Antibiotics Resistance

Almost all bacteria that were once susceptible to antibiotics are resistant to at least one, if not more antibiotics today. Antibiotics resistance in bacteria may either be intrinsic or acquired. Intrinsic resistance means that the bacteria were resistant to antibiotic even before the antibiotic was introduced (natural resistant to a specific antimicrobial because they are impermeable to it or they do not possess the molecular target of the drug). Acquired resistance means the bacterium that was previously sensitive to an antibiotic has now turned resistant (occurs through mutation or the acquisition of new genetic material).

Mechanisms of resistance

1-Drug inactivation

Enzymes secreted by typically Gram positive bacteria destroy the antibiotic before it reaches the organism.

- *Staphylococcus aureus* resistance to penicillin.

Enzymes concentrated in the periplasmic space of Gram negative bacteria destroy the antibiotic when it enters the organism.

- β-lactamase hydrolysis of the β-lactam ring before it can bind to PBP's.
- aminoglycosides modifying enzymes
- choramphenicol estrases.

2- Target modification

Modification of the antimicrobial target results in reduced the affinity for the drug.

- β- lactam antibiotics are unable to bind to the altered PBP's of Methicillin resistant *Staphylococcus aureus*.

- Alteration of the topoisomerase IV structure prevents the action of quinolones.
- Changes to ribosomal protein subunits prevent the action of aminoglycosides and macrolides.

3- Reduction of the antibiotic concentration at the target site.

The outer membrane of Gram negative bacteria acts as an inherent permeability barrier to antibiotics. Repression of porins channels in the cell membrane reduces antibiotic entry into the cell.

4- Efflux pumps

Efflux mechanism involves the removal of materials (waste products or toxins) from the microbial cell and provide a very efficient means for antibiotic resistance. Some pathogens have plasma membrane translocases, called efflux pumps, that expel drugs. They are non specific and pump many different drugs, thus they called multi-drug resistance pumps.

Finally, resistant bacteria may either use an alternative pathway to bypass the sequence inhibited by the agent or increase the production of the target metabolite. For examples, some bacteria are resistant to sulfonamides simply because they use performed folic acid from their surroundings, rather than synthesize it themselves. Other strains increase their rate of folic acid production and thus counteract sulfonamide inhibition.

Characteristic of the ideal antimicrobial agents

1-Selectively toxic to the microbe but nontoxic to host cell.

2-Microbicidal rather than microbistatic.

3-Realtively soluble, functions even when highly diluted in body fluid.

4-Remian potent long enough to act and is not breakdown or excreted prematurely.

5-Doesn’t lead to the development of antimicrobial resistance.

6- Complement or assists the activities of the host’s defenses.

7-Remian active in tissues and body fluids.

8-Readily delivered to the site of infection.

9-Reasonably priced.

10-Doesn’t disrupt the host’s health by causing allergies or predisposing the host to other infections.