Fundamentals of Antibiotic

Antibiotics

Antibiotics are chemical substances produced by living organisms which inhibit or kill bacteria.

- The first antibiotic that inhibited bacterial growth were natural products.
- Over time, these natural antibiotics have been modified.
- Several types of semi-synthetic antibiotics have been derived from these molecules

Antibiotics

- **Penicillin** was the first antibiotic which discovered accidentally by Alexander Fleming
- Bactericidal antibiotic
- Natural antibiotic produced by Penicillium fungi
- Narrow spectrum (G +ve).
- Inhibit cell wall synthesis by interfering with the synthesis and cross linking of peptidoglycan.
- Destroyed by β-lactimase enzyme which produced by some bacteria.
- Cause allergic reaction lead to anaphylactic shock

1. Natural Antibiotics:

- **Are produced by certain molds and bacteria usually living in the soil.**
- Penicillin and cephalosporin are examples of antibiotics produced by molds.
- Bacitracin, eryhtromycin and chloramphenicol are examples of antibiotics produced by bacteria.

2. Semisynthetic Antibiotics:

- **Chemically modified antibiotics**
- e.g. semisynthetic penicillin such as ampicillin and carbenicillin

3. Synthetic Antibiotics:

- **Chemically designed in the lab**

Antimicrobial agents

They are chemical substances that kill or inhibit the growth of microorganisms.

Antimicrobial agents include:

- **Antibacterial Agent (Antibiotic)>>** Drugs used to treat bacterial infections.
- **Antifungal Agent>>** Drugs used to treat fungal infections.
- **Antiprotozoal Agent>>** Drugs used to treat protozoal infections.
- **Antiviral Agent>>** Drugs used to treat viral infections.

Chemotherapeutic agent

It is a drug when given to the patient reach the blood circulation and exert selective inhibition or killing to the infectious agents with minimum side effect to the host.

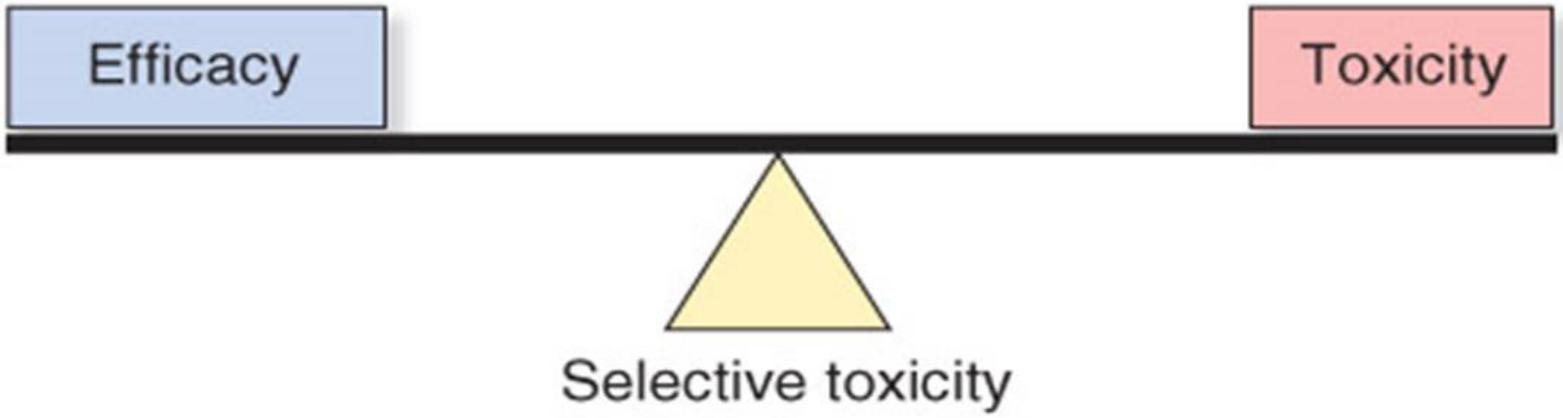
Selective toxicity: drugs that kill harmful microbes without damaging (low side effect) the host

Therapeutic Index (TI):

- TI is the ratio between toxic dose and therapeutic dose.
- High TI means the medicine very safe, and low TI means the medicine not safe.

- If the toxic dose of a medicine is small this mean medicine is not safe (toxic). But if the toxic dose is big>> medicine is safe

- If the therapeutic dose is small>> medicine is safe. But if the therapeutic dose is big>> medicine is not safe



$$\text{Chemotherapeutic index} = \frac{\text{Toxic dose}}{\text{Therapeutic dose}}$$

Ideal Qualities of Antimicrobial Agent

Characteristics of a good Drug:

- Kill or inhibit the growth of pathogens.
- Cause no damage to the host.
- Cause no allergic reaction in the host.
- Stable to store in solid or liquid form.
- Stay in target tissues for a long time to be effective.
- Kill the pathogen before they become resistant to it.

Antimicrobial agents are classified according to:

1. According to the kind of organism affected:

EX: Antibacterial, Antiviral… etc

2. According to their effect on the organism:

a) Microbicidal:

killing effect on the organism. EX: bactericidal, virocidal, fungicidal

b) Microbiostatic:

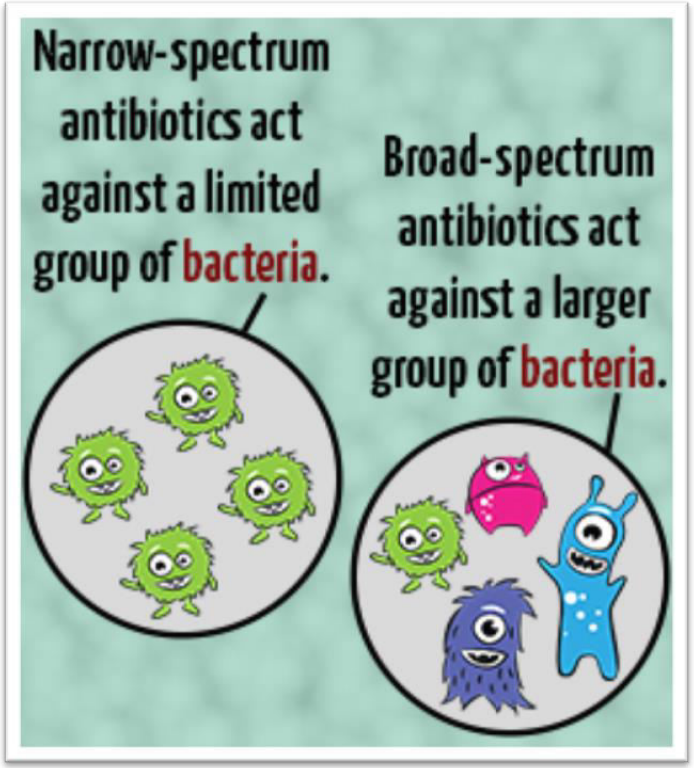
Inhibition of organism multiplication allowing the body defense mechanism to deal with them. EX: bacteriostatic

3. According to the antibiotics spectrum:

a) Narrow-spectrum Antibiotics

- Antibiotics that can kill or inhibit either Gram positive or Gram negative bacteria.
- EX: **Vancomycin** work on Gram positive bacteria only.

Colistin work on Gram negative bacteria only.



b) Broad-spectrum Antibiotics

- Antibiotics that can kill or inhibit Both Gram positive and Gram negative bacteria.
- EX: **Ampicillin.**

4. According to mechanisms of action (Target site) of antibiotics are:

a) Inhibition of the cell wall synthesis (production).

b) Damage to the cell membrane.

c) Inhibition of the nucleic acid synthesis (DNA or RNA).

d) Inhibition of protein synthesis.

e) Inhibition of enzyme activity.

How Antimicrobial Agents Work?

The antimicrobial agent must target a metabolic process or structure present in the pathogen and not in the host.

5. According to chemical structure of the antibiotic

Antibiotic Class	Description	Example
β-lactam	-Largest group of Antibiotic -All members have a β-lactam ring (3 carbon + 1 nitrogen)	Penicillins Cephalosporins Monobactams Carbapenems
Aminoglycoside	bactericidal	Gentamicin, sterptomycin
Glycopeptide	very improtant antibiotic for gram+ve cocci especially (MRSA) and colestridum defficile, bactericidal	Vancomycin
Tetracyclines	Broad-spectrum, bacteriostatic	minocycline
Macrolides	Bacteriostatic at lower dose and bactericidal at higher doses	Erythromycin
Polypeptide	bactericidal	Polymyxins

Multidrug Therapy

- The simultaneous use of two or more drugs to kill all the pathogens and prevent resistant pathogens from growing.
- EX: Treatment of Tuberculosis (Tb)>> 4 drugs are used.

- Simultaneous use of two or more drugs can cause>>

Synergism effect: combination is better than single A.B.

or **Antagonism effect:** combination is worse than single A.B.

Antifungal and Antiprotozoal Agents

Antimicrobial drugs against fungal and protozoal pathogens are difficult to use because they are eukaryotic cells like our cells so they tend to be toxic to the patient.

Mechanisms of action of Antifungal Agents are:

- Binding to cell membrane sterols
- Inhibiting sterols synthesis.
- Inhibiting nucleic acid synthesis.
- e.g. Amphotericin B

Mechanisms of action of Antiprotozoal Agents are:

- Inhibiting nucleic acid synthesis.
- Inhibiting protozoal metabolism.
- e.g. Metronidazole

Antiviral Agents

- Until recent years there were no drugs for the treatment of viral diseases.
- Antiviral drugs are specially very difficult to produce because viruses are intracellular pathogens.
- Only few drugs have been found to be effective in certain viral diseases. They work by inhibiting viral replication within cells.
- e.g.: **Acyclovir** for the treatment of HSV.

Resistance of Bacteria

Intrinsic Resistance:

Some bacteria have natural resistance to some drugs because the drug cannot enter the bacterial cells or the bacteria doesn't have the target site specific to the drug.

Acquired Resistance:

1. Chromosomal Mutation

- During bacterial reproduction an accidental alteration in the gene can be happen (mutation) and leads to alters the gene product.

2. Gen transfer

- Genes encoding resistance to antibiotic can spread to different strains, species, and even genera by Plasmids.

Multidrug Resistance (Superbugs)

- **When microorganisms (mainly bacteria) become resistant to many different antimicrobial drugs.**

Examples:

- **MRSA:** Methicillin Resistant *Staphylococcus aureus*.
- **VRSA:** Vancomycin Resistant *Staphylococcus aureus*.
- **MRTB:** Multi-drug Resistant *Mycobacterium tuberculosis*.
- β-Lactamase resistant *Streptococcus pneumoniae*.
- **Note: some viruses, fungi , parasites have also shown resistance**

- When penicillin G was first introduced, <3% of *Staphylococcus aureus* strains were resistant to it.

- Now 90% or more are resistant to it!

Effect of Antibiotics on Normal Flora

- Broad-spectrum antibiotics also kill healthy bacteria which normally live in the intestines and the vagina
- Antibiotics alter the normal flora in the gastrointestinal system, killing off the bad as well as the good bacteria.
- If the flora is severely altered (in which too many beneficial bacteria die), it can even lead to life-threatening colitis
- Antibiotics alter the normal vaginal flora and often bring about vaginal yeast infections

Slowing Down Emergence and Spread of Antimicrobial Resistance

- **Responsibilities of Physicians:** must work to identify microbe and prescribe suitable antimicrobials, must educate patients

- **Responsibilities of Patients:** need to carefully follow instructions

- **Educate Public:** must understand appropriateness and limitations of antibiotics; antibiotics not effective against viruses

Global Impacts: organism that is resistant can quickly travel to another country

- in some countries antibiotics available on non-prescription basis
- antibiotics fed to animals can select for drug- resistant organisms