# Protein Synthesis Inhibitors:

- Exert antimicrobial specific effects by targeting bacterial cytoplasmic ribosome

*High levels may cause toxicity due to resemblance between mitochondrial & bacterial mitochondria.

**30 S Ribosomal subunit**
- tetracyclines: end in -cycline
- aminoglycosides: gentamycin, neomycin, amikacin, tobramycin, streptomycin

**50S ribosomal subunit**
- macrolides: end in mycin
- chloramphenicol, clindamycin, lincomycin, linezolid, Quinupristan / Dalfopristin

## Tetracyclines: ~cycline

- Bacteriostatic
- Blocks attachment to amino-acyl tRNA = no translation (A site)
- $G^+$, $G^-$, spirochetes, amoeba
- absorption impaired by:
  1. Dairy products
  2. antacids
  3. Fe salts
  4. Bismuth subsalicylate
- crosses placenta, no to preg patients.
- minocycline can cross blood-brain barrier.
- Adverse effects:
  1. GI upset: superinfections w/ staph or C. Diff
     - ↳ control w/ foods
  2. Tooth pigmentation & enamel hypoplasia
     - ↳ no for little kids
  3. minocycline - vestibular disturbances
  4. Phototoxicity: tetra, doxy, deme-.
  5. Pseudotumor cerebri - intracranial HTN
  6. Fatal hepatotoxicity in pregnant women
  7. Fanconi if expired

## macrolides: ~mycin

- Bacteriostatic
- MOA: bind reversibly to a site (23s) on 50S subunit of bacterial ribosome → inhibiting translocation step of protein syn.
  - ↳ close or identical for: lincomycin, clindamycin, chloramphenicol
- Erythromycin
  - $G^+$ cocci & bacilli
    - ↳ not active w/ $G^-$ bac
- Clarithromycin:
  - Good against intracellular pathogens
  - H. influenzae
- azithromycin:
  - H. influenzae, moraxella catarrhalis
- DOC:
  1. mycoplasma pneumoniae
  2. Legionnaires' disease
  3. Community acquired pneumonia from atypical pathogens.
- distributes everywhere but CNS
  - ↳ concentrates in neutrophils, macrophages, fibroblast
- Erythro & clarithro-:
  - ↳ interact w/ CP450, inhibiting ox of
    1. theophylline

- contraindications
  1. Doxy- only w/ renal insufficiency
- omadacycline: extremely broad spectrum.
  ↳ N/V so fasting required before(4H) & after(2H) taking oral tablets
- demeclocycline:
  • induces nephrogenic diabetes insipidus
  • t(x): syndrome of inappropriate ADH(SIADH)

**aminoglycosides**: GNATS
- 3 linked sugars
- Bactericidal
- irreversible 30S binders
  1. Inhibit initiation complex form
  2. Premature mRNA translation termination
  3. misread of genetic code
- G- aerobes
- IM/IV: poor absorption
- High accumulation in renal cortex
  ↳ can lead to ototoxicity & nephro-
- cross placenta
- therapeutic concentrations are close to toxic concentration
  ↳ once daily dosing
- 8th cranial nerve ototoxicity
  ↳ monitor closely for
  • risk ↑ w/ concurrent loop-diuretic usage
- Neomycin: topical & bowel usage only
- neuromuscular paralysis:
  ↳ results from ↓ Ach release & ↓ postsynaptic sensitiv to transmitter
  ↳ administer $Ca^{2+}$ gluconate or neostigmine to reverse
- streptomycin: tuberculosis + penicillin or vanc (endocarditis)
- gentamicin, tobramycin, amikacin

2. warfarin
3. carbamezepine
4. cyclosporine

- Azithro doesn't undergo metabolism
  ↳ concentrated in bile w/ Erythro.
- Adverse effects:
  1. Epigastric distress
  2. cholestatic jaundice esp w/ estolate form of erythromycin
  3. QT prolongation & cardiac arrhythmias w/ azithro.
  4. Clarithro: ↑ risk of mortality & morbidity in patients w/ ♡ disease.
- Fidaxomicin: t(x) of C. Diff associated diarrhea >18.
  ↳ bactericidal against
  • narrow spectrum
  • adverse: N/V, abdominal pain, GI hemorrhage, anemia & neutropenia.
- Chloramphenicol
  • toxicity restricts to only life threatening infections.
  • static or cidal
  • Broad spectrum
  • very active against anaerobes.
  • MOA: binds 50S & prevents peptide bond formation.
    1. Inhibits peptidyl transferase
    2. prevents tRNA bind
    - also inhibits mammalian protein synthesis.
  • therapeutic uses:
    1. meningococcal meningitis
    2. Pneumococcus
    3. H. influenzae
    4. Vibrio cholera
  • converted to glucoronide

↳serious infections of unknown etiology (G-)
- amikacin for serious resistant nosocomial infections

combination therapy
- Beta lactam + aminoglycoside
- Diseases
  1. Entercoccal endocarditis
  2. Staphylococcal endocarditis
- MoA:
  - CW inhibitor disrupts integrity
  - ↑ aminoglycoside access

in liver
- adverse:
  1. Bone marrow ↓
  2. Gray baby syndrome: poor feeding, depressed breathing, CV collapse, cyanosis & death
  3. GI disturbances
  4. Superinfections

- Clindamycin: bacteriostatic
  - MoA: inhibits aminoacyl translocation step
  - narrow spectrum
    ↳ aerobic bacteroides fragilis - abdominal trauma infections
  - adverse effects
    1. diarrhea
    2. Potentially fatal pseudomembranous colitis (PMC) caused by toxin sec by C. diff resistant strains
- Quinupristin/dalforpristin:
  - Bacteriocidal
  - MoA: 50s - inhibits chain elongation, promotes release
  - use: MRSA, VRE
  - adverse
    1. Phlebitis
    2. Hyperbilirubinemia
    3. arthralgia, myalgia
    4. Inhibit CYP3A4
- Linezolid
  - Bacteriostatic
  - MoA: prevents form of ribosome initiation complex
  - reserved for resistant bac
  - adverse effects
    1. Reversible thrombocytopenia
    2. Bone marrow suppression
    3. ocular & peripheral neuritis
- Pleuromutilins
  - t(x) of CAP
  - PO/IV
  - MoA: binds @ different

molecular site than different than antibiotic classes

- G+ & fastidious org
- adverse:
  1. Headache, nausea, diarrhea
  2. QT- prolongation
  3. IV pain, erythema, phlebitis
  4. PO: GI disorders