal Impairment

Prescribing antibiotics to patients with impaired kidney function requires a highly cautious and strategic approach to prevent serious health risks. When kidney function declines, the body's ability to eliminate drugs—particularly those primarily cleared by the kidneys—is significantly reduced. This reduction in excretory capacity can lead to an accumulation of antibiotics in the bloodstream, increasing the likelihood of drug toxicity. This is especially concerning for antibiotics with a narrow therapeutic window, where even slight overdosing can lead to harmful consequences. Medications like *aminoglycosides* and *vancomycin* are especially problematic in such cases due to their reliance on renal clearance. If dosages are not properly adjusted, these drugs can reach toxic levels and result in severe side effects such as *kidney damage (nephrotoxicity)*, *hearing loss (ototoxicity)*, and other systemic complications. Therefore, it is essential to assess renal function before initiating treatment, using indicators such as *serum creatinine* and *estimated glomerular filtration rate (eGFR)* to guide decisions. To prevent toxicity, clinicians must tailor the antibiotic regimen by *modifying the dosage or extending the dosing intervals* based on the patient's level of renal function. Additionally, *therapeutic drug monitoring* may be necessary to ensure drug levels remain within the safe and effective range. Not all antibiotics carry the same risk. Drugs like *doxycycline* and *clindamycin*, which are either minimally eliminated by the kidneys or metabolized differently, are safer alternatives for patients with renal impairment [27]. These options help achieve therapeutic goals while reducing the risk of drug buildup. Ultimately, managing antibiotics in renal-impaired patient's demands careful drug selection, individualized dosing, and vigilant monitoring. By doing so, healthcare providers can treat infections effectively without compromising patient safety.

6. Patients with Hepatic Impairment

Administering antibiotics to patients with hepatic impairment necessitates a thoughtful and individualized approach due to the liver's central role in drug metabolism. In patients with compromised liver function, the body's ability to process and eliminate medications that are metabolized hepatically is significantly reduced. This impaired metabolism can lead to drug accumulation, prolonged half-life, and an increased risk of adverse effects, especially in antibiotics with a narrow therapeutic index or known hepatotoxicity. Several antibiotics, such as *erythromycin* and *rifampin*, are extensively metabolized in the liver. In patients with liver dysfunction, these drugs may require *dose reduction* or extended dosing intervals to prevent toxic buildup. Without proper adjustments, there is a risk of systemic toxicity or exacerbation of liver damage. Therefore, careful assessment of liver function is crucial prior to initiating therapy. One of the most widely used tools to guide dosing decisions in hepatic impairment is the *Child-Pugh score*, which classifies liver disease severity into classes A, B, or C based on clinical and laboratory parameters [28]. This scoring system aids in determining whether standard dosing is appropriate or if modifications are necessary. In patients with significant liver impairment, it is also essential to *avoid antibiotics that have hepatotoxic potential*, as they can worsen liver injury or cause life-threatening complications. For example, *isoniazid*, a cornerstone drug in the treatment of tuberculosis, is known for its potential to induce liver inflammation and should be avoided in individuals with *active liver disease* unless the benefits clearly outweigh the risks. Additionally, *routine monitoring of liver function tests (LFTs)*, including levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin, is essential throughout the course of antibiotic therapy. These markers provide insight into the liver's ability to handle medications and offer early warnings of hepatic stress or toxicity [29]. Beyond dosage and drug selection, clinicians must also consider the patient's overall condition, comorbidities, and other medications that may interact with prescribed antibiotics or place further burden on the liver. A comprehensive, multidisciplinary approach involving pharmacists, hepatologists, and infectious disease specialists can be invaluable in managing complex cases.

7. Immunocompromised Patients

Treating infections in *immunocompromised patients*—including individuals living with *HIV/AIDS*, those undergoing *cancer chemotherapy*, and *organ transplant recipients*—requires a highly strategic and protective approach. These populations face a heightened vulnerability to infections due to their weakened immune defenses, making infections not only more frequent but also more severe and potentially life-threatening. As such, *timely, effective, and appropriately tailored antibiotic therapy* becomes a critical component of their medical management. In these high-risk patients, *broad-spectrum antibiotics* are often necessary as first-line treatment because they offer immediate coverage against a wide range of potential pathogens [30]. Immunocompromised individuals are more susceptible not only to common bacterial infections but also to *opportunistic pathogens*, including fungi and atypical organisms, which can quickly progress without a robust immune response to combat them. Therefore, empirical broad-spectrum therapy is frequently initiated even before a pathogen is identified, especially in cases of fever or systemic signs of infection. In addition to active treatment, *prophylactic antibiotics* play a vital role in preventing infections in immunocompromised individuals. For example, *trimethoprim-sulfamethoxazole (TMP-SMX)* is commonly prescribed to prevent *Pneumocystis jirovecii pneumonia (PJP)*, a life-threatening opportunistic infection in patients with severe immune suppression, particularly in those with advanced HIV or post-transplant immunosuppression [31]. This preventive approach can significantly reduce morbidity and mortality in vulnerable patients. However, while aggressive antibiotic use is often necessary, it must be carefully managed to avoid long-term consequences such as *antimicrobial resistance*. Overuse or inappropriate selection of antibiotics can promote the emergence of resistant organisms, which pose an even greater threat to immunocompromised patients. Therefore, treatment regimens should be *personalized* based on infection risk, underlying conditions, and microbiological data whenever available. Importantly, *live vaccines are contraindicated* in many immunocompromised individuals due to the risk of vaccine-induced infection [32]. This further underscores the importance of infection prevention through antibiotics and other non-vaccine methods. Multidisciplinary coordination, involving infectious disease specialists, oncologists, or transplant teams, is essential for optimizing outcomes in these complex cases.

REFERENCES

1. Konstantopoulou, A., 2016. "Systematic study and investigation of use and misuse of antibiotics in public health. Interdepartmental postgraduate training." Program of Medicinal Chemistry,
2. Leonard Katz, Richard H Baltz, Natural product discovery: past, present, and future, *Journal of Industrial Microbiology and Biotechnology*, Volume 43, Issue 2-3, 1 March 2016, Pages 155–176,
3. Katz L, Baltz RH: Natural product discovery: past, present, and future. *J Ind Microbiol Biotechnol* 2016, 43:155-176.
4. Prescott JF: The resistance tsunami, antimicrobial stewardship, and the golden age of microbiology. *Vet Microbiol* 2014, 171:273-278.
5. Mohr KI. History of antibiotics research. How to overcome the antibiotic crisis: facts, challenges, technologies and future perspectives. 2016 Oct 15:237-72.
6. Walsh CT, Wencewicz TA: Prospects for new antibiotics: a molecule-centered perspective. *J Antibiot* 2014, 67:7-22.
7. Clardy J, Fischbach MA, Currie CR. The natural history of antibiotics. *Current biology*. 2009 Jun 9;19(11):R437-41.
8. Neil JO: Report on Antimicrobial Resistance. 2016 [https:// amr-review.org](https://amr-review.org).
9. Payne DJ, Gwynn MN, Holmes DJ, Pompliano DL: Drugs for bad bugs: confronting the challenges of antibacterial discovery. *Nat Rev Drug Discovery* 2006, 6:29-40.
10. Haas LF: Papyrus of Ebers and Smith. *J Neurol Neurosurg Psychiatr* 1999, 67:572-578.
11. Harrison F, Roberts AEL, Gabriliska R, Rumbaugh KP, Lee C, Diggle SP: A 1,000-year-old antimicrobial remedy with antistaphylococcal activity. *mBio* 2015, 6:e01129
12. R.B. Ghooi, S.M. Thatte: Inhibition of cell wall synthesis - is this the mechanism of action of penicillins *Medical Hypotheses*, Volume 44, Issue 2, 1995, Pages 127-131, ISSN 0306-9877,
13. Bhattacharjee MK, Bhattacharjee MK. Antibiotics that inhibit cell wall synthesis. *Chemistry of Antibiotics and Related Drugs*. 2016:49-94.
14. McCoy LS, Xie Y, Tor Y. Antibiotics that target protein synthesis. *Wiley Interdisciplinary Reviews: RNA*. 2011 Mar;2(2):209-32.
15. Arenz S, Wilson DN. Bacterial protein synthesis as a target for antibiotic inhibition. *cold spring harbor perspectives in medicine*. 2016 Sep 1;6(9):a025361.
16. Bhattacharjee MK. Antibiotics that inhibit nucleic acid synthesis. In *Chemistry of antibiotics and related drugs* 2022 Aug 23 (pp. 125-148). Cham: Springer International Publishing.
17. Fritzsche H, Waehnert U, Chaires JB, Dattagupta N, Schlessinger FB, Crothers DM. Anthracycline antibiotics. Interaction with DNA and nucleosomes and inhibition of DNA synthesis. *Biochemistry*. 1987 Apr 1;26(7):1996-2000.
18. Bu'Lock JD. Intermediary metabolism and antibiotic synthesis. In *Advances in applied microbiology* 1961 Jan 1 (Vol. 3, pp. 293-342). Academic Press.
19. Martin JF, Demain AL. Control of antibiotic biosynthesis. *Microbiological reviews*. 1980 Jun;44(2):230-51.
20. Franklin TJ, Snow GA, Franklin TJ, Snow GA. Antiseptics, antibiotics and the cell membrane. *Biochemistry and molecular biology of antimicrobial drug action*. 1998:43-59.
21. Vazquez-Muñoz R, Meza-Villezas A, Fournier PG, Soria-Castro E, Juarez-Moreno K, Gallego-Hernández AL, Bogdanchikova N, Vazquez-Duhalt R, Huerta-Saquero A. Enhancement of antibiotics antimicrobial activity due to the silver nanoparticles impact on the cell membrane. *PloS one*. 2019 Nov 8;14(11):e0224904.
22. Sime FB, Roberts MS, Roberts JA. Optimization of dosing regimens and dosing in special populations. *Clinical Microbiology and Infection*. 2015 Oct 1;21(10):886-93.
23. Pernet A. Temafloxacin: a safe antibiotic for the elderly, patients with comorbidities, and other special populations. *The American journal of medicine*. 1991 Dec 30;91(6):S162-5.
24. Grigoryan L, Germanos G, Zoorob R, Juneja S, Raphael JL, Paasche-Orlow MK, Trautner BW. Use of antibiotics without a prescription in the US population: a scoping review. *Annals of internal medicine*. 2019 Aug 20;171(4):257-63.
25. Beckett CL, Harbarth S, Huttner B. Special considerations of antibiotic prescription in the geriatric population. *Clinical Microbiology and Infection*. 2015 Jan 1;21(1):3-9.
26. Zayyad H, Eliakim-Raz N, Leibovici L, Paul M. Revival of old antibiotics: needs, the state of evidence and expectations. *International journal of antimicrobial agents*. 2017 May 1;49(5):536-41.
27. Jhaveri R. Anti-infective Dosing in Special Populations. *Clinical Therapeutics*. 2016 Sep 1;38(9):1928-9.
28. Karunaratna I, Hapuarachchi T, Gunasena P, Ekanayake U, Rajapaksha S, Gunawardana K, Aluthge P, Bandara S, Jayawardana A, Kapila De Alvis S. Amoxicillin in Special Populations: Dosage Adjustments and Monitoring.
29. Gould FK. Linezolid: safety and efficacy in special populations. *Journal of antimicrobial chemotherapy*. 2011 May 1;66(suppl_4):iv3-6.
30. Sime FB, Roberts MS, Roberts JA. Optimization of dosing regimens and dosing in special populations. *Clinical Microbiology and Infection*. 2015 Oct 1;21(10):886-93.
31. Pereira JQ, Silva MT, Galvão TF. Use of antibiotics by adults: a population-based cross-sectional study. *Sao Paulo Medical Journal*. 2018 Sep;136:407-13.
32. Lajunen TJ. Antibiotic Use in Communities. *Antibiotics*. 2024 May 13;13(5):438.