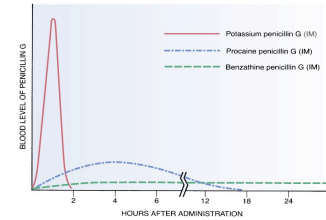


ANTI-INFECTIVES

BACTERIA:

Inhibits cell wall synth/ Beta-Lactum ring (Azetronam on list, but not covered)



Drug	Coverage	Admin/MOA/kinetics	AEs	Misc
Penicillins	Gram+ Gram- (some) anaerobes Bacteremia	Oral; Short half-life Protein bound X cross BBB well Benz & proc Pen G is IM; extended release Varying resist to BL Exc by kidney	GI symptoms/Suprainfections Overdose → neurologic problems Probenecid (gout; urine exc) prolongs the half-life Synergistic with aminoglycoside antibiotics (but can NOT go in same IV line).	Rash or anaphylaxis. @ 1 st or repeated dose. Cross-allergy to other beta-lactam antibiotics is common. Skin testing no good. Combine w/ BL inhibitor for resistance
Cephalosporins (4 generations)		Similar to Pen 1 st & 2 nd do not cross BBB	Cef -xol, -zone & -tan + warfarin leads to increased bleeding b/c interference w/ Vit K production Disulfiram-like effects cause alcohol intolerance	3 rd & 4 th should be reserved for serious cases
Carbapenems (s.a. imipenem & meropenem)	gram+ gram- anarobes.	IV only (no PO absorption)	Suprainfection Cross allergies w/ penicillin	Broad spectrum Good for mixed infections
Vancomycin	gram+ infections in pen-resistant pts.	NOT a beta lactam Poor penetration to CSF Rapid infusion bad (60 min good)	Synergist w/ aminoglycosides Otototoxicity or nephrotoxicity Multiple drug interactions w/ hyperlipidemic drugs, muscle relaxants, and ototoxic drugs Thrombophlebitis (use large vein and change IV site often).	Big guns → potentially toxic Clostridium difficile (GI suprainfection) & other bowel infections: Admin orally, no absorption into blood

PROTEIN synth inhibitors (bacteriostatic) (Chloramphenicol mentioned, but not covered)

Drug	Coverage	Admin/MOA/kinetics	AEs	Misc
Tetracyclines	Rickettsial diseases (Rocky mtn) & <i>Chlamydia</i> , acne & periodontal disease.	Bind to the 30S peptide chain elongation. Mainly PO, rare IV. Poor CSF penetration Some have bad absorption	Form insolues w/ Ca,Fe, Mg, Al, Zn Don't give w/ antacids, dairy, iron Suprainfection (GI and candida)	Doxycycline, minocycline and others Broad spectrum (resistance problems)
Macrolides	Gram +/- Alternative for penicillin in allergic patients.	Inhibit 50 S ribosomal subunit. Poor CSF penetration	Some Erythromycin corrosive to the GI tract; erosive esophagitis. Hepatotoxicity	Erythromycin +/-some -, clarithromycin, azithromycin. Erythromycin & clarithromycin are P450 inhibitors
Clindamycin	Anaerobes Gram+ aerobes.	Inhibits 50S ribosomal subunit; don't use w/ macrolide. Poor penetration of the brain. IV infusion must be <u>SLOW</u> .		Big guns. Suprainfection with <i>Clostridium difficile</i>
Aminoglycosides (BACTERIOCIDAL)	Gram - No activity against anaerobes.	Bind to the 30S Promote the formation of bad proteins/kill cell Charged drug → use IV. Topical use to sterilize gut, skin (neomycin) or eye.	Qd infusions Low levels inbetween → washout → less toxicity. Graph of washout pg 48 Ototoxic and nephrotoxic	Tobramycin, gentamycin, amakacin, etc.

NA synth: inhibit synth of folic acid needed for DNA, RNA + proteins

Drug	Coverage	Admin/MOA/kinetics	AEs	Misc
Sulfamethoxazole-trimethoprim (Bactrim): Synergists	Broad spectrum UTI and for <i>Pneumocystis carinii</i> pneumonia of AIDS	S blocks synth of Dihydropteroic Acid T blocks synth of Tetrahydrofolic Acid. (by blocking bact Both steps are required to make Tetrahydrofolic Acid-needed for DNA,RNA, and protein synth	Hypersensitivity Rash Trimethoprim- blood dyscrasias (abnormal state). Crystalluria – remain hydrated CNS effects – headache, psychosis	Drug blocks enzyme dihydrofolate reductase
Fluoroquinolones	Aerobic, most gram- and some gram+	Inhibit an enzyme (DNA gyrase) → DNA repl. Cations s.a. Al, Fe, Ca, Zn interfere w/ absorption	Tendon/joint problems. Photosensitivity. <i>Candida</i> suprainfections; oropharynx. CNS effects.	Ciprofloxacin, oxofloxacin, etc. Can increase plasma levels of theophyllin (resp disease drug) and warfarin (watch prothrombin time).
Metronidazole (Flagyl)	Aneorobic organisms; parasites and bacteria		Darkening of the urine CNS adverse effects Caution during pregnancy, avoid during lactation P450 interactions	A prodrug; activated in anaerobic cells.

TUBERCULOSIS (myobacteria)

Recall: gram+ but waxy cell wall (mycolic acid)

Drug	Admin/MOA/kinetics	AEs*	Misc
Isoniazid	Inhibits mycobacterial cell wall formation → highly specific for TB. Widely distributed to all body tissues; crosses BBB. Alone w/ latent TB. W/ 1+ for active.	Peripheral neuropathy (give pyridoxine/vitamin B ₆). Hepatotoxic (esp in elderly). Avoid alcohol. Increases levels of phenytoin (AED).	
Rifampin	MOA: inhibits RNA synth. Used w/ 1+ for active TB Distributed to the CSF. Hepatic metabolism.	Hepatotoxic and increases the hepatotoxicity of isoniazid and pyrazinamide. Induces P450 → decreases levels of OCs, seizures meds, etc. Turns body fluids red!	
Pyrazinamide	MOA unknown	Hepatotoxic	Often combined with isoniazide, rifampin, and ethambutol.
Ethambutol	MOA: disrupts mycolic acid (of mycobacteria) Distributed widely but doesn't penetrate the brain	Can cause optic neuritis (recall –itis=inflammation). Allergic reactions NOT hepatotoxic!	

*Watch serum level of liver enzymes for all.

ANTIFUNGALS

Fungal infection can be systematic or superficial. Systematic is more dangerous and can be opportunistic (e.g. immunosuppressed pts) or nonopportunistic (uncommon). Treatment is difficult, prolonged and often toxic.

Drug	Coverage	Admin/MOA/kinetics	AEs
Amphotericin B; aka Amphoterrible!	Systemic fungal infections.	Binds to sterols in the fungal membrane; increases permeability. Dose reduction when w/ flucytosine; too synergistic.	Toxic to mammalian cells b/c cholesterol (a sterol) in cell membranes. Phlebitis and systemic symptoms (fever, chills, rigors, nausea and headache) if given IV. Nephrotoxic – like aminoglycosides
Ketoconazole	systematic & superficial	Inhibits the synth of a sterol. Oral alt to amphotericin B for systemic fungal infections.	P450s inhibitor – use with extreme caution Rare hepatic necrosis.

ANTI-VIRALS:

HSV can infect genitalia, mouth or face. VZV Σ → Chicken Pox and Shingles

NOTE – immunization for chicken pox and shingles (both are manifestations of herpes zoster) is available

Drug	Coverage	Admin/MOA/kinetics	AEs/Misc.
Acyclovir	For herpes viruses – HSV, VZV & CMV (most CMV resist)	MOA: X synth of viral DNA – but must be activated by viral enzyme-thymidine kinase. Topical, oral, and IV.	Nephrotoxic – hydrate well to dilute drug in renal tubules. Resistance if thymidine kinase deficiency.
Valacyclovir (Valtrex)			Prodrug of acyclovir – but it is more bioavailable.
Ganciclovir	All herpes viruses, including CMV (immunocompromised pts)	Poor oral bioavailability; inc w/ food. Excreted unchanged in the urine – decrease dose for patients with renal impairment.	Serious toxicities Granulocytopenia and thrombocytopenia (platlet decrease); monitor blood counts. Teratogenic and embryotoxic – USE OCs.

INFLUENZA Drugs: Immunization is key!

Drug	Coverage	Notes
Amantadine and rimantadine	Prophylaxis & treatment (only for influenza A)	For both A & B. More effective, better tolerated and have lower risk of resistance. Must be taken very soon after the first flu symptoms appear.
Oseltamivir (Tamiflu)	Prophylaxis or shortens duration of flu	Neuraminidase inhibitors Oral
Zanamivir (Relenza)	Works similarly to oseltamivir – not approved for prophylaxis.	Neuraminidase inhibitors Inhaled

HIV Drug Type	Drugs	MOA	AEs:	Notes
Nucleoside Reverse Transcriptase Inhibitors	Zidovudine	Suppresses synth of DNA; early term of DNA strand.	Toxic to human cell division Lactic acidosis→Hepatomegaly (big liver). GI toxicity – stomatitis, nausea, diarrhea, etc.	Bone marrow depression, anemia, neutropenia.
Non-Nucleoside Reverse Transcriptase Inhibitors	Nevirapine, delavirdine, efavirenz.	Bind to active site of reverse transcriptase; direct inhibition.	P450 interactions. Avoid St. John’s wort. Rash & hepatotoxicity severe.	DO NOT affect human DNA.
Protease Inhibitors	Indinavir, ritonavir, saquinavir, lopinavir,...	Inhibit viral protease (4 protein catabolism), needed 4 viral maturation/cutting	Hyperglycemia/diabetes. Fat redistribution. Hyperlipidemia. Increased bleeding. Reduced bone mineral density. Elevation of liver enzymes. Avoid St. John’s wort and garlic Metabolized by P450 enzymes GI side effects similar to the NNRTIs & NRTIs	
Fusion Inhibitor	Enfuvirtide (only one!)	Inhibits entry of HIV into CD4 positive cells.	Resist: gp41 mutates to alter its shape so the drug can’t bind. Injection-site reactions (pain & tenderness). Risk of bacterial pneumonia is increased.	For last efforts. \$\$ + inconvenient. Manufacture slow; supply limited.

