Antibiotics

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Pharmacology

Antibiotics

- Antibiotics are the substances which are derived from one microorganism in order to kill another microorganism. Antibiotics are effective against bacterial, fungal and parasitic infections. But, antibiotics are not helpful against viral infections.
- The development of chemical synthesis has helped to produce the synthetic components which act as an antimicrobial agent against the pathogenic bacteria. These synthetic components are also called as antibiotics. Pathogenic bacteria can be killed by synthetic components at low concentrations. Examples: Ampicillin and amoxicillin.
- In 1908, a German bacteriologist, Paul Ehrlich had developed a synthetic component from an arsenic-based structure for the treatment of syphilis, which is called as arsphenamine or salvarsan.
- Then, in 1929, Alexander Fleming discovered Penicillin from the fungus *Penicillium notatum*. Penicillin is used to treat different types of bacterial infections.

Types of antibiotics

- Two types of antibiotics are commonly available. These are as follows:
- ***Bactericidal antibiotics*** **–** These antibiotics had killing effects on bacteria. Example: Penicillin, Aminoglycosides, Ofloxacin.
- ***Bacteriostatic antibiotics*** **–** These antibiotics have an inhibitory effect on bacteria. Example: Erythromycin, Tetracycline, Chloramphenicol.
- Depends on the spectrum of action, antibiotics are further classified into three types. These are as follows:
- **Broad-spectrum antibiotics:** These antibiotics are widely used to kill or inhibit the Gram-positive and Gram-negative bacteria. Example: Chloramphenicol
- **Narrow spectrum antibiotics:** These antibiotics are widely effective against specific groups of bacteria. Example: Penicillin G
- **Limited spectrum antibiotics:** These antibiotics are effective against a single organism or a single disease. Example: Dysidazirine.

Difference between antimicrobials and antibiotics

- There are many different compounds that can inhibit the growth of microorganisms, and many terms that are used to categorize such compounds. ‘Antimicrobials‘, ‘antibacterials’ and ‘antibiotics’ are commonly used terms that can sometimes be used interchangeably, but there are important differences between these words:
- ***Antimicrobials*** is a wider term that includes all agents that act against microorganisms, namely bacteria, fungi, viruses and protozoa.
- ***Antibacterials*** act only on bacteria. Broadly defined, this term encompasses all compounds that act against bacteria, including antibiotics. Today the term is sometimes used for different types of disinfectants that are not used as medicine, such as alcohol or triclosan.

- ***Antibiotics*** are produced naturally by microorganisms and kill or inhibit the growth of other microorganisms, mainly bacteria.
- The word comes from the Greek words ‘anti’, meaning ‘against’, and ‘biotikos’, meaning ‘concerning life’. Strictly speaking, antibiotics do not include agents that are produced by chemical or biochemical synthesis. However for simplicity, synthetic or semi-synthetic variants (such as quinolones) are usually included under the term antibiotics.
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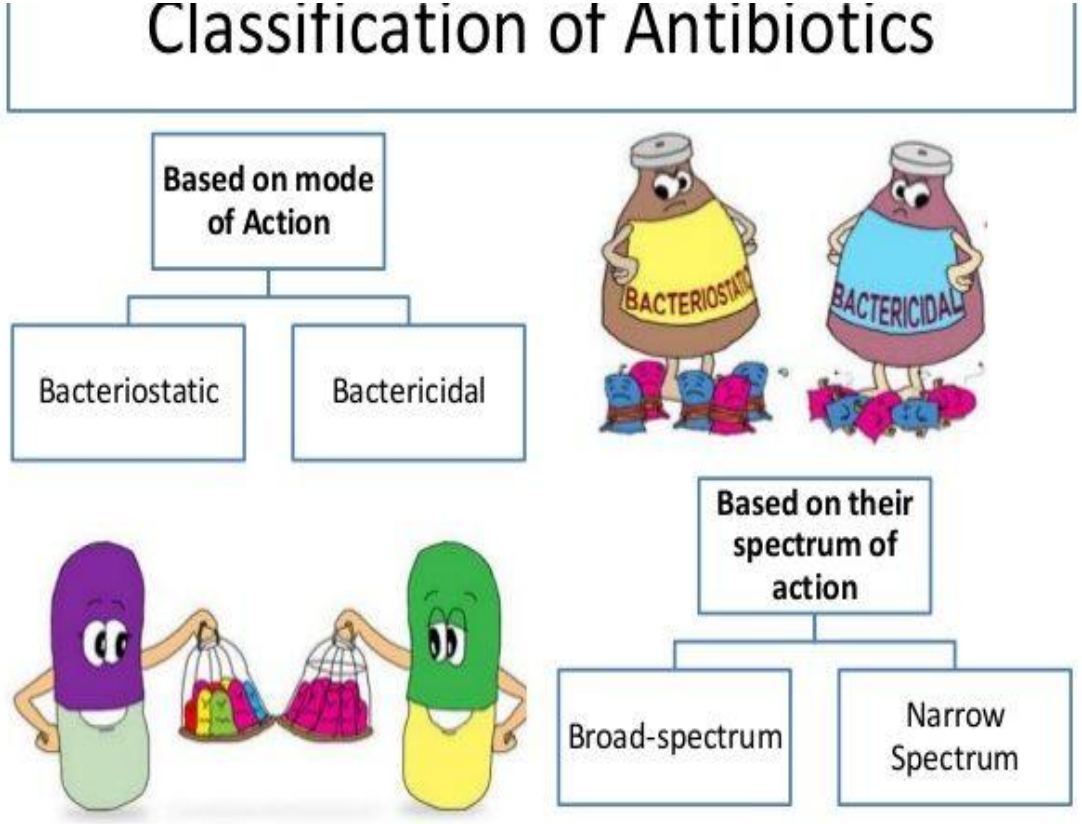
Antiseptics and disinfectants

- Antiseptics and disinfectants are the chemical components which are used as antimicrobial agents.
- Antiseptics are applied to the injured tissues, cuts, and infected skin surfaces. Antiseptics are not prescribed to be taken orally. A few examples are given below:
- **Dettol –** It is a mixture of chloroxylenol and terpineol. It is used to apply in the wounds.
- **Iodine tincture and iodoform –** It has very good antiseptic properties.
- **Boric acid** – It is used as an antiseptic agent for eyes.
- Disinfectants are used to destroy the pathogenic microorganisms in the non-living objects such as floors and drainage systems.
- Example: Chlorine and sulphur dioxide at low concentration.

- **Classification of antibiotics**
- **A] On the basis of chemical structure**
- **B] On the basis of origin**
- **C] On the basis of range of activity (spectrum of activity)**
- **D] On the basis of mode of action**
- **E] On the basis of effects of their activity**
- **F] On the basis of route of administration**



Classification of antibiotics on the basis of origin:

- **1.Microbial origin:**
- **i. Bacterial origin:**
- *Bacillus polymyxa*: Polymyxin
- *Chromobacter violaceum*: Bacitracin
- *Micromonospora* spp: Gentamycin
- **ii. Fungal origin:**
- *Penicillium notatum*: Penicillin
- *Cephalosporin* spp: Cephalosporin
- **iii. Actimomycetes origin:**
- *Streptomyces* griseus: Streptomycin
- **2. Semi-synthetic antibiotics:**
- Examples: Amoxycillin, Ampicillin, Doxycycline, Tigecycline, Sulfonamide etc
- **3. Synthetic antibiotics:**
- Examples: Chloramphenicol (* it was extracted from *Streptomyces venzuelae* but now produced synthetically), 4-quinolones, Sulfonamide

Antibiotic Classes

Antibiotics	Aminoglycosides	Streptomycin Gentamicin	Gram (-)	Inhibit Protein Synthesis (30s)	Bacteremia, Abdominal Infections
Can	Cephalosporins	Ceftriaxone Cefepime	Gram (+)/(-)	Inhibit Cell Wall Synthesis	Skin, Urinary, Resp. Infections
Terminate	Tetracyclines	Tetracycline Doxycycline	Gram (+)/(-)	Inhibit Protein Synthesis (30s)	Lyme Disease, PID, STIs
Protein	Penicillins	Ampicillin Amoxicillin	Gram (+)/(-)	Inhibit Cell Wall Synthesis	ENT, Skin, Urinary Infections
Synthesis	Sulfonamides	Sulfasalazine Sulfamethoxazole	Gram (+)/(-)	Inhibit Folate Synthesis	UTIs, Burns, Eye Infections
For	Fluoroquinolones	Ciprofloxacin Levofloxacin	Gram (+)/(-)	Inhibit DNA Replication	Respiratory & Urinary Infections
Microbial	Macrolides	Azithromycin Erythromycin	Gram (+)	Inhibit Protein Synthesis (50s)	Pneumonia, Sinus, ENT, STIs
Cells	Carbapenems	Meropenem Ertapenem	Gram (+)/(-)	Inhibit Cell Wall Synthesis	Urinary, Abdom. Infections
Like	Lincosamides	Clindamycin	Gram (+)	Inhibit Protein Synthesis (50s)	Skin, Bone, Lung Infections
Germs	Glycopeptides	Vancomycin	Gram (+)	Inhibit Cell Wall Synthesis	MRSA, Skin, Endocarditis

- You can use the following EZmed mnemonic to remember these main classes:
- **“Antibiotics Can Terminate Protein Synthesis For Microbial Cells Like Germs”.**
- This mnemonic is useful because it not only helps you remember the main antibiotic classes, but it also reminds you that inhibition of protein synthesis is the mechanism of action for many antibiotics

- **“Antibiotics Can Terminate Protein Synthesis For Microbial Cells Like Germs”**
- **A**ntibiotics = **A**minoglycosides
- **C**an = **C**ephalosporins
- **T**erminate = **T**etracyclines
- **P**rotein = **P**enicillins
- **S**ynthesis = **S**ulfonamides
- **F**or = **F**luoroquinolones
- **M**icrobial = **M**acrolides
- **C**ells = **C**arbapenems
- **L**ike = **L**incosamides
- **G**erms = **G**lycopeptides

Antibiotic Classes

Mnemonic

“Antibiotics Can Terminate Protein Synthesis For Microbial Cells Like Germs”

1. Aminoglycosides
2. Cephalosporins
3. Tetracyclines
4. Penicillins
5. Sulfonamides
6. Fluoroquinolones
7. Macrolides
8. Carbapenems
9. Lincosamides
10. Glycopeptides

Image: Use the above mnemonic to remember the 10 main antibiotic classes.

Antibiotics classes

- **Aminoglycosides**
- ***Drug Names***: Examples of aminoglycosides include streptomycin and gentamicin. These drug names typically end in “mycin/micin”.
- ***Gram Coverage***: Aminoglycosides primarily cover aerobic gram-negative bacteria and do not cover anaerobes. While they are particularly active against gram-negatives, they can act synergistically against certain gram-positive organisms.
- ***Mechanism of Action***: Aminoglycosides inhibit protein synthesis.
- Ribosomes function to synthesize proteins in cells, and bacterial ribosomes are made up of a 30s and 50s subunit.

- Aminoglycosides bind to the 30s ribosomal subunit of bacteria thereby disrupting protein synthesis (human ribosomes have a 40s and 60s subunit and are not affected by the antibiotic as a result).
- ***Example Indications***: Aminoglycosides are highly potent, broad-spectrum antibiotics and can be used for bacteremia, **intra-abdominal** infections, and other life-threatening infections that may progress to **shock** if untreated.

Cephalosporins

- ***Drug Names***: Examples of **cephalosporins** include ceftriaxone and cefepime. These drug names typically begin with “cef/ceph”.
- ***Gram Coverage***: Cephalosporins cover both gram-positive and gram-negative bacteria.
- ***Mechanism of Action***: Cephalosporins inhibit cell wall synthesis.
- Peptidoglycan is a major component of bacterial cell walls and is necessary to maintain the cell wall integrity.
- Peptidoglycan synthesis is facilitated by penicillin-binding proteins (PBPs).
- Cephalosporins (along with penicillins and carbapenems) contain a beta-lactam ring in their structure and are classified as beta-lactam antibiotics as a result.
- Beta-lactam antibiotics bind to, and inhibit, PBPs thereby preventing peptidoglycan synthesis and cross-linking. As a result, the bacterial cell wall is disrupted.

- ***Example Indications***: Cephalosporins can be used for skin, urinary, and respiratory infections among others.
- There are 5 generations of cephalosporin medications based on their spectrum of coverage.

Tetracyclines

- ***Drug Names***: Examples of tetracyclines include tetracycline and doxycycline. These drug names usually end in “cycline”.
- ***Gram Coverage***: Tetracyclines cover both gram-positive and gram-negative bacteria.
- ***Mechanism of Action***: Tetracyclines are similar to aminoglycosides in that they inhibit protein synthesis, specifically by binding to the 30s subunit of the bacterial ribosome.
- ***Example Indications***: Tetracyclines can be used for Lyme disease, pelvic inflammatory disease (PID), and some sexually transmitted infections (STIs) among others

Pencillins

- ***Drug Names***: Examples of penicillins include ampicillin and amoxicillin. These drug names typically end in “cillin”.
- ***Gram Coverage***: Penicillins cover both gram-positive and gram-negative bacteria, especially the later generation penicillins.
- ***Mechanism of Action***: Penicillins are beta-lactam antibiotics, and therefore they inhibit cell wall synthesis similar to cephalosporins.
- ***Example Indications***: Penicillins can be used for various ear, nose, throat (ENT), skin, and urinary infections among others.
- Later generations can also be used for intra-abdominal infections such as **gallbladder/biliary** infections among others

Sulfonamides

- **Sulfonamides**
- ***Drug Names***: Examples of sulfonamides include sulfasalazine (can be used as an anti-inflammatory) and sulfamethoxazole. These drug names typically begin with “sulfa”.
- ***Gram Coverage***: Sulfonamides cover both gram-positive and gram-negative bacteria.
- ***Mechanism of Action***: Sulfonamides inhibit folate synthesis.
- Bacteria have the unique ability to generate their own folate, whereas humans must obtain folate from their diet.
- Therefore, sulfonamides act on this unique bacterial function by inhibiting folate synthesis.
- ***Example Indications***: Sulfonamides can be used for ***burns***, eye infections, and urinary tract infections (UTIs) among others.
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Fluoroquinoloes

- ***Drug Names***: Examples of fluoroquinolones include ciprofloxacin and levofloxacin. These drug names typically end in “floxacin”.
- ***Gram Coverage***: Fluoroquinolones cover both gram-positive and gram-negative bacteria.
- ***Mechanism of Action***: Fluoroquinolones inhibit DNA synthesis and replication.
- They inhibit enzymes such as DNA gyrase and topoisomerase, and DNA is unable to unwind and/or replicate as a result.
- ***Example Indications***: Fluoroquinolones can be used for respiratory and urinary infections among others.

Macrolides

- ***Drug Names***: Examples of macrolides include azithromycin and erythromycin. These drug names typically end in “thromycin”.
- ***Gram Coverage***: Macrolides cover primarily gram-positive bacteria, with some gram-negative coverage.
- ***Mechanism of Action***: Macrolides inhibit protein synthesis.
- However, rather than binding to the 30s subunit of bacterial ribosomes (like we saw with aminoglycosides and tetracyclines), macrolides bind to the 50s subunit.
- ***Example Indications***: Macrolides can be used for pneumonia, sinusitis, ENT infections, and STIs among others.

Carbapenems

- ***Drug Names***: Examples of carbapenems include meropenem and ertapenem. These drug names typically end in “penem”.
- ***Gram Coverage***: Carbapenems cover both gram-positive and gram-negative bacteria.
- ***Mechanism of Action***: Carbapenems inhibit cell wall synthesis similar to cephalosporins and penicillins as they are also beta-lactam antibiotics.
- ***Example Indications***: Carbapenems are broad-spectrum antibiotics and can be used for urinary and abdominal infections among others.
- **Appendicitis**, especially if complicated (perforated, abscess, etc), is one example in which carbapenems could be used.

Lincosamides

Drug Names: Examples of lincosamides include clindamycin, lincomycin, and pirlimycin. Some of these drug names, but not all, end in “mycin”.

- ***Gram Coverage***: Lincosamides primarily cover gram-positive bacteria as they are unable to pass through the outer membrane of gram-negative organisms.
- ***Mechanism of Action***: Lincosamides inhibit protein synthesis, specifically by targeting the 50s subunit of the bacterial ribosome as we saw with macrolides.
- ***Example Indications***: Lincosamides can be used for skin, bone, and lung infections among others

Glycopeptides

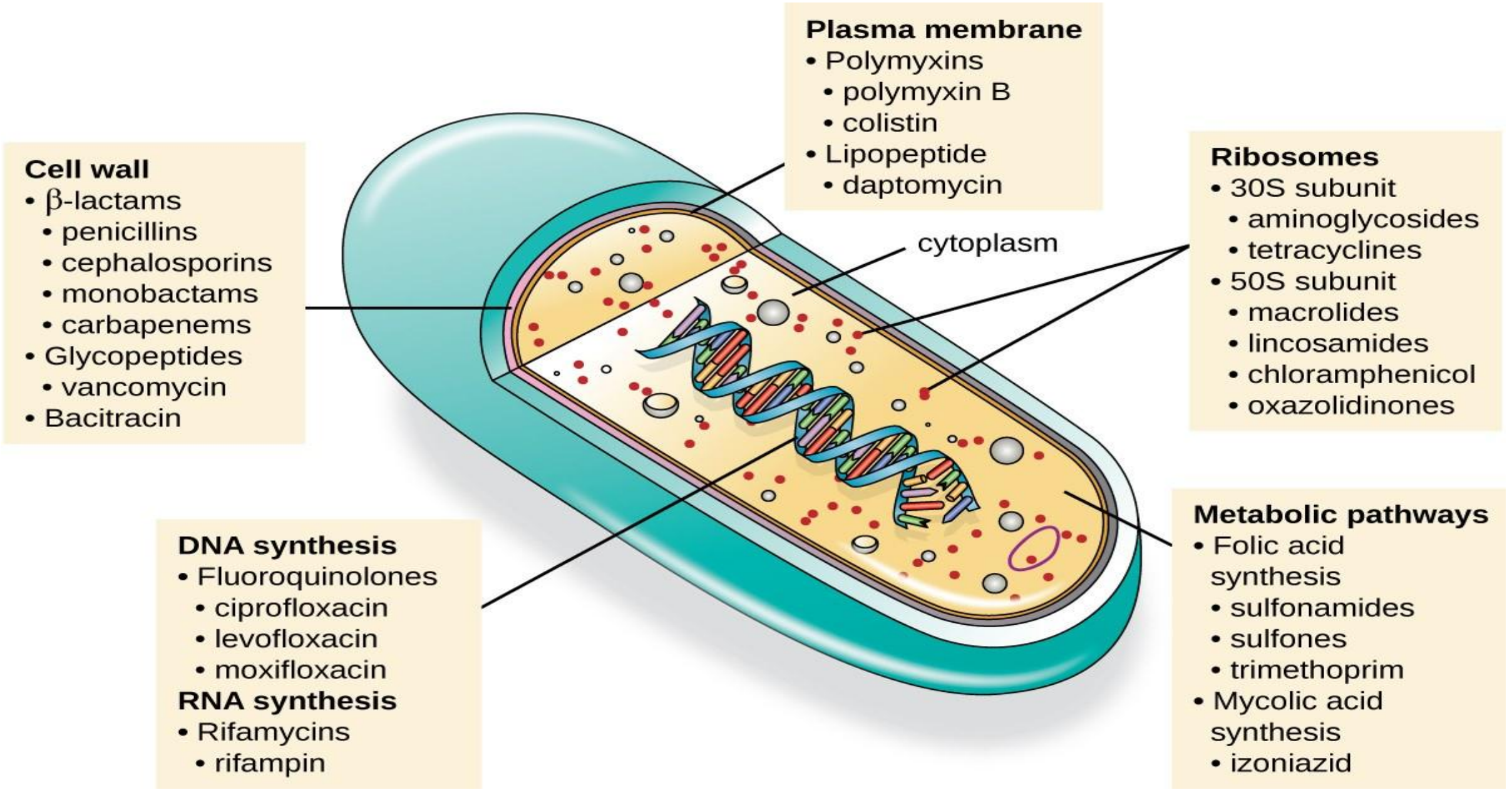
- ***Drug Names***: Vancomycin is an example of a glycopeptide. Most of these drug names end in “in” with some ending in “mycin”.
- ***Gram Coverage***: Glycopeptides primarily cover gram-positive bacteria as they are large and cannot pass through the porin channels found in the outer membrane of gram-negative bacteria.
- ***Mechanism of Action***: Glycopeptides inhibit cell wall synthesis.
- ***Example Indications***: Glycopeptides can be used for methicillin-resistant Staphylococcus aureus (MRSA), skin infections, and endocarditis among others.

How do antibiotics work?

- Antibiotics work by blocking vital processes in bacteria, killing the bacteria or stopping them from multiplying. This helps the body's natural immune system to fight the bacterial infection. Different antibiotics work against different types of bacteria.
- Antibiotics that affect a wide range of bacteria are called broad spectrum antibiotics (eg, amoxicillin and gentamicin).

- Antibiotics that affect only a few types of bacteria are called narrow spectrum antibiotics (eg, penicillin).

- Different types of antibiotics work in different ways. For example, penicillin destroys bacterial cell walls, while other antibiotics can affect the way the bacterial cell works.
- Doctors choose an antibiotic according to the bacteria that usually cause a particular infection. Sometimes your doctor will do a test to identify the exact type of bacteria causing your infection and its sensitivity to particular antibiotics.

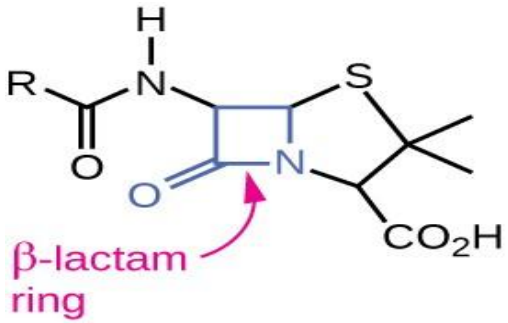


There are several classes of antibacterial compounds that are typically classified based on their bacterial target.

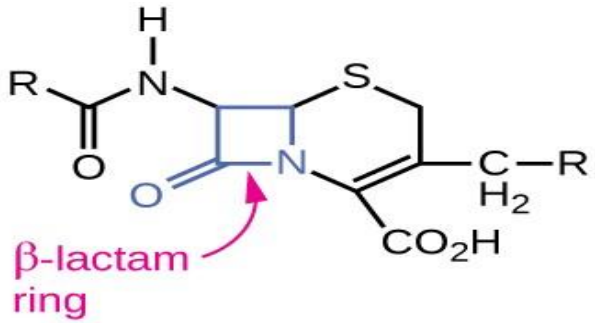
Common Antibacterial Drugs by Mode of Action……VIT		
Mode of Action	**Target**	**Drug Class**
Inhibit cell wall biosynthesis	Penicillin-binding proteins	β-lactams: penicillins, cephalosporins, monobactams, carbapenems
	Peptidoglycan subunits	Glycopeptides
	Peptidoglycan subunit transport	Bacitracin
Inhibit biosynthesis of proteins	30S ribosomal subunit	Aminoglycosides, tetracyclines
	50S ribosomal subunit	Macrolides, lincosamides, chloramphenicol, oxazolidinones
Disrupt membranes	Lipopolysaccharide, inner and outer membranes	Polymyxin B, colistin, daptomycin
Inhibit nucleic acid synthesis	RNA	Rifamycin
	DNA	Fluoroquinolones
Antimetabolites	Folic acid synthesis enzyme	Sulfonamides, trimethoprim
	Mycolic acid synthesis enzyme	Isonicotinic acid hydrazide
Mycobacterial adenosine triphosphate (ATP) synthase	Mycobacterial ATP synthase	Diarylquinoline

1. Inhibitors of Cell Wall Biosynthesis

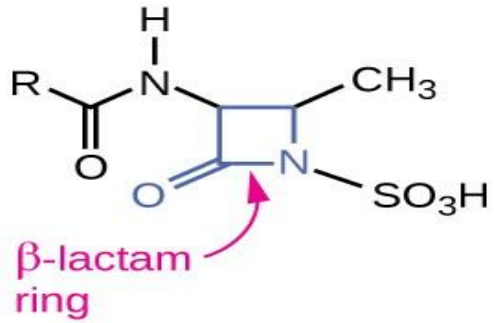
- Several different classes of antibacterials block steps in the biosynthesis of **peptidoglycan**, making cells more susceptible to osmotic lysis . Therefore, antibacterials that target cell wall biosynthesis are bactericidal in their action. Because human cells do not make peptidoglycan, this mode of action is an excellent example of selective toxicity.
- Penicillin, the first antibiotic discovered, is one of several antibacterials within a class called **β-lactams**. This group of compounds includes the **penicillins**, **cephalosporins**, **monobactams**, and **carbapenems**, and is characterized by the presence of a **β-lactam ring** found within the central structure of the drug molecule . The β-lactam antibacterials block the crosslinking of peptide chains during the biosynthesis of new peptidoglycan in the bacterial cell wall. They are able to block this process because the β-lactam structure is similar to the structure of the peptidoglycan subunit component that is recognized by the crosslinking **transpeptidase** enzyme, also known as a **penicillin-binding protein (PBP)**.



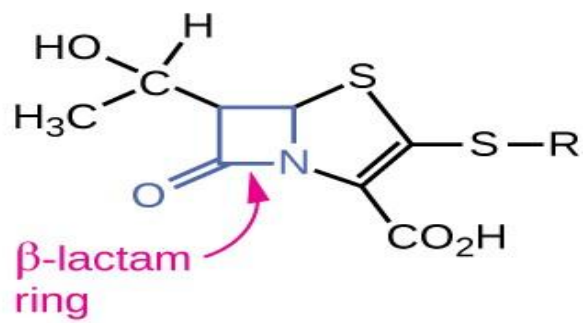
penicillin



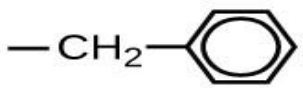
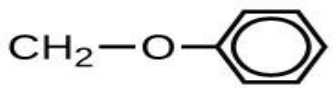
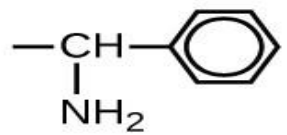
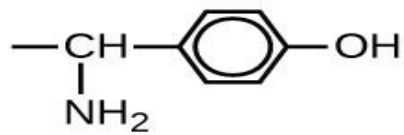
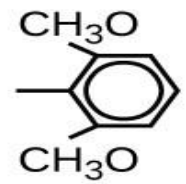
cephalosporin

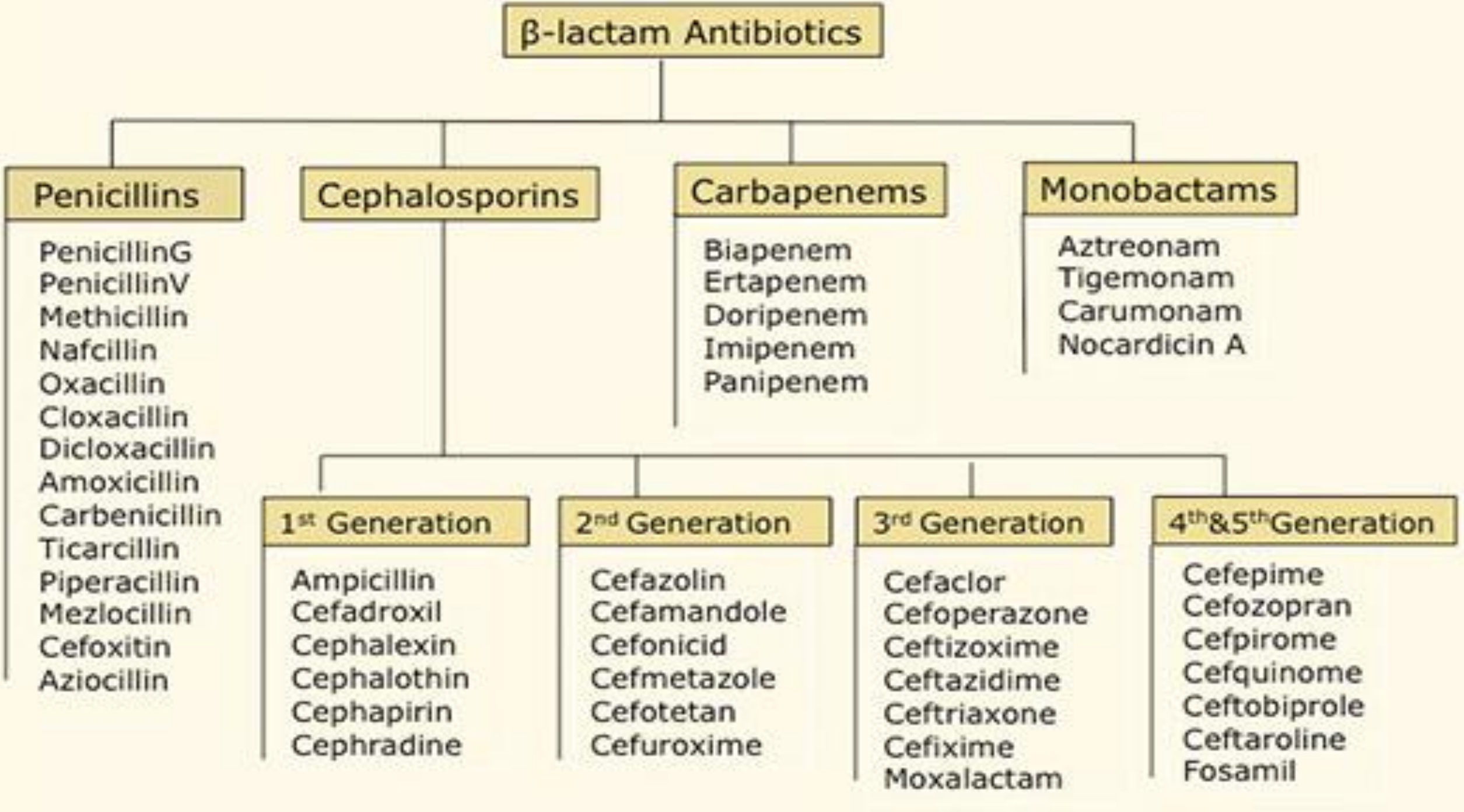


monobactam



carbapenem

R group					
Drug name	penicillin G	penicillin V	ampicillin	amoxicillin	methicillin
Spectrum of activity	G+ and a few G−	similar to penicillin G	G+ and more G− than penicillin	similar to ampicillin	G+ only, including β-lactamase producers
Route of administration	parenteral	oral	parenteral and oral	oral (better than ampicillin)	parenteral


β-lactam Antibiotics
Penicillins
PenicillinG
PenicillinV
Methicillin
Nafcillin
Oxacillin
Cloxacillin
Dicloxacillin
Amoxicillin
Carbenicillin
Ticarcillin
Piperacillin
Mezlocillin
Cefoxitin
Aziocillin
Cephalosporins
1st Generation
Ampicillin
Cefadroxil
Cephalexin
Cephalothin
Cephapirin
Cephradine
2nd Generation
Cefazolin
Cefamandole
Cefonicid
Cefmetazole
Cefotetan
Cefuroxime
3rd Generation
Cefaclor
Cefoperazone
Ceftizoxime
Ceftazidime
Ceftriaxone
Cefixime
Moxalactam
4th&5th Generation
Cefepime
Cefozopran
Cefpirome
Cefquinome
Ceftobiprole
Ceftaroline
Fosamil
Carbapenems
Biapenem
Ertapenem
Doripenem
Imipenem
Panipenem
Monobactams
Aztreonam
Tigemonam
Carumonam
Nocardicin A

2. Inhibitors of Protein Biosynthesis

- The cytoplasmic **ribosomes** found in animal cells (80S) are structurally distinct from those found in bacterial cells (70S), making protein biosynthesis a good selective target for antibacterial drugs. Several types of protein biosynthesis inhibitors are discussed in this section and are summarized in Figure.

A. Protein Synthesis Inhibitors That Bind the 30S Subunit

- Aminoglycosides are large, highly polar antibacterial drugs that bind to the 30S subunit of bacterial ribosomes, impairing the proofreading ability of the ribosomal complex. This impairment causes mismatches between codons and anticodons, resulting in the production of proteins with incorrect amino acids and shortened proteins that insert into the cytoplasmic membrane. Disruption of the cytoplasmic membrane by the faulty proteins kills the bacterial cells. The **aminoglycosides**, which include drugs such as **streptomycin**, **gentamicin**, **neomycin**, and **kanamycin**, are potent broad-spectrum antibacterials. However, aminoglycosides have been shown to be nephrotoxic (damaging to kidney), neurotoxic (damaging to the nervous system), and ototoxic (damaging to the ear).

Inhibitors of Protein Biosynthesis . Cont.

- Another class of antibacterial compounds that bind to the 30S subunit is the **tetracyclines**.
- In contrast to aminoglycosides, these drugs are bacteriostatic and inhibit protein synthesis by blocking the association of tRNAs with the ribosome during translation. tetracyclines produced by various strains of ***Streptomyces*** were first discovered in the 1940s, and several semisynthetic tetracyclines, including **doxycycline** and **tigecycline** have also been produced.

Inhibitors of Protein Biosynthesis. Cont.

B. Protein Synthesis Inhibitors That Bind the 50S Subunit

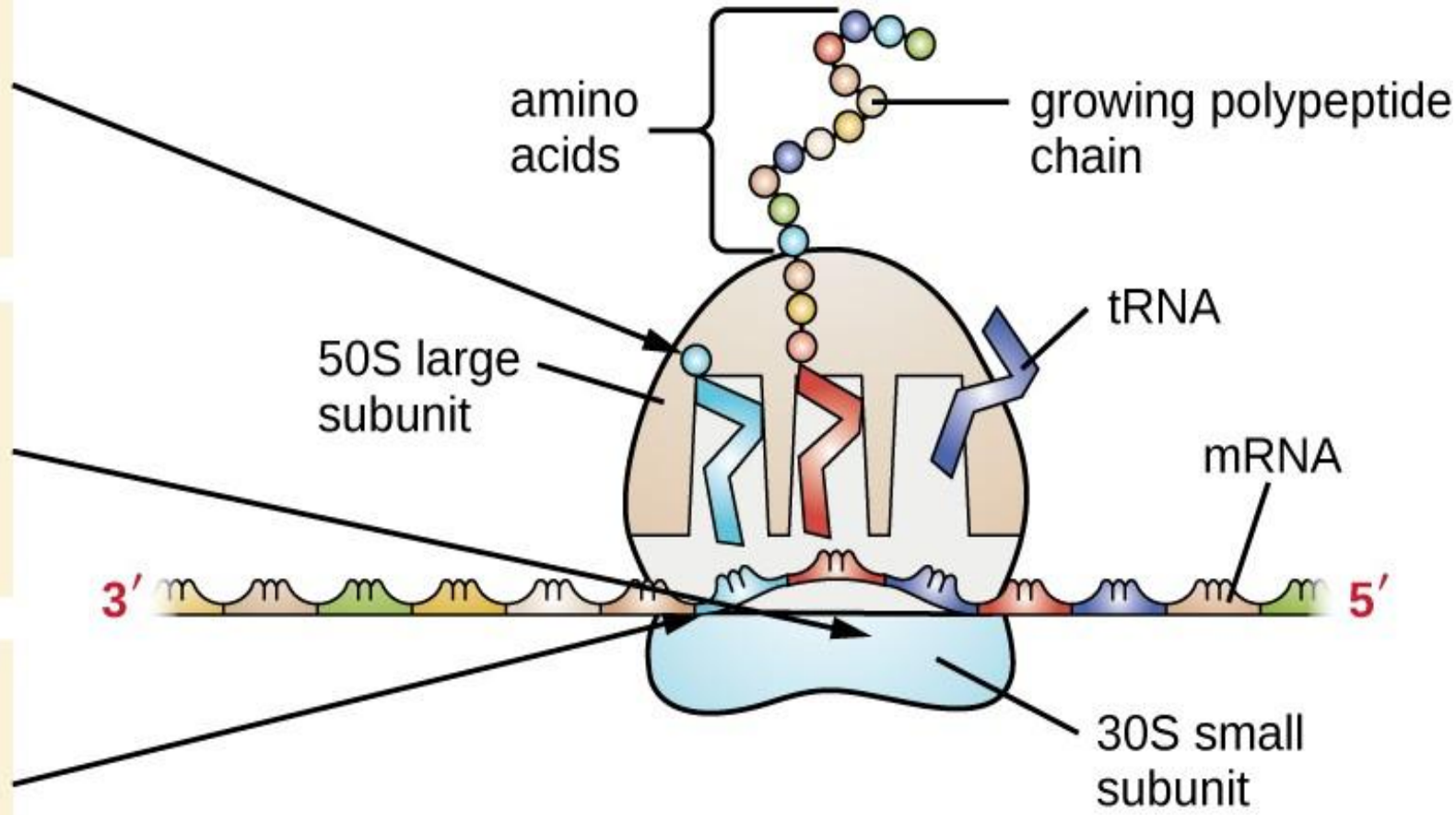
- There are several classes of antibacterial drugs that work through binding to the 50S subunit of bacterial ribosomes. The macrolide antibacterial drugs have a large, complex ring structure and are part of a larger class of naturally produced secondary metabolites called **polyketides**, complex compounds produced in a stepwise fashion through the repeated addition of two-carbon units by a mechanism similar to that used for fatty acid synthesis.
- Macrolides are broad-spectrum, bacteriostatic drugs that block elongation of proteins by inhibiting peptide bond formation between specific combinations of amino acids. The first macrolide was **erythromycin**. It was isolated in 1952 from ***Streptomyces erythreus*** and prevents translocation. Semisynthetic macrolides include azithromycin and telithromycin.,

Major classes of protein synthesis–inhibiting antibacterials

Chloramphenicol, macrolides, and lincosamides
- Bind to the 50S ribosomal subunit
- Prevent peptide bond formation
- Stop protein synthesis

Aminoglycosides
- Bind to the 30S ribosomal subunit
- Impair proofreading, resulting in production of faulty proteins

Tetracyclines
- Bind to the 30S ribosomal subunit
- Block the binding of tRNAs, thereby inhibiting protein synthesis



3. Inhibitors of Membrane Function

- A small group of antibacterials target the bacterial membrane as their mode of action .
- The **polymyxins** are natural polypeptide antibiotics that were first discovered in 1947 as products of *Bacillus polymyxa*; only polymyxin B and polymyxin E (**colistin**) have been used clinically.

Drugs That Inhibit Bacterial Membrane Function

Mechanism of Action	Drug Class	Specific Drugs	Spectrum of Activity	Clinical Use
Interacts with lipopolysaccharide in the outer membrane of gram-negative bacteria, killing the cell through the eventual disruption of the outer membrane and cytoplasmic membrane	Polymyxins	Polymyxin B	Narrow spectrum against gram-negative bacteria, including multidrug-resistant strains	Topical preparations to prevent infections in wounds
		Polymyxin E (colistin)	Narrow spectrum against gram-negative bacteria, including multidrug-resistant strains	Oral dosing to decontaminate bowels to prevent infections in immunocompromised patients or patients undergoing invasive surgery/procedures.
				Intravenous dosing to treat serious systemic infections caused by multidrug-resistant pathogens

4. Inhibitors of Nucleic Acid Synthesis

- Some antibacterial drugs work by inhibiting nucleic acid synthesis
- For example, **metronidazole** is a semisynthetic member of the nitroimidazole family that is also an antiprotozoan. It interferes with DNA replication in target cells.
- The drug **rifampin** is a semisynthetic member of the **rifamycin** family and functions by blocking RNA polymerase activity in bacteria.
- The RNA polymerase enzymes in bacteria are structurally different from those in eukaryotes, providing for **selective toxicity** against bacterial cells.
- It is used for the treatment of a variety of infections, but its primary use, often in a cocktail with other antibacterial drugs, is against mycobacteria that cause **tuberculosis**.
- Despite the selectivity of its mechanism, rifampin can induce liver enzymes to increase metabolism of other drugs being administered (antagonism), leading to **hepatotoxicity** (liver toxicity) and negatively influencing the bioavailability and therapeutic effect of the companion drugs.

Drugs That Inhibit Bacterial Nucleic Acid Synthesis

Mechanisms of Action	Drug Class	Specific Drugs	Spectrum of activity	Clinical Use
Inhibits bacterial RNA polymerase activity and blocks transcription, killing the cell	Rifamycin	Rifampin	Narrow spectrum with activity against gram-positive and limited numbers of gram-negative bacteria. Also active against *Mycobacterium tuberculosis*.	Combination therapy for treatment of tuberculosis
Inhibits the activity of DNA gyrase and blocks DNA replication, killing the cell	Fluoroquinolones	Ciprofloxacin, ofloxacin, moxifloxacin	Broad spectrum against gram-positive and gram-negative bacteria	Wide variety of skin and systemic infections

5. Inhibitors of Metabolic Pathways

- Some synthetic drugs control bacterial infections by functioning as **antimetabolites**, competitive inhibitors for bacterial metabolic enzymes.
- The **sulfonamides** (**sulfa drugs**) are the oldest synthetic antibacterial agents and are structural analogues of *para*-aminobenzoic acid (PABA), an early intermediate in folic acid synthesis By inhibiting the enzyme involved in the production of dihydrofolic acid, sulfonamides block bacterial biosynthesis of folic acid and, subsequently, pyrimidines and purines required for nucleic acid synthesis.
- This mechanism of action provides bacteriostatic inhibition of growth against a wide spectrum of gram-positive and gram-negative pathogens.
- Because humans obtain folic acid from food instead of synthesizing it intracellularly, sulfonamides are selectively toxic for bacteria.
- However, allergic reactions to sulfa drugs are common. The **sulfones** are structurally similar to sulfonamides but are not commonly used today except for the treatment of **Hansen's disease** (**leprosy**).

6. Inhibitor of ATP Synthase

- Bedaquiline, representing the synthetic antibacterial class of compounds called the **diarylquinolones**, uses a novel mode of action that specifically inhibits mycobacterial growth.
- Although the specific mechanism has yet to be elucidated, this compound appears to interfere with the function of **ATP** synthases, perhaps by interfering with the use of the hydrogen ion gradient for ATP synthesis by **oxidative phosphorylation**, leading to reduced ATP production.
- Due to its **side effects**, including **hepatotoxicity** and potentially lethal heart arrhythmia, its use is reserved for serious, otherwise untreatable cases of **tuberculosis**.

Antibiotic Classes

Mechanism of Action

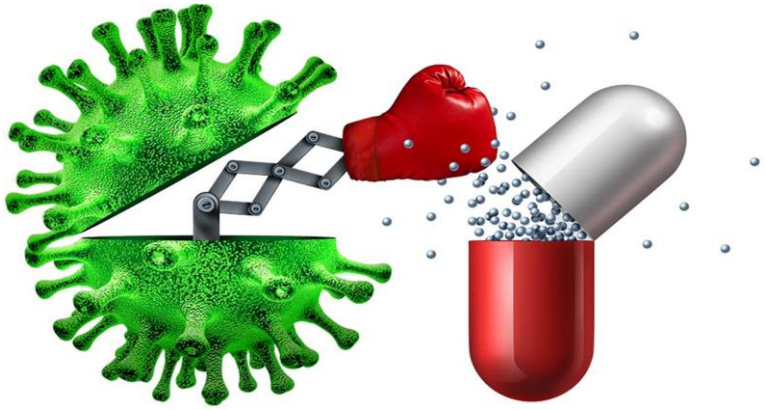
1. Aminoglycosides - Inhibit Protein Synthesis
2. Cephalosporins - Inhibit Cell Wall Synthesis
3. Tetracyclines - Inhibit Protein Synthesis
4. Penicillins - Inhibit Cell Wall Synthesis
5. SulFOnamides - Inhibit FOlate Synthesis = "FO"
6. FluoroQUINolones - Inhibit DNA Replication = QUINtuplets
7. Macrolides - Inhibit Protein Synthesis
8. Carbapenems - Inhibit Cell Wall Synthesis
9. Lincosamides - Inhibit Protein Synthesis
10. Glycopeptides - Inhibit Cell Wall Synthesis

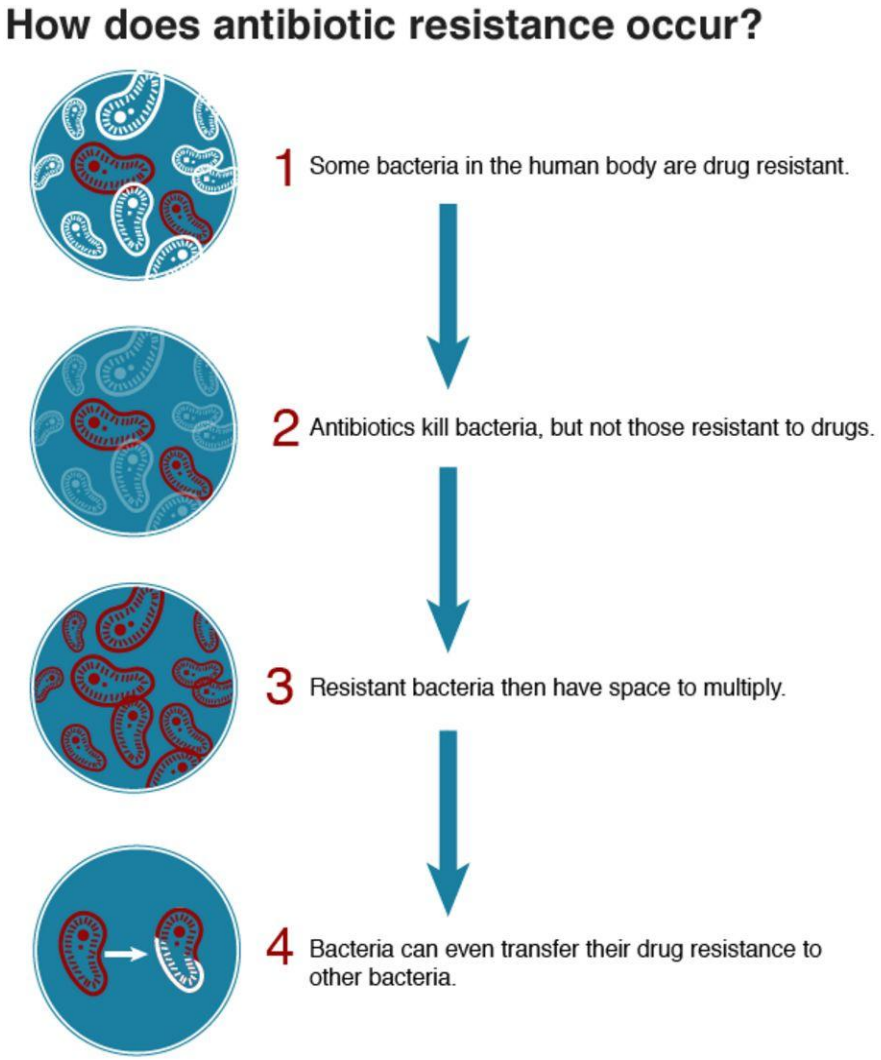
MALT = Protein

Macrolides
Aminoglycosides
Lincosamides
Tetracyclines

Image: You can use the above tricks to remember the mechanism of action for each antibiotic class.

- **Resistance**
- Antibiotics are very effective at killing most, but not all, bacteria. Some bacteria acquire genes that protect them from the drug's attack.
- They survive treatment and reproduce themselves, spreading the key genes more widely so the drug becomes ever less effective.
- **What are 'superbugs'?**
- Superbugs' are bacteria that are resistant to several different antibiotics such as methicillin-resistant Staphylococcus aureus (MRSA) bacteria - commonly found in hospitals - and the bacteria that cause tuberculosis (Mycobacterium tuberculosis).
- These are now very hard to treat because of antibiotic resistance. To help prevent antibiotic resistance:

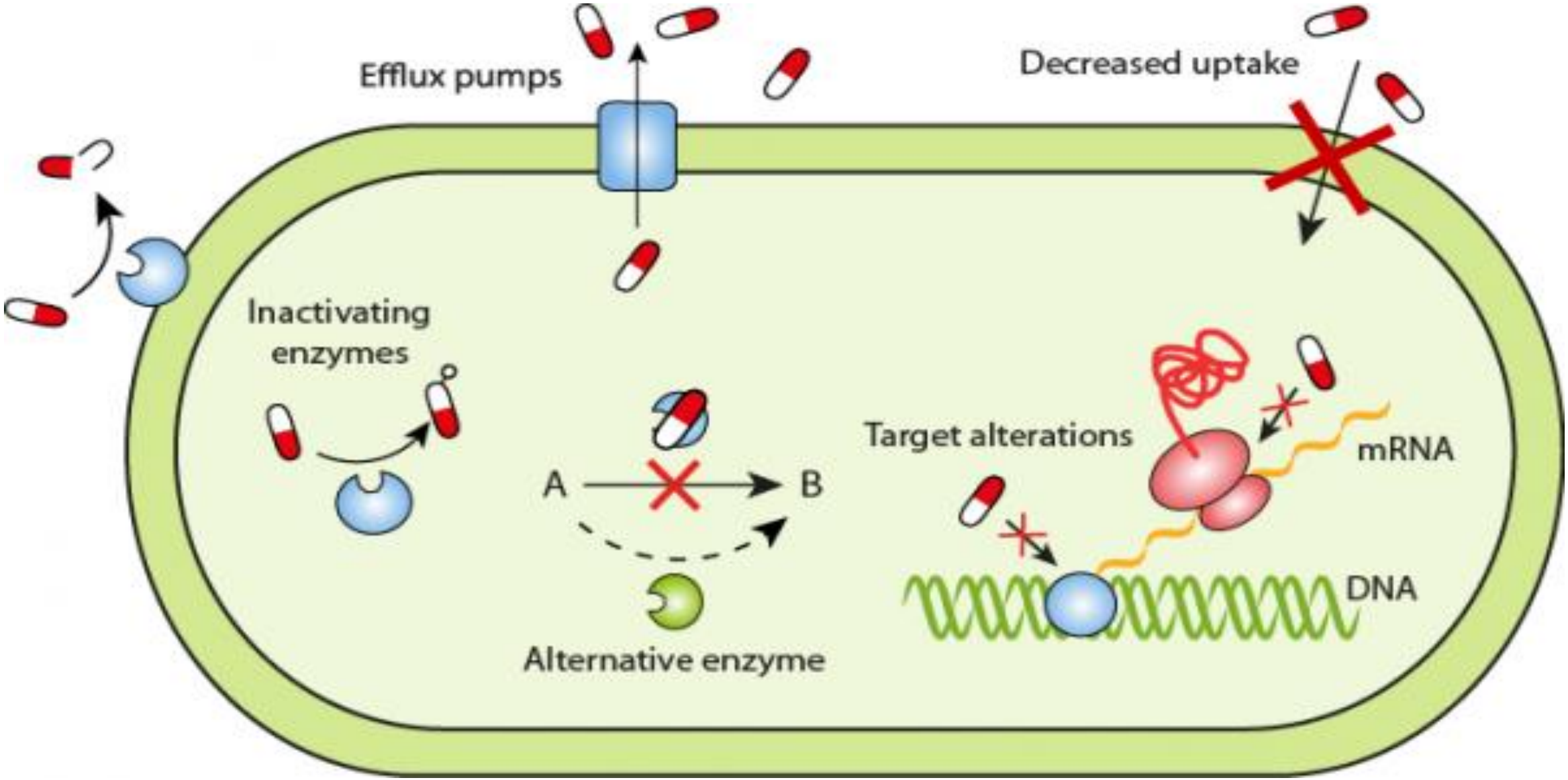




Antibiotic resistance mechanisms

❑1. Stop the antibiotic from reaching its target

- **A. Pump the antibiotic out from the bacterial cell.** Bacteria can produce pumps that sit in their membrane or cell wall. These so-called efflux pumps are very common in bacteria and can transport a variety of compounds such as signal molecules and nutrients.
- **B. Decrease permeability of the membrane that surrounds the bacterial cell.** Certain changes in the bacterial membrane make it more difficult to pass through. In this way, less of the antibiotic gets into the bacteria.
- **C. Destroy the antibiotic.** There are bacterial enzymes that can inactivate antibiotics. One example is β-lactamase that destroys the active component (the β-lactam ring) of penicillins, extremely important antibiotics for treating human infections. In later years, bacteria that produce extended-spectrum β-lactamases, so called ESBL-producing bacteria, have become a major problem.
- **D. Modify the antibiotic.** Bacteria can sometimes produce enzymes that are capable of adding different chemical groups to antibiotics. This in turn prohibits binding between the antibiotic and its target in the bacterial cell.


Efflux pumps
Decreased uptake
Inactivating enzymes
A
B
Alternative enzyme
Target alterations
mRNA
DNA

2. Modify or bypass the target of the antibiotic

- **A. Camouflage the target.** Changes in the composition or structure of the target in the bacterium (resulting from mutations in the bacterial DNA) can stop the antibiotic from interacting with the target. Alternatively, the bacteria can add different chemical groups to the target structure, in this way shielding it from the antibiotic.
- **B. Express alternative proteins.** Some bacteria are able to produce alternative proteins that can be used instead of the ones that are inhibited by the antibiotic. For example, the bacterium *Staphylococcus aureus* can acquire the resistance gene *mecA* and produce a new penicillin-binding protein. These proteins are needed for bacterial cell wall synthesis and are the targets of β-lactam antibiotics. The new penicillin-binding protein has low affinity to β-lactam antibiotics and is thus resistant to the drugs, and the bacteria survive treatment. This type of resistance is the basis in MRSA (methicillin-resistant *Staphylococcus aureus*).
- **C. Reprogram target.** Sometimes bacteria can produce a different variant of a structure it needs. For example, Vancomycin-resistant bacteria make a different cell wall compared to susceptible bacteria. The antibiotic is not able to interact as well with this type of cell wall.

Antibiotic Therapy in Dentistry

- The physiological changes of pregnancy can affect the condition of the oral cavity such as increasing the risk of gingivitis and pyogenic granuloma
- Preventive or therapeutic interventions during this period should be carried out to preserve the health of both mother and her neonate, enhance maternal oral health, and reduce children's future oral problems
- In this regard, it has been mentioned that the mothers with poor oral hygiene who have a higher number of microorganisms in their saliva, especially *Streptococcus mutans*, can easily transmit the infection to the infant causing several serious problems for them.
- It should be also noted that most of the dental procedures are not emergencies and can be postponed after delivery; however, acute dental infections should be managed during pregnancy

Antibiotic Use in Pediatric Dentistry

Agent	Situation	Dose	Maximum dose	Available forms
Amoxicillin	First choice in dental infection	20–40 mg/kg/day, e8 h	2 g/day	Tablet 125 mg, capsule 250 mg and 500 mg, and oral suspension 125 mg/5 ml and 250 mg/5 ml
Amoxicillin + clavulanic acid	Failure of first choice antibiotic		1000–2800 mg amoxicillin/143–400 mg clavulanic acid	Tablet 375 mg, 625 mg, and 1000 mg and oral suspension 228.5 mg/5 ml
Clindamycin	Penicillin hypersensitivity	10–20 mg/kg/day, e6 h		Suspension 75 mg/5 ml
Cephalexin	Necessity of broad-spectrum action	25–100 mg/kg/day, e6_8 h		Tablet 125 mg, 250 mg, and 500 mg, capsule 250 mg, 500 mg, and 750 mg, and oral suspension 125 mg/5 ml and 250 mg/5 ml
Metronidazole	Anaerobic bacteria	30 mg/kg/day, 8 h	2 g/day	Tablet 200 mg, 250 mg, 400 mg, and 500 mg,


Thank You !