Pocket Guide for Antibiotic Pharmacotherapy

Antibiotic Pharmacokinetics & Pharmacodynamics

Bacteriostatic versus Bactericidal

"ECSTaTiC for bacteriostatic"

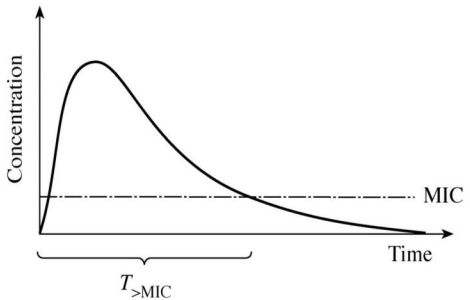
- **E**rythromycin (macrolides)
- **C**lindamycin (lincosamides)
- **S**ulfonamides
- **T**rimethoprim
- **T**etracyclines
- **C**hloramphenicol

"Very Proficient For Complete Cell Murder"

- **V**ancomycin
- **P**enicillins
- **F**luoroquinolones
- **C**ephalosporins
- **C**arbapenems
- **M**etronidazole

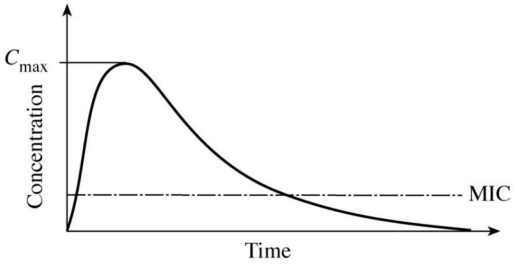
Time-dependent

- Optimize killing by maximizing time above MIC
- More frequent administration or extended-infusion increases efficacy by extending T>MIC
- Ex: beta-lactam antibiotics



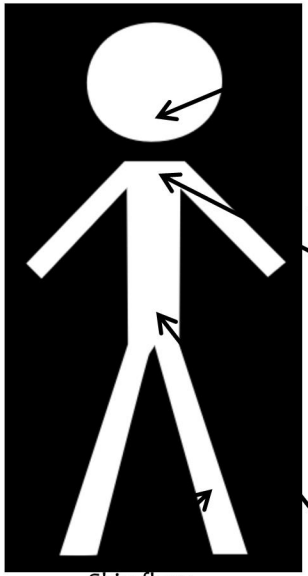
Concentration-dependent

- Optimize killing by maximizing peak concentrations
- Less frequent but higher doses increases efficacy by maximizing Cmax:MIC ratio
- Ex: aminoglycosides, daptomycin



Microbiome Man

"Where bacteria normally live"



Oral flora

Streptococci
Staphylococci
Lactobacillus spp.
Diphtheroids
Porphyromonas spp.
Fusobacterium spp.
Actinomyces spp.

Respiratory flora

Streptococci
Staphylococci
Diphtheroids
Neisseria spp.
Haemophilus spp.
Moraxella spp.
Yeasts

Gut flora

Enterobacteriaceae
Bacteroides spp.
Clostridium spp.
Lactobacillus spp.
Candida spp.
Streptococci
Enterococci
Staphylococci

Skin flora

Staphylococci
Streptococci
Diphtheroids
Micrococci
Propionibacterium spp.
Peptostreptococci

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Spectrum of Activity Against Common Bacteria

Refer to hospital antibiogram for susceptibility rates of specific organisms

Bug \ Drug	Penicillin G	Oxacillin	Ampicillin	Amox-Clav	Amp-Sulb	Pip-Tazo	Cefazolin	Cefuroxime	Cefoxitin	Ceftriaxone	Ceftazidime	Cefepime	Ceftaroline	Ertapenem	Imipenem	Meropenem	Aztreonam	Aminoglycosides	Ciprofloxacin	Moxifloxacin	Levofloxacin	Doxycycline	Minocycline	Tigecycline	Polymyxins	Vancomycin	Daptomycin	Linezolid	Quinu/Dalfo	Clindamycin	TMP-SMX	Metronidazole	Nitrofurantoin	Azithromycin	Clarithromycin
Beta-hemolytic streptococci	*	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				+	+	±	+	+		+	+	+	+	+	±			+	+
Viridans group streptococci	+		+	+	+	+		+	+	+		+	+	+	+	+				+	+	+	+	+		+	+	+	+	+	+			+	+
Streptococcus pneumoniae	+		+	+	+	+		+	+	+		+	+	+	+	+				+	+	+	+	+		+	+	+	+	+	+			+	+
Staphylococcus aureus (MSSA)	±	*		+	+	+	*	+	+	+		+	+	+	+	+				+	+	+	+	+		+	+	+	+	+	+		+	+	+
Staphylococcus aureus (MRSA)													+							+	+	+	+	+		*	+	+	+	+	+		+	±	±
Enterococcus faecalis	+		*	+	+	+									+				+	+	+	+	+	+		+	+	+					+		
Enterococcus faecium																			±	+	+	+	+	+		+	+	+	+				+		
Escherichia coli			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+							+	+		
Klebsiella spp.				+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+							+			
Enterobacter spp.						+				+	+	*	+	+	+	+	+	+	+	+	+	+	+	+	+							+			
Citrobacter spp.						+				+	+	*	+	+	+	+	+	+	+	+	+	+	+	+	+							+			
Serratia spp.						+				+	+	*	+	+	+	+	+	+	+	+	+	+	+	+								+			
Proteus spp.			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+											+			
Acinetobacter spp.					+	+					+	+			+	+	+	+	+	+	+	+	+	+	+							+			
Pseudomonas aeruginosa						+					+	+			+	+	+	+	+	+	+				+										
Stenotrophomonas maltophilia											±									+	+		+								*				
Bacteroides spp.				+	+	+			+					+	+	+				+		±	±	+		+	+	+	+	+		+			
Prevotella spp.				+	+	+			+					+	+	+				+		+	+	+		+	+	+	+	+		+			
Clostridium spp.	+		+	+	+	+	±	±	+	±	±	±	±	+	+	+				+		±	±	+		+	+	+	+	+		+			
Peptostreptococcus spp.	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+				+		+	+	+		+	+	+	+	+		±			
Atypicals																			+	+	+	+	+	+										+	+

* = drug of choice

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Antibiotic Pharmacotherapy by Class

Refer to Guidelines for Dosing in Renal Failure for both dosing in normal renal function and renal dose adjustments

Antibiotic	Adverse Reactions	Drug Interactions	Clinical Pearls
Penicillins *Penicillin G, oxacillin, ampicillin, amoxicillin*	GI upset (nausea, diarrhea) Hypersensitivity reactions Leukopenia, thrombocytopenia (rare) Neurologic (altered mental status, seizures) Interstitial nephritis Hepatotoxicity (oxacillin)	None	Generally drugs of choice for bacteria once susceptibility known (e.g. MSSA, penicillin-susceptible *S. pneumoniae*, ampicillin-susceptible enterococci)
Beta-lactam inhibitor combinations *amoxicillin-clavulanate, ampicillin-sulbactam, piperacillin-tazobactam*		None	Excellent anaerobic activity Sulbactam has unique activity against *Acinetobacter* spp. (doses based on sulbactam, >6 g/day) Consider amox-clav 500-125 mg q8h dosing for gram-negative, anaerobic, or mixed infections (more clavulanate needed)
Cephalosporins *Cefazolin, ceftriaxone, ceftazidime, cefepime, ceftaroline*		None	Cross-reactivity with penicillin allergy <5% Caution with third generation cephalosporins (e.g. ceftriaxone) and SPACE bugs+ (ampC producers)
Carbapenems *Ertapenem, imipenem, meropenem, doripenem*		None	Generally reserved for multidrug resistant gram-negatives (MDR-GN) Drug of choice for ESBL producers Excellent anaerobic activity Cross-reactivity with penicillin allergy <5%
Monobactams *Aztreonam*		None	Generally reserved for <u>severe</u> penicillin allergy (e.g. anaphylaxis), but may cross-react with ceftazidime allergy
Fluoroquinolones *Ciprofloxacin* *Moxifloxacin* *Levofloxacin*	GI upset (nausea, vomiting, diarrhea) Neurologic (dizziness, AMS, seizures) Phototoxicity Tendonitis, cartilage erosion QT prolongation Dysglycemia Peripheral neuropathies	Caution with cations (reduced bioavailability) Inhibits 1A2 (cipro)	Increasing resistance may limit use, particularly with *E. coli* Higher dose for *P. aeruginosa* (e.g. cipro 750 mg q12h, levo 750 q24h) Highly bioavailable, PO = IV Moxifloxacin = poor urine penetration (not used for UTIs) QT prolongation risk = moxi > levo >> cipro
Tetracyclines *Doxycycline* *Minocycline* *Tigecycline*	GI upset (nausea, vomiting, epigastric distress) Photosensitivity Teeth discoloration Vertigo (minocycline)	Caution with cations (reduced bioavailability)	Highly bioavailable, PO = IV (doxy, mino) Tige = severe nausea, may need scheduled antiemetics pre-dose Mino, tige = has activity against multidrug resistant organisms (even if tetra or doxy resistant)
Macrolides *Erythromycin, azithromycin, clarithromycin*	GI upset (nausea, vomiting, diarrhea) QT prolongation	Inhibits 3A (ery > clari >> azi)	QT prolongation risk = ery >> clari > azi
Glycopeptides *Vancomycin*	Red man syndrome Nephrotoxicity Neutropenia (rare)	None	Red man syndrome can be prevented by slowing infusion rates or premedicate with diphenhydramine IV vanc for systemic infections, PO vanc for *C. difficile* infection
Cyclic Lipopeptide *Daptomycin*	Skeletal muscle toxicity Eosinophilic pneumonia	None	Generally reserved for severe, resistant gram-positive infections (e.g. MRSA, VRE) if vancomycin failure or resistant Not for pulmonary infections (deactivated by lung surfactant)
Oxazolidinone *Linezolid*	Thrombocytopenia Peripheral neuropathies	Inhibits MAO (weak) p-glycoprotein substrate	Generally reserved for severe, resistant gram-positive infections (e.g. MRSA, VRE) if vancomycin failure or resistant Highly bioavailable, PO = IV Higher toxicity risk with long-term therapy (>2 weeks) Higher risk for serotonin syndrome with due to MAO inhibition with serotonergic agents (e.g. SSRIs, TCAs) and foods (e.g. red wine)
Lincosamide *Clindamycin*	GI upset (diarrhea > nausea, vomiting) Elevated LFTs (minor)	None	Increasing resistance in *S. aureus* and streptococci may limit use Increasing resistance in anaerobes, particularly *Bacteroides* spp.
Sulfonamides *Trimethoprim-sulfamethoxazole*	Hypersensitivity reactions Leukopenia, anemia Hyperkalemia, renal failure	None	Highly bioavailable, PO = IV Dose for severe infections = 15 mg/kg/day based on TMP component (e.g. PCP, *Nocardia* spp.)
Nitroimidazole *Metronidazole*	GI upset (nausea) Peripheral neuropathy Taste disturbances (metallic)	None	Highly bioavailable, PO = IV Excellent anaerobic activity Avoid alcohol due to disulfiram reaction Higher risk for peripheral neuropathies with long-term therapy
Nitrofurans *Nitrofurantoin*	Peripheral neuropathy Pulmonary toxicity Hepatotoxicity (rare)	None	Only used for UTIs, but without pyelonephritis Do not use with poor renal function (low urinary penetration) Low resistance = good option for multidrug resistant organisms
Aminoglycosides *Gentamicin, tobramycin, amikacin*	Nephrotoxicity Ototoxicity Vestibular toxicity	None	Tobramycin preferred for *P. aeruginosa* infections May be used synergistically for severe gram-positive infections Ami = may have activity even if gent or tobra resistant
Polymyxins *Colistin, polymyxin B*	Nephrotoxicity Neurotoxicity (oral/peripheral paresthesias)	None	Last line for MDR-GNs due to high toxicity risk and limited efficacy Consider polymyxin B for systemic infections and colistin for UTIs

+ SPACE bugs = *Serratia marcescens*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Citrobacter freundii*, *Enterobacter* spp.

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