



PRINCIPLES OF ANTIMICROBIAL THERAPY

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What is chemotherapy?

CHEMO

THERAPY

WHAT IS CHEMOTHERAPY?

The use of chemical substances to treat diseases.

Chemotherapy can be used to eliminate microorganisms e.g: Bacteria, virus, fungi, helminthes (worms) and malignant tumors.

Antimicrobial therapy

✕ kills or inhibits the growth of microorganisms such as bacteria, fungi, viruses or protozoa.

ANTIMICROBIAL AGENT

✗ is any chemical substance which kills the organism or inhibits its growth e.g:
Sulphonamides, quinolones

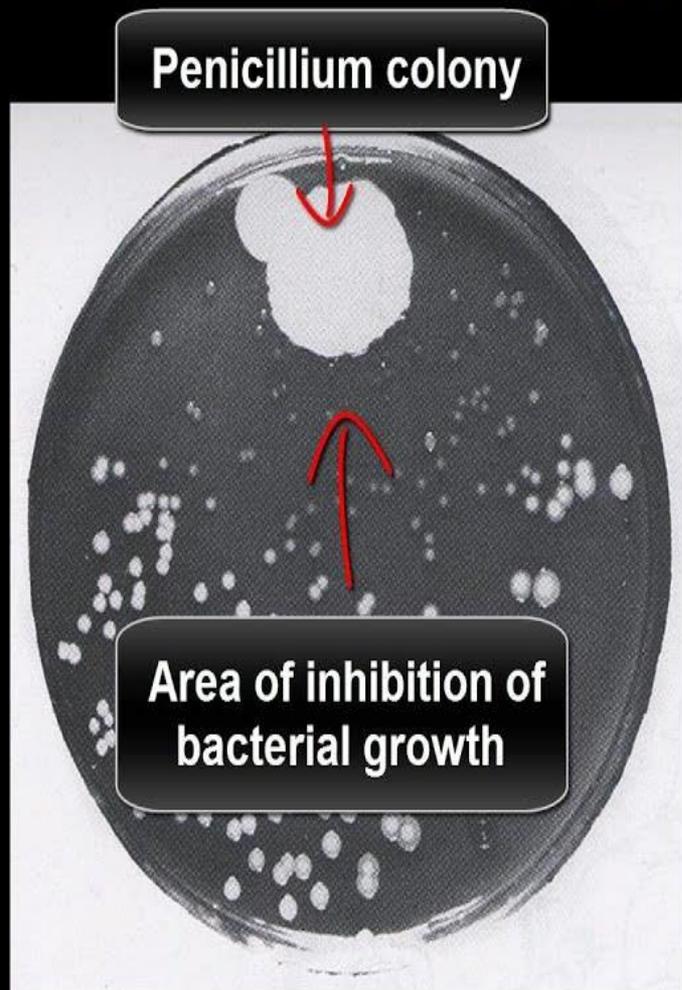
ANTIBIOTIC

✗ is a substance produced by living microorganisms to inhibit or kill another living microorganisms e.g: Penicillins, cephaloporins , tetracyclines and chloramphicol.

28th September 1928



Discovery of penicillin



Fleming came to the conclusion that something in the fungus was inhibiting the growth of the bacteria.

- Despite Flemings' discovery, it wasn't until the 1940s that the true potential of penicillin was realized when it was used to save thousands of lives in World War Two.

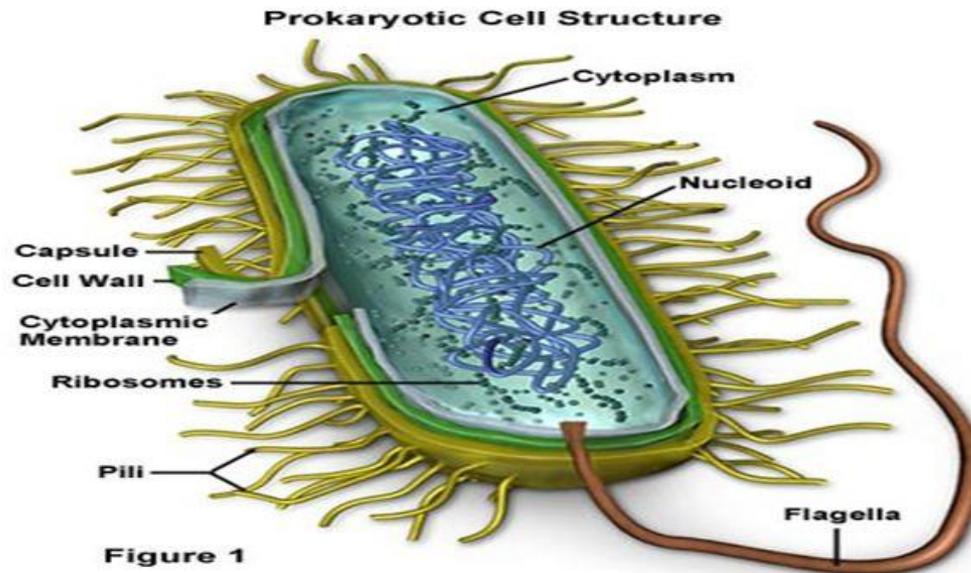


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- ✘ To be effective and safe, antimicrobial agent must have **selective toxicity**

SELECTIVE TOXICITY

SELECTIVE TOXICITY

- The ability to kill or inhibit the growth of a microorganism without harming the host cells.



SELECTIVE TOXICITY

The drug must be toxic to the pathogen more than toxic to the host.



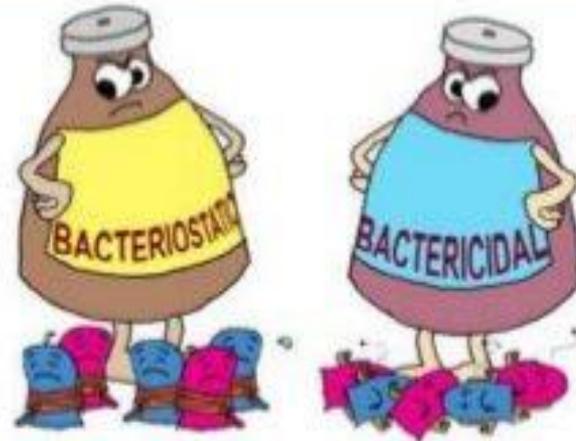
Selective toxicity is due to the difference in structure or metabolism between the pathogen and the host.

Classification of Antibiotics

Based on mode of Action

Bacteriostatic

Bactericidal



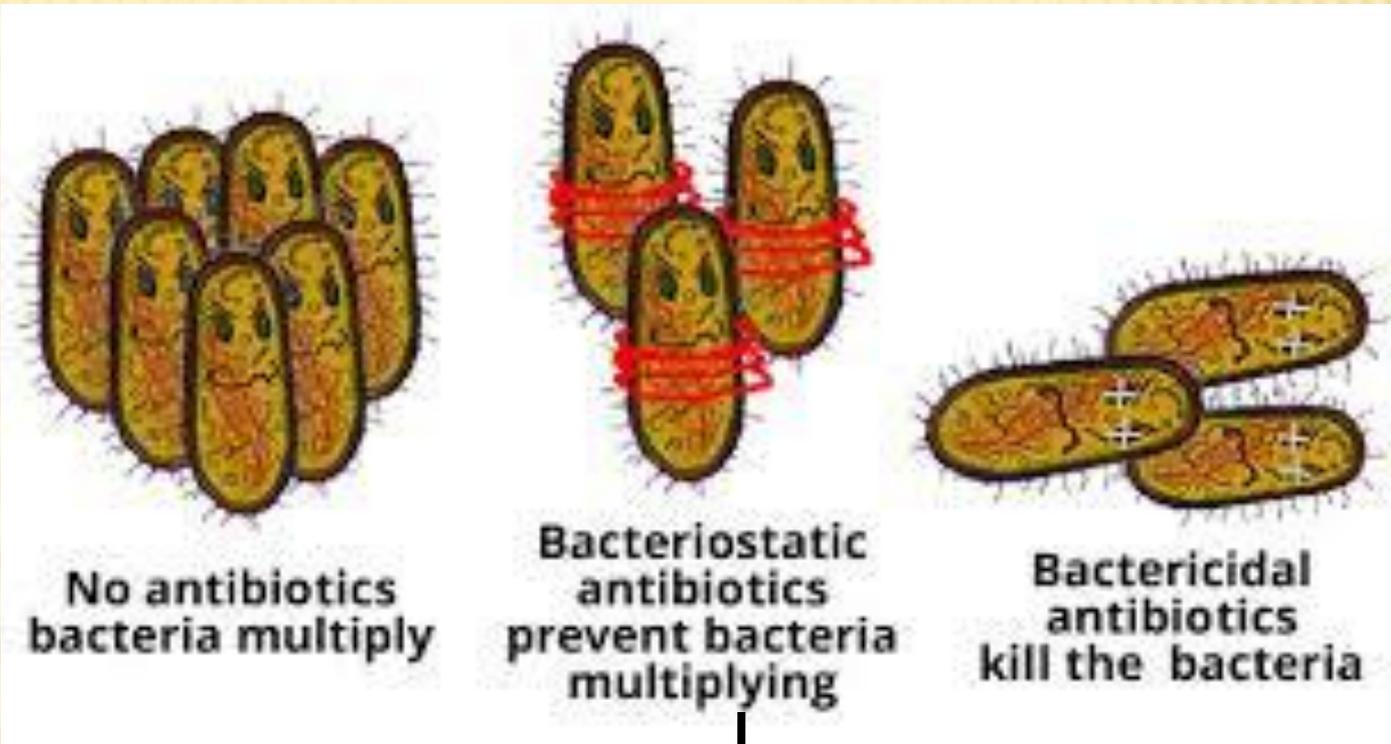
Based on their spectrum of action

Broad-spectrum

Narrow Spectrum



CLASSIFICATION OF ANTIMICROBIAL AGENTS ACCORDING TO THEIR MODE OF ACTION:



Once stopped bacterial multiplication resumed

BACTERICIDAL

Kill microorganisms by direct effect e.g. B-lactam antibiotics, Aminoglycosides, Quinolones, Rifampicin.



Effective in immunosuppressed host.

BACTERIOSTATIC

Inhibit growth of
microorganism. e.g.
Sulphonamides,
chloramphenicol & tetracyclines
Host immune system does the
killing

Not effective in
immunosuppressed host.

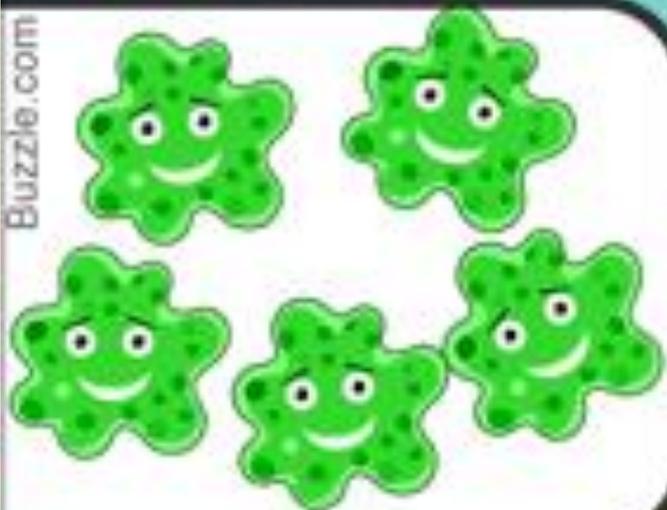
BACTERIOSTATIC AND CIDAL

according to concentration e.g:
Erythromycin and Isoniazide.

Location and severity of infection
affect choice of antibiotic:

E.g. CNS infection calls for
bactericidal treatment

CLASSIFICATION OF ANTIMICROBIAL AGENTS ACCORDING TO THE SPECTRUM:



Narrow-spectrum
antibiotics act
against a limited
group of bacteria.



Broad-spectrum
antibiotics act
against a larger
group of bacteria.

BROAD SPECTRUM ANTIBIOTICS

Effective against multiple gram +ve & -ve organisms e.g:
Emepenem,
tetracycline, quinolones
,chloramphicol.

Used as initial empirical treatment till culture and sensitivity results appear.

Q e t c

NARROW SPECTRUM ANTIBIOTICS

Effective against specific organisms e.g:
Antimicrobial against gram +ve bacteria: vancomycin and Penicillin G.

Antimicrobial against gram -ve bacteria:
polymixine, bacitracin and aminoglycosides.

Used in treatment of susceptible organisms based on culture and sensitivity results.

MODERATE SPECTRUM ANTIBIOTICS

- ✘ Moderate spectrum: e.g: Macrolids

EXTENDED-SPECTRUM ANTIBIOTICS

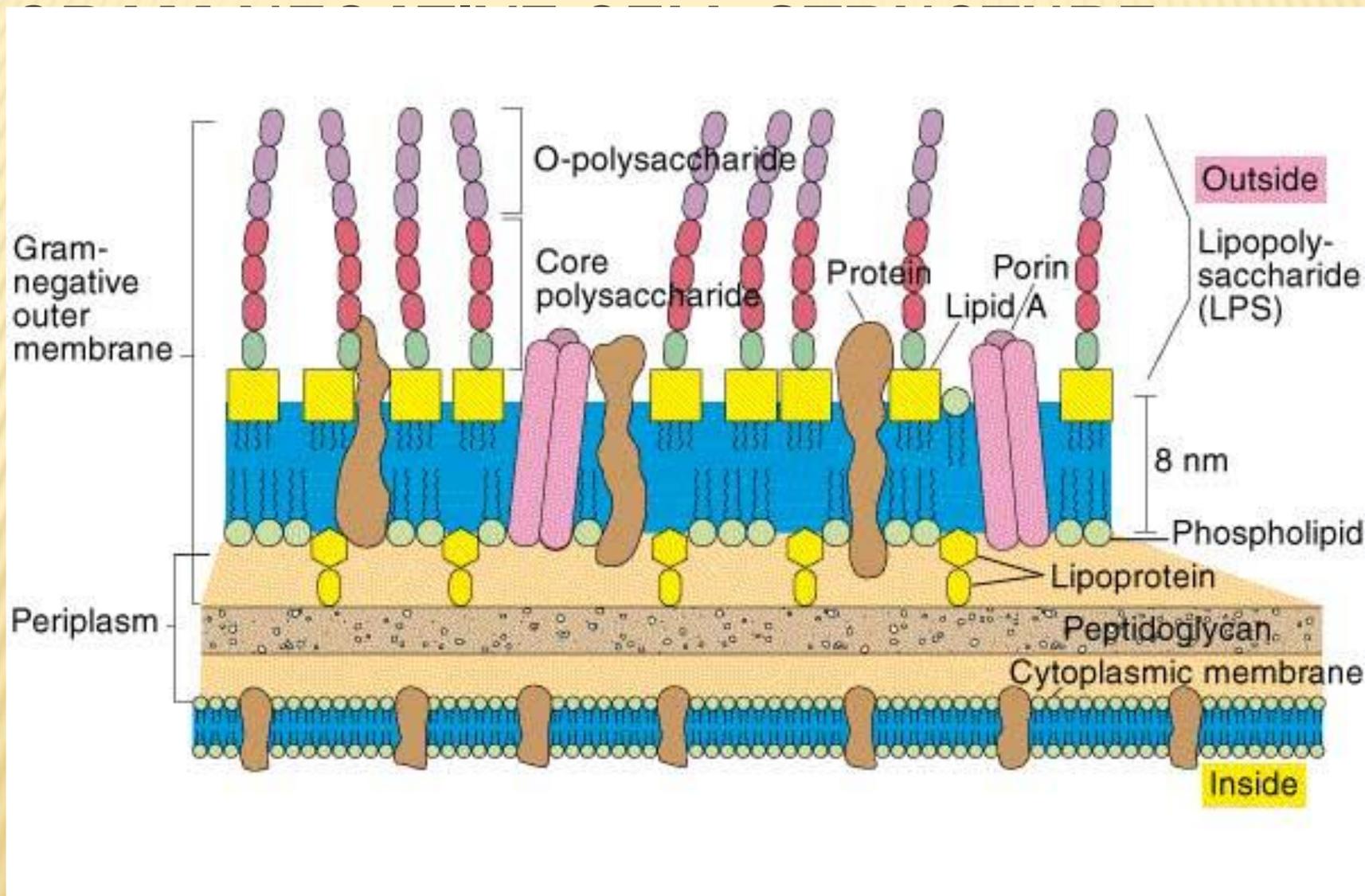
Extended spectrum is the term applied to antibiotics that are modified to be effective against gram-positive

organisms and also against a significant number of gram-negative bacteria.

For example, *ampicillin*

GRAM POSITIVE & GRAM NEGATIVE

- ✘ Gram positive bacteria have a thick cell wall
 - + Peptidoglycan directly accessible from environment
- ✘ Gram negative bacteria have a different wall
 - + Thin layer of peptidoglycan
 - + Surrounded by an **outer membrane** composed of **lipopolysaccharide, phospholipids, and proteins**
 - + Outer membrane is a barrier to diffusion of molecules including many antibiotics
 - ✘ Some hydrophobic antibiotics may diffuse in.
 - ✘ Porins allow passage of only some antibiotics



G-NEGATIVE BACTERIA



CLASSIFICATION OF ANTIMICROBIAL AGENTS ACCORDING TO SITE OF MECHANISM OF ACTION:

Mechanisms of Antibiotics

Inhibit Cell Wall Synthesis or Function

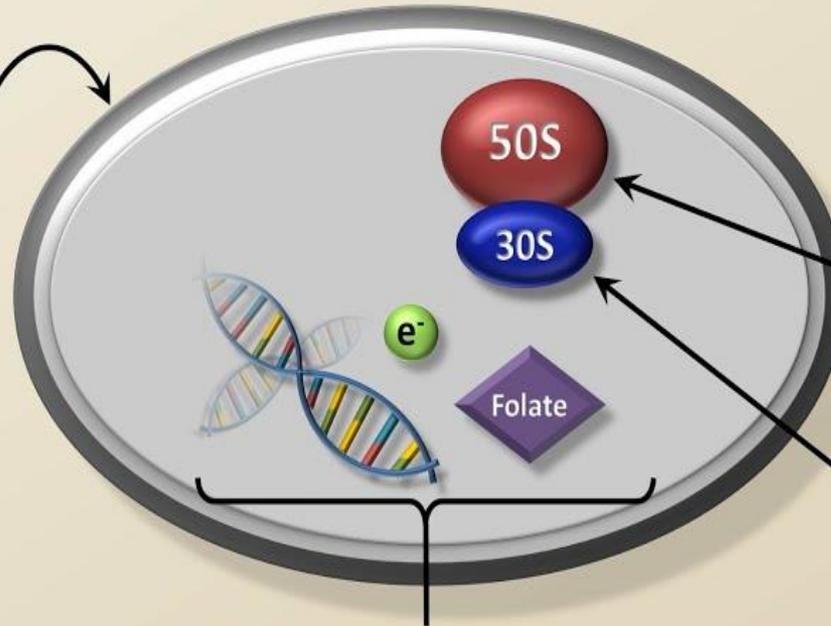
Beta Lactams

Penicillins
Cephalosporins
Carbapenems
Monobactams

Vancomycin

Daptomycin

Polypeptides



Inhibit Protein Synthesis

Inhibit 50S subunit

Macrolides
Clindamycin
Linezolid
Streptogramins
Chloramphenicol

Inhibit 30S Subunit

Aminoglycosides
Tetracyclines
Tigecycline

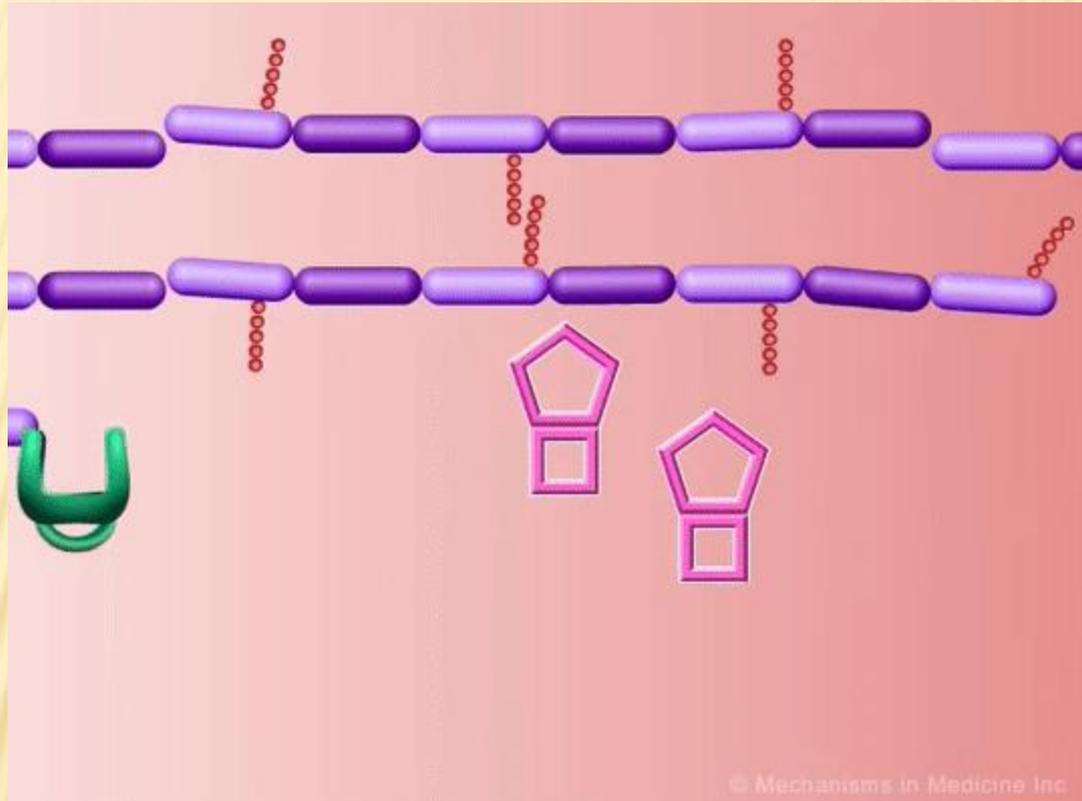
Inhibit Nucleic Acid Synthesis or Function

Inhibit DNA Gyrase +/- Topoisomerase IV: Quinolones

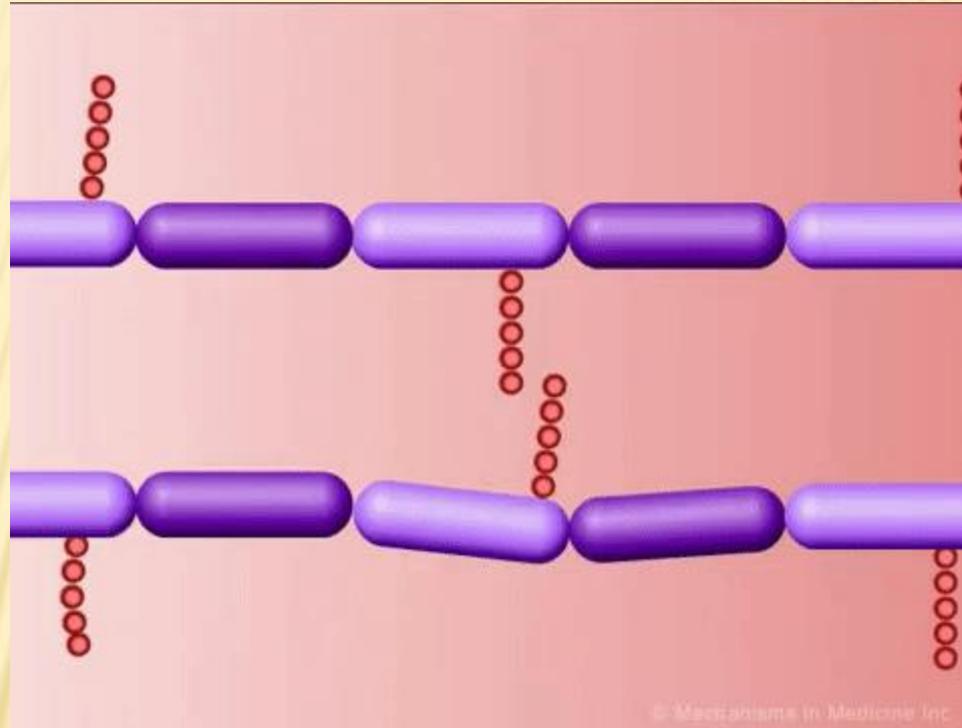
Inhibits Folate Synthesis: Trimethoprim / Sulfamethoxazole

Create Free Radicals: Metronidazole, Nitrofurantoin

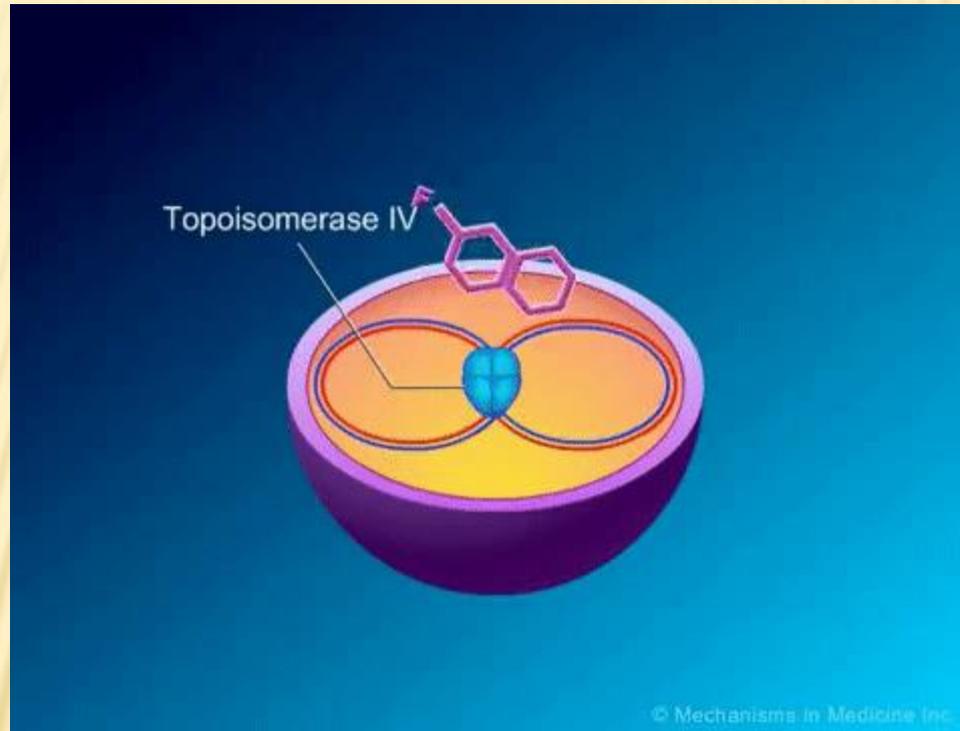
CELL WALL SYNTHESIS IN BACTERIA



CELL WALL SYNTHESIS INHIBITORS



MECHANISM OF QUINOLONES ACTION



ANTIMICROBIAL RESISTANCE

The ability of a microbe (germ) to resist the effects of a drug.

Antimicrobial-resistant germs are not killed by the drugs that are typically used against them and may continue to multiply.

Antimicrobial resistance includes antibacterial, antifungal, and antiviral resistance.

Drug resistance may be present before treatment is given or may occur during or after treatment with the drug.

CAUSES OF THE ANTIBIOTIC RESISTANCE

1- Overuse

2- Antibiotics are unregulated and available over the counter without a prescription

3- Incorrectly prescribed antibiotics

4- Extensive Agricultural Use

5- Availability of Few New Antibiotics

What is drug resistance types?

Antimicrobial resistance mechanisms fall into four main categories:

(1) limiting uptake of a drug

(2) modifying a drug target

(3) inactivating a drug

(4) active drug efflux

MAIN SIDE EFFECTS OF CHEMOTHERAPEUTIC AGENTS & ANTIBIOTICS:

HYPERSENSITIVITY

- ✘ Fever, skin rash, angioedema and anaphylactic reactions e.g. penicillins & cephalosporins



DIRECT TOXICITY

(According to age, sex, genetic background, hepatic & renal status).

Hemopoietic disorders: (chloramphenicol)

G-6-PD: (sulphonamide)

Hepatic toxicity: (ketoconazole).

Renal toxicity: (outdated tetracyclines).

Dental discoloration (tetracyclines).

Taste disturbances (metronidazole)

Pseudomembranous colitis (tetracyclines)

Ototoxicity (aminoglycosides).

Peripheral neuropathy (INH).

SPECIFIC TOXICITY:

Streptomycin: Deafness & vertigo (8th nerve affection)

Chloramphenicol: Bone marrow depression, Grey baby syndrome.

Tetracyclines : Teratogenic & G.I.T. irritation (nausea, vomiting) Teeth (enamel hypoplasia, yellow discolouration)



POSITIVE OUTCOMES OF ANTIBIOTIC THERAPY

Early recognition and treatment of infection

Selection of appropriate antibiotic

Use the right DOSE using Pharmacodynamic principles

Use the right dosing that would allow for the minimization of drug resistance

HOW TO SELECT AN ANTIBIOTIC?

**THROUGH ANSWERING THE FOLLOWING
QUESTIONS:**

1.

- ✘ Is an antibiotic indicated on the bases of clinical findings?

2.

- ✘ A clinical specimen has been obtained, examined and cultured?

3.

- ✘ What pathogens are most likely to be causing the infection?

4.

✘ If multiple antibiotics are available to treat this organism, which agent is best for a given patient? (This question involves such factors as drug of choice, pharmacokinetics of agents, toxicology, cost and bactericidal compared with bacteriostatic agents.)

5.

✘ Is an antibiotic combination good?

6.

- ✘ Does the patient have any of the following conditions or other specific conditions?
 - + Renal diseases?
 - + Liver dysfunction?
 - + Allergies?
 - + Pregnancy?
 - + Lactation
 - +?

7.

✘ What is the best route of administration?

8.

✘ What is the appropriate dose?

9.

- ✘ Will initial therapy require modification after culture data are returned?

10.

- ✘ What is the optimal duration of treatment?

EMPIRIC ANTIBIOTIC THERAPY

- ✘ Empiric antibiotic therapy is antibiotic therapy started before the identification of the causative micro-organism.
- ✘ Identification and susceptibility testing of bacteria from clinical specimens is not available for 48-72 hours after collection of the specimen from the patient

EMPIRIC ANTIBIOTIC THERAPY

✘ Empiric antibiotic therapy should be initiated only if there is clear clinical reason, otherwise therapy should be postponed until susceptibility testing of bacteria from clinical specimens is available

EXAMPLES

BACTERIAL (TONSILO)PHARINGITIS

- ✘ Group A beta-hemolytic streptococcus
- ✘ a throat culture or a rapid antigen detection test (RADT) if clinical signs are not sufficient to exclude other conditions
- ✘ Drug of choice **penicillin** (V p.o., G i.v.)
- ✘ Macrolides are alternative drugs for patients who are allergic to penicillin
- ✘ 10-day course

ACUTE SINUSITIS, OTITIS MEDIA

Streptococcus pneumoniae,
Hemophilus influenzae, Moraxella catarrhalis

Drug of choice -
Amoxicillin/clavulanic acid, ampicillin/sulbactam

Alternative agents –
macrolides,
clindamycin

Thank you