

ANTI-VIRAL DRUGS

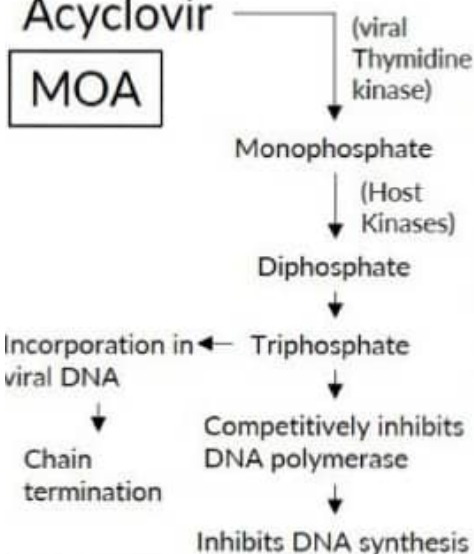
Anti-Herpes Drugs

(Her Father Got A cycle)

- Foscarnet 3rd choice
- Guanythidine 2nd choice
- Acyclovir 1st choice

Acyclovir

MOA



Clinical Uses

- Mucocutaneous and genital herpes
- Prophylaxis in AIDS
- Organ transplant
- IV for encephalitis

Toxicity

(Cycle Has Two New Designs)

Acyclovir side effects

- Hypotension
- Tremors
- Nephrotoxicity
- Delirium

(Valacyclovir is prodrug of Acyclovir)

Drugs used for HIV

1. Nucleoside RT inhibitors

(Abba Didi Emi Lambi Ziddi Satai)

- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Zalcitabine
- Zidovudine

2. Non-Nucleoside RT inhibitors

(DEEN T)

- Delavirdine
- Efavirenz
- Etravirine
- Nevirapine
- Tenofovir

3. Protease Inhibitors

(FRIAANDS LiTe)

- Fosamprenavir
- Ritonavir
- Indinavir
- Amprenavir
- Atazanavir
- Nelfinavir
- Darunavir
- Saquinavir
- Lopinavir
- Tipranavir

4. CCR-5 antagonist

- Maraviroc

5. Fusion inhibitor

- Enfuvirtide

(Drugs that can be used in Pregnancy)

Drugs used in Influenza

M2 Inhibitors

1. Amantadine
 2. Rimantadine
- Prevents uncoating by binding M2 protein channel
 - Use: Influenza A virus
 - Resistant Strains: H1N1, H3N2, Avian & Porcine Influenza

Toxicity

- GI irritation
- Dizziness
- Ataxia
- Slurred Speech

NA Inhibitors

1. Zanamivir
 2. Oseltamivir
- Inhibitors of neuraminidases, cleave sialic acid residues from viral proteins and surface proteins of infected cells, impede viral spread
 - Uses: Influenza A & B, H3N2, H1N1 Strains

Toxicity

- Zanamivir (Inhaler)
- Cough, Throat discomfort, Bronchospasm in Asthma
- Oseltamivir (Oral)
- GI symptoms

Drugs used in Hepatitis

Hepatitis B

(Adela In Entry Test)

- Adefovir
- Lamivudine
- IFN (Interferon) alpha
- Entecavir
- Tenofovir

Hepatitis C

(Rabia In China)

- Ribavirin
- IFN alpha (Hepatitis C)

IFN (Interferon) Alpha

MOA

- Act through JAK-STAT pathway and form antiviral proteins
- Activates host cell ribonuclease that degrades viral mRNA
- Promotes formation of Natural Killer Cells that kill infected liver cells

Uses

- Hepatitis B & C
- Kaposi's sarcoma - HHV-8
- Papillomatosis - HPV
- Topically for genital warts (Combination with Ribavirin - Prevents HCV)

Toxicity

(GC WoN FooT Ball)

- GIT irritation
- CNS toxicity
- Weight loss
- Neutropenia
- Fatigue, Flu-like Syndrome
- Thyroid dysfunction
- Bone Marrow Toxicity

(Contraindicated in Pregnancy)

Ribavirin

MOA

- Nucleoside Resemblance
- Incorporated into RNA
- Cause mutation and death

Use

- It is used adjunctively with IFN- α in chronic HCV.

Toxicity

- Conjunctival and bronchial irritation
- Hemolytic Anemia

Contraindication

- Pregnancy

(RBC Hemolysis)

- Ribavirin
- Better to avoid in Pregnancy
- Conjunctival and Bronchial irritation
- Hemolytic Anemia

ANTI-MALARIAL DRUGS

(Prima Queen Celebrated many festivals)

- Primaquine
- Quinine
- Chloroquine
- Mefloquine
- Anti-folates

Tissue Schizonticide

- Primaquine

Blood Schizonticide

- Other drugs

Plasmodium

- P. vivax
- P. ovale
- P. malariae
- P. falciparum

(Have Hepatic dormant stage. Responsible for recurrent infections and relapses)

Mechanism of Actions

Chloroquine

- Accumulate in food vacuole of plasmodia
- Prevent polymerization of Heme into Hemozoin
- Accumulation of Heme is toxic to the parasite

Quinine

- Complexes with double stranded DNA
- Prevent strand separation of DNA
- Prevent Replication and Transcription

Mefloquine

- Its Mechanism of Action is not known

Primaquine

- Converted to Electrophiles
- Generates Reactive oxygen species (ROS)
- Interferes with oxygen transport
- Also act as Gametocide that prevents malarial transmission

Anti-Folates

- Sulfonamides → PABA → Dihydropteroate synthase → Dihydropteroic acid
- Proguanil (Chloroguanide) → Dihydrofolate synthase → Dihydrofolic acid
- Cycloquanil → Dihydrofolate reductase → Tetrahydrofolic acid
- Primaquine → Dihydrofolate reductase → Tetrahydrofolic acid

Mechanism of Resistance

Chloroquine

- Decrease intracellular accumulation by increased activity of membrane pumps (efflux)
- pfcr1 (Plasmodium falciparum Chloroquine resistance transporter)

Anti-Folates

- Target enzyme modification

Clinical Uses

Chloroquine

- Non-falciparum and Sensitive falciparum Malaria treatment

Quinine

- Chloroquine resistant falciparum Malaria treatment
- Used with doxycycline and clindamycin (to shorten toxicity duration and limit toxicity)
- Shouldn't be used for prophylaxis (to delay resistance emergence)

Mefloquine

- Chloroquine resistant Malaria prophylaxis
- Alternative to Quinine in acute attacks
- Uncomplicated infection of P. falciparum

Primaquine

- Eradicate liver stages of P. vivax and P. ovale
- Used in conjugation with Blood schizonticides
- 14 day treatment after chloroquine treatment
- Alternative for primary prevention

Anti-Folates

- Blood schizonticide against P. falciparum
- Fensidar (Primaquine + Sulfadoxine); Chloroquine resistant falciparum treatment
- Malarone (Primaquine + Atovaquone): Chloroquine resistant falciparum prophylaxis

Traveler's Malaria

- Chloroquine – Prophylaxis
- Mefloquine – Chloroquine resistant
- Doxycycline & Malarone – Multidrug resistant
- Primaquine – Terminal prophylaxis of P. vivax & P. ovale

Adverse Effects (Toxicity)

Chloroquine

(G RANA Sahib)

GI irritation, Retinal damage, Auditory damage, Neuropathies, Attack of porphyria, Skin rash & lesions

Quinine

(Black Chandia got his TV)

- Black water fever (Hematotoxicity)
- Cinchonism (GI disturbances, headache, tinnitus, blurred vision)

Mefloquine

(Psycho Cat Has Some Gastric Disease)

Psychiatric diseases, CVS disorders, Headache, Skin rash, GI disturbances, Dizziness

Primaquine

GI disturbances, Pruritus, Headache, Methemoglobinemia, Mild anemia, Cyanosis, Hemolysis in G6PD patients. Not given in Pregnancy and G6PD patients

Anti-Folates

(HINGE)

Hemolysis, Drug interactions, Nephrotic damage, GIT distress

OTHER ANTI-MALARIAL DRUGS

- Doxycycline – Tetracycline – Chemoprophylactic
- Amodiaquine (Low Cost) – Chloroquine resistant falciparum
- Atovaquone – Disrupt mitochondrial electron transport
- Halofantrine (Halo – Whole) – Active against erythrocytic stage of all 4 forms of malaria
- Artemisinins – Reliable against quinine resistant

ANTI-FUNGAL DRUGS

Alter Membrane Permeability

- Azoles
- Polyenes
- Terbinafine

- Amphotericin B
- Nystatin

Block B-Glucan Synthesis

- Echinocandins

Block Nucleic Acid Synthesis

- Flucytosine

Disrupt Microtubule Functions

- Griseofulvin

Systemic drugs for Mucocutaneous Infections

Topical Drugs

Nystatin

- MOA similar to Amphotericin B
- DOC for Oropharyngeal, Cutaneous, Vulvovaginal candidiasis
- Toxicity includes GI irritation and Skin rashes

Griseofulvin (Fungistatic)

- **MOA:** It inhibits mitotic spindle formation.
- **Resistance:** Decrease in uptake of drug via Energy-dependent transport mechanism
- **Spectrum:** Dermatophytes
- **Toxicity:** Disulfiram-like reaction with ethanol
- **Interaction:** CYP450 inducer. Increase metabolism of drugs e.g. Anticoagulants
- **Contraindication:** Pregnancy and Porphyria

Terbinafine (Fungicidal)

- **MOA:** Inhibits Squalene epoxidase
- **Resistance:** Target enzyme modification
- **Spectrum:** Dermatophytes, Candida
- **Toxicity:** GI Disturbances, Rashes, Headache, Visual and taste disturbances
- **Contraindication:** Nursing mothers, Renal or hepatic dysfunction

Drugs for Systemic Fungal Infections

- Amphotericin B
- Flucytosine
- Azoles
- Echinocandins

Systemic drugs for Mucocutaneous Infections

- Griseofulvin
- Terbinafine

Topical Drugs

- Nystatin
- Miconazole
- Clotrimazole

Drugs for Systemic Fungal Infections

Amphotericin B

MOA

Binds ergosterol - Produce artificial pores - Alters cell membrane permeability

Resistance

Decrease level of / Structural change in Ergosterol

Spectrum (ABCHM)

- Aspergillus
- Blastomyces
- Cryptococcus, Candida Albicans
- Histoplasma
- Mucor

(Induction Regimens before Follow-up treatment with Azole)

Toxicity

(Chill MS Has Fever, Vomiting)
(And Killing Throbbing Heartbeat)

Infusion Related

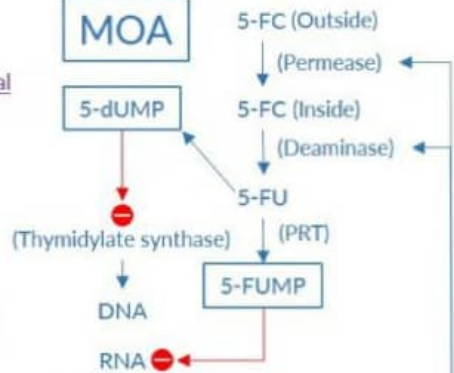
- Chills
- Muscle Spasm
- Hypotension
- Fever
- Vomiting

Dose limiting

- Anemia
- Kidney disorder
- Thrombophlebitis
- Heart abnormalities

Flucytosine

MOA



Resistance

Modification of

Spectrum (Triple C)

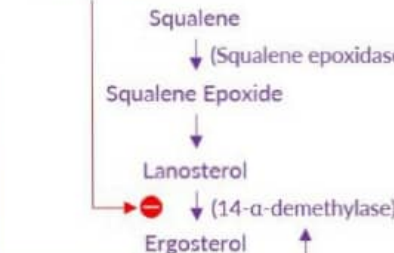
In combination with Amphotericin B for Fungi causing:

- Candidiasis
- Cryptococcosis
- Chromoblastomycosis

Toxicity

- Reversible Bone Marrow depression
- Alopecia
- Reversible hepatic dysfunction (↑ALT, ↑AST)
- Severe enterocolitis, GI disturbances

Azoles



Resistance

Decrease sensitivity due to long-term use

Classification

Imidazole

- Ketoconazole

Triazoles

- Fluconazole
- Itraconazole - DOC for Meningitis caused by C. neoformans
- Voriconazole
- Posaconazole

Toxicity

- Vomiting, Diarrhea, Rash
- Hepatotoxicity

Drug Interactions

- (CYP450 inhibitor)
- Warfarin, Phenytoin, Cyclosporin, Oral hypoglycemics
- Drugs that affect Gastric pH
- Proton pump inhibitors

- Blastomyces
- Paracoccidioidomycosis
- Histoplasmosis
- Sporothrix

Echinocandins

MOA

- Inhibit the synthesis of β(1,3) d-glucan
- Prevents fungal cell wall synthesis

Resistance

Modification of β(1,3) d-glucan synthase

Drug Interactions

- Increase in daily dose of Caspofungin is required with CYP450 inducers
- Echinocandins with cyclosporin raise hepatic transaminases

Spectrum

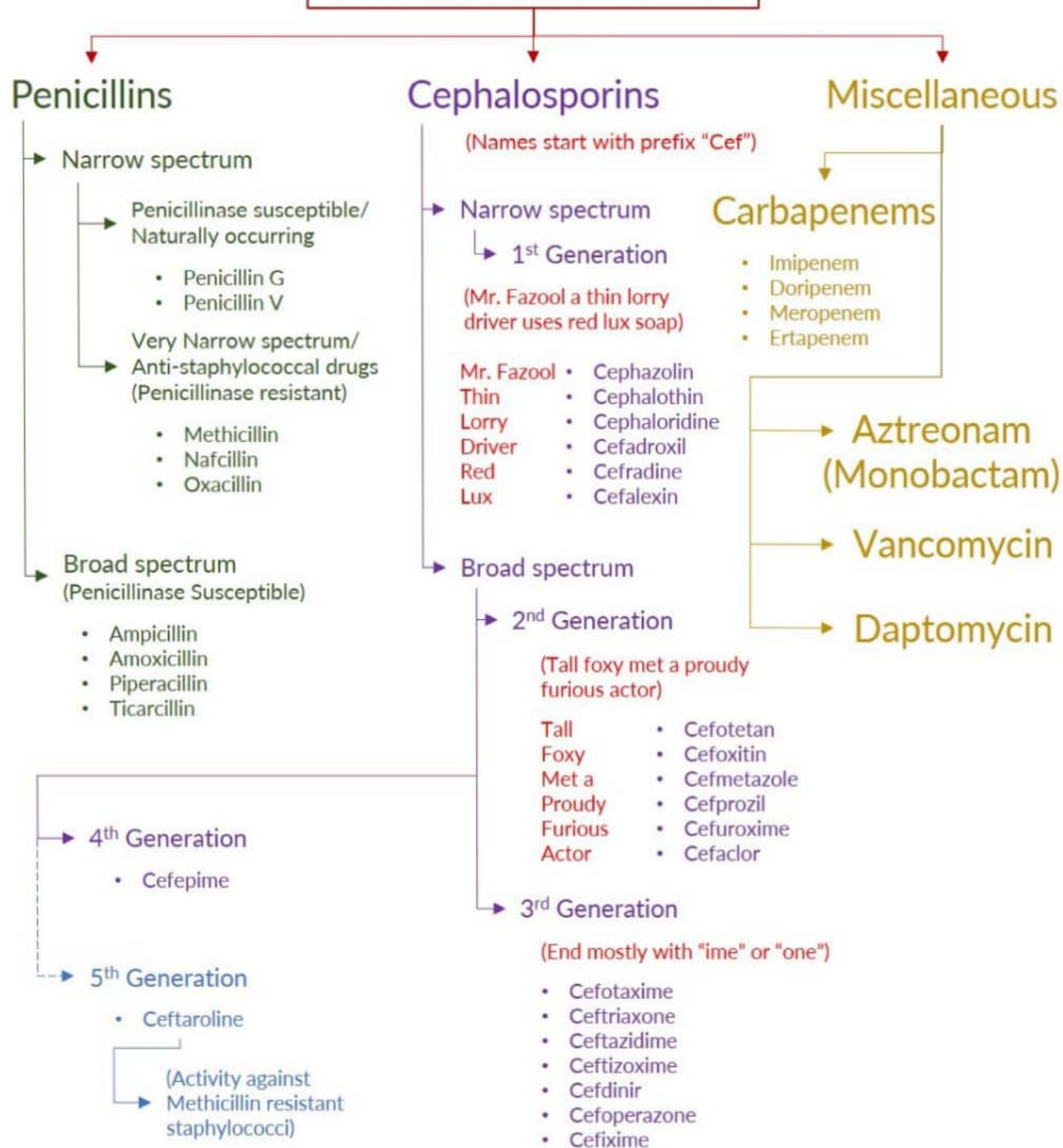
- Caspofungin
- Amphotericin resistant candidiasis
- 2nd line drug for invasive aspergillosis
- Micafungin
- Mucocutaneous candidiasis
- Prophylaxis for candida
- Anidulafungin
- Esophageal and Invasive candidiasis

Toxicity

- Toxicity is Uncommon
- Fever, rash, nausea phlebitis
- Histamine-like reaction (flushing) when infused too rapidly

BETA-LACTAM ANTIBIOTICS AND CELL WALL SYNTHESIS INHIBITORS

Classification and Names



ANTI-MALARIAL DRUGS

(Prima Queen Celebrated many festivals)

- Primaquine
- Quinine
- Chloroquine
- Mefloquine
- Anti-folates

Tissue Schizonticide
• Primaquine

Blood Schizonticide
• Other drugs

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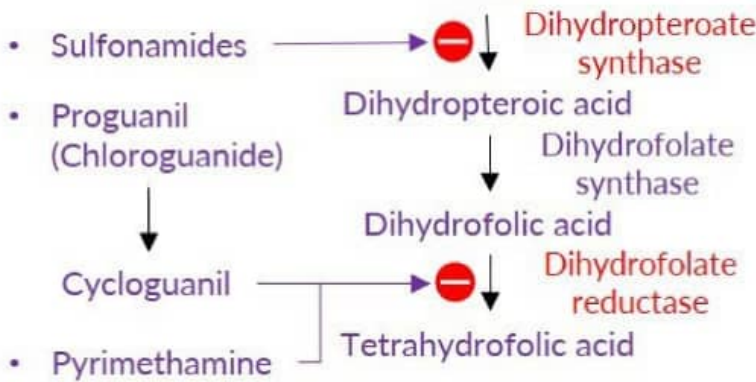
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Primaquine

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- Interferes with oxygen transport
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Anti-Folates



Mechanism of Resistance

Chloroquine

- Decrease intracellular accumulation by increased activity of membrane pumps (efflux)
- *pfcr* (*Plasmodium falciparum* Chloroquine resistance transporter)

Anti-Folates

- Target enzyme modification

PROTEIN SYNTHESIS INHIBITORS

- Broad-Spectrum**
- Aminoglycosides
 - Chloramphenicol
 - Tetracyclines

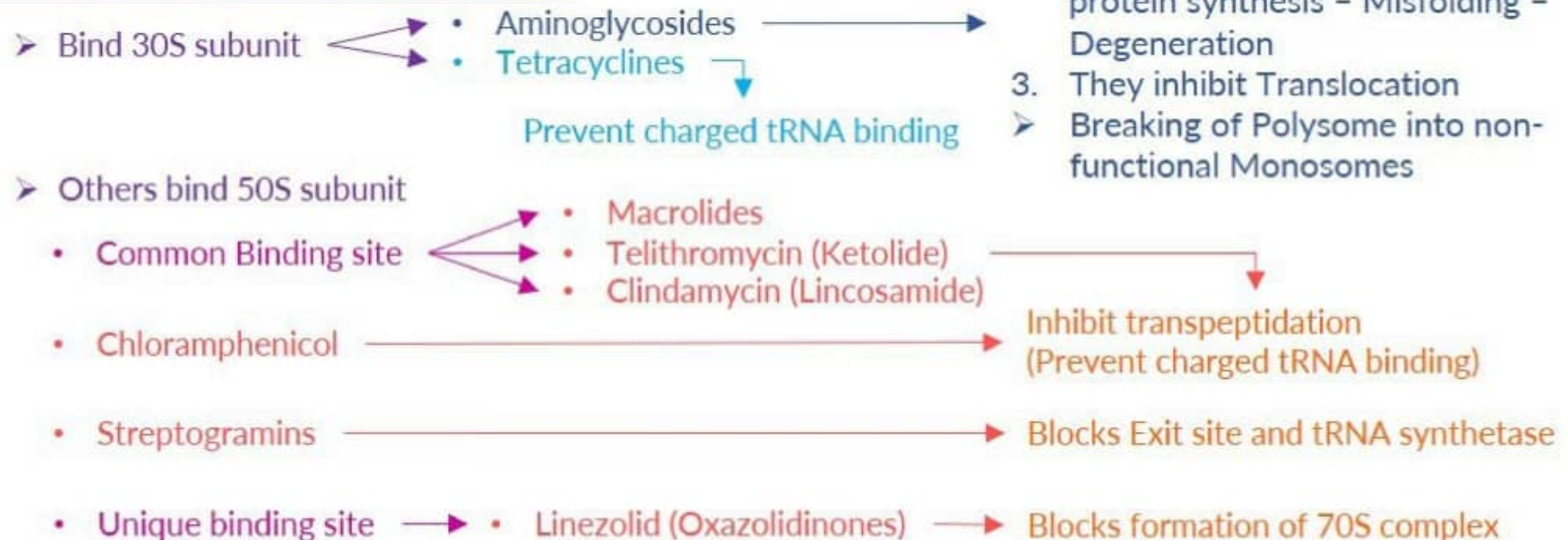
- Moderate-Spectrum**
- Macrolides
 - Ketolides (Telithromycin)

- Narrow-Spectrum**
- Lincosamides (Clindamycin)
 - Streptogramins
 - Oxazolidinones (Linezolid)

All Protein synthesis inhibitors are Bacteriostatic EXCEPT;

- Aminoglycosides
- Streptogramins
- Macrolides (at high dose only)

Mechanism of Action



ANTI-MYCOBACTERIAL DRUGS



Drugs used in Tuberculosis

Drugs used in Leprosy

Drugs used for Atypical Mycobacteria

1st line drugs

Alternative drugs

(PRISE)

(PACE)

(DARC)

(AtypiCle Mycobacteria)

- Pyrazinamide
- Rifampin
- Isoniazid
- Streptomycin
- Ethambutol

- p-Aminosalicylate
- Amikacin
- Ciprofloxacin
- Ethionamide

- Dapsone
- Acedapsone
- Rifampin
- Clofazimine

- Azithromycin
- Clarithromycin
- Moxifloxacin

Aminoglycosides

Names

(STANG K)

Streptomycin
Tobramycin
Amikacin
Neomycin (oral)
Gentamycin
Kanamycin

- ➔ No protein synthesis
- ➔ Action on gram Negative
- ➔ Nephrotoxic, Ototoxic
- ➔ Not used in pregnancy (teratogenic)
- ➔ Not used alone (combined with B-Lactams)
- ➔ No Oral Absorption
- ➔ Neomycin - Oral

Spectrum

(KEEP STaPled CaSh in PurSe)

(Gentamycin, Tobramycin, Amikacin)
K - Klebsiella
E - Enterobacter
E - E Coli
P - Proteus, Pseudomonas
S - S Agalactiae
Ta - TB, Tularemia
Pled - Plague (Yersinia Pestis)
Ca - Catarrhalis
Sh - Shigella
in - H. Influenza
Pur - Providentia
Se - Serratia

Streptomycin + Penicillins

- Enterococcal carditis
- TB (1st line), Plague, Tularemia

Neomycin, Kanamycin

Topical and Oral use only

- Bowel flora
- Skin infection (prior to colorectal surgery)

➔ Nephrotoxic

Mechanism of Action

1. Binds to 30S and interferes with initiation complex
2. Misreading of codon - Faulty protein synthesis - Misfolding - Degeneration
3. They inhibit Translocation
 - Breaking of Polysome into non-functional Monosomes

Bactericidal

Post Antibiotic Effect

Conc. Dependent Killing

Mechanism of Resistance

- Efflux pumps
- Blocked penetration
- Plasmid associated enzyme inactivation (Group Transferases)

Toxicity

(NONS)

- Disruption of Ca channels in proximal tubular cells
- Neuromuscular Paralysis
 - Ototoxicity (Auditory - Amikacin, Vestibular - Gentamycin, tobramycin)
 - Nephrotoxicity
 - Skin Reactions / Contact dermatitis