VIVEKANANDA COLLEGE
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NAAC ACCREDITED ‘A’ GRADE

Topic	: Drug Resistance
Course Title	: Basic Microbiology and Microbial Genetics
Paper	: CC 10
Unit	: II
Semester	: 4
Name of the Teacher	: Dr. Kakali Roy
Name of the Department	: Biochemistry

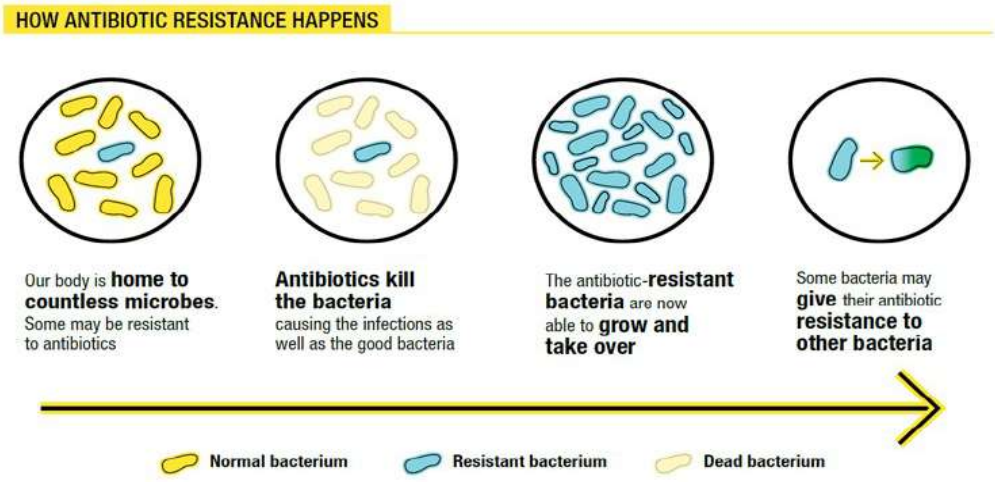
Drug Resistance

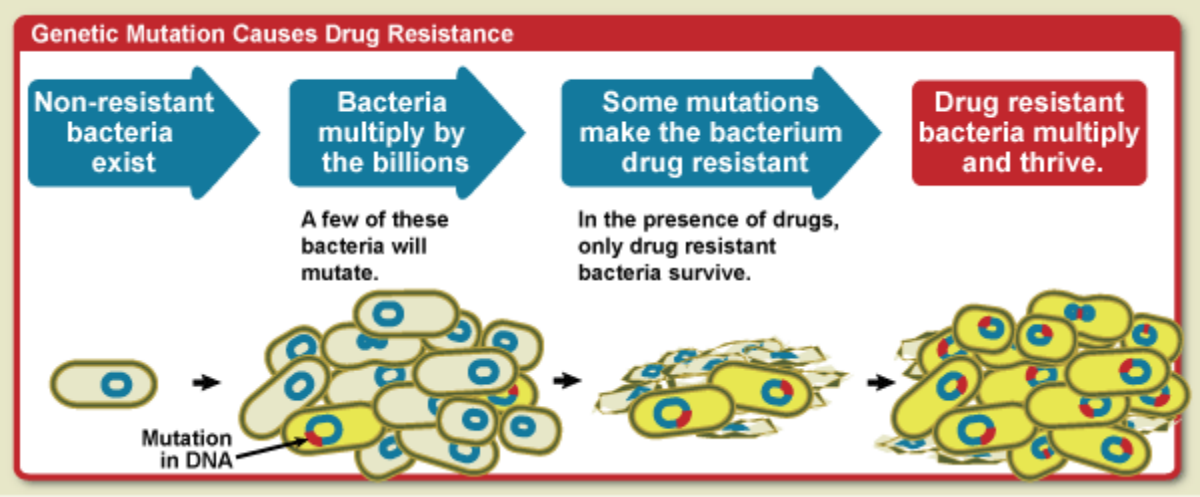
- It is a **phenomena** when the bacteria changes and becomes resistant to the antibiotics used to treat the infections they cause

Phenomena of resistance

- Resistant organism can be of the following three types-

1. Drug tolerant
2. Drug destroying
3. Drug impermeable

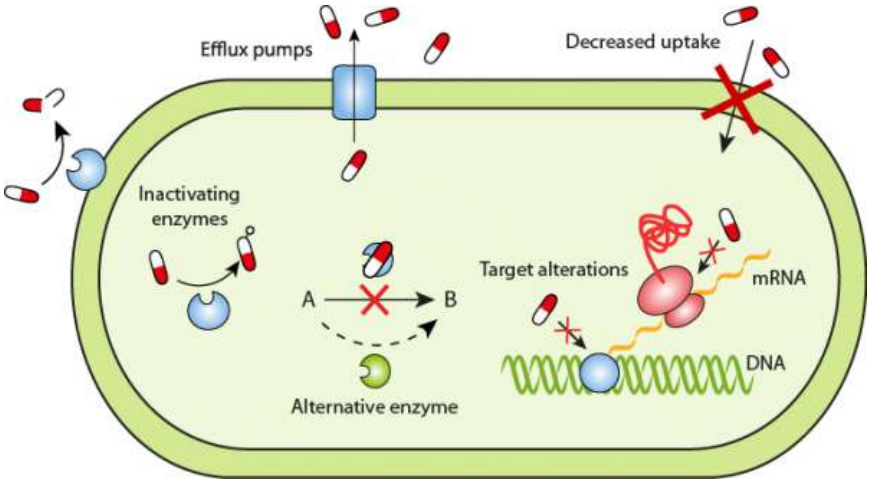




Drug resistance Mechanism

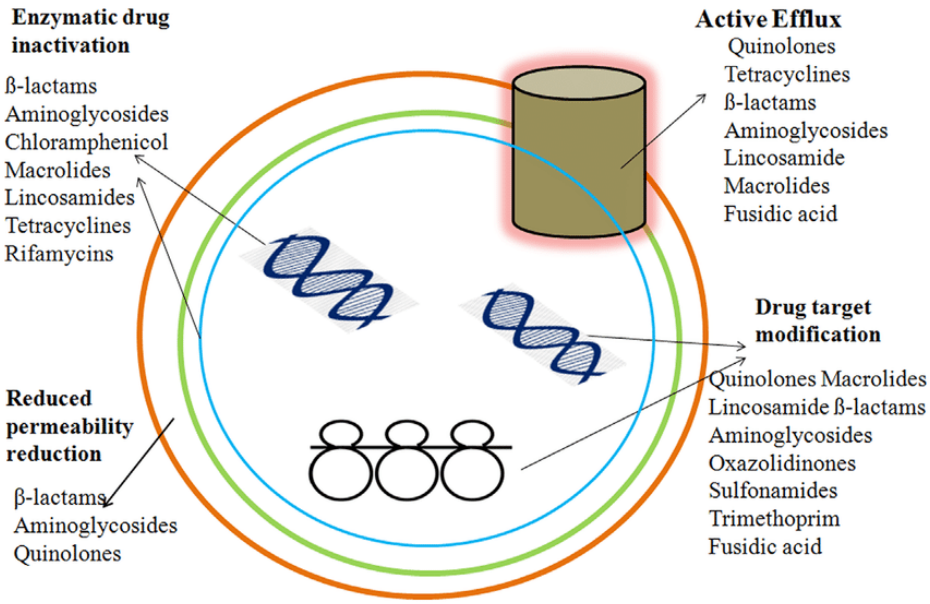
- No therapeutic drug (antibiotic) inhibits all microbial pathogens
- Some microbial pathogens possess natural ability to resist to certain antibiotics.

Bacteria acquire drug resistance using resistance mechanisms :



Mechanisms of antibiotic resistance:

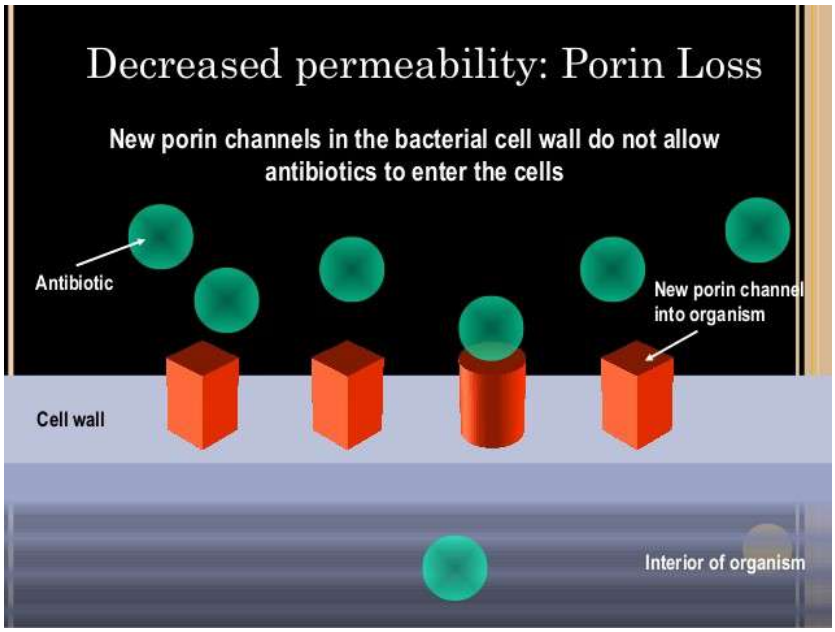
- Reduced permeability or uptake
- Enzymatic inactivation
- Enhanced efflux
- Alternation or over expression of target
- Loss of enzymes involved in drug metabolism
- **Enzymatic inactivation - β-lactamase(EC No 3.5.2.6)** releases the β-lactam ring and inactivates the β-lactam antibiotics.



Reduced Permeability to Antibiotic

- Bacteria often develop impermeability and become resistant by preventing entrance of the drug.
- Many gram-negative bacteria are unaffected by penicillin G because the drug fails to penetrate the envelope's outer membrane.

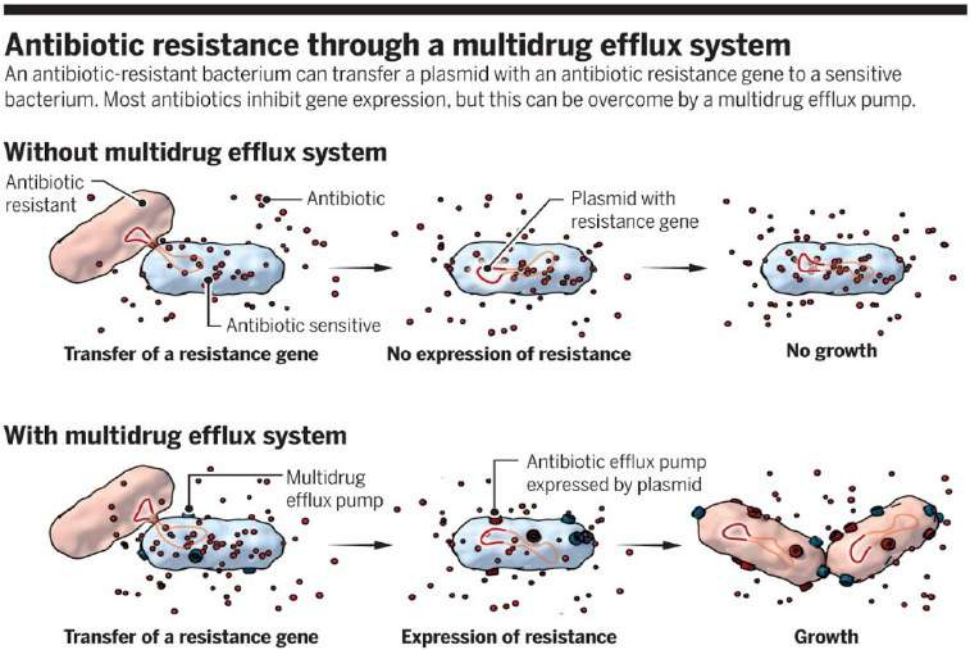
- Modifications in penicillin binding proteins also render a cell resistant.
- A decrease in permeability in bacterial pathogens can lead to resistance against sulphonamide.
- Antibiotics normally enter bacterial cells via porin channels in the cell wall
- Decrease in permeability also can occur as a result of loss of porin proteins.



Efflux (Pumping Antibiotic Out of the Cell)

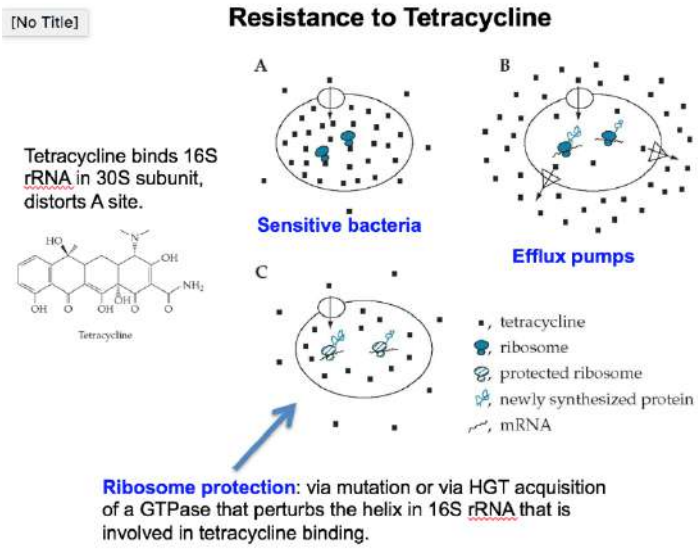
- Microbial pathogens possess resistance strategy by which they pump the drug out of the cell after it has entered.
- Some pathogens have plasma membrane translocases ----called **efflux pumps** that expel drugs.

- They are relatively nonspecific and can pump many different drugs -----so these transport proteins are often called **multidrug-resistance pumps**.



- Gram-positive and gram-negative bacteria that become resistant to **tetracycline** commonly overproduce related membrane proteins that act as **efflux pump**.

- Tetracycline resistant bacterial cell takes up the drug as rapidly as do sensitive ones but differ in being able to pump it out again.

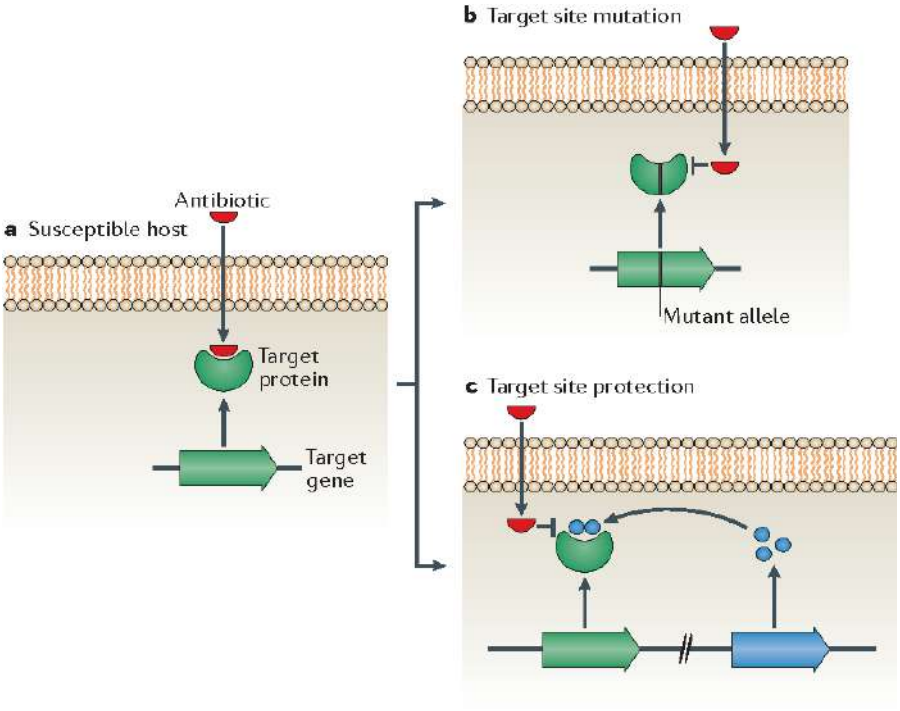


Importance of efflux pump

- Promotes the excretion of drugs and chemicals.
- To protect microorganisms against antibiotics and chemicals, toxins, stress and protect
- For the survival of microorganisms in different environments.
- For the supply of materials for the synthesis of bacterial surface structures involved.

Modification of the Target Site

- Each chemotherapeutic agent acts on a specific target
- Resistance arises when the target enzyme or organelle is modified so that it is no longer susceptible to the drug.



Modification/Protection of the Target site

Resistance resulting from altered target sites :

Target sites	Resistant Antibiotics
Ribosomal point mutation	Tetracyclines,Macrolides , Clindamycin
Altered DNA gyrase	Fluoroquinolones
Modified penicillin binding proteins (Strepto.pneumonia)	Penicillins
Mutation in DNA dependant RNA polymerase (M.tuberculosis)	Rifampicin

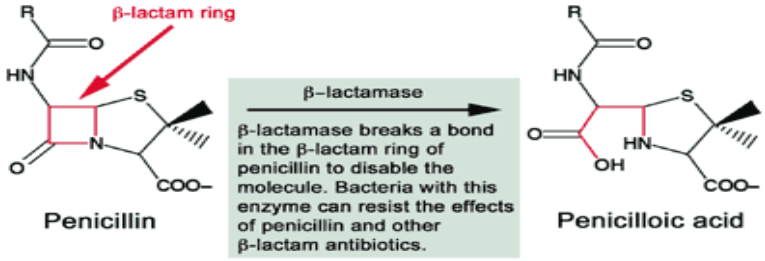
Drug Inactivation through Chemical Modification

- Many bacterial pathogens show resistance to drug by inactivating drugs through chemical modification.

Mechanisms of Antibacterial Resistance

- Antibiotic inactivation
  - Bacteria acquire genes encoding enzymes that inactivate antibiotics
- Examples include:
  - β-lactamases
  - Aminoglycoside - modifying enzymes
  - Chloramphenicol acetyl transferase

Penicillin Resistance



Development of a Resistant Biochemical Pathway

Use of alternative pathways for metabolic / growth requirements

- Resistance can also occur by alternate pathway that bypasses the reaction inhibited by the antibiotic.
- Sulfonamide resistance can occur from overproduction of PABA

SN	Mechanism	Examples of affected antimicrobials
1	**Destruction, modification, or inactivation of the antimicrobial.**	β-lactam antibiotics Chloramphenicol Aminoglycosides
2	**Multidrug efflux pumps.**	Tetracycline
3	**Target site alteration.**	β-lactam antibiotics Chloramphenicol streptomycin Quinolones Fusidic acid Erythromycin Glycopeptides Rifampicin
4	**Reduction in the cell surface permeability or access of the antimicrobial to the cell interior.**	Tetracyclines Quinolones β-lactam antibiotics Aminoglycosides Chloraphenicol
5	**New metabolic bypass mechanism.**	Rrimethoprim Sulphonamides

Reference

1. Biologydiscussion.com/medical-microbiology
2. Researchgate.net/mechanisms of antibiotic resistance
3. Bio News central.com/antibiotic resistance
4. www.google.com