Tishk International University- Nursing
Microbiology
Antimicrobials

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Lec.7-8

Antimicrobial Drug:

- Antimicrobial drug is a drug used to treat a microbial infection. "Antimicrobial" is a general term that refers to a group of drugs that includes antibiotics, antifungals, antiprotozoals, and antivirals.

Antibiotics

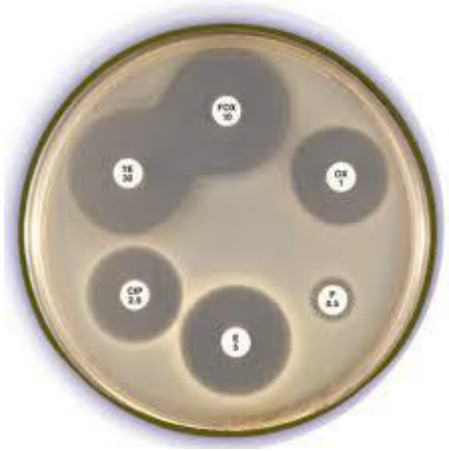
Antibiotics are drugs that kill or inhibit the growth of bacteria and are used to treat bacterial infections. They are produced in nature by soil bacteria and fungi.

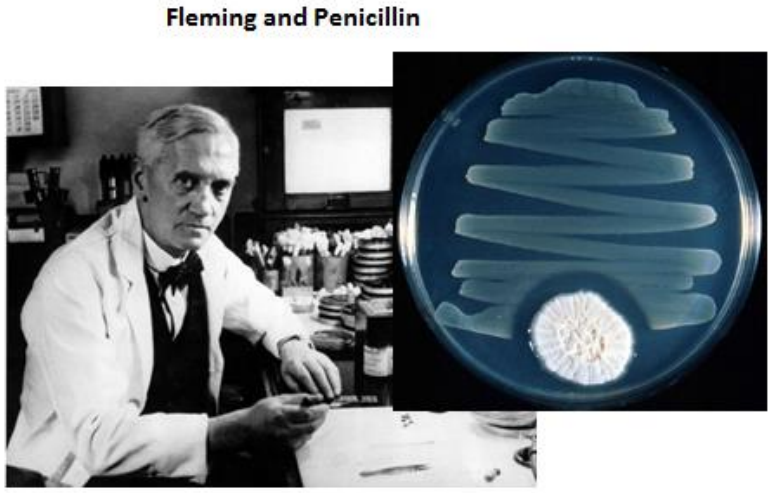
Antibiotics

- Fight pathogens
- Interfere with formation of cell walls
- Many obtained from bacteria or fungi
- Others produced synthetically

History

-The discovery of the first antibiotic was an accident. In **1928**, sir **Alexander Fleming**, , a Scottish biologist accidentally contaminated a plate with a fungus.
-He observed a clearly defined region of no bacterial growth where the fungi had contaminated the plate.



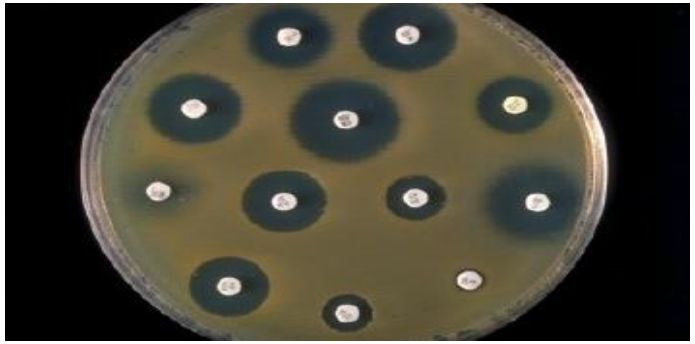


Zone of inhibition

- If an antibiotic stops the bacteria from growing or kills the bacteria, there will be an area around discs. where the bacteria have not grown enough to be visible. This is called a zone of inhibition.

- The area around the fungus was eventually referred to as a zone of inhibition

- Zone of inhibition due to the diffusion of a substance with antibiotic properties from the microorganism



Narrow and Broad Spectrum antibiotics

Narrow-spectrum drugs affect only a select group of microbes—gram-positive cells, for example (Clarithromycin, Clindamycin, Erythromycin.

•**Advantages :**

- The narrow-spectrum antibiotic will not kill as many of the normal microorganisms in the body as the broad spectrum antibiotics. So, It has less ability to cause superinfection.
- The narrow spectrum antibiotic will cause less resistance of the bacteria as it will deal with only specific bacteria.

•**Disadvantages :**

-Narrow spectrum antibiotics can be used only if the causative organism is identified.
- If you don't choose the drug very carefully, the drug may not actually kill the microorganism causing the infection.

- **Broad-spectrum drugs** affect a large number of microbes. Example :Azithromycin, Amoxicillin, Vancomycin, Levofloxacin,Streptomycin
- Tetracycline,Chloramphenicol

•**ADVANTAGES** :

- A clear advantage to the use of broad-spectrum antibiotics is that there is less of a need (as compared with narrow-spectrum antibiotics) to identify the infecting pathogen with real certainty before commencing treatment.

•**DISADVANTAGES :**

- Children who receive broad-spectrum antibiotics during their first year of life are at increased risk of developing childhood asthma.
- Broad Spectrum antibiotics may give rise to drug resistance.

How do antibiotics work?

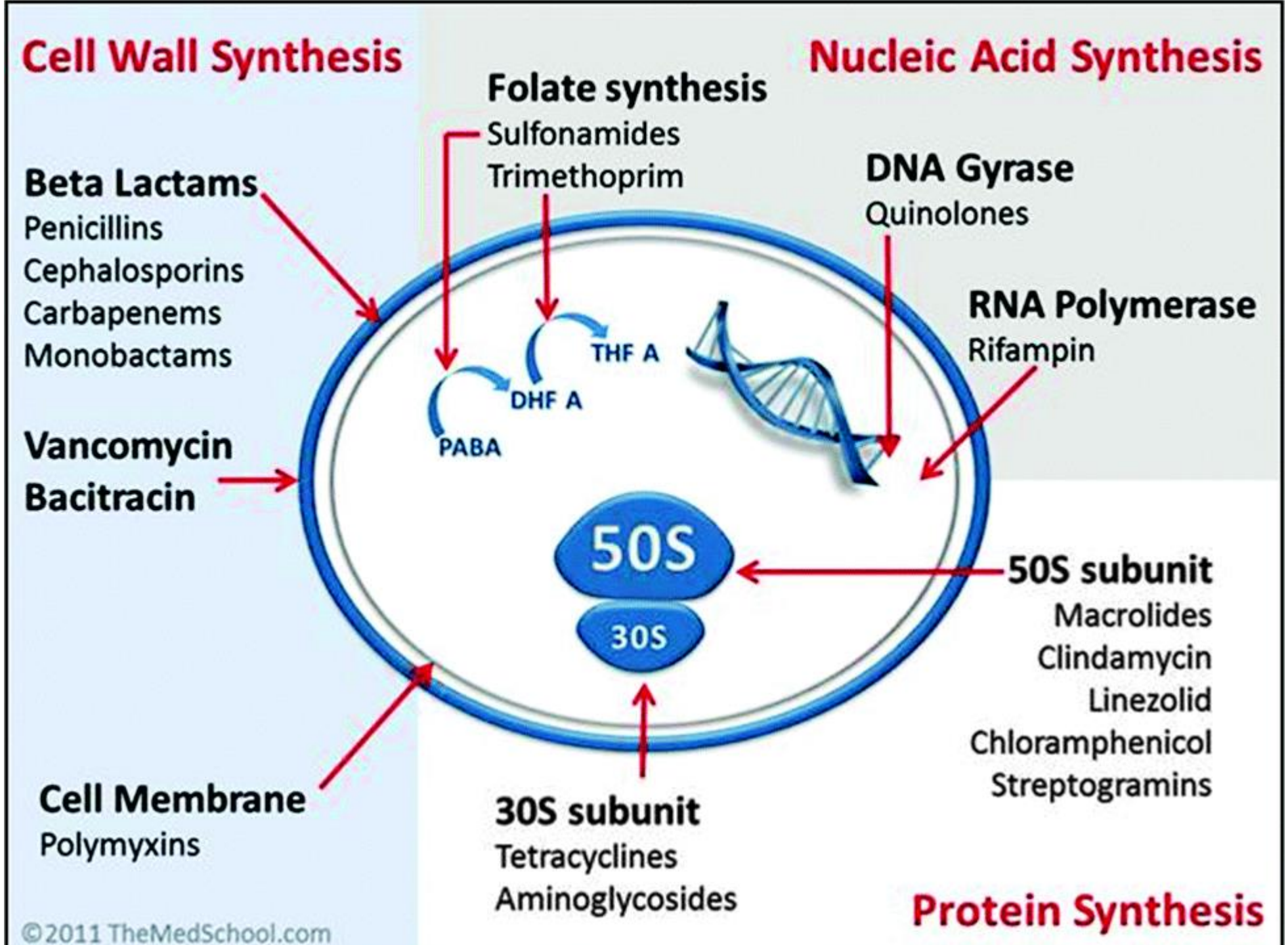
- Antibiotics take advantage of the difference between the structure of the bacterial cell and the host's cell.

- They either prevent the bacterial cells from multiplying so that the bacterial population remains the same.
- allowing the host's defense mechanism to fight the infection or kill the bacteria, for example stopping the mechanism responsible for building their cell walls.

Antibiotic targets

Antibiotic targets can be subdivided into five major groups:

- The bacterial cell wall
- The bacterial plasma membrane
- Synthesis of bacterial proteins
- Bacterial nucleic acids and metabolism


Cell Wall Synthesis
Nucleic Acid Synthesis
Folate synthesis
Sulfonamides
Trimethoprim
Beta Lactams
Penicillins
Cephalosporins
Carbapenems
Monobactams
DNA Gyrase
Quinolones
RNA Polymerase
Rifampin
THF A
DHF A
PABA
Vancomycin
Bacitracin
50S
30S
50S subunit
Macrolides
Clindamycin
Linezolid
Chloramphenicol
Streptogramins
Cell Membrane
Polymyxins
30S subunit
Tetracyclines
Aminoglycosides
Protein Synthesis
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Antibacterial Antibiotics:

- Inhibitors of Cell Wall Synthesis and Injury to plasma membrane:

1. All penicillin contain a b-lactam ring. Penicillin inhibit peptidoglycan synthesis.
2. Natural penicillin produced by *Penicillium* are effective against gram-positive coccus and spirochetes.
3. Some bacteria produce Penicillinases (b -lactamases) which are bacterial enzymes that destroy natural penicillin's.

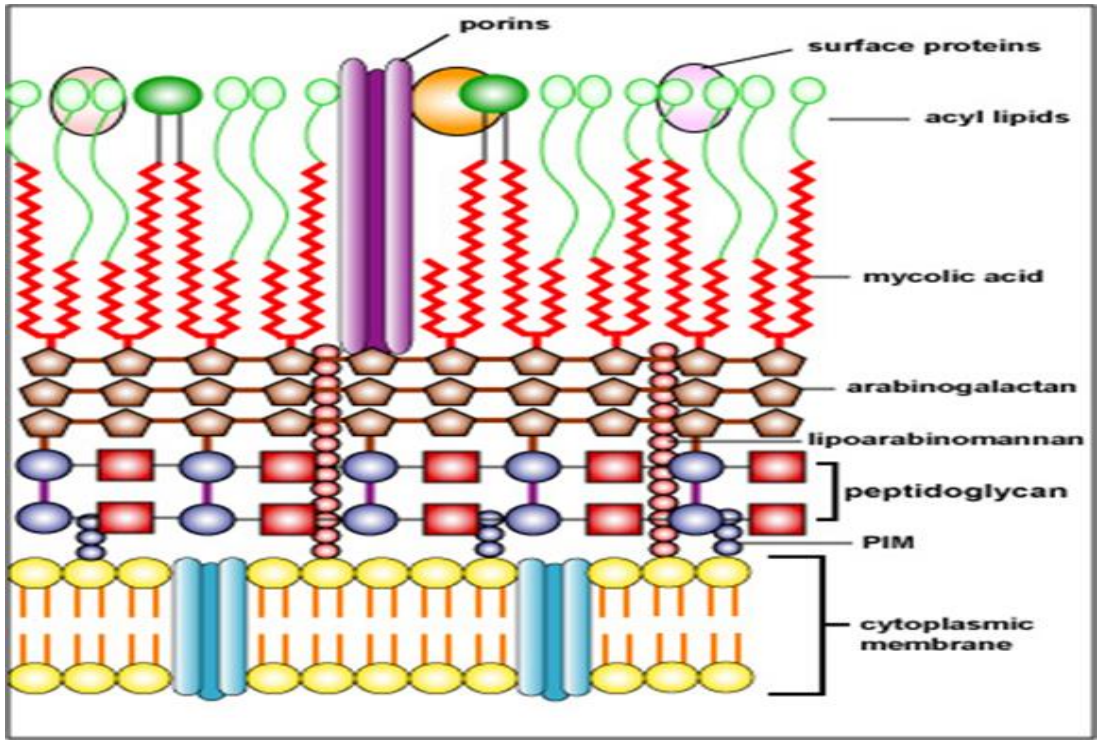
4- semisynthetic penicillin are made in the laboratory by adding different side chains onto the b -lactam ring made by the fungus. Semisynthetic penicillins are resistant to penicillinases and have a broader spectrum of activity than natural penicillins.

5. Cephalosporins inhibit cell wall synthesis and are used against penicillin-resistant strains.

6. Bacitracin and polymyxin B (colisin) are applied topically to treat superficial infections. Bacitracin inhibits cell wall synthesis primarily in gram-positive bacteria. Polymixin B are used in the treatment of Gram-negative bacterial infections. They work mostly by breaking up the bacterial cell membrane.

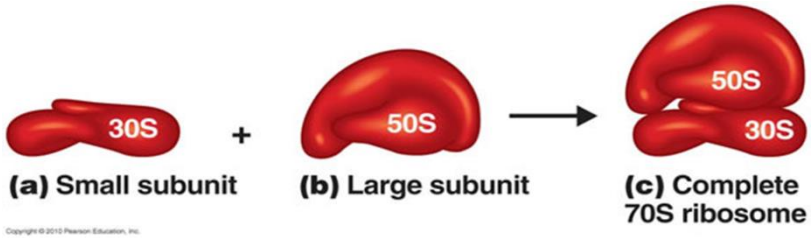
7. Vancomycin inhibits cell wall synthesis and may be used to kill penicillinase-producing Staphylococci.

8. Isoniazid (INH) inhibits mycolic acid synthesis in mycobacteria. INH is administered with rifampin or ethambutol to treat tuberculosis.



- Inhibitors of Protein Synthesis:

Aminoglycosides, tetracyclines, chloramphenicol, and **macrolides inhibit protein synthesis** at 70S ribosomes.



- Inhibitors of Nucleic Acid (DNA/RNA) Synthesis

1. **Rifamycin inhibits mRNA synthesis**; it is used to treat **tuberculosis (Mycobacterium tuberculosis)**.

2. **Quinolones** and **fluoroquinolones inhibit DNA gyrase** for treatment **of urinary tract infections**

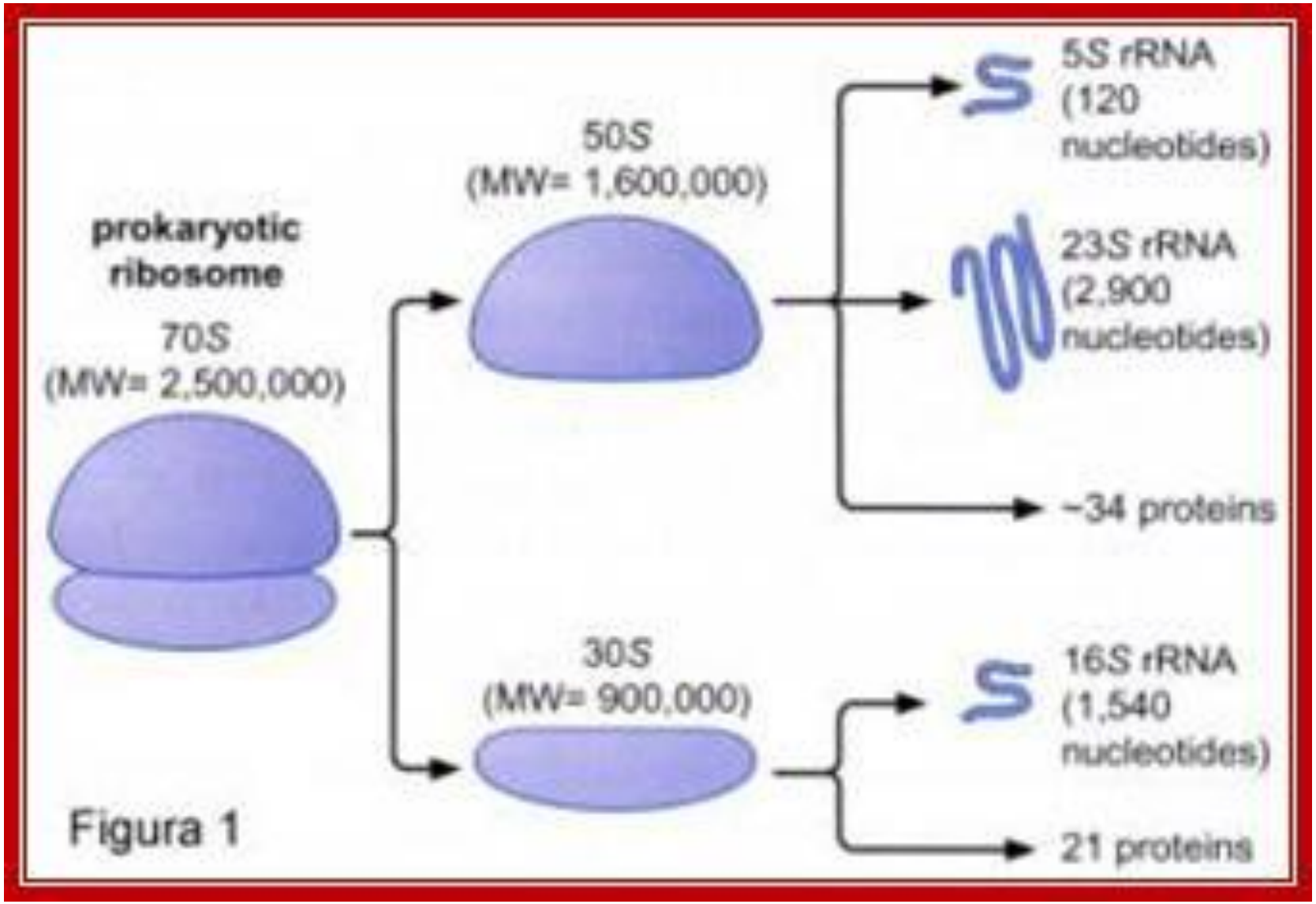

prokaryotic ribosome
70S
(MW= 2,500,000)
50S
(MW= 1,600,000)
30S
(MW= 900,000)
5S rRNA
(120 nucleotides)
23S rRNA
(2,900 nucleotides)
~34 proteins
16S rRNA
(1,540 nucleotides)
21 proteins

Figura 1

Resistance to antibiotics

Bacteria are constantly finding ways to counteract antibiotics.

One of the most important bacterial defense mechanisms is the production of enzyme β-lactamase.

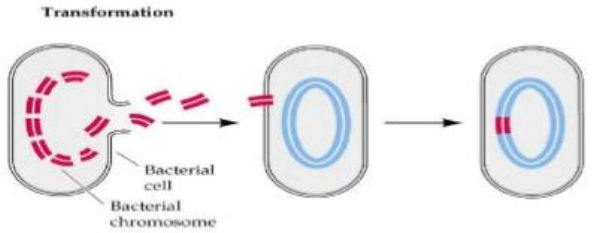
Organisms that produce β-lactamase are resistant to penicillin.

How is resistance spread?

Antibiotic resistance can either be inherent or acquired.

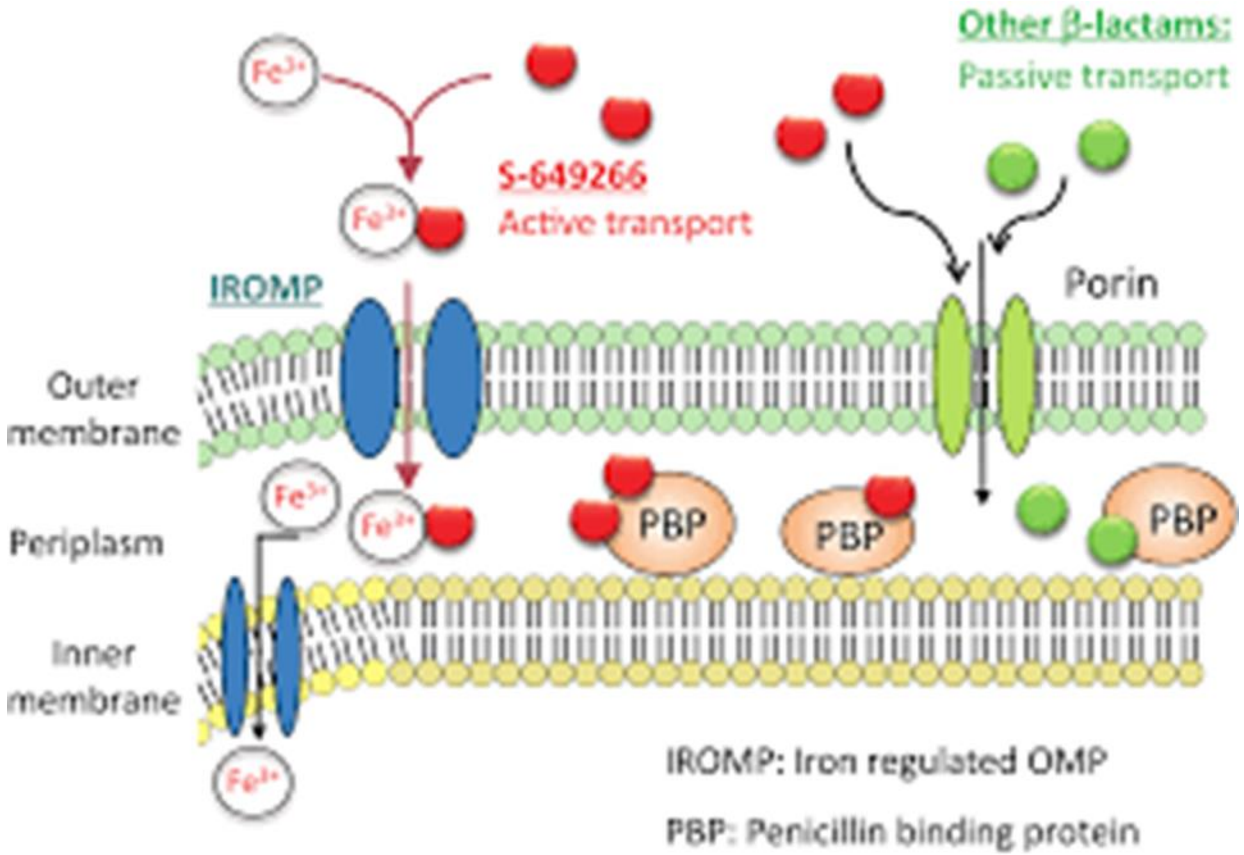
Inherent resistance: Some bacteria are naturally resistant to some antibiotics due to their physiological characteristics.

Acquired resistance occurs when a bacterium that was originally sensitive to an antibiotic develops resistance. For example resistance genes can be transferred from one plasmid to another plasmid or chromosome, or resistance can occur due to a random spontaneous chromosomal mutation.



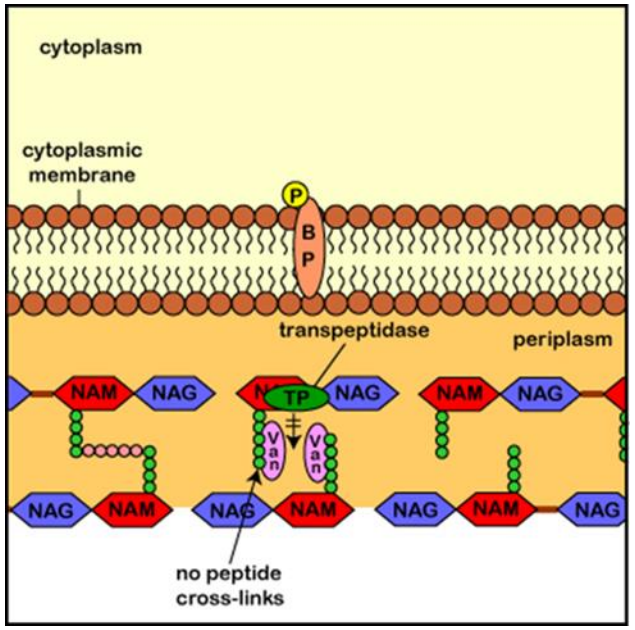
1- Production of Enzymes

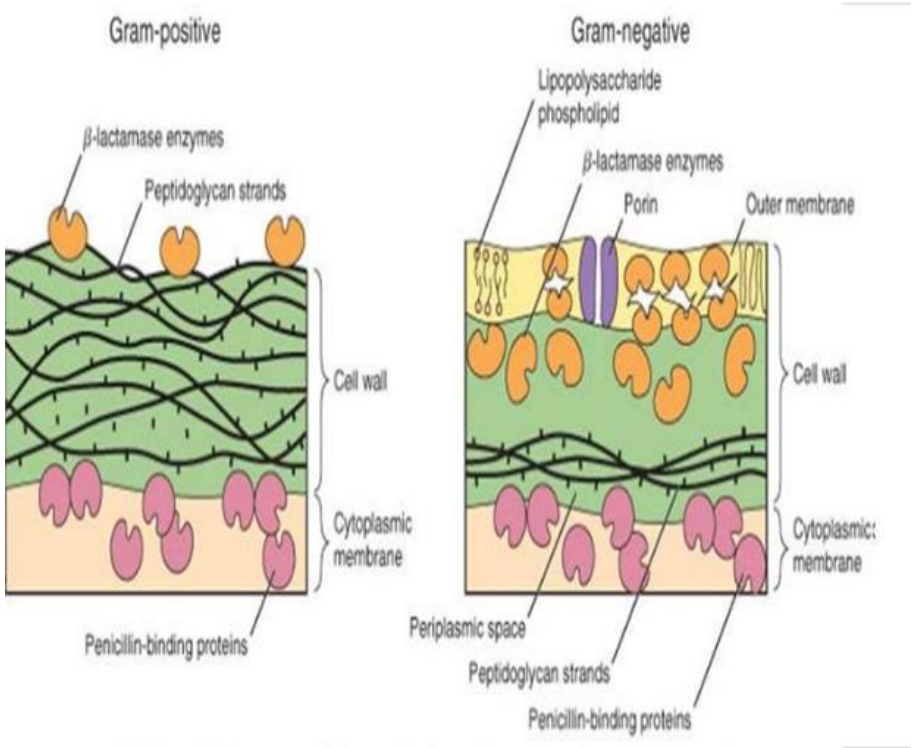
a- **Beta-lactamases**: are enzymes that hydrolyze beta-lactam drugs. As a result the cell is resistant to the action of the beta lactam drugs.



In gram-negative bacteria the beta lactam drugs enter the cell through the porin channels and encounter beta-lactamases in the periplasmic space. The beta-lactamases destroy the beta-lactam molecules before they have a chance to reach their PBP(**Penicillin-binding proteins)** targets.

-In gram-positive bacteria the beta-lactamases are secreted extracellularly into the surrounding medium and destroy the beta-lactam molecules before they have a chance to enter the cell.





• b-Aminoglycoside-modifying enzymes: Gram-negative bacteria may produce adenylating, phosphorylating or acetylating enzymes that modify an aminoglycoside so that it is no longer active.

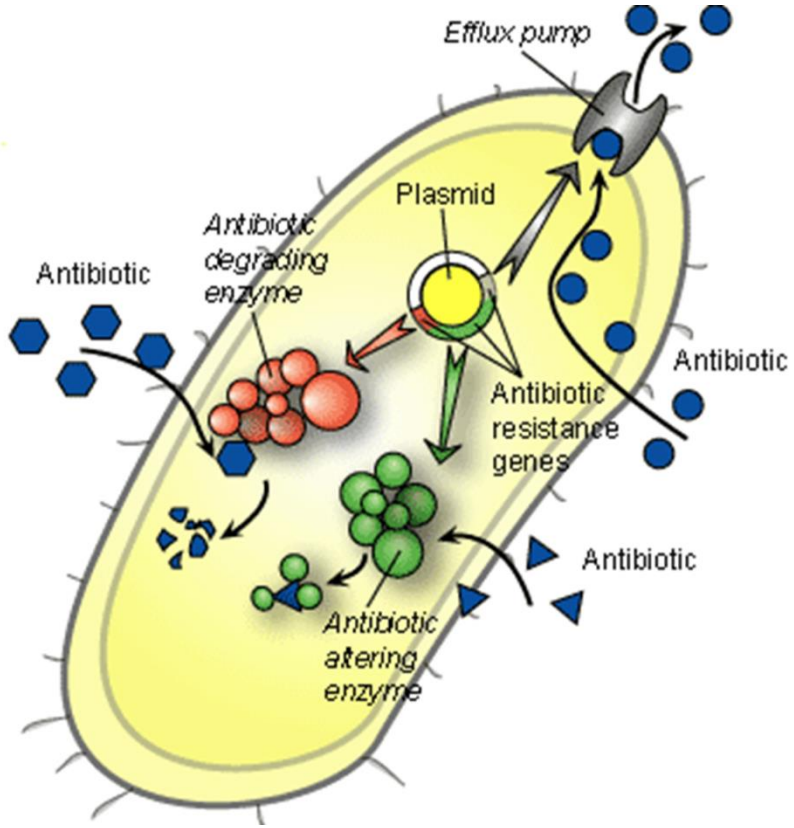
c- Chloramphenicol acetyl transferase: Gram-negative bacteria may produce an acetyl transferase that modifies chloramphenicol so that it is no longer active. Bacterial Outer Membrane Impermeability

2- PBPs in both gram-positive and gram-negative bacteria may be altered through mutation so that beta lactams can no longer bind to them; thus the cell is resistant to these antibiotics.

3- Mutation in DNA gyrase and topoisomerase: Mutations in the chromosomal genes for DNA gyrase and topoisomerase IV confer quinolone resistance.

4- Efflux Pumps

• A wide variety of efflux pumps provide antimicrobial resistance in both gram positive and gram-negative bacteria. Active efflux of antibiotics is mediated by trans-membrane proteins inserted in the cytoplasmic membrane and, in the case of gram-negative organisms, in the outer membrane and the periplasm.



Allergy testing - skin

Allergy skin tests are used to find out which substances cause a person to have an allergic reaction.
Such as skin pick test and batch test

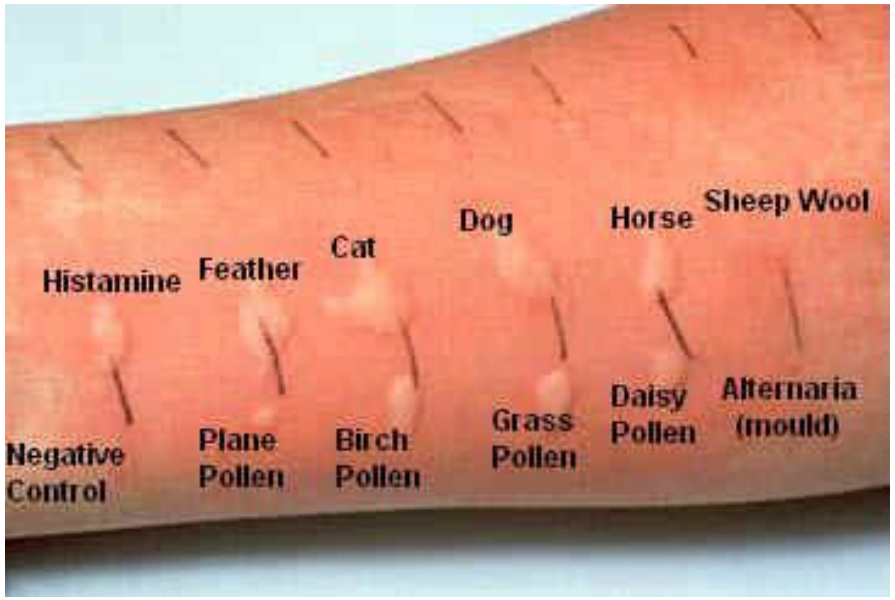
- The skin prick test involves:

•Placing a small amount of substances that may be causing your symptoms on the skin, most often on the forearm, upper arm, or back.

•The skin is then pricked so the allergen goes under the skin's surface.

•The health care provider closely watches the skin for swelling and redness or other signs of a reaction. Results are usually seen within 15 to 20 minutes.

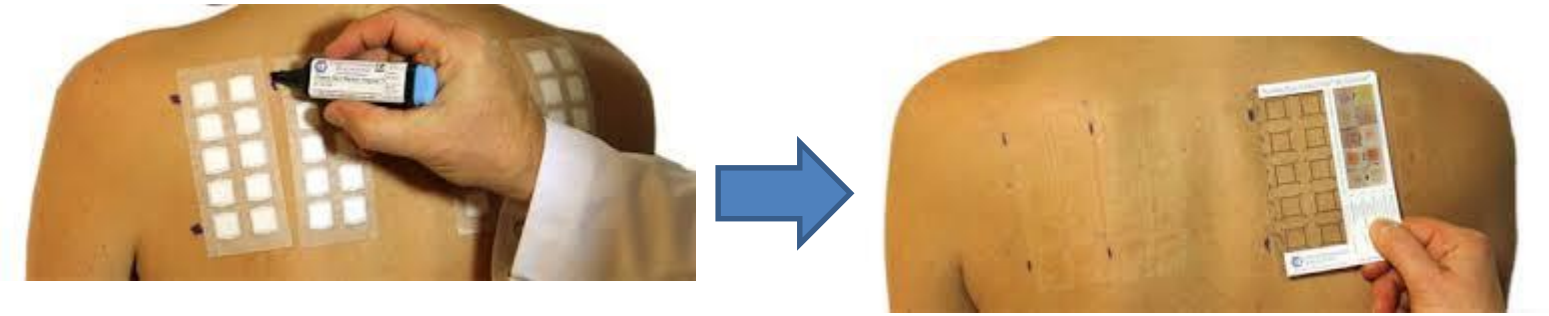
•Several allergens can be tested at the same time.



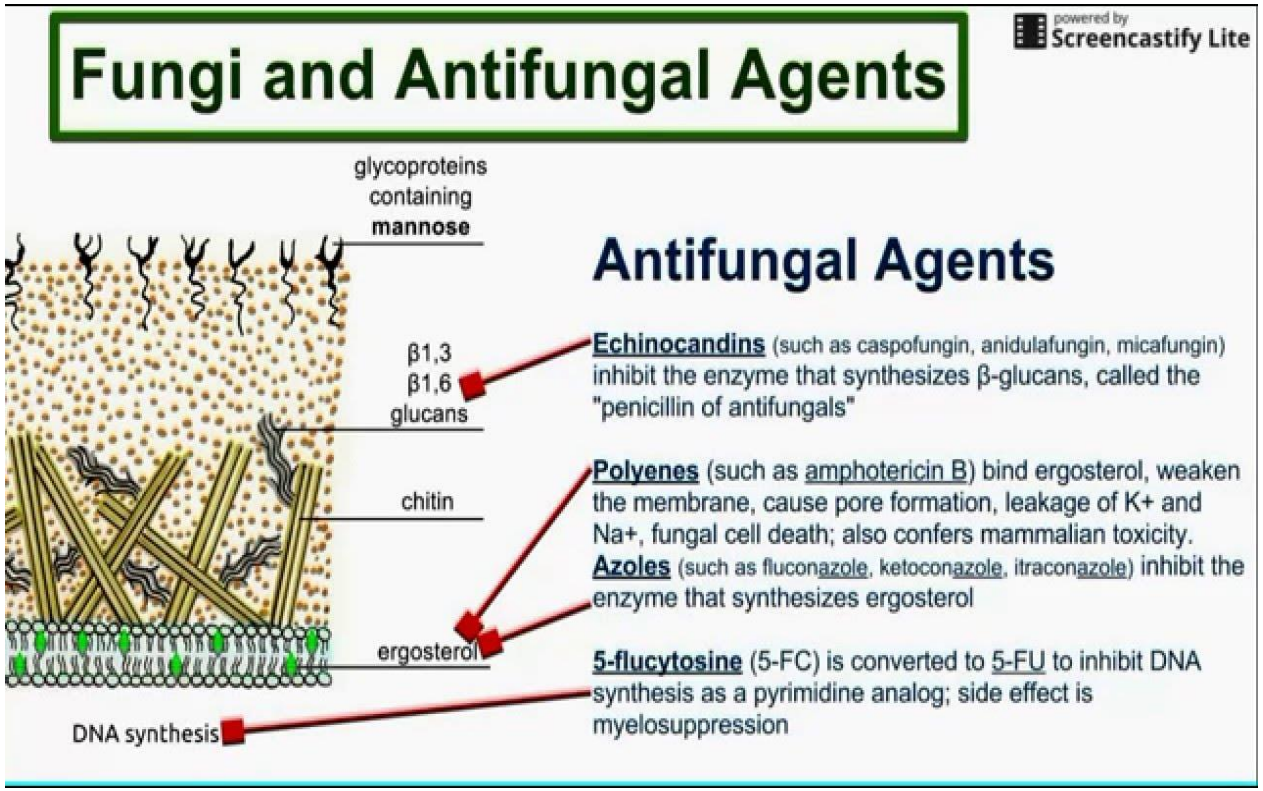
Patch testing is a method to diagnose the cause of skin reactions that occur after the substance touches the skin:

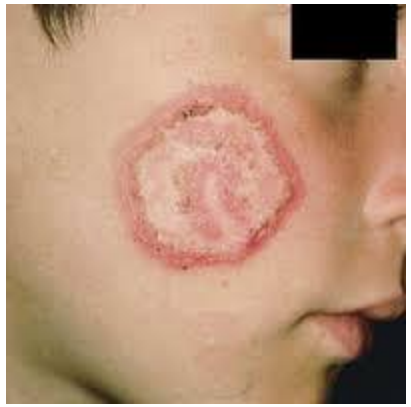
•Possible allergens are taped to the skin for 48 hours.

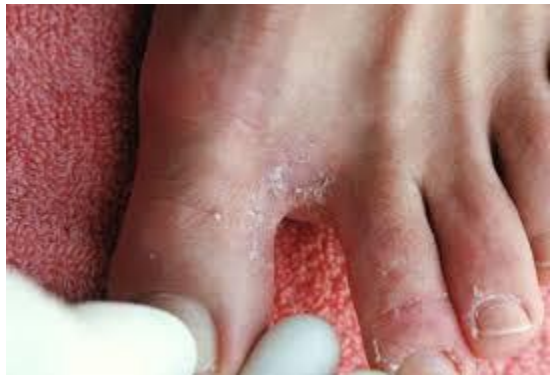
•The health care provider will look at the area in 72 to 96 hours.

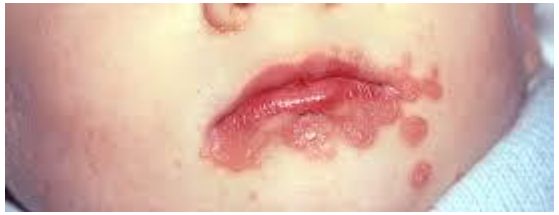


Antifungal Drugs: An antifungal medication is a pharmaceutical fungicide or fungistatic used to treat and prevent mycoses such as athlete's foot, ringworm, candidiasis (thrush), serious systemic infections such as cryptococcal meningitis, and others. Such drugs are usually obtained by a doctor's prescription, but a few are available OTC (over-the-counter).

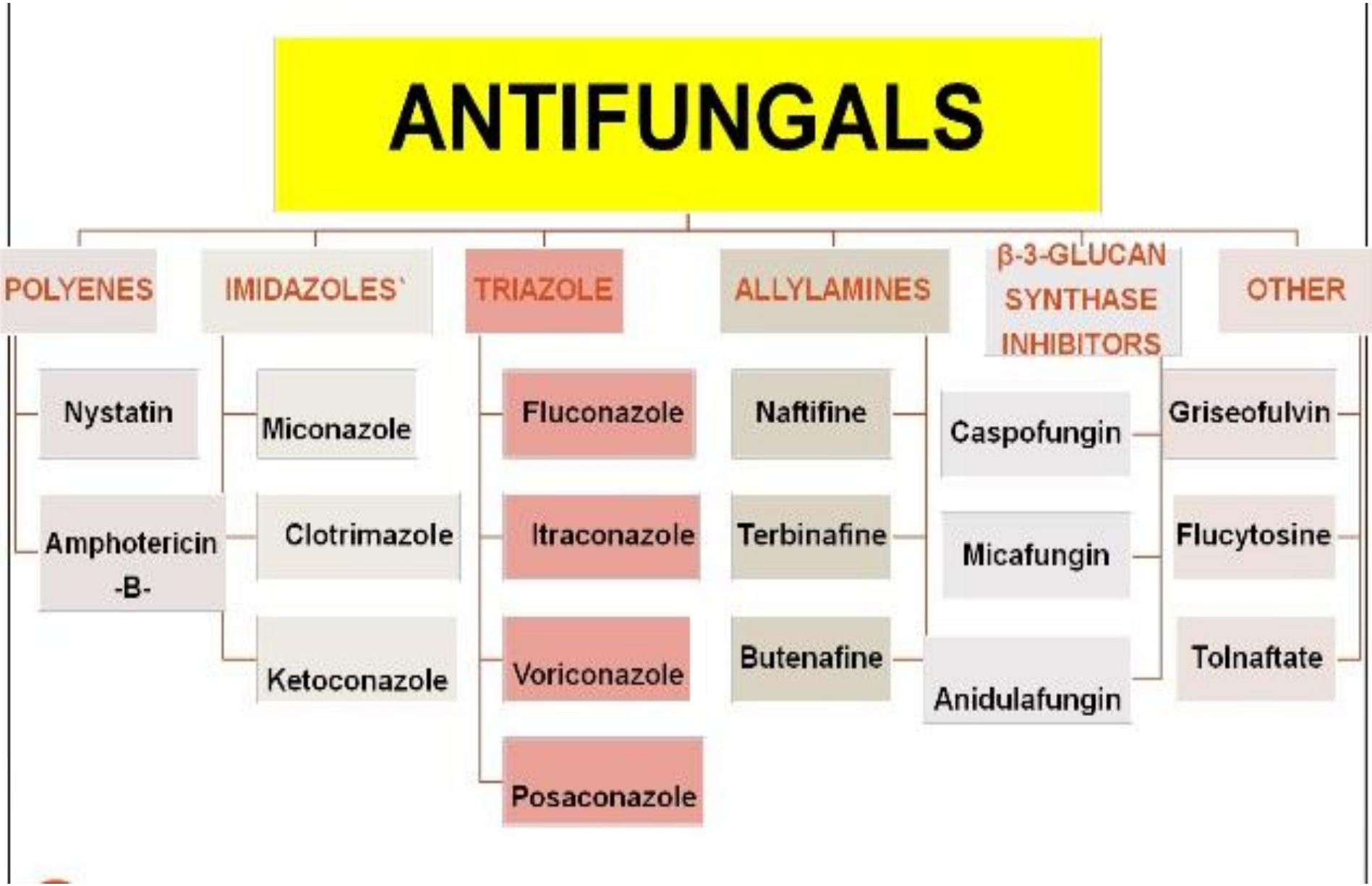









Cryptococcal Meningitis
Cryptococcus gattii


ANTIFUNGALS
POLYENES
IMIDAZOLES`
TRIAZOLE
ALLYLAMINES
β-3-GLUCAN SYNTHASE INHIBITORS
OTHER
Nystatin
Amphotericin -B-
Miconazole
Clotrimazole
Ketoconazole
Fluconazole
Itraconazole
Voriconazole
Posaconazole
Naftifine
Terbinafine
Butenafine
Caspofungin
Micafungin
Anidulafungin
Griseofulvin
Flucytosine
Tolnaftate

Antiviral drugs

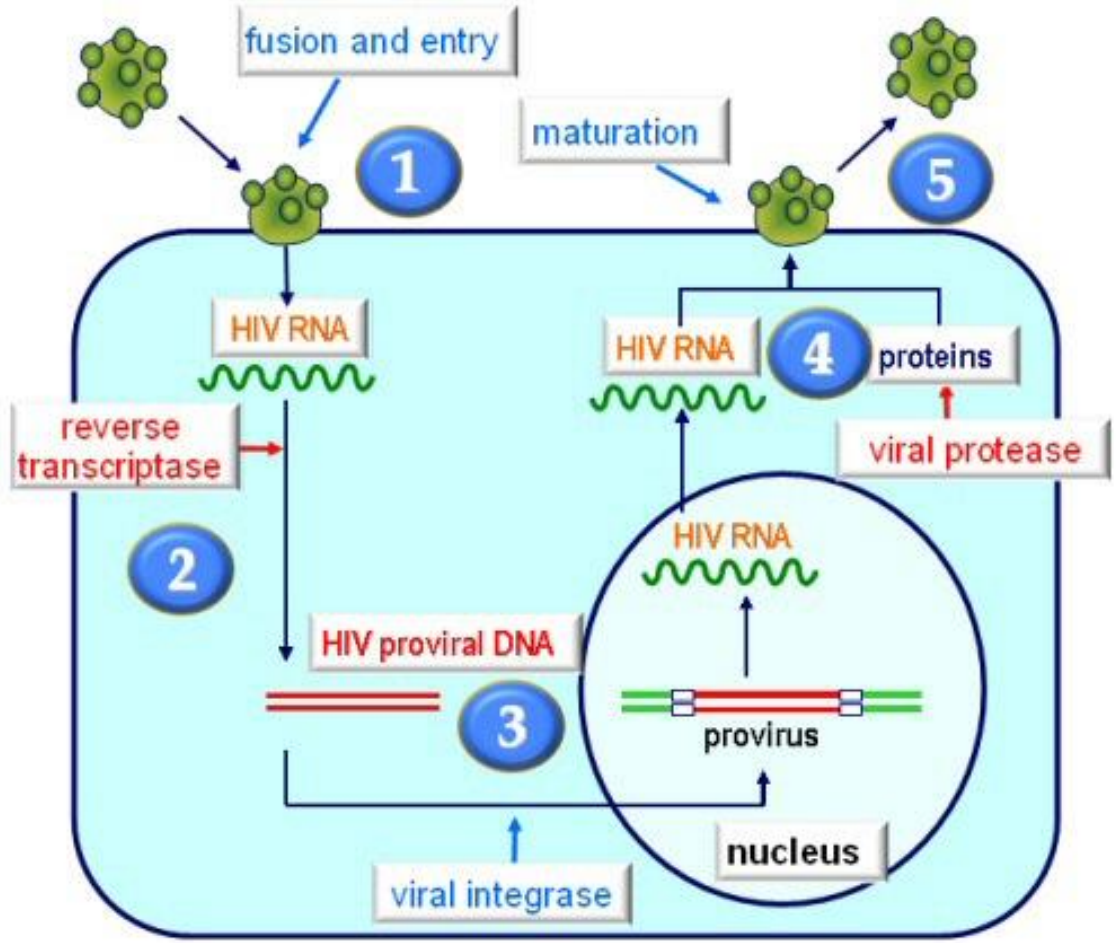
- Antiviral chemotherapy is still in its infancy.
- Viruses are more difficult ‘targets’ than bacteria: they are most vulnerable during reproduction, but all use host cell organelles and enzymes to do this, so that antiviral compounds are often as toxic to host cells as to virus.

Antiretroviral Agents

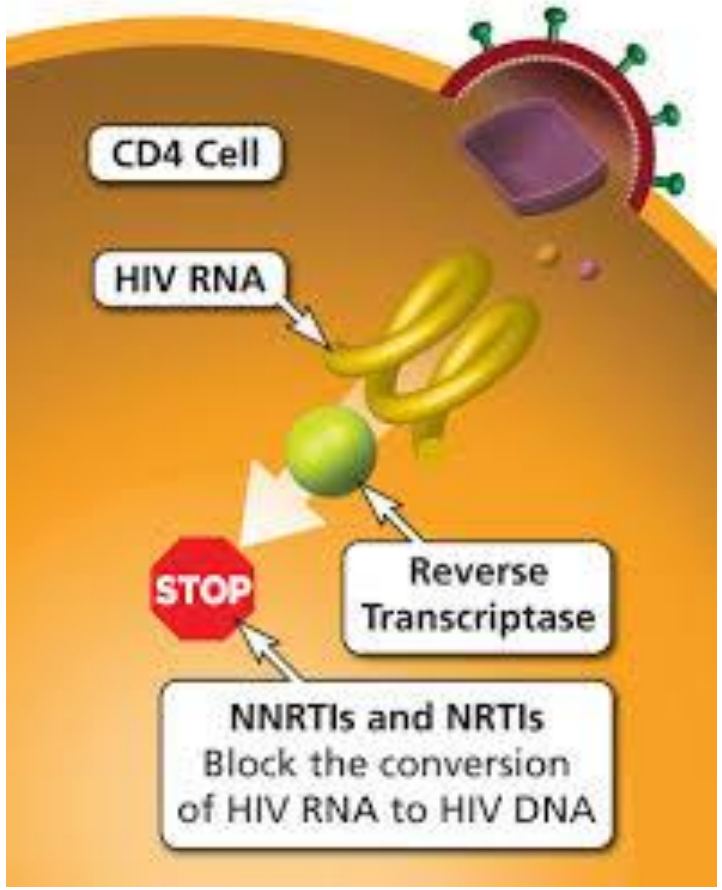
- There are five classes of antiretroviral drugs, each of which targets one of four viral processes. These classes of drugs are:

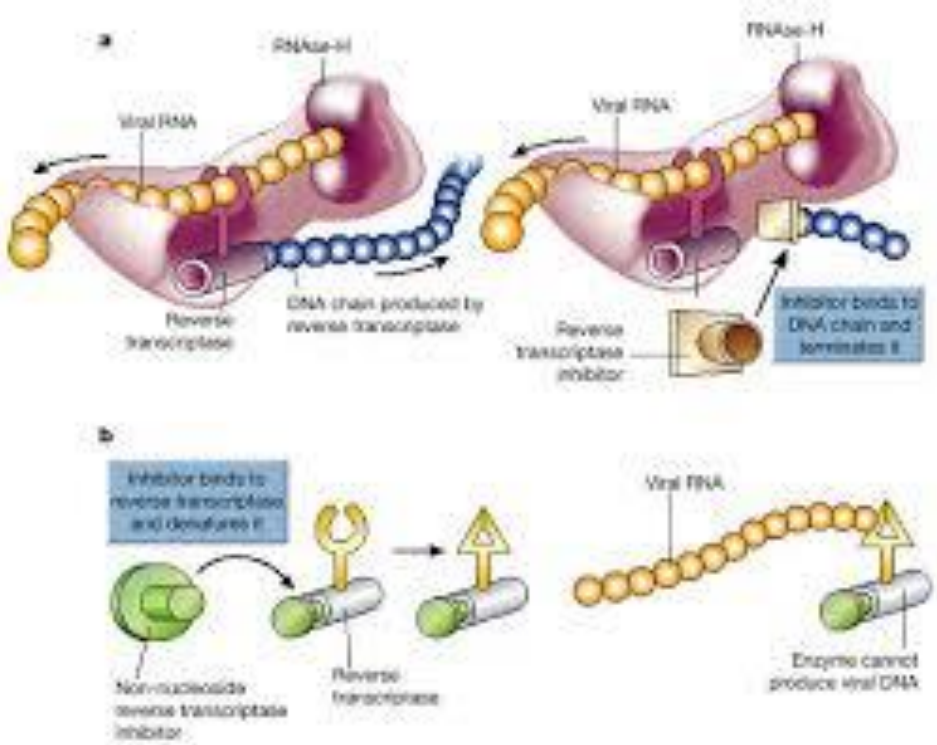
1. Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs),
2. Non-nucleoside reverse transcriptase inhibitors (NNRTIs),
3. Protease inhibitors,
4. Entry inhibitors
5. Integrase inhibitors.

Traditional HIV Therapeutic Targets



Approach: Drugs that block the assembly of virus


CD4 Cell
HIV RNA
STOP
Reverse Transcriptase
NNRTIs and NRTIs
Block the conversion of HIV RNA to HIV DNA


a
RNAse-H
Viral RNA
Reverse transcriptase
DNA chain produced by reverse transcriptase
Viral RNA
Reverse transcriptase inhibitor
b
Viral RNA
Enzyme cannot produce viral DNA

Classification of Antiviral Drugs

Information

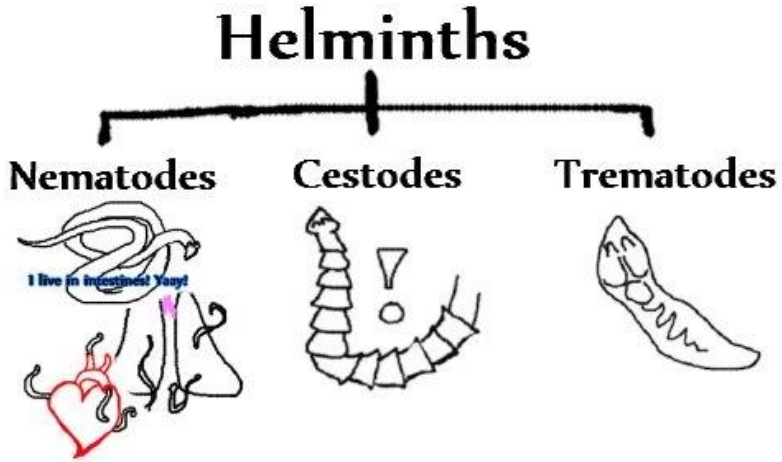
CLASSES	DRUGS
1. Anti-Herpes virus	Idoxuridine, Trifluridine Acyclovir, Valacyclovir, Famciclovir Ganciclovir, Valganciclovir Cidofovir Foscarnet Fomivirsen
2. Anti-influenza virus	Amantadine, Rimantadine Oseltamivir, Zanamivir
3. Anti-Hepatitis virus/Nonselective antiviral drugs	
a. Primarily for Hepatitis B	Lamivudine, Adefovir dipivoxil, Tenofovir
b. Primarily for Hepatitis C	Ribavirin, Interferon α

Antiprotozoan and Antihelminthic Drugs

Chloroquine and **quinacrine stop DNA synthesis** by intercalation between base pairs.

metronidazole(is an antibiotic that is used to treat a wide variety of infections. It works by stopping the growth of certain bacteria and parasites.)

Antihelminthic drugs include **niclosamide(is effective against cestodes that infect humans and many other animals.),**



Bacteriocins are proteinaceous toxins produced by bacteria to inhibit the growth of similar or closely related bacterial strain(s). They are structurally, functionally, and ecologically diverse. Applications of bacteriocins are being tested to assess their application as narrow-spectrum antibiotics

Bacteriocins were first discovered by A. Gratia in 1925.He was involved in the process of searching for ways to kill bacteria, which also resulted in the development of antibiotics and the discovery of bacteriophage, all within a span of a few years. He called his first discovery a colicine because it killed *E. coli.*