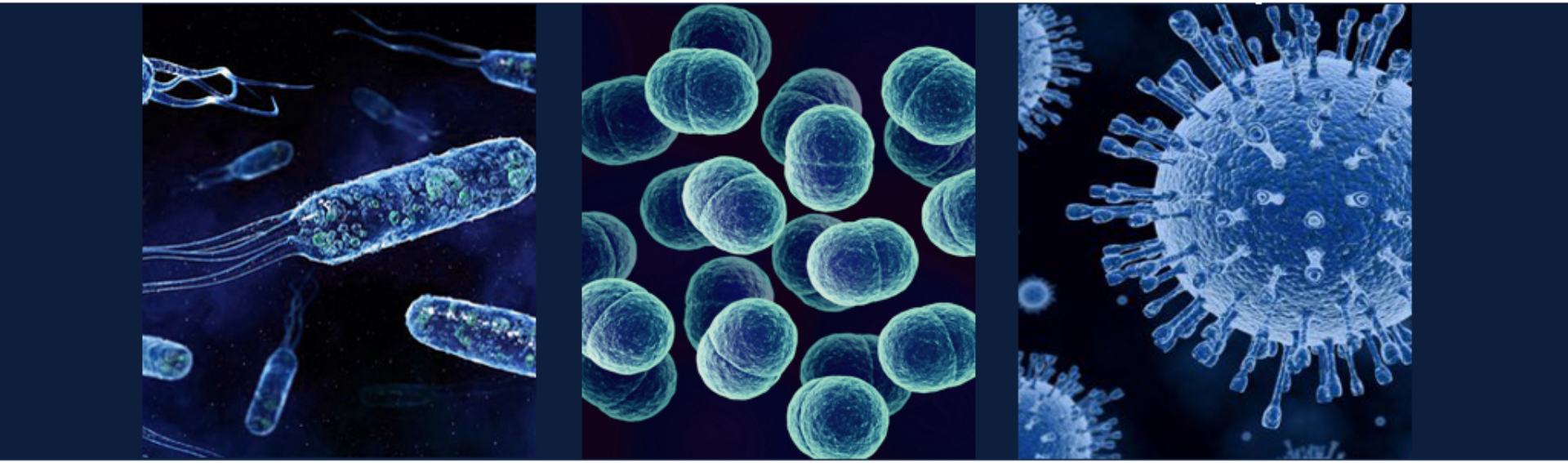
MICROBIOLOGY TEAM 435

هذا العمل لا يغني عن المرجع الأساسي للمذاكرة



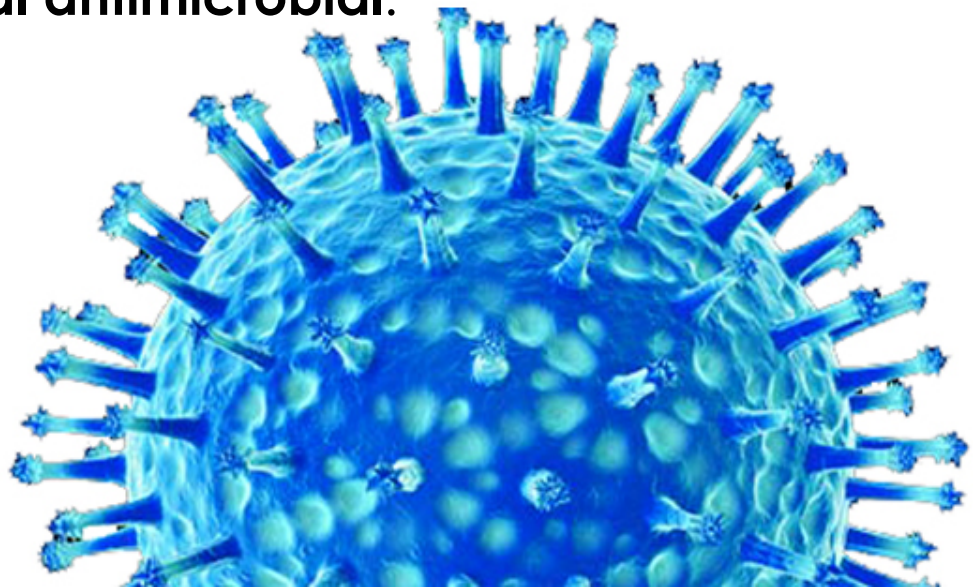
Lecture 13

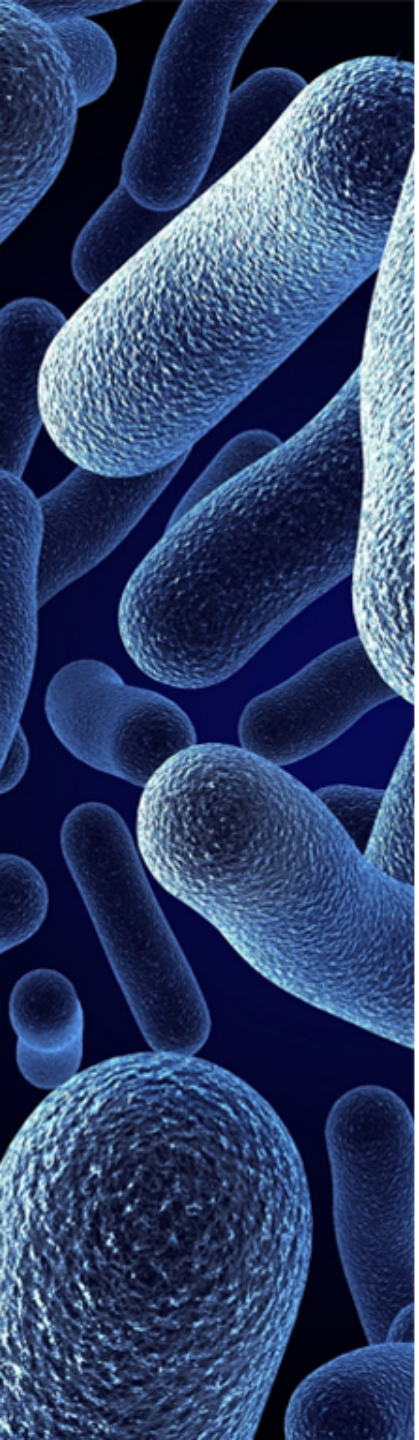
Antibiotics

● Important ● Term ● Extra explanation ● Additional notes

Objectives

- Define **antibiotic** ,**chemotherapy** and **selective toxicity**.
- Describe the difference between **bactericidal & bacteriostatic** antibiotics.
- Recognize the narrow and broad **spectrum antibiotics**.
- Define the **therapeutic index**.
- Know the **mechanism of action of antimicrobial agents**.
- Recognize the various **classes of antimicrobial agents** (action, spectrum and side effects)
- Explain the **criteria for an ideal antimicrobial**.





Antibiotic ,chemotherapy, selective toxicity, and therapeutic index

Both are antimicrobial agents

a) Antibiotics:
Natural compounds produced by microorganism which inhibit the growth of other microorganism .

b) Chemotherapy:
- **Synthetic compounds.**

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

Therapeutic index:
The **Ratio** of Toxic dose to human / Therapeutic dose against bacteria.

Examples:
Penicillin: High , good to human.
Aminoglycosides: low.
Polymyxin B: the lowest, toxic to human.

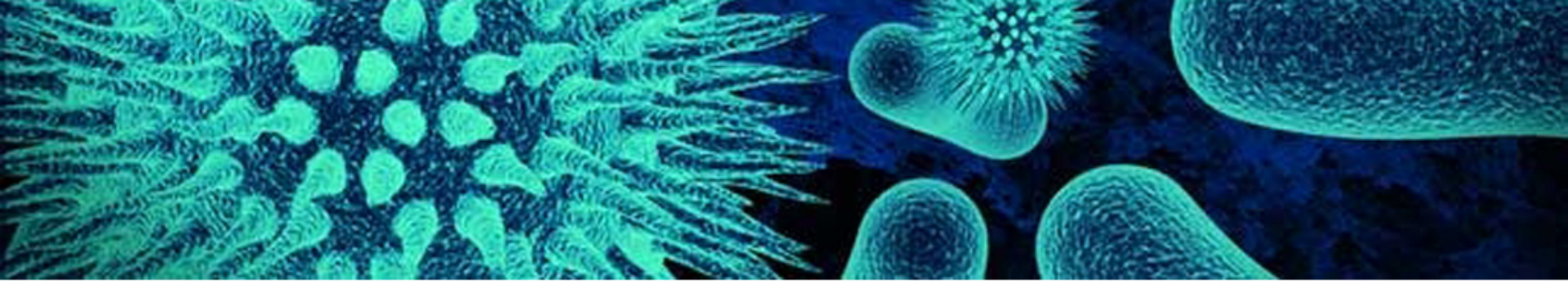
Mechanism of action of antimicrobial agents

1) Inhibition of cell wall synthesis.
2) Alteration of cell membrane
3) Inhibition of protein synthesis
4) Inhibition of nucleic acid synthesis
5) Anti-metabolite OR competitive antagonism.

Bactericidal & bacteriostatic antibiotics

bactericidal	bacteriostatic
kills bacteria	prevents multiplication

Spectrum of activity
Broad spectrum : affects gram positive & Gram negative bacteria
Narrow spectrum : affects selected organism.



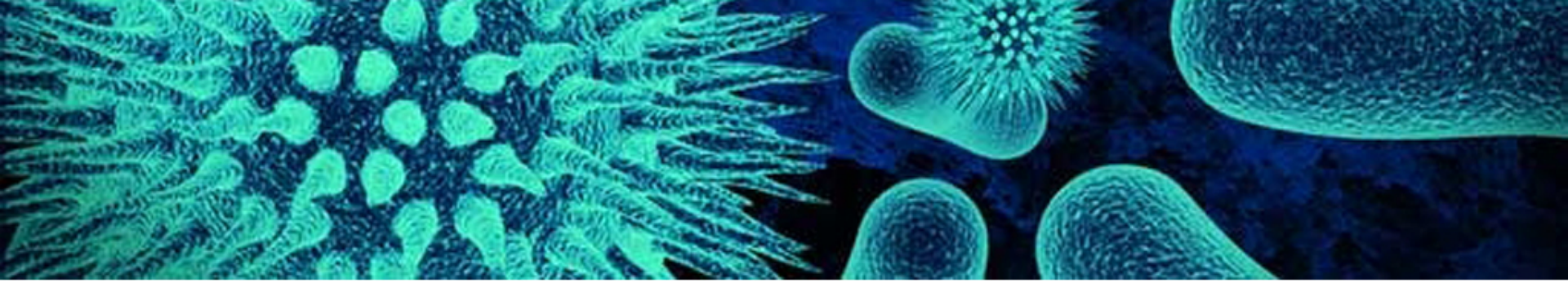
Antimicrobials that inhibit cell wall synthesis

A- Beta-Lactam antimicrobial agents

1-Penicillins
2-Cephalosporins
3-Carbapenems (imipenem & meropenem)
4-Monobactama (aztreonam)

B- Vancomycin

Teicoplanin



β - Lactam antibiotics

*Composed of: Beta-lactin ring and organic acid
*It can be natural or semi-synthetic
*Bactericidal
*Bind to penicillin binding protein (PBP) and interfere with trans-peptidation reaction
*Toxicity: mainly
1/allergy(common)
2/Anaphylaxis
3/Diarrhea

Penicillins

1-Benzyl penicillin: acts mainly on gram positive bacteria,
Examples:
Penicillin V, Procaine penicillin, Benzathine penicillin
2-Isoxazolyl penicillin: effective for staphylococcus aureus
Example: Cloxacillin
3-Amino-penicillin: effective for Enterobacteria
Example: Ampicillin
4-Acylaminopenicillin: effective for Pseudomonas
Example: Piperacillin & mezlocillin

Vancomycin

*Glycopeptides
*inhibit cell wall synthesis.
*Bactericidal
* Acts on Gram positive bacteria only (narrow spectrum).
*Given by injection only.
Used for methicillin resistant S.aureus systemic infections (MRSA) , emperical treatment of Gram positive infections & pseudomembranous colitis.
Side effects:
Red man syndrome , phlebitis, nephrotoxic & ototoxic.

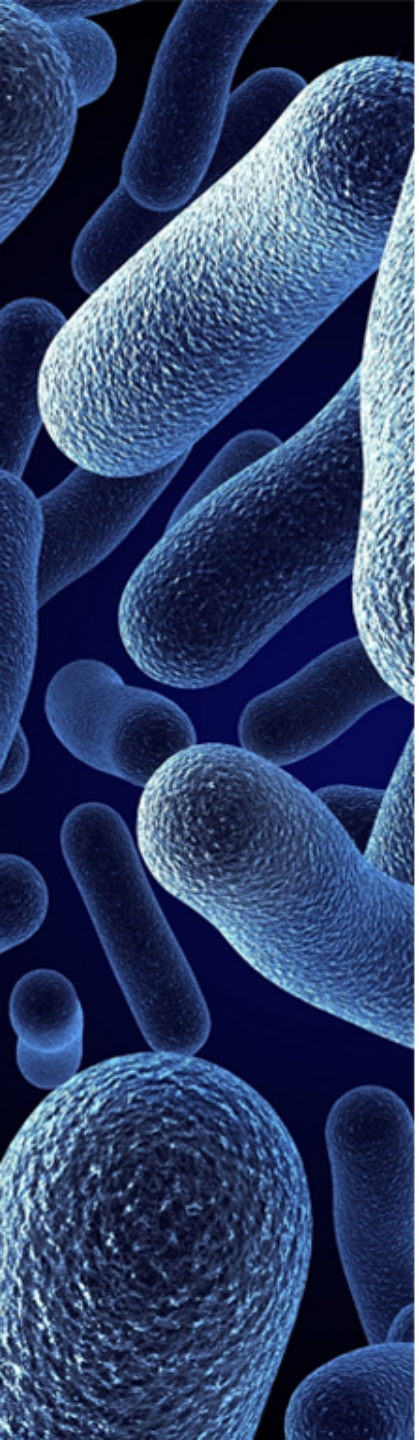
Cephalosporins

First generation:
Cephradine
Ceohalexime

Second generation:
Cefuroxime
Cephamycin (Cefoxitin)

Third generation:
expanded spectrum
Examples:
Ceftriaxone
Ceftazidime

Fourth generation:
Cefepim
Cefexime



ANTIBIOTICS THAT ALTER CELL MEMBRANES

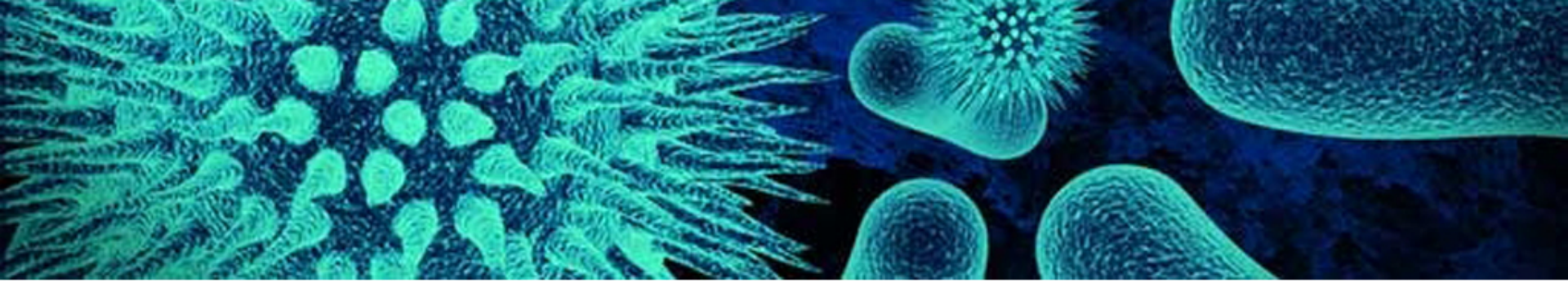
Polymyxin B and Colistin

Polymyxin B : a Peptide active against Gram **negative bacteria only**.

Bactericidal.

Only used ***locally*** due to serious **nephrotoxicity** when used systemically.

Colistin used for the treatment of multi-resistant organisms (MRO) such as ;*Pseudomonas* and *Acinetobacter* infections.



ANTIBIOTICS THAT INHIBIT PROTIEN SYNTHESIS

MACROLIDES

- Erythromycin & Clindamycin
- Bacteriostatic
- Good activity on :Legionella, Camylobacter, Gram negative and positive infections for patients allergic to Penicillins and Cephalosporins.
- Clindamycin acts on anaerobes as well
- Side effects : GIT disturbance, Pseudomembraneous colitis (mainly *clindamycin*)
- New Macrolides :
- Azithromycin & Clarithromycin . Less side effects , better penetration and longer half life.

CHLORAMPHENICOL

- Broad spectrum & bactericidal
- Side effects : it affects bone marrow cells and cause aplastic anemia
- Used only for severe infections not responding to treatment by other antimicrobials , also for the treatment of Rickettsial diseases
- Used also *topically* for eye and ear infections.

TETRACYCLINES

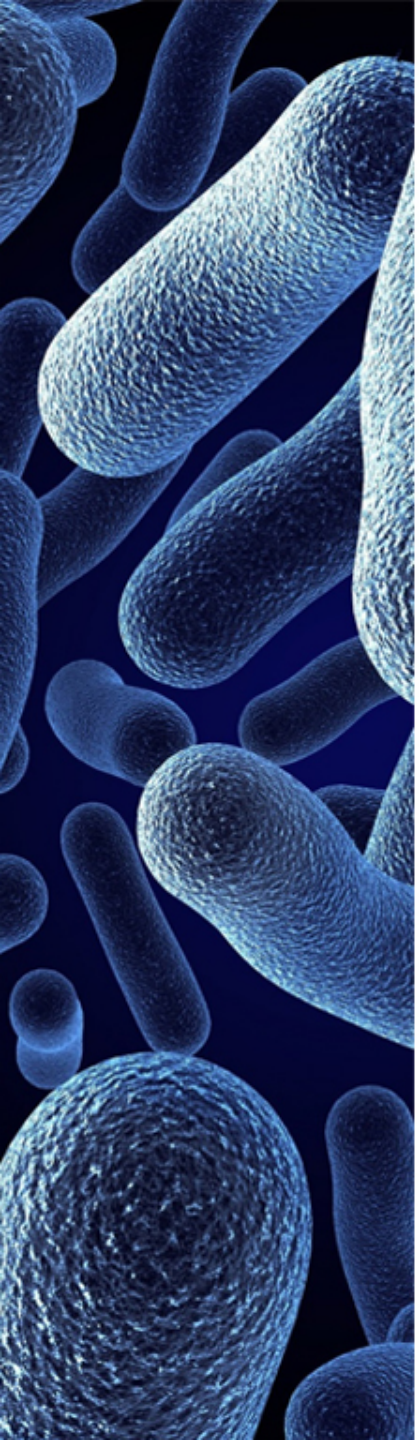
- Broad spectrum , bacteriostatic, not used for children under 8 yrs. or pregnant women. Oral absorption.
- Effective for Intracellular organisms eg. *Mycoplasma, Chlamydia ,Brucella* also for *V. cholera & Nocardia*

Classes

- Short acting: Tetracycline
- Long acting: Minocycline , Doxycycline (good CSF penetration).
- New tetracycline : Tigycycline *(covers MRSA,MSSA, some Gram negative bacteria and anaerobes.*
- Side effects :
- Permanent teeth discoloration , GIT disturbance

AMINOGLYCOSIDES

- Bactericidal
- Acts only on Gram negative bacteria(*narrow spectrum*)
- Streptococci & anaerobes are naturally resistant
- Examples: Gentamicin ,Amikacin , Neomycin ,
- Given by injection .
- Side effects : Nephrotoxic & Ototoxic - dose related.



ANTIMICROBIALS THAT ACT ON NUCLEIC ACID

Rifampicin

Metronidazole

Quinolones

Rifampicin

- Semi-synthetic, bactericidal , acts on Gram positive bacteria and selected Gram negative bacteria.
- Reserved for Tuberculosis
- Resistance develops quickly
- Used in combination
- Side effects :Causes discoloration of body fluids & hepatotoxicity.

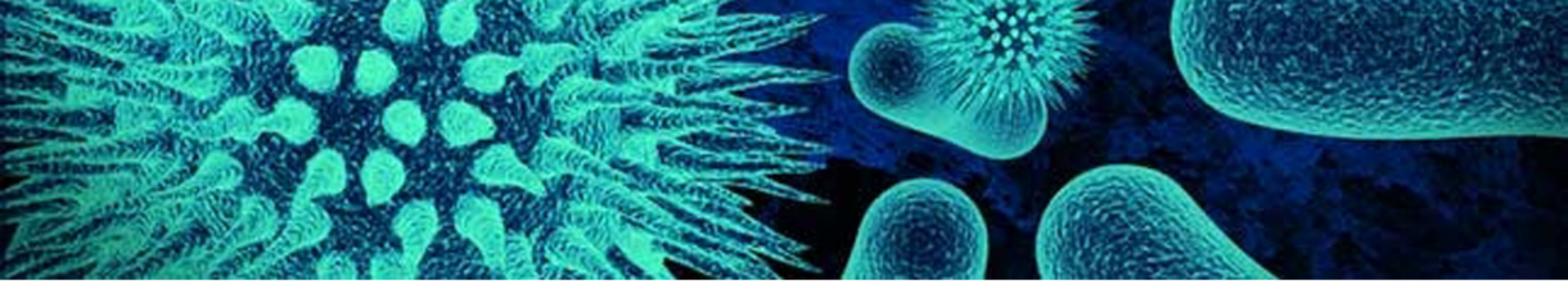
Metronidazole

- Nitroimidazole active on anaerobic bacteria and also parasite.
- Causes DNA breakage.
- Used for the treatment of infections due to
- B.fragilis , Trichomonas vaginalis and also for amoebiasis and giardiasis.

Quinolones

- Synthetic, bactericidal, inhibit DNA Gyrase and /or Topoisomerase.
- Generations:
- first generation: Nalidexic acid –locally acting
- Second generation: Fluoroquinolones eg. Ciprofloxacin, Norfloxacin, Ofloxacin,Levofloxacin
- Third generation: Sparfloxacin, Gatifloxacin
- Fourth generation: Moxifloxacin, Trovafloxacin

Side effects: affects cartilage (animals) & heart



ANTIMETABOLITES (folate inhibitors)

Trimethoprim-Sulfamethoxazole (TMP-SMX)

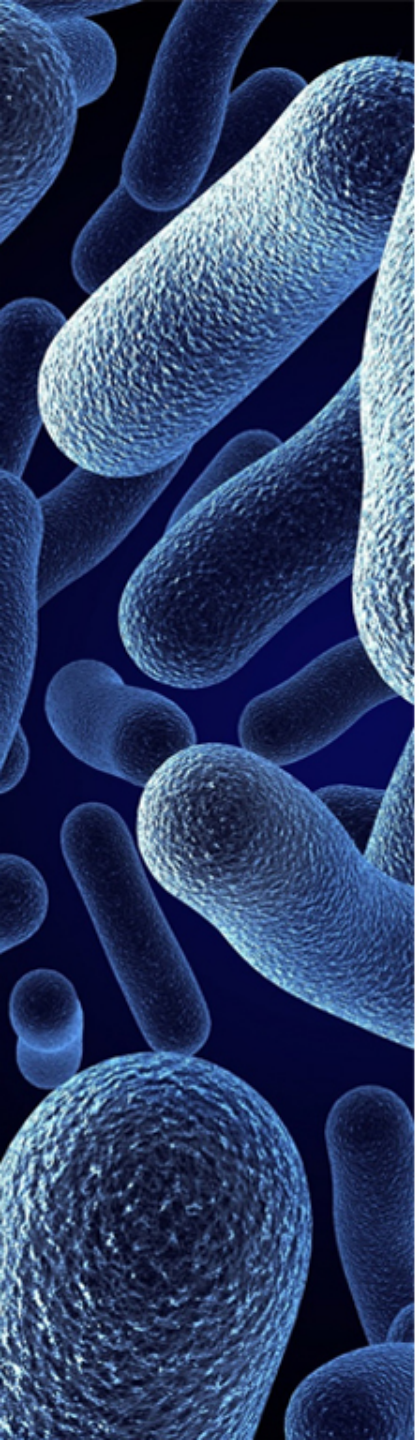
Combination of TMP-SMX called :
Bactrim / Septrin

Block sequential steps in folic acid synthesis

Effective of infections caused by *:*
Nocardia, Chlamydia, Protozoa & Pneumocystis caranii infections

Used for the treatment of:
upper & lower respiratory tract infections , otitis media, sinusitis & infectious diarrhea.

Side effects:
GIT, hepatitis , bone marrow depression& hypersensitivity



Anti-tuberculosis agents

First line agents

- Isoniazid (INH)
- Rifampicin
- Ethambutol
- Pyrazinamide

A combination of 4 drugs used for 6 months. eg. INH+ Rifampicin + Ethambutol for 2 months then continue INH+ Rfampicin for 4 months.

Second line agents

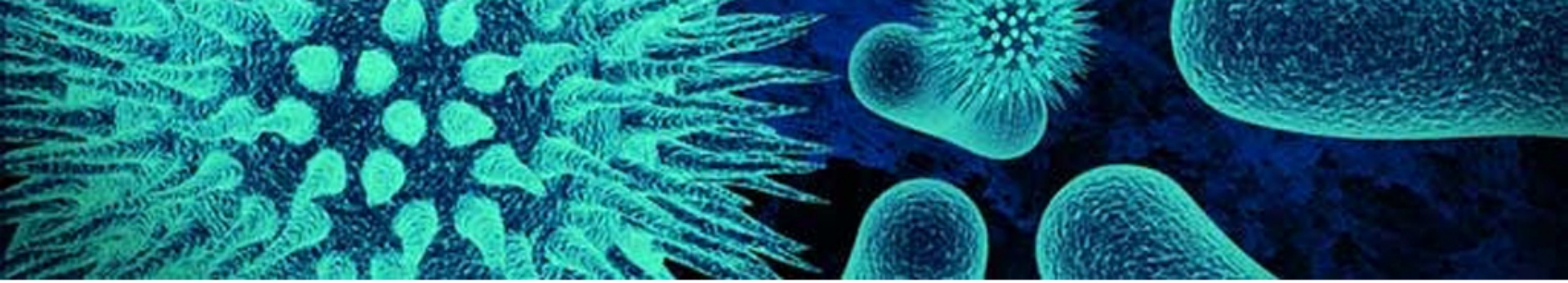
- Sterptomycin
- Para amino salicylic acid (PASA)
- Cycloserine
- Capreomycin

Used for resistant cases or cases not responding to first line drugs.

- **Isoniazid (INH)**
  - Bactericidal
  - Affects mycobacteria at different sites of the lung tissues.
  - Used for the treatment and prophylaxis of tuberculosis.
  - Side effects: peripheral neuritis &liver toxicity

- **Ethambutol**
  - Bactericidal
  - Concentrated in the phagolysosomes of alveoli
  - Side effect: optic neuritis

- **Pyrazinamide**
  - Acts on acid environment of macrophages
  - Side effects: hepatitis and arthralgia



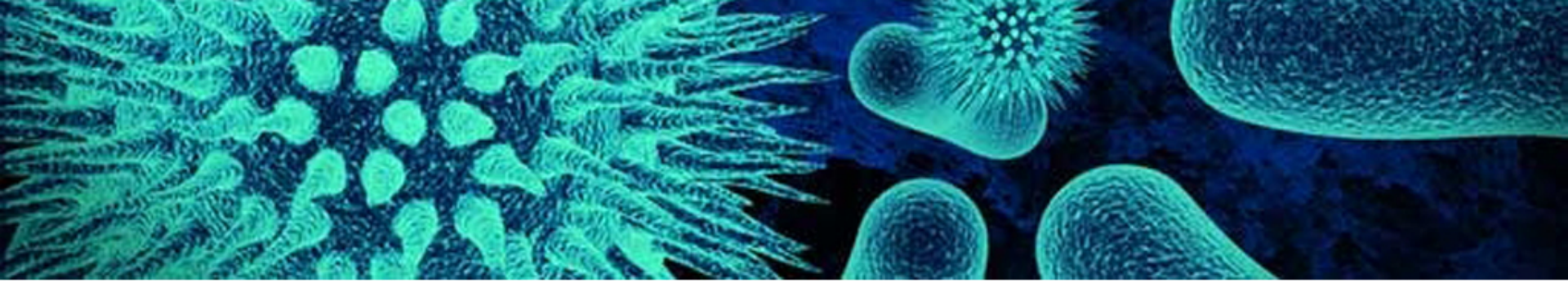
ANTIBIOTIC RESISTANCE IN BACTERIA

*Due to indiscriminate use of antimicrobials.*Selective advantage of antibiotics.

ANTIBIOTIC RESISTANCE IN BACTERIA

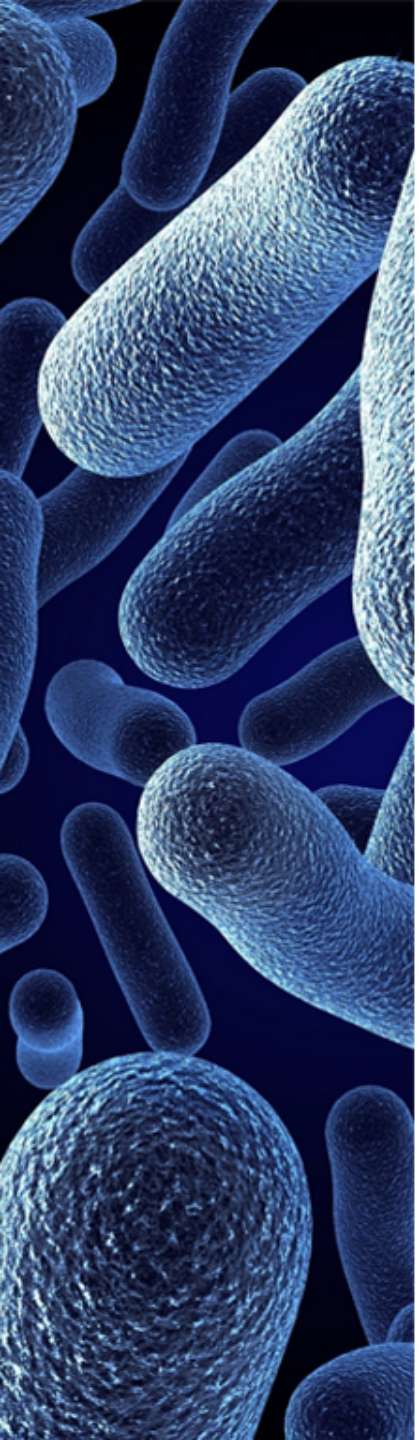
Types of resistance

Innate resistance	Acquired resistance due to :		Cross resistance	Dissociate resistance
e.g. *Streptococcus* & anaerobes are naturally resistant to gentamicin.	1- Mutation: *Mycobacterium tuberculosis* resistant to streptomycin	2- Gene transfer: plasmid mediated or through transposons	Resistance to one group confer resistance to other drug of the same group . e.g. resistance to erythromycin and clindamycin	e.g. resistance to gentamicin does not confer resistance to tobramicin .



ANTIBIOTIC RESISTANCE IN BACTERIA cont.

Mechanisms of resistance	Principles of antimicrobial therapy	Criteria for ideal antimicrobial agent
1- Permeability changed 2- Modification of site of action, e.g. Mutation. 3- Inactivation by enzymes . E.g. Beta- Lactamase & aminoglycoside inactivating enzymes. 4- Passing blocked metabolic reaction e.g. *PABA (para amino benzoic acid)* → folic acid , and is plasmid mediated.	▪Indication ▪Choice of drug ▪Route ▪Dosage ▪Duration ▪Distribution ▪Excretion ▪Toxicity ▪Combination use as in tuberculosis ▪ Prophylaxis Short term: ▪Meningitis Long term: ▪Tuberculosis, recurrent urinary tract infections , rheumatic fever	▪ Has selective toxicity ▪ Causes no hypersensitivity ▪ Penetrate tissues quickly ▪ Resistance does not develop quickly ▪ Has no effect of normal flora ▪ Broad spectrum



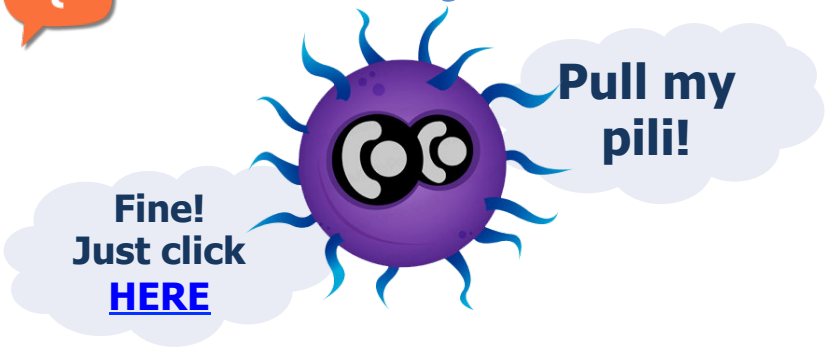
REMEMBER….

Antibiotics can do harm and develop resistance **so must be used judiciously**.

Antibiotics potentiate (increase strength) the function of human immune system to fight microbes.

We must know the toxicity , pharmacokinetics, and spectrum of activity of antimicrobials to make best guess of use.

Online Quiz



Videos

Video 1
http://youtu.be/IVBCrzjOI40
Video 2
http://youtu.be/057phDG4mKU

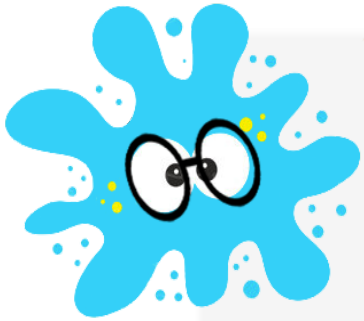
Books that could help you

Lippincott's Illustrated Reviews

MiCRObiology

TEAM 435

We do things better



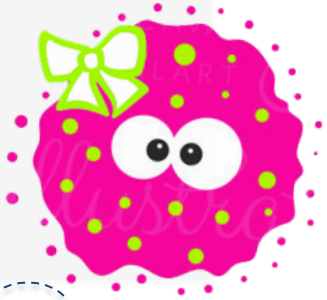
Boys Team

- Ali Alzahrani
- Khalid Sharahily
- Ahmad Alzahrani
- Zeyad Alsalem
- Muhammad Dossary
- Meshal Alhazmy
- Hamzah Alfiar

Girls Team

- Lamya Alsaghan
- Nojood Alhaidri
- Monera Alayuni
- Alanoud AlOmair
- Shahad Alenezi
- Aisha Al-Sabbagh
- Bodour Julaidan
- Noura AlTawil
- Deema AlFaris
- Sara Al-Hussein
- Suha Alenezy
- Latifah Alsukait
- Dalal Alhuzaimi
- Reema Allhaidan

Girls power!



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Contact us!

إن أصبنا فمن **الله** عز وجل، وإن أخطأنا فمن **أنفسنا والشيطان**