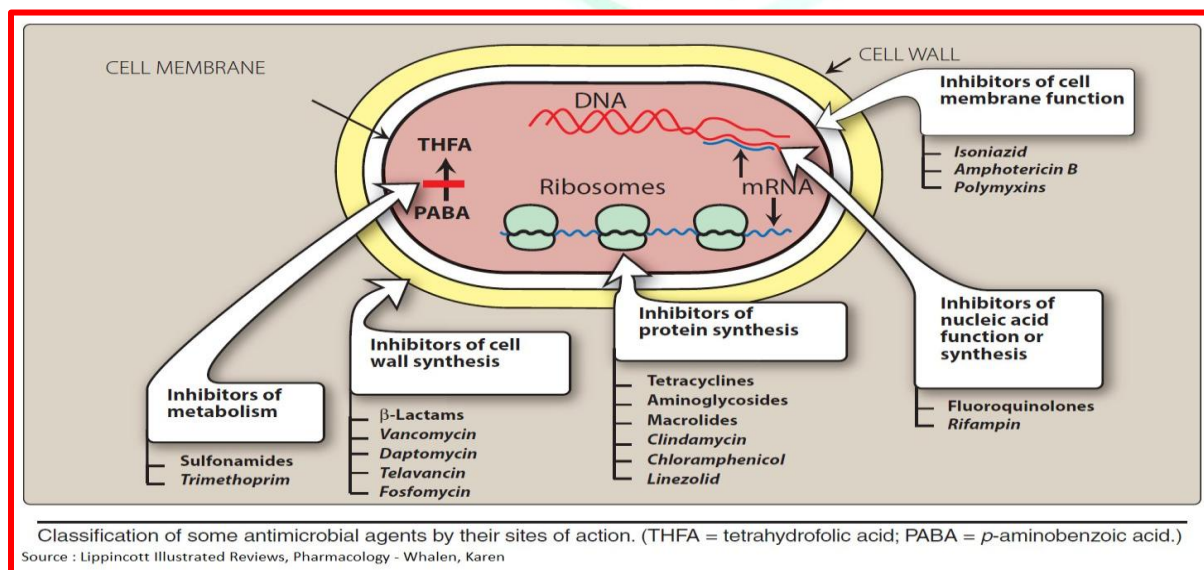


Modes of Action of Antibacterial Agents

Antibacterial agents eliminate or inhibit the growth of bacteria by targeting vital cellular structures and biochemical processes. Their actions can be classified into five major mechanisms:

1. **Inhibition of cell wall synthesis:** Some agents block the formation of peptidoglycan, an essential component of the bacterial cell wall, leading to cell lysis.
2. **Disruption of cell membrane integrity:** Certain drugs alter membrane permeability, causing leakage of cellular contents and ultimately cell death.
3. **Inhibition of protein synthesis :** These agents bind to bacterial ribosomes and prevent the production of proteins required for growth and replication.
4. **Interference with metabolic pathways:** Some antibacterial disrupt essential enzymatic reactions involved in bacterial metabolism.
5. **Inhibition of nucleic acid synthesis :** These drugs prevent the replication or transcription of DNA and RNA, thereby stopping bacterial multiplication.

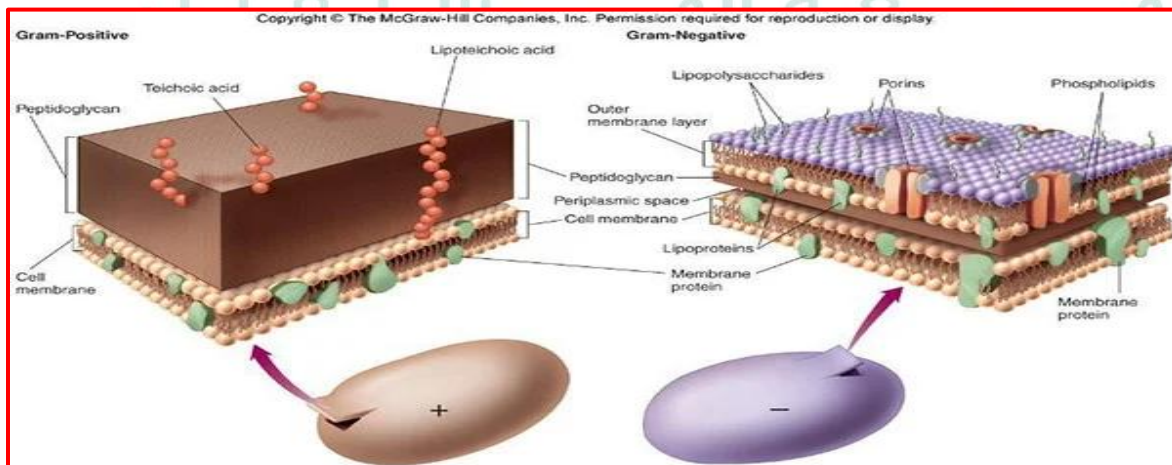


Inhibition the Cell Wall Synthesis:

Certain antibacterial medications specifically target the formation of the bacterial cell wall, a structure not found in human cells. This wall is mainly built from peptidoglycan, a complex polymer consisting of long glycan strands that are linked together through peptide bridges. These drugs are most effective when the bacteria are actively multiplying, since cell wall production occurs during growth and division.

Key agents in this class include the β -lactam antibiotics, so named because they contain a β -lactam ring essential for their antibacterial action. This category encompasses penicillins, cephalosporins, monobactams, and carbapenems. Additional important inhibitors of cell wall synthesis are vancomycin and daptomycin.

Both gram-positive and gram-negative bacteria share two main components in their cell envelope: the cytoplasmic membrane and the cell wall. However, the cell wall in gram-positive bacteria is significantly thicker than in gram-negative bacteria. In addition, gram-negative bacteria possess an outer membrane as part of their envelope, a feature absent in other bacterial types. This membrane contains unique molecules, such as **lipopolysaccharides (LPS)**, which contribute to the bacteria's defense against harmful substances like antibiotics and detergents.



Inhibitors of Cytoplasmic Membrane Function

The cytoplasmic membrane, present in all living cells, serves several essential functions. It acts as a selectively permeable barrier, facilitates active transport, and thereby regulates the cell's internal composition. If the membrane's integrity is compromised, macromolecules and ions can leak out, leading to cellular damage or even cell death.

The cytoplasmic membranes of bacteria and fungi differ structurally from those of animal cells, making them more susceptible to disruption by certain antimicrobial agents. This structural difference allows for selective chemotherapy, as drugs can target microbial cells without significantly affecting host cells.

Antibiotics that act on cell membranes are typically selective for specific groups of microorganisms due to variations in membrane lipid composition. Among the most notable are the polymyxins, which function like detergents. They bind to membrane phospholipids, leading to disruption and dissolution of the bacterial cell membrane.

Some other antimicrobial agents, such as the polyene antifungals **amphotericin B** and **nystatin**, exert their effect by attaching to specific sterols (**Ergosterol**) found in fungal cell membranes. This interaction disrupts membrane integrity and increases permeability.

Polymyxins are ineffective against fungi, while polyene antifungals do not have activity against bacteria, reflecting the structural differences between bacterial and fungal cell membranes.

Inhibition of Protein Synthesis

Bacterial cells contain 70S ribosomes, while mammalian cells possess 80S ribosomes. The differences in their subunits, chemical structure, and functional characteristics are significant enough to allow antimicrobial agents to selectively inhibit protein synthesis in bacteria with minimal impact on mammalian cells.

During normal protein synthesis in microorganisms, multiple ribosomes simultaneously translate a single mRNA strand. These clusters of ribosomes attached to the same mRNA molecule are known as polysomes.

Several antibiotic classes exert their effects by interfering with protein synthesis, including macrolides (such as erythromycins), lincosamides (lincomycins), tetracyclines, glycylyclines, aminoglycosides, and chloramphenicol.

Inhibition of Nucleic Acid Synthesis

Antibacterial agents that interfere with nucleic acid synthesis act by targeting key enzymes involved in genetic processes. They may inhibit DNA polymerase or DNA helicase, thereby preventing DNA replication, or block RNA polymerase, which disrupts transcription.

Because the mechanisms of nucleic acid synthesis are relatively similar in bacteria and eukaryotic cells, these drugs tend to exhibit lower selective toxicity compared to other classes of antibiotics.

Antibacterial drugs that inhibit nucleic acid synthesis exert their effects through three principal mechanisms:

1. **Inhibition of precursor synthesis** : These agents interfere with the production of essential components required for nucleic acid formation. Examples include **sulfonamides** and **trimethoprim**, which disrupt folate metabolism necessary for DNA synthesis.
2. **Inhibition of DNA replication** : These drugs prevent the duplication of bacterial DNA. The main representatives of this group are the **quinolones**.
3. **Inhibition of RNA polymerase** : These agents block the transcription process by targeting bacterial RNA polymerase. An important example is **rifampicin**.

Inhibition of Essential Metabolite Synthesis

An antimetabolite is a substance that interferes with a cell's normal metabolic processes, thereby preventing it from completing vital biochemical reactions.

Antimetabolites exert their effects through two main mechanisms:

1. **Competitive enzyme inhibition** : They resemble the natural substrate of an enzyme and compete with it for binding, thereby blocking the normal metabolic reaction.

Some **sulfonamide drugs (sulfonamides)** resemble **PABA (para-aminobenzoic acid)** in bacteria, so they compete with it and inhibit the synthesis of **folic acid**, which is essential for bacterial growth.

2. **Erroneous incorporation into nucleic acids** : They may be mistakenly incorporated into DNA or RNA in place of normal components, resulting in defective nucleic acid synthesis and impaired cellular function.

This principle is commonly used in the treatment of cancer and viral infections to stop the replication of cells or viruses. Some chemotherapy drugs, such as nitrogenous base analogs (antimetabolites), work through this mechanism.

