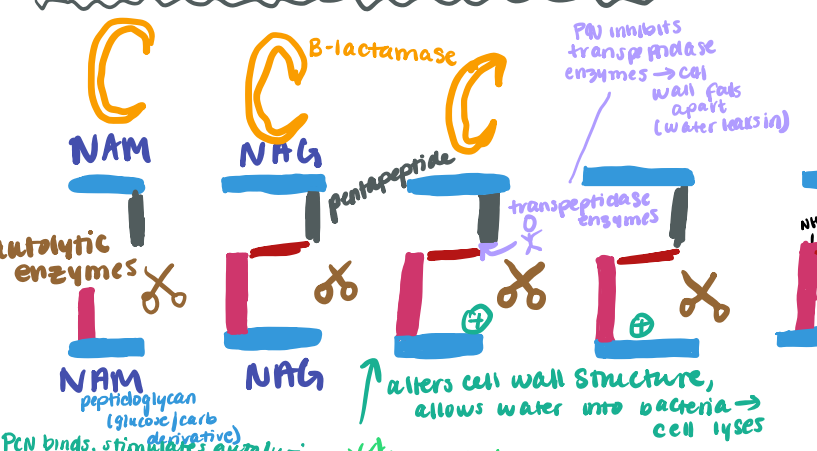


# CELL WALL SYNTHESIS INHIBITORS



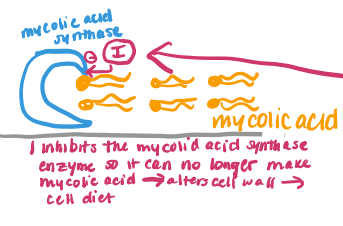
## glycopeptides

### Vancomycin (non-β-lactam)

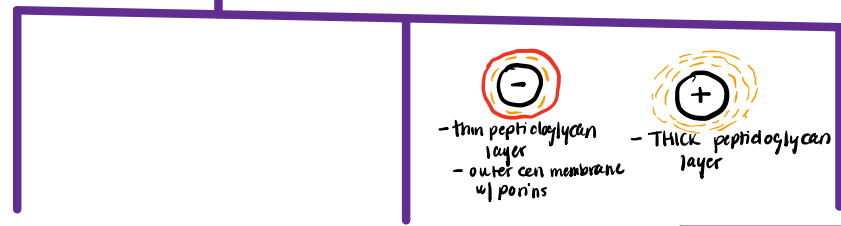
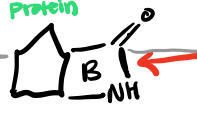
- MRSA > gram ⊕
- C. diff > gram ⊕
- resistant coagulase ⊖ bacteria
- vanco binds on to COO<sup>-</sup> end → allosterically alters → NH<sub>2</sub> group can't form peptide bond

## Isoniazid

- inhibits synthesis of mycolic acids (essential components of mycobacterial cell walls)
- penetrates into macrophages
- paired w/ Rifampin to tx most strains of tuberculosis



## β-lactam



## PENICILLINS

- PEN G
- PEN G proline
- PEN VK
- Piperacillin
- Amoxicillin
- Ampicillin
- gram + / - \*more resistant
- streptococcal
- syphilis

## AMOXICILLIN

- ← very susceptible to β-lactamases, give w/ clavulonic acid (β-lactamase inhibitor)
- UTIs
- RTIs
- meningitis
- salmonella
- otitis media

## CEPHALOSPORINS

- 1st gen Cephalixin > gram ⊕
- 2nd gen Cefuroxime > gram ⊕
- 3rd gen Ceftriaxone > gram ⊖
- 4th gen Cefepime > gram ⊖
- 5th gen Ceftaroline - MRSA
- S. aureus
- Strep pyogenes
- Pseudomonas
- meningitis
- Klebsiella (pneumonia)
- enterobacteria

## ETHAMBUTOL

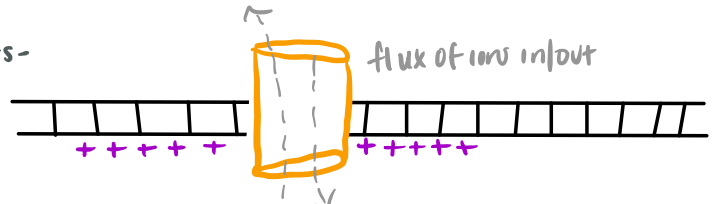
- inhibits mycobacterial arabinosyl transferases → involved in polymerization of arabinoglycan (essential component of mycobacterial cell wall)
- tuberculosis, always given w/ other anti-TB's

## CARBAPENEMS

- Imipenem-cilastatin
- Meropenem
- Ertapenem
- β-lactam ring highly resistant to β-lactamases
- broad spectrum
- gram + cocci
- gram - rods AND resistant
- gram - rods
- ↳ pseudomonas
- ↳ enterobacter
- anaerobes

## MONOBACTAM

- Aztreonam
- prevent peptidoglycan cross-linking by binding to PBP3
- gram ⊖
- \* Pseudomonas



## DAPTOMYCIN

- gram ⊕
- ↳ S. aureus, MRSA, VRE
- forms pore in bacterial cell wall → flux of ions moving in & out → depolarization of inside membrane

- inhibits DNA synthesis
- inhibits ribosome protein synthesis
- inhibits RNA synthesis
- \* bactericidal

## β-LACTAMASE INHIBITORS

- \* DO NOT WORK ON:
- 1. chromosomal β-lactamases
- ↳ enterobacter
- ↳ citrobacter
- ↳ indole-positive proteus
- ↳ actinobacter
- ↑ expression of AmpC gene regulated by presence of substrates like 3rd gen cephalosporins

- S - Serratia marcescens
- P - Proteus (indole-+)
- A - Actinobacter baumannii
- C - Citrobacter freundii
- E - Enterobacter spp.
- low level constitutive production of AmpC β-lactamase

- 2. extended spectrum (ESBL)
- ↳ E. coli
- ↳ Klebsiella spp.

# PROTEIN SYNTHESIS INHIBITORS

## other 50s inhibitors

### MACROLIDES

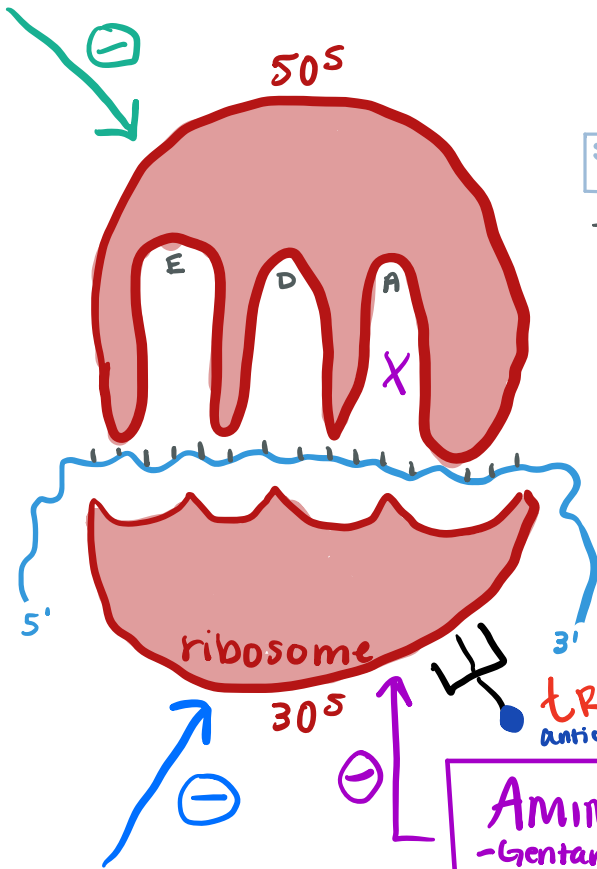
- Erythromycin
- Azithromycin
- Clarithromycin (-)

- inhibit ribosome from elongating peptide chain / reading the mRNA → can't synthesize functional proteins

\* **BACTERIOSTATIC**  
\* **50S**

\* doesn't cause cell to die, inhibits cell from carrying out specific fxns

- pneumonia
  - ↳ legionella
  - ↳ mycoplasma
- H. pylori
  - ↳ peptic ulcers
- GI infections
  - ↳ Campylobacter
- STIs
  - ↳ Chlamydia
  - ↳ gonorrhoea



### OXAZOLIDINONES

- Linezolid
- \* **bactericidal / bacteriostatic**
- binds to 50s ribosomal subunit → inhibit protein synthesis
- very narrow spectrum
- treatment of RESISTANT gram (+) cocci
  - ↳ MRSA
  - ↳ VRE

### LINCOSAMIDES

- Clindamycin
- \* **bacteriostatic!**
- inhibits peptidyl transfer by binding 50s
- narrow spectrum
- gram (+) cocci
  - ↳ MRSA (↑ resistance)
  - ↳ anaerobes
  - ↳ B. fragilis
- \* skin infections / dental infections
  - ↳ penetrates abscesses

### STREPTOGRAMINS

- Quinupristin/dalfopristin
- \* **bactericidal / bacteriostatic**
- forms complex w/ ribosomal actions to inhibit protein synthesis
- Selective: gram (+) aerobic bacteria
  - ↳ MRSA
  - ↳ VRE

### CHLORAMPHENICOL

- \* **bacteriostatic**
- binds 50s & blocks aminoacyl binding to acceptor site → blocks peptidyl transferase reaction + translation
- gram +/-
- **bactericidal against**
  - ↳ H. influenzae
  - ↳ S. pneumoniae
  - ↳ IV. meningitidis
- VRE
- rocky mtn spotted fever
- outside US: bacterial meningitis

### TETRACYCLINES

- Doxycycline

- Borrelia Burgdorferi
  - ↳ Lyme disease
- Chlamydia
- P. acnes
- rosacea
- Yersinia pestis
  - ↳ bubonic plague
- Anthrax
- pneumonia
  - ↳ legionella (gram -)

\* **30s subunit**

- binds to 30s, prevents tRNA from coming into A site & read codons in mRNA

\* **bacteriostatic!**

### AMINOGLYCOSIDES

- Gentamicin
- Amikacin
- Tobramycin

\* **30s subunit**

- blocks TRNA from binding to A site → inhibits protein synthesis

- CAUSE cell death

\* **bactericidal!**

- gram -
  - ↳ pseudomonas
  - ↳ aerobic (-) bacteria
  - ↳ Enterobacteria
- UTIs
- pneumonia
- meningitis
- Peritonitis

- blocks tRNA from coming into A site  
tRNA anticodons specific to mRNA codons

# DNA & RNA SYNTHESIS INHIBITORS

- DNA gyrase inhibitors

## FLUROQUINOLONES

- Ciprofloxacin<sup>2nd</sup> - Moxifloxacin<sup>4th</sup>
- Levofloxacin<sup>3rd</sup>

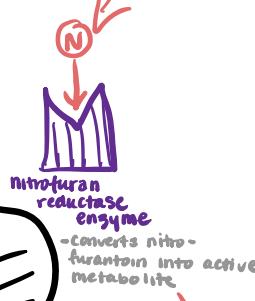
\* type II topoisomerase  
↳ gram ⊖

- stimulate cutting part of enzyme → inhibits fusing component → DNA fragmentation
- gram - / ⊕?
- pyelonephritis
- prostatitis
- osteomyelitis



## NITROFURANTOIN

- gram - / +
- \* UTI
- E. coli (gram -)
- Enterococci (gram +)
- binds to nitrofurantoin reductase enzyme → converts nitrofurantoin into active metabolite → produces reactive intermediate which
  - damages DNA
  - damages RNA
  - inhibits RNA protein synthesis
  - damages cell wall
- \* bactericidal!



reactive intermediate

damages DNA

damages RNA

## RIFAMPICIN

- tuberculosis
- MRSA
- inhibits RNA polymerase → inhibits transcription / protein synthesis
- \* bactericidal

RNA polymerase

inhibits RNA + protein synthesis

DNA fragmentation



## METRONIDAZOLE

- gram - / +
- anti-protozoan action
  - ↳ Giardia
  - ↳ Entamoeba histolytica
- H. Pylori
- bacterial vaginosis
- disrupts normal helical structure of DNA → exposes it to undergo fragmentation (by nucleases)
- \* bactericidal

## RIFAXIMIN

- inhibits RNA polymerase
- \* bacteriostatic!
- travelers diarrhea
- hepatic encephalopathy
- IBS / IBD

# FOLIC ACID PATHWAY INHIBITORS

para-**amino benzoic acid (PABA)** + **Pteridine**

**Dihydro Pteric Acid**

**dihydro folic acid**  
**DHF**

**tetrahydrofolic acid**  
**THF**

**Purines & pyrimidines**  
(components of DNA)

**Celconimides**

**Sulfa-methoxazole**

- inhibit folate metabolism

- toxoplasmosis
- Nocardiosis
- UTIs
- \* bacteriostatic

dihydro synthetase enzyme

dihydrofolate reductase enzyme

**trimethoprim**

- inhibit enzyme dihydrofolate reductase

- enterobacteria (gram -)
- \* bacteriostatic

**BACTRIM**  
(sulfa-methoxazole + trimethoprim)

\* broad spectrum  
\* bactericidal

- pneumocystis carini \*
- UTIs
- respiratory infections (rare)
- salmonella
- septicemia
  - ↳ listeria monocytogenes
- toxoplasmosis
- neutropenic pts → prophylaxis

# HELPFUL MNEUMONICS

## 10 main classes

<b>A</b> ntibiotics	—	<b>A</b> minoglycosides	→	"-mycin"	- inhibit 30 protein synthesis
<b>C</b> an	—	<b>C</b> ephalosporins	→	"cef-"	- inhibit cell wall synthesis
<b>T</b> erminate		<b>T</b> etracyclines	→	"-cycline"	- inhibit 30s protein synthesis
<b>P</b> rotein		<b>P</b> enicillins	→	"-cillin"	- inhibit cell wall synthesis
<b>S</b> ynthesis		<b>S</b> ulfonamides	→	"Sulfa"	- inhibit folate synthesis
<b>F</b> or		<b>F</b> luoroquinolones	→	"-floxacin"	- inhibit DNA replication
<b>M</b> icrobial		<b>M</b> acrolides	→	"-thromycin"	- inhibit 50s protein synthesis
<b>C</b> ells		<b>C</b> arbapenems	→	"-penem"	- inhibit cell wall synthesis
<b>L</b> ike		<b>L</b> incosamides	→	clindamycin	- inhibit 50s protein synthesis
<b>G</b> erms		<b>G</b> lycopeptides	→	vancomycin	- inhibit cell wall synthesis

## antibiotics w/o gram + AND - coverage

- G**lycopeptides → gram +
- L**incosamides → gram +
- A**minoglycosides → gram -
- M**acrolides → gram +

## Inhibit protein synthesis

**M**  
**A**  
**L**  
**T**

# Protein Synthesis Inhibitors

## AMINOGLYCOSIDES

- Gentamicin - Amikacin
- Tobramycin (IV)

### \* 30s subunit

- blocks TRNA from binding to A site → inhibits protein synthesis
- CAUSE cell death

### \* bactericidal!

### Bugs

#### - gram -

↳ pseudomonas

↳ aerobic (-) bacteria

↳ Enterobacteria

- Complicated UTIs
- Septicemia

### adverse effects/toxicities

- \* ototoxicity
- nephrotoxicity
- neuromuscular blockade

### \* adjust renal dose!

\* M. gravis → complete contraindication

## MACROLIDES

- Erythromycin (PO)
- Azithromycin (IV or PO)
- Clarithromycin (-)

- inhibit ribosome from elongating peptide chain / reading the mRNA → can't synthesize functional proteins

### \* BACTERIOSTATIC

### \* 50S

\* doesn't cause cell to die, inhibits cell from carrying out specific fxns

### BUGS

## TETRACYCLINES

- Doxycycline (PO)

### \* 30s subunit

- binds to 30s, prevents tRNA from coming into A site & read codons in mRNA

### \* bacteriostatic!

### BUGS

- tick borne diseases

\* Chlamydia

\* Rickettsia

\* Mycoplasma

- gonococcal dz

- anthrax, malaria, tularemia

- alternate for:

↳ MRSA

↳ VRE

- acne, rosacea

### adverse effects

- GI upset
- photosensitivity
- effects on calcified tissues
- superinfections
  - ↳ candida
  - ↳ C. diff
- vestibular

\* contra. in:

- pregnancy
- kids < 8

\* only Doxy for pts w/ renal insufficiency

## CHLORAMPHENICOL

### \* bacteriostatic

- binds 50S & blocks aminoacyl binding to acceptor site → blocks peptidyl transferase reaction + translation

### BUGS

- gram +/-

- bactericidal against

↳ H. influenzae

↳ S. pneumoniae

- VRE

- rocky mtn spotted

- pneumonia
  - ↳ legionella
  - ↳ mycoplasma
- H. pylori
  - ↳ peptic ulcers
- GI infections
  - ↳ Campylobacter
- STIs
  - ↳ chlamydia
  - ↳ gonorrhoea

- ↳ N. meningitidis
- adverse effects:
  - grey baby syndrome
  - bone marrow suppression
  - anemia
  - pancytopenia

fever  
- outside US: bacterial meningitis

## LINCOSAMIDES - Clindamycin

\* bacteriostatic!

- inhibits peptidyl transfer by binding 50s

- narrow spectrum

- gram (+) cocci

↳ MRSA (↑ resistance)

↳ anaerobes

• B. fragilis

\* skin infections/dental infections

↳ penetrates abscesses

adverse effects

- diarrhea, nausea, vomiting

- rash

\* causes C Diff

adverse effects

\* well tolerated

- some GI upset

- erythro-faunice from cholestatic hepatitis

\* avoid in pts w/ hepatic dysfunction

\* CYP3A4 inhibitor → warfarin

## STREPTOGRAMINS

- Quinupristin/dalfopristin

\* bacteriocidal

- forms complex w/ ribosomal actions to inhibit protein synthesis

BUGS

- selective: gram ⊕ aerobic bacteria

↳ MRSA

↳ VRE

adverse effects

- arthralgia

- myalgia

## OXAZOLIDINONES

- Linezolid

\* bacteriocidal / bacteriostatic

- binds to 50s ribosomal subunit → inhibit protein synthesis

- very narrow spectrum

• treatment of RESISTANT gram ⊕ cocci

↳ MRSA

↳ VRE

adverse effects

- dose dependent thrombocytopenia

- serotonin syndrome → antidepressants

# DNA GYRASE INHIBITORS

## FLUROQUINOLONES

- Ciprofloxacin<sup>2nd</sup> - Moxifloxacin<sup>4th</sup>
- Levofloxacin<sup>3rd</sup>

\*type II topoisomerase  
↳ gram ⊖

- stimulate cutting part of enzyme → inhibits fusing component → DNA fragmentation

## BUGZ

1st: Norfloxacin (not in use)

2nd: Ciprofloxacin

- gram ⊖
  - ↳ Pseudomonas!
- Staph (MSSA)
- atypicals
  - ↳ chlamydiae
  - ↳ mycoplasma
  - ↳ legionella

4th: Moxifloxacin

- gram ⊖
- \* anaerobes!
- NO pseudomonas!

3rd: Levofloxacin

- γ activity
- better against:
  - ↳ Strep
  - ↳ atypicals

## adverse effects

- mild GI effects
- CNS → headache, dizzy, insomnia
  - ↳ confusion in elderly
- phototoxicity
- neuromuscular blockade
- tendinopathy/rupture
- QT prolongation - avoid in pts w/ arrhythmias

\*contra. in:

- \* kids!
- \* pregnancy
- \* myasthenia gravis