Cell wall synthesis inhibitors

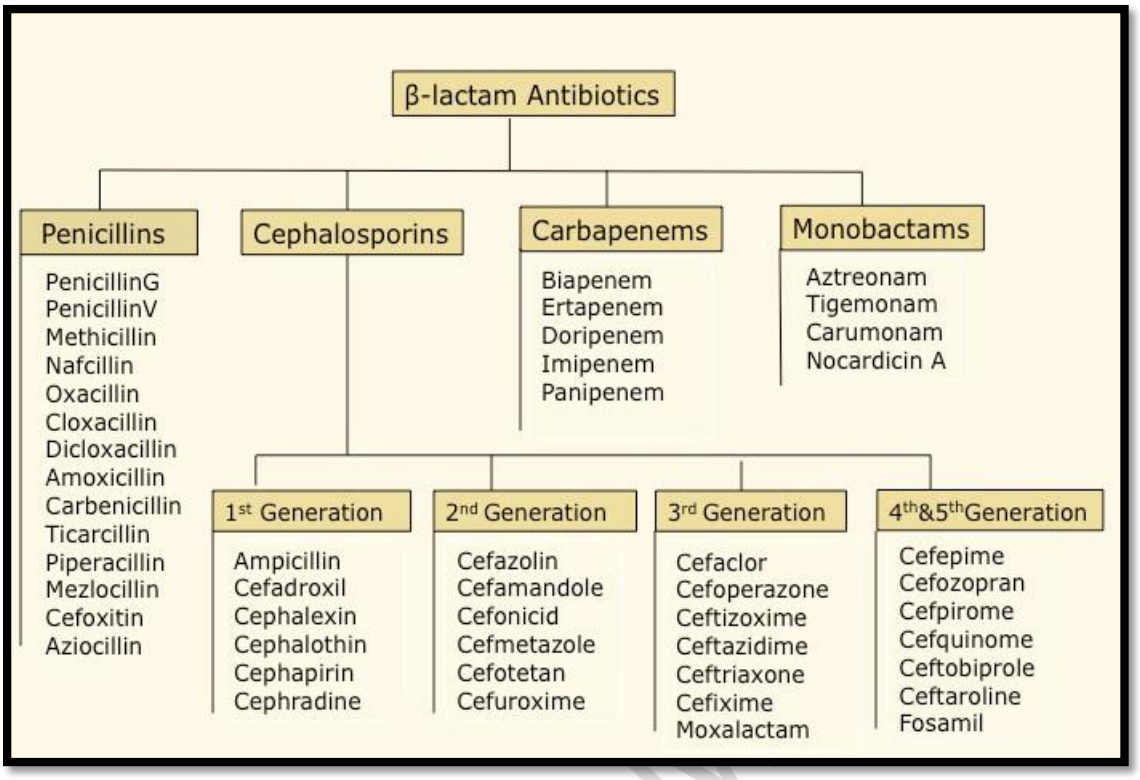


Figure (1): show the classification of β-Lactam drugs

A-Penicillin : The penicillin are among the most widely effective and the least toxic drugs known, but increased resistance has limited their use.

M.O.A: The penicillin interfere with the last step of bacterial cell wall synthesis resulting in exposure of the osmotically less stable membrane, cell lysis can then occur.

Types of Penicillin:

1-Natural penicillins: Natural penicillins (**penicillin G and penicillin V)**

2-Antistaphylococcal penicillin: (Methicillin, nafcillin oxacillin, and dicloxacillin) are β-lactamase (penicillinase)-resistant penicillin.

3- Extended-spectrum penicillin: Ampicillin and Amoxicillin have an antibacterial spectrum similar to that of penicillin G but are more effective against gram-negative bacilli.

Note: Resistance to these antibiotics is now a major clinical problem, so Formulation with a **β-lactamase inhibitor** such as clavulanic acid or sulbactam , protects amoxicillin or ampicillin, respectively from enzymatic hydrolysis to produce **(Augmentin)** known to their wide antibacterial spectrum.

4-Antipseudomonal penicillins: Piperacillin and ticarcillin called antipseudomonal penicillins because of their activity against *Pseudomonas aeruginosa.*

Nursing Considerations of penicillins: The role of the nurse in drug therapy with penicillins involves**:**

1. it is essential to assess previous drug reactions to penicillin prior to administration, If the client has a history of severe penicillin-allergic reactions, cephalosporin should be avoided due to the risk for cross-sensitization.
2. After parenteral administration of penicillins, the client should be observed for 30 minutes for possible allergic reactions, especially with the first dose
3. Clients with impaired renal function may require smaller doses because the majority of penicillin is excreted through the kidneys.

B-Cephalosporin: Most cephalosporins are produced semi synthetically by the chemical attachment of side chains to 7-aminocephalosporanic acid. Cephalosporins have the same mode of action as penicillins, and they are affected by the same resistance mechanisms. Cephalosporins are generally the treatment of choice for clients with gram-negative infections.

Administration: Many of the cephalosporins must be administered IV or IM , because of their poor oral absorption.

Classification of Cephalosporins:

1-First generation (Cefadroxil, Cephalexin): They are resistant to the staphylococcal penicillinase and also have activity against **Proteus mirabilis, E. coli, and Klebsiella. Pneumonia.**

2-Second generation(Cefazolin, Cefamandole): Appear greater activity against three additional gram-negative organisms: **H. influenzae, Enterobacter aerogenes, and some Neisseria species.**

3-Third generation(Ceftriaxone, Cefixime): third-generation cephalosporins have enhanced activity against gram-negative **bacilli and Serratia marcescens**. Ceftriaxone and cefotaxime have become agents of choice in the treatment of meningitis.

4-Fourth generation: (Cefepim, Cefozopran): Cefepime must be administered parenterally. Cefepime has activity against streptococci and staphylococci, Cefepimeis also effective against aerobic gram-negative bacteria.

5-Advanced generation (Ceftaroline, Fosamil): ceftaroline fosamil. It is indicated for the treatment of complicated skin and skin structure infections and community-acquired pneumonia.

Resistance of microorganisms to penicillin and cephalosporin: Natural resistance to the penicillins occurs as follows

1. β -Lactamase enzyme activity.

2. Decreased permeability to the drug.
3. Altered penicillin-binding protein PBPs.

The adverse effect of penicillin and cephalosporin: Hypersensitivity, Diarrhea, Nephritis, Neurotoxicity, Hematologic toxicities.

C- Other β-Lactam drugs:

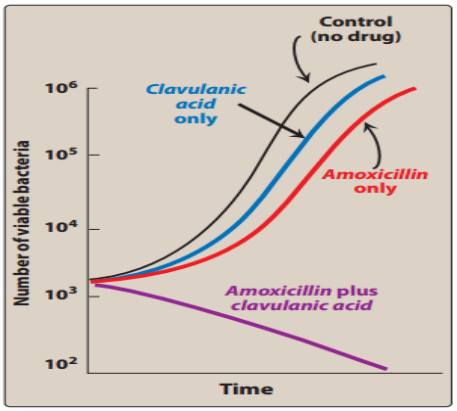
1-Carbapenems: These are synthetic β-lactam antibiotics that differ in structure from the penicillins, **Which include (Imipenem, meropenem doripenem, and ertapenem).**

Antibacterial spectrum: This drug plays a role in empiric therapy because it is active against β-lactamase–producing gram-positive and gram-negative organisms.

2-**Monobactams:** which also disrupt bacterial cell wall synthesis, are unique because the β-lactam ring is not fused to another ring. **Aztreonam,** which is the only monobactam has antimicrobial activity directed primarily against gram-negative pathogens.

β-Lactamase inhibitors: β-Lactamase inhibitors, such as **clavulanic acid, sulbactam and tazobactam** contain a β-lactam ring but, by themselves, do not have significant antibacterial activity or cause any significant adverse effects. Instead, they bind to and inactivate β-lactamases, thereby protecting the antibiotics that are normally substrates for these enzymes. The β-lactamase inhibitors formulated in combination with β-lactamase–sensitive antibiotics.

Figure (3): show the effect of clavulanic acid and amoxicillin in the inhibition of E.coli



Protein synthesis inhibitor drugs

A number of antibiotics exert their antimicrobial effects by targeting bacterial ribosomes and inhibiting bacterial protein synthesis.

Bacterial ribosomes are composed of the 30S and 50S subunits while mammalian ribosomes have 40S and 60S subunits).

*** This group includes (Aminoglycosides, Macrolides, chloramphenicol, clindamycin, and tetracycline).

1-Aminoglycosides: (gentamycin, Streptomycin, Amikacin):

Are effective for the majority of aerobic gram-negative bacilli, including those that may be multidrug-resistant, such as ***Pseudomonas. aeruginosa, Klebsiella pneumonia,*** **and** ***Enterobacter*** **spp.**

Mechanism of action: they bind the 30S ribosomal subunit, where they interfere with the assembly of the functional ribosomal apparatus and/or cause the 30S subunit of the completed ribosome to misread the genetic code.

Note: Antibiotics that disrupt protein synthesis are generally bacteriostatic except aminoglycoside which is bactericidal.

Adverse effects: Ototoxicity, Nephrotoxicity, Neuromuscular paralysis, Allergic reactions.

2-Macrolides: (erythromycin, Azithromycin, clarithromycin):

The macrolides are a group of antibiotics with a macrocyclic lactone structure to which one or more deoxy sugars attached.

A. Mechanism of action: The macrolides bind irreversibly to a site on the 50S subunit of the bacterial ribosome, thus inhibiting translocation steps of protein synthesis.

Antibacterial spectrum:

1. **Erythromycin:** This drug is effective against many of the same organisms as penicillin G Therefore; it could be use in patients with penicillin allergy.
2. **Azithromycin:** Although less active against streptococci and staphylococci than erythromycin, azithromycin is far more active against respiratory infections like **H. influenza and Moraxella catarrhalis.** Azithromycin is the preferred therapy for **urethritis caused by Chlamydia trachomatis.**

Adverse effects and interaction:
Gastric distress and motility, Cholestatic jaundice, Ototoxicity.
Interactions:

1. Anesthetic agents and anticonvulsant drugs may interact with erythromycin to cause serum drug levels to rise and result in toxicity
2. This drug interacts with cyclosporine, increasing the risk for nephrotoxicity.
3. It may increase the effects of warfarin. Because macrolides may decrease warfarin metabolism and excretion**.**

3-Chloramphenicol: The use of chloramphenicol a broad-spectrum antibiotic, is restricted to life-threatening infections for which no alternatives exist. is active against many types of microorganisms including **chlamydiae, rickettsiae, spirochetes, and anaerobes**. The drug is primarily bacteriostatic, but depending on the dose and organism, it may be bactericidal.

Mechanism of action: It binds reversibly to the bacterial 50S ribosomal subunit and inhibits protein synthesis at the peptidyl transferase reaction.

Adverse effects:

1. Anemia 2-Gray baby syndrome

5-Tetracycline: (Demeclocycline, Doxycycline, Minocycline):

Bacteriostatic antibiotics are effective against a wide variety of organisms, including gram-positive and gram-negative bacteria, protozoa, **spirochetes, mycobacteria, and atypical species**.

Mechanism of action: The drugs bind reversibly to the 30S subunit of the bacterial ribosome. This action prevents the binding of tRNA to the mRNA–ribosome complex, thereby inhibiting bacterial protein synthesis.

Adverse effects: 1-Gastric discomfort 2-Effects on calcified tissues 3-discoloration of the teeth 4-Phototoxicity 5-Vestibular dysfunction

Drugs that Affect Nucleic Acid Synthesis

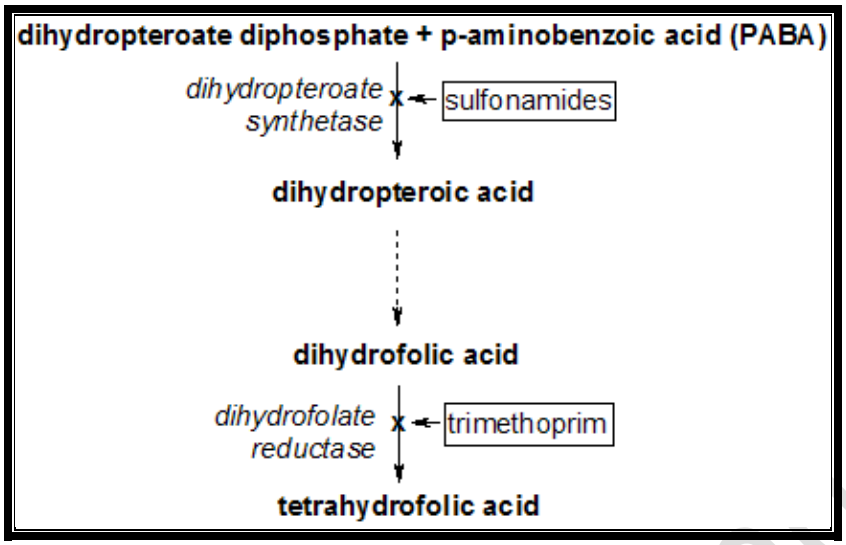
Fluoroquinolones:(Norfloxacin,Ciprofloxacin,Levofloxacin)

They are effective against gram-negative organisms (**Escherichia coli, P. aeruginosa, Haemophilus influenzae)**, atypical organisms **(Legionellaceae, Chlamydiaceae)**, gram-positive organisms (**streptococci**), and some mycobacteria (**Mycobacterium tuberculosis**). Fluoroquinolones are typically not used for the treatment of Staphylococcus aureus or enterococcal infections.

Mechanism of action: Inhibition of DNA gyrase, thus interfering with the separation of newly replicated DNA.

Drugs inhibit Folic acid synthesis

Sulfonamides and Trimethoprim: These drugs are seldom prescribe alone except in developing countries, where they still employed because of their low cost and efficacy.



Mechanism of action of sulfonamides and trimethoprim