

The high yield



Bacterial Protein Synthesis Inhibitors

AMINOGLYCOSIDES

Ribosomes: site of protein synthesis

• Prokaryotic ribosomes are 70S:

Large subunit: 50S

33 polypeptides

Small subunit: 30 S

21 polypeptides

• Eukaryotic are 80S

acting at the ribosomal level taking the advantage of major difference prokaryotic and eukaryotic ribosome structure

(Amikacin , Gentamicin , Neomycin , Streptomycin)

Action: (cidal)

Irreversible binding to 30S subunit

Not :
absorbed orally (MW > 500)
pass BBB
pass placenta and breast milk

Not metabolized

Excreted unchanged in urine: active in alkaline urine

N.B
The B-lactams inhibit cell wall synthesis
and thereby increase the permeability of the
aminoglycosides.

Indications:

1- UTIs (use is not common; nephrotoxicity)

2- Septicemia , meningococcal
meningitis: gentamicin

3- T.B streptomycin (1st line)

4- Plague (Y. pestis): (1st line)

5- oral for gut decontamination, hepatic
coma (neomycin)

6- Gentamicin: combined with:

- Infective endocarditis with
vancomycin

- Peritonitis with penicillin and
metronidazole

7- eye drops (Tobramycin)

Adverse effects:

1- Nephrotoxicity (old age
cephalosporins)

2- Nerve toxicity: 8th cranial nerve:
ototoxicity: reversible if early

3- Neuromuscular blocking

MACROLIDES/KETOLIDES

(Azithromycin , Clarithromycin , Erythromycin ,
Telithromycin)

Action: (static but increasing concentration turns the
drug into cidal)

Binding of 50S subunit: (weak reversible binding)

Poor oral absorption (MW > 500)

Not pass BBB

Pass placenta but not teratogenic (safe in pregnancy:
erythromycin, zithromycin)

Pass to most body fluids in good concentration
Concentrated in macrophages and polymorphs

Metabolism: liver

Excretion: bile, enterohepatic circulation

Indications

1- G+ve infections respiratory and ENT infections:
(2nd choice after penicillins and cephalosporins)

2- Clarithromycin: eradication of H. pylori in peptic
ulcer: 10 days

3- Syphilis: 2nd choice after penicillin and
cephalosporins

4- Atypical infections: eye and genital infections of
chlamydia, atypical pneumonia, Legionnaires' disease

5- Toxoplasmosis

Adverse effects:

1- GIT upset

2- Cholestatic Hepatitis

3- Enzyme inhibitor

4- Prolongation of QT interval: (sudden cardiac death)

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Chlaramphenicol

- # Action: (Static)
- # Binding (weak) to 50S subunit.
- # Well-absorbed; (MW < 500)
- # Pass BBB
- # Widely distributed: high Vd
- # Pass placenta, in breast milk
- # Metabolized by glucuronidation in liver: glucuronyl transferase phase II
- # Excreted in urine: inactive metabolites

Indications

- 1- Atypical microorganisms: after macrolides and doxyeycline: 3rd choice
- 2- Meningitis: after penicillins, cephalosporins 3rd choice
- 3- Cholera: ampicillin, 3rd generation cephalosporins, floroquinolones 4th choice
- 4- Eye infections; eye drops

Adverse effects

- 1- Fatal anemia: rare (immunologica): not dose dependent, irreversible, after stopping the drug
- 2- Bone marrows depression reversible, mild, dose-dependent, Curing treatment
- 3- Hepatic enzyme inhibitor
- 4- Teratogenic: Grav baby Syndrome

Teratogenicity of Chloramphenicol administration late in pregnancy

Low capacity to glucuronyl transferase enzyme and underdeveloped renal function → a decreased ability to excrete the drug → drug accumulates to levels that interfere with the function of mitochondrial ribosomes
»»»
poor feeding, depressed breathing, cardiovascular collapse, cyanosis ("grey baby") and death.

N.B
only 2 -OH groups, 2 Cl atoms
Not used nowadays except topically for eye infections

N.B
Contraindications/ blood diseases, pregnancy, lactation, children less than 2y

Clindamycin

- # Action: (Static)
- # Binding to 50S subunit.
- # Rapid complete oral absorption (MW < 500)
- # pass BBB in Small amounts
- # Penetrates bone, tissue fluids including prosta
- # Pass placenta: (not teratogenic)
- # Indications
 - 1- Dental infections
 - 2- Bone , joint infection: osteomyelitis
 - 3- Toxioshock, syndrome :Nafcillin, Oxacillin, Vancomycin or gentamicin
 - 4- Topical :acene
 - 5- Toxoplasmosis, malaria (off-label)
- # Adverse effects pseudomembranous colitis: 2-20% most serious may be fatal by Clostridium difficile Treatment: oral metronidazole for 7-10 days or oral (vancomycin)

Tetracyclines

- # Action: (Static)
- # Reversible (weak) binding to 30S subunit
- # Partially absorbed (MW < 500 except tigecycline parenteral)
- # Absorption decreased with: food, milk, antacid, iron (binds to heavy metals)
- # Incomplete passage to BBB
- # Pass placenta (teratogenic) and breast milk (high affinity to Ca)
Contraindications: pregnancy, lactation, children < 8 y



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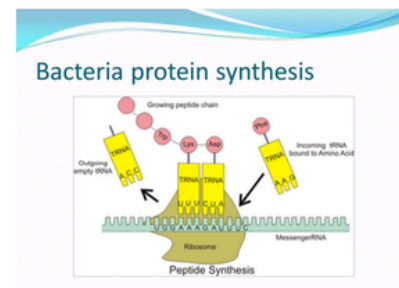
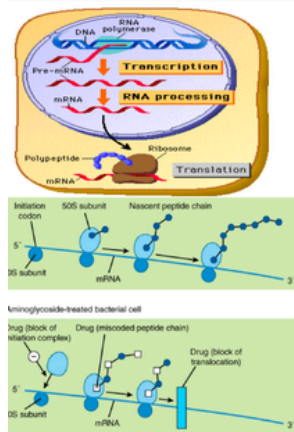
Tetracyclines

- # **Metabolism:** extensive in liver
- # **Excreted in urine (80% inactive), more than in bile (enterohepatic circulation)**

- # **Indications**
 - 1- calm my leg: 2nd choice after macrolides
 - 2- BRC: 1st choice, 2nd choice: macrolides:
borrelia: tick-born spirochetes:
Lyme disease: doxycycline 100mg twice daily for 14 days
Rickettsia: rocky mountain fever: 100mg doxycycline twice daily for 7-10 days
Coxiella: Q fever: 100mg doxycycline twice daily for 14 days
 - 3- Cholera: 300 mg doxycycline single oral dose)
 - 4- Acne: doxycycline oral with topical clindamycin)
 - 5- SIADH: DEMECLOCYCLINE

- # **1- Teeth, bone: Discoloration and deformity in growing teeth and bone (contraindicated in pregnancy, lactation and in children < 8 years)**
- 2- Renal impairment (should be also avoided in renal disease)**
- 3- GIT upset: peptic ulcer**
- 4- liver: liver cell failure. cholestatic jaundice**
- 5- kidney: nephrogenic DI, Fanconi syndromne (outdated tetracyclines)**
- 6- Photosensitivity**

N.B
doxycycline and minocycline : nearly complete oral absorption, 50% renal excretion, 50% in bile: can be used in renal impairment



تذكرونا بدعوة ولا تنسو إخواننا في غزة ولبنان من الدعاء "اللهم يا مفرج الهموم فرج همهم وانصرهم على اعدائهم واعدئنا واعداء الامة الاسلامية جمعاء"

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