



Microbiology – Antibiotics

TEAM 437

Everything the doctor
focused on is in red

Red: important

Green : doctor notes

Black : original slides

Grey: extra information

In this link, you will find any corrections or notes unmentioned in the team's work. Please check the link below **frequently**.

https://docs.google.com/presentation/d/1yIQt3G8UDFG6xYMRhXkTk-dS54NeTfhJaPe_y0M-kjk/edit?usp=sharing



Objectives

- By the end of this lecture the student should be able to:
- Define antibiotic ,chemotherapy and selective toxicity
- Describe the difference between bactericidal and 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

Antimicrobial agents



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ANTIBIOTICS:

- Natural compounds produced by microorganism which inhibit the growth of other microorganism .

CHEMOTHERAPY:

- Synthetic compounds .
- Antimicrobial agents.

SELECTIVE TOXICITY:

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

Activity

BACTERICIDAL: kills bacteria

BACTERIOSTATIC: prevents multiplication.

Spectrum of activity

- Broad spectrum : Gram positive & Gram negative bacteria
- Narrow spectrum : selected organism.

THERAPEUTIC INDEX:

- The **RATIO** of the dose toxic to the host to the effective therapeutic dose.
- *Examples:*
 - Penicillin: High
 - Aminoglycosides : low
 - Polymyxin B : the lowest

Mechanism of action

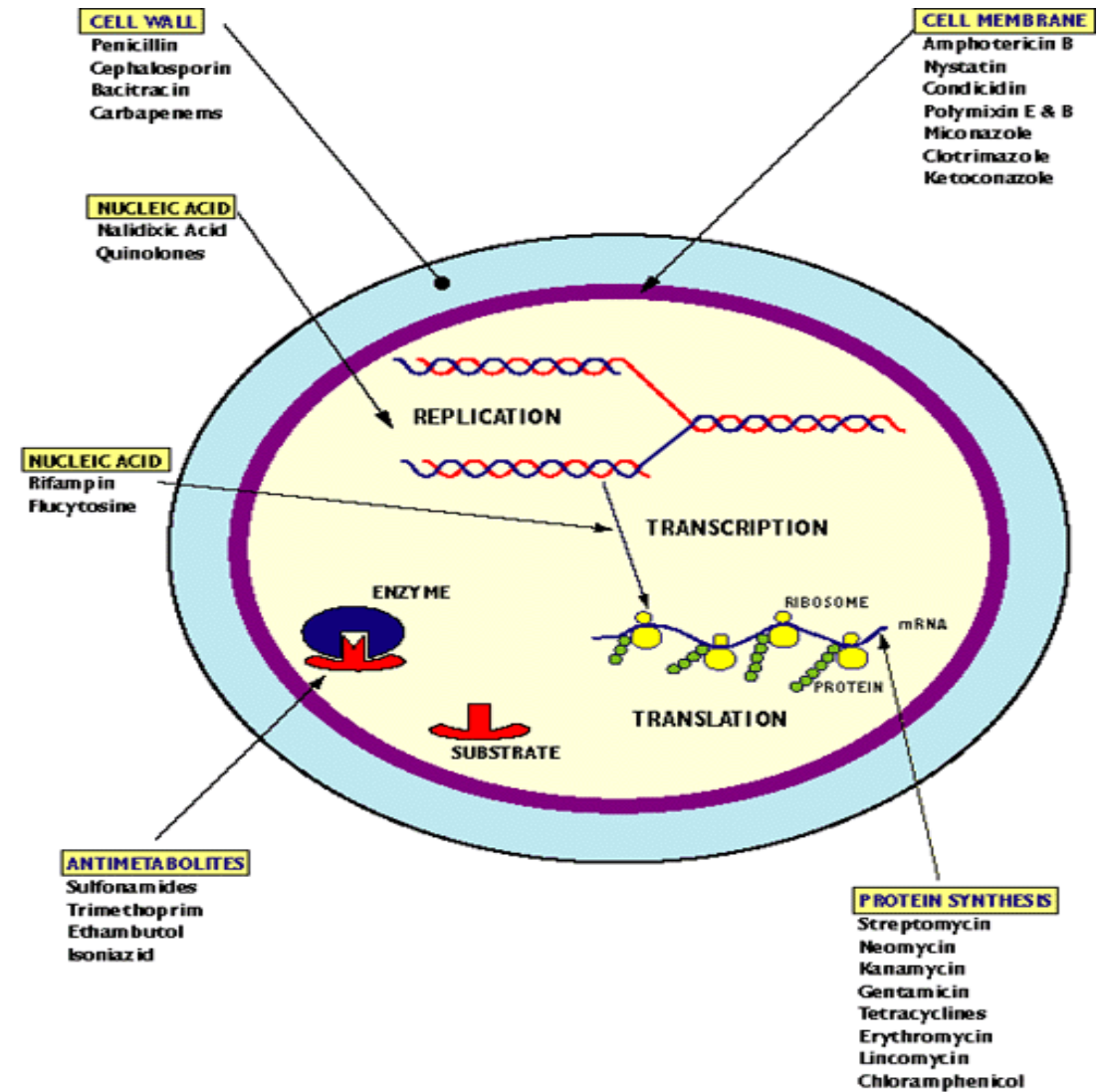
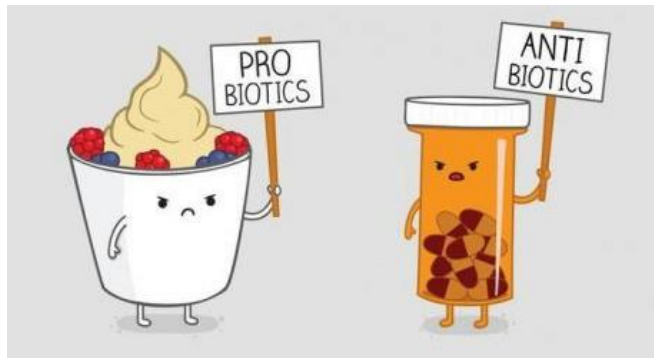


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Antibiotics can harm the microorganism by one of the following ways:

- 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.



Antimicrobials that inhibit cell wall synthesis



1-Beta Lactam Antimicrobial Agents

- Contain : Beta- Lactam ring & organic acid.
- Natural & Semi-synthetic
- **Bactericidal**
- Bind to PBP, interfere with trans-peptidation reaction
- Toxicity: mainly :
 - **hypersensitivity (type 1)**
 - Anaphylaxis
 - Diarrhea, ..etc
- They include :
 - Penicillins
 - Cephalosporins
 - Cephamycin
 - Carbapenems (imipenem & meropenem)
 - Monobactam (aztreonam)
 - Beta-lactamase inhibitors

2-Vancomycin (Teicoplanin) (huge molecule)

- Glycopeptides
- **Bactericidal.**
- **Acts on Gram positive bacteria only.(narrow spectrum**
- Inhibit cell wall synthesis
- Given by **injection** only.
- Used for :
 - **MRSA (Methicillin-resistant Staphylococcus aureus)**
 - S.epidermidis
 - pseudomembranous colitis.
- Side effects : **Red man syndrome** ,phlebitis, nephrotoxic & ototoxic.

β ~ LACTAM ANTIBIOTICS



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Penicillins

1. Benzyl penicillin: acts mainly on gram positive bacteria.
 - e.g.: Penicillin V, Procaine penicillin, Benzathine penicillin.
2. Isoxazolyl penicillin: **effective for staphylococcus aureus.**
 - e.g.: Cloxacillin
3. Amino-penicillin: **effective for Enterobacteria.**
 - e.g.: Ampicillin (acts on gram positive and gram negative bacteria and on anaerobes.)
4. Acylaminopenicillin: **effective for Pseudomonas.**
 - e.g.: Piperacillin & mezlocillin

Cephalosporins

- First Generation :
 - Cephradine
 - Ceohalexine
- Second Generation:
 - Cefuroxime
 - Cephamycin (Cefoxitin)
- Third Generation :
 - Expanded Spectrum
 - Examples :
Ceftriaxone
Ceftazidime
- Fourth Generation :
 - Cefepim
 - Cefexime

β-Lactamase inhibitors

- β-Lactams with **no antibacterial activity.**
- **Irreversibly bind to β-lactamase enzyme.**
- Examples : Clavulanic acid, Sulbactam, Tazobactam
- Effective on staph. Penicillinases and broad spectrum β-lactamases.
- Examples of antibiotics used with inhibitors : amoxicillin/clavulanic acid, ticarcillin /clavulanic acid and piperacillin /tazobactam.

β-Lactamase is an enzyme in bacteria that breaks the beta-lactam ring in antibiotics (such as penicillin). To inhibit that enzyme β-Lactamase inhibitors are used. even though they have little to no antibacterial activity , they prevent bacterial degradation of beta-lactam rings , and as a result allow antibiotics with beta lactam rings to work on the bacteria.



Antibiotics that alter cell membranes

PolymyxinB:

- a Peptide
- active against **Gram negative** bacteria only.
- **Bactericidal.**
- Only used **LOCALLY** due to serious **nephrotoxicity**

Colistin:

- active against **Gram negative** bacteria only.
- **Bactericidal.**
- Causes **nephrotoxicity**
- used for the treatment of multi-resistant organisms (MRO) such as :Pseudomonas and Acinetobacter infections.

Antibiotics that inhibit protein synthesis



MACROLIDES (50 Sub Unit of 23 rRNA):	AMINOGLYCOSIDES (S30S ribosomal subunit):	TETRACYCLINE (S30S ribosomal subunit):	CHLORAMPHENICOL <small>MICROBIOLOGY</small> (50 Sub Unit of 23 rRNA). ⁴³⁷
<ul style="list-style-type: none"> ❖ Types:Erythromycin & Clindamycin ❖ Bacteriostatic ❖ Legionella, Camylobacter, Gram negative and positive infections for patients allergic to Penicillins and Cephalosporins. ❖ Clindamycin acts on anaerobes as well ❖ Cause GIT disturbance, Pseudomembraneous colitis. ❖ New types Macrolides : Azithromycin & Clarithromycin . (Less side effects , better penetration and longer half life.) 	<ul style="list-style-type: none"> ❖ Bactericidal ❖ Acts only on Gram negative bacteria ❖ Streptococci & anaerobes are naturally resistant ❖ Examples: Gentamicin ,Amikacin , Neomycin , ❖ Given by injection . ❖ Nephrotoxic & Ototoxic - dose related 	<ul style="list-style-type: none"> ❖ Bacteriostatic ❖ Broad spectrum ❖ Oral absorption ❖ Intracellular organisms eg. Mycoplasma, Chlamydia ,Brucella also for V. cholera & Nocardia ☐ Classes: <ul style="list-style-type: none"> ▪ Short acting: Tetracycline ▪ Long acting: Minocycline , Doxycycline (CSF penetration). ▪ New tetracycline : Tigycycline (MRSA,MSSA, some Gram negative bacteria and anaerobes.) ☐ Side effects : <ul style="list-style-type: none"> ▪ Teeth discoloration , GIT disturbance ✓ Should not be given to pregnant women or children under 7 years. 	<ul style="list-style-type: none"> ❖ Broad spectrum (effective against all bacteria that cause meningitis) ❖ Bacteriostatic ❖ Affects bone marrow cells and cause aplastic anemia ❖ Used for severe infections not responding to treatment , also for Rickettsial diseases.



Antimicrobials that act on nucleic acid

Rifampicin

Quinolones

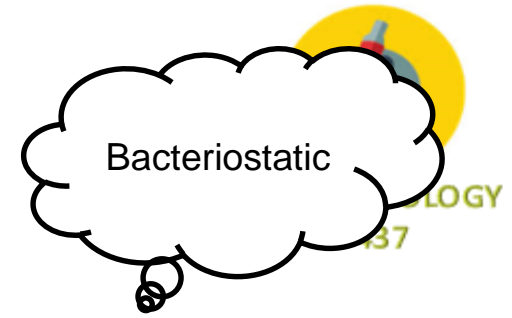
Metronidazole

- Characters
 - Semi-synthetic
 - **Bactericidal**
- Acts on
 - **Gram positive bacteria and selected Gram negative bacteria**
- Reserved for
 - **Tuberculosis** and Brucella
- Resistance
 - **Develops quickly**
- Used in
 - **Combination**
- Cause
 - Discoloration of body fluids
 - **hepatotoxicity**

- Characters
 - Synthetic
 - **Bactericidal**
- Acts on
 - Narrow spectrum and Active **on Gram negative bacteria**
- Inhibit
 - DNA Gyrase and/or topoisomerase
- Generations
 - **Four generations** (no need to memorize the examples in each generation. Just know that there are 4 generations)
- 1st Generation
 - Nalidixic acid – Locally acting
- 2nd Generation
 - Fluoroquinolones eg. Ciprofloxacin, Norfloxacin, Ofloxacin, Levofloxacin
- 3rd Generation
 - Sparfloxacin, Gatifloxacin
- 4th Generation
 - Moxifloxacin, Trovafloxacin
- Side effects
 - On Cartilage & Heart
- Can't be used
 - With children and pregnant

- **Bactericidal**
- **Active on Anaerobic bacteria, and Parasite**
- Cause
 - DNA Breakage
- Used for
 - B.fragilis(Bacteroids Fragilis)
 - Trichomonas vaginalis
 - Amoebiasis
 - Giardiasis
- Side effects
 - Alcohol + Metronidazole = Hypersensitivity

ANTIMETABOLITES (folate inhibitors):



- Bacteria makes their own folic acid , and the antimetabolites causes multiple problems in the folic acid metabolism in the bacteria .
- Work by suppressing the bacteria and they can also degrade the DNA
- They are **board spectrum**

هذه صورة تركها
الدكتور تشرح ان فيه
واحد يشتغل early
واحد late



• Trimethoprim-Sulfamethoxazole (TMP-SMX)

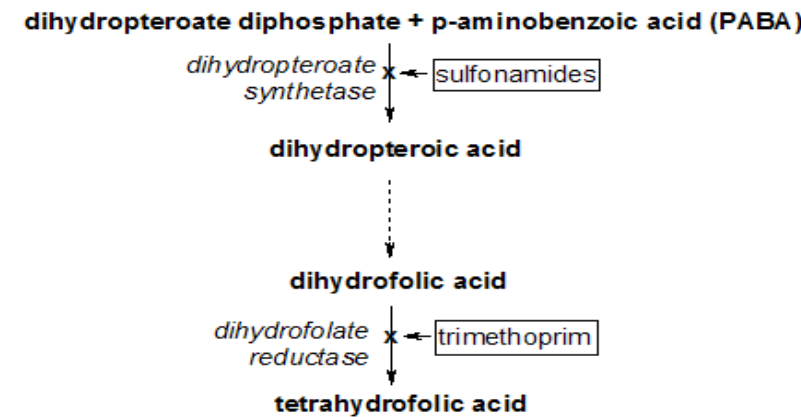
• Combination of TMP-SMX called : Bactrim / Septrin

• Block sequential steps in folic acid synthesis

• Used to treat : **Nocardia, Chlamydia, Protozoa & P.cranii**

• UTI, LRTI, OM., Sinusitis, infectious diarrhea.

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



ما ركز على ال early وال late
بس ذكرها عالسريع

Late

Early



Antituberculous agents

First line:

Isoniazide (inh):

- Bactericidal
- Affects mycobacteria at different sites of lung tissues
- Used for the treatment & prophylaxis of tuberculosis
- Cause peripheral neuritis (pyridoxine (vitamin B6 deficiency))

Rifampicin:
-Causes hepatotoxicity

Ethambutol:
-Causes color blindness
-Bactericidal
-Concentrated in phagolysosome of alveoli
-Optic neuritis

Pyrazinamide:
-Causes gout
-Acid environment of macrophages
-Hepatitis & arthralgia

Second line:

Streptomycin

Pasa

Cycloserine,

Capreomycin

الدكتور قال ما راح يسال عنهم الا ببلوك
الريسبايروتيري

ANTIBIOTIC RESISTANCE IN BACTERIA



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- 1- Indiscriminate use of antimicrobials
- 2- Selective advantage of antibiotics

Types of resistance:

A) Innate

e.g. Streptococcus & anaerobes are resistant to gentamicin.

b) acquired resistance :

- 1- mutation: mtb resistant to streptomycin
- 2- gene transfer: plasmid mediated or through transposons

C) Cross resistance :

Resistance to one drug confers resistance to other drugs of the same group .
e.g. Resistance to erythromycin and clindamycin

D) Dissociate resistance:

resistance to gentamicin does not confer resistance to tobramycin .

Mechanisms of resistance:

1- Permeability changed

2- modification of site of action, e.g. MUTATION

3- passing blocked metabolic reaction. e.g. PABA-----
---folic acid , plasmid mediated

4- inactivation by enzymes . e.g. Beta- Lactamase & aminoglycoside inactivating enzymes



Principles of antimicrobial therapy:

- Indication
- Choice of drug
- Route
- Dosage
- **Prolaphaxis**
- Duration
- Distribution
- Excretion
- Toxicity
- Combination

a) Short term:

-Meningitis

B) long term:

-Tuberculosis, ,
-RHEUMATIC FEVER

CRITERIA FOR IDEAL ANTIMICROBIAL:

- ✓ SELECTIVE TOXICITY
- ✓ NO HYPERSENSITIVITY
- ✓ PENETERATE TISSUES QUICKLY
- ✓ RESISTANCE NOT DEVELOP QUICKLY
- ✓ NO EFFECT ON NORMAL FLORA
- ✓ BROAD SPECTRUM



Questions

1- Which of these results in teeth discoloration?

- a) *Aminoglycosides* b) *Tetracycline* c) Polymyxin B d) Penicillin

2- An example of beta-lactamase inhibitor?

- a) Penicillin b) Amoxicillin c) Clavulanic Acid d) ticarcillin

3- Bactericidal prevent bacterial multiplication

- a) True b) *False*

4- Aplastic anemia is caused by?

- a) Chloramphenicol b) Vancomycin c) HBV d) Metronidazole

5- Broad spectrum kills gram +ve and gram -ve bacteria?

- a) True b) False

6- Antibiotic that shouldn't be used during pregnancy?

- a) Rifampicin b) Quinolones c) Macrolides

1-B 2-C 3-B 4-A 5-A 6-B



MED437
KING SAUD UNIVERSITY

لا يقوى الإنسان في الحياة على هذه الأرض من دون أن يعاونه النَّاس ويقفوا معه.



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