Drug	Mechanism of Action	Mechanism of Resistance	Spectrum of Activity	Pharmacology	Indications for Use	Toxicity
Penicillin	•binds penicillin binding proteins (transpeptidases, carboxypeptidases); enzymes involved in cell wall (peptidoglycan) biosynthesis	•beta-lactamase cleaves beta-lactam ring and inactivates drug (chromosomal or plasmid mediated) •Gram- can change porin channel permeability preventing drug from reaching receptor site •efflux pumps •alteration of PBPs (esp. in Gram+)	bactericidal •Gram+ streptococci, enterococci, meningococci, treponema pallidum (syphilis), most anaerobes •poor activity against Gram- rods	•some oral use •minor metabolism •excreted by kidneys via tubular secretion (probenecid will block) •well distributed to lungs, liver, kidney, muscle, bone and placenta •high urinary and bile concentrations		•hypersensitivity (rash; anaphylaxis) act as haptens to combine with human proteins major determinant= penicilloyl (uticaria and late rxns) minor determinant= benzylpenicilloate (anaphylaxis and accelerated rxns)
Ampicillin (aminopenicillins)	•binds pencillin binding proteins (transpeptidases, carboxypeptidases); enzymes involved in cell wall biosynthesis •better penetration through outer mb of Gram- than penicillin G and better binding to PBPs	•beta-lactamase cleaves beta-lactam ring and inactivates drug (chromosomal or plasmid mediated) •Gram- can change porin channel permeability preventing drug from reaching receptor site •efflux pumps •alteration of PBPs (esp. in Gram+)	bactericidal •Gram+ streptococci, enterococci (unless they express beta-lactamases) •Gram- hemophilus, e.coli, salmonella, shigella (but many Gram- have plasmid mediated resistance)	•oral and IV		•rash is common
Semisynthetic penicillinase-resistant penicillins (Nafcillin, Oxacillin, Methicillin)	•binds penicillin binding proteins (transpeptidases, carboxypeptidases); enzymes involved in cell wall (peptidoglycan) biosynthesis •bulky side chains inhibit action of staph beta-lactamases	•bulk prevents them from getting through Gram- porins	bactericidal •used primarily for staphylococci •Gram+ pneumococci, streptococci, NOT enterococci	•Methicillin – least protein bound of the group •Nafcillin – high biliary excretion •Isoxazolyl penicillins (parenteral and IV forms)	•serious staphylococcus aureus infections (cellulites, endocarditis, sepsis)	

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Beta-lactamase inhibitors Sulbactam Clavulanic acid Tazobactam	•high affinity for plasmid-mediated beta-lactamases					
Combination: (penicillin + beta-lactamase inhibitor **Piperacillin + Tazobactam**	•binds PBPs; enzymes involved in cell wall biosynthesis •beta-lactamase inhibitors (tazobactam) high affinity for plasmid mediated enzymes	•Gram- can change porin channel permeability preventing drug from reaching receptor site •efflux pumps •alteration of PBPs (esp. in Gram+)	bactericidal ; broad spectrum •Gram+ streptococci, enterococci, meningococci, treponema pallidum (syphilis), most anaerobes •Gram- pseudomonas aeruginosa, bacteroides, proteus			
Carbapenems Imipenem Meropenem	•binds PBP-2 •permeability through porin channels	•STABLE to beta-lactamase; but alternate enzymes that can hydrolyze •alteration of porin channels	bactericidal; HUGE spectrum kills most Gram+, Gram-, and anaerobic bacteria including pseudomonas aeruginosa; does NOT kill: MRSA, enterococcus, c. difficile			•allergic rxns similar to penicillin •(?) Imipenem may lower seizure threshold
Monobactams Aztreonam	•only binds Gram- PBPs	•STABLE to beta-lactamase	bactericidal; NARROW spectrum ONLY aerobic Gram- rods; including p. aeruginosa		•can use in place of an aminoglycoside •can use in penicillin allergic pts (little cross-reactivity)	

Drug	Mechanism of Action	Mechanism of Resistance	Spectrum of Activity	Pharmacology	Indications for Use	Toxicity
1st Generation Cephalosporins Cefazolin, Cephalothin, Cephalexin (oral), Cefaclor (oral)	•like penicillins, inhibit enzymatic rxns needed for stable bacterial wall synthesis by binding to PBPs	•permeability – failure of cephalosporins to reach receptor sites •destroyed by beta-lactamase •alteration of PBPs	bactericidal •Gram+ cocci s. pneumoniae, s. aureus, NOT enterococci •Gram- rods e. coli, klebsiella, proteus mirabilis	•hydrophilic molecules that achieve excellent drug levels in lung, kidney, muscle, bone, placenta, interstitial, synovial, and peritoneal fluids, and in urine •eliminated via kidney (probenecid blocks secretion of some compounds)	•common infections •surgical prophylaxis •skin and soft tissue infections	•hypersensitivity (rash, urticaria, eosinophilia, fever, anaphylaxis – rare) •leukopenia and rarely hemolytic anemia •superinfection with fungi or resistant Gram- organisms •phlebitis, false+ tests (Coombs, glucose)
2nd Generation Cephalosporins Cefuroxime Cefoxitin Cefotetan	•like penicillins, inhibit enzymatic rxns needed for stable bacterial wall synthesis by binding to PBPs	•permeability – failure of cephalosporins to reach receptor sites •destroyed by beta-lactamase (cefuroxime is STABLE to plasmid mediated penicillinases) •alteration of PBPs	bactericidal •Gram+ cocci s. pneumoniae, less s. aureus, NOT enterococci •Gram- rods e. coli, klebsiella, proteus mirabilis •cefuroxime covers h. influenzae •cefoxitin and cefotetan increased anaerobe coverage, bacteroides	•parenteral drugs •hydrophilic molecules that achieve excellent drug levels in lung, kidney, muscle, bone, placenta, interstitial, synovial, and peritoneal fluids, and in urine •eliminated via kidney (probenecid blocks secretion of some compounds)	•upper respiratory tract infections (h. influenzae) •GI tract flora infections	•hypersensitivity (rash, urticaria, eosinophilia, fever, anaphylaxis – rare) •leukopenia and rarely hemolytic anemia •superinfection with fungi or resistant Gram- organisms •phlebitis, false+ tests (Coombs, glucose)
3rd Generation Cephalosporins cefotaxime ceftriaxone ceftazidime	•like penicillins, inhibit enzymatic rxns needed for stable bacterial wall synthesis by binding to PBPs	•permeability – failure of cephalosporins to reach receptor sites •STABLE to plasma mediated beta-lactamases •alteration of PBPs	bactericidal •cefotaxime: highly active against s. pneumoniae; n. meningitides, h. influenzae, e. coli, klebsiella, NOT p. aeruginosa •ceftriaxone: s. pneumoniae, n. gonorrhea, b. burgdorferi •ceftazidime: less Gram+ activity but can kill p. aeruginosa	•cefotaxime and ceftriaxone achieve good CSF levels; ceftazidime adequate CSF levels •ceftriaxone longer half-life and more active than cefotaxime; a single IM does can kill for 12-24 hrs	•cefotaxime= drug of choice for meningitis •ceftriaxone= outpatient coverage of septic pneumococcal pts, n. gonorrhea, and CNS lyme disease	•hypersensitivity (rash, urticaria, eosinophilia, fever, anaphylaxis – rare) •leukopenia and rarely hemolytic anemia •superinfection with fungi or resistant Gram- organisms •phlebitis, false+ tests (Coombs, glucose)

Drug	Mechanism of Action	Mechanism of Resistance	Spectrum of Activity	Pharmacology	Indications for Use	Toxicity
Vancomycin	•targets d-ala-d-ala petapeptide; blocks 2 steps in cell wall synthesis at an earlier step than beta-lactams	•problem in enterococcus fecium – has plasmid-mediated, readily transferable resistance (plasmids have been shown capable of replicating in s. aureus) •transposable element that allows organism to sense vancomycin and activate transcription leading to replacement of d-ala-d-ala with d-ala-d-lactate	bactericidal •most Gram+ including beta-lactamase producers and methicillin resistant staph aureus; streptococcus, clostridia, listeria, bacillus	•parenteral •wide tissue distribution and infected pleural, pericardial, synovial, ascitic fluids and meninges •excreted by kidneys	•serious Gram+ infections in penicillin allergic pts •infections due to resistant s. pneumoniae or MRstaph	•low risk of nephrotoxicity •phlebitis (frequent) •red man syndrome: when given in too rapid an infusion get generalized rash, uticaria (due to histamine release) •(?) ototoxicity

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Chloramphenicol	•binds peptidyl transferase, a component of the 50s ribosome	•presence of enzyme chloramphenicol transacetylase (acetylates the drug)	Mostly bacteriostatic may be bacteriocidal against pneumococcus and neisseria •broad spectrum aerobic Gram+ most Gram- most anaerobes ricksettsia	•higher levels with ORAL vs IV •well distributed throughout body; CSF levels 30-50% of serum w/o inflammation •metabolized to inactive metabolite in liver	•NOT drug of choice for any infection; used more in developing world •typhoid fever (s. typhi) •meningitis in penicillin allergic pts (pneumococcus, hemophilus, neisseria) •rickettsial infections	•dose related bone marrow depression •(rare) aplastic anemia •in neonates get gray baby syndrome (vasomotor collapse, abdominal distention, cyanosis)
Quinolones	•bind DNA-DNA gyrase (topoisomerase II) complex and blocks further DNA replication •blocks topoisomerase IV inteferes with separation of interlocked replicated DNA molecules •other sites of action (?) RNA and protein synthesis (?)	•mutations in topoisomerase II or IV •resistance is chromosomal (rather than plasmid) •can emerge quickly during therapy esp. with s. aureus, or p. aeruginosa; a single mutation leads to resistance •active efflux system in Gram+ and Gram-	bactericidal **1st generation** (nalidixic acid) •Gram- enterics (UTIs) **2nd generation** (norfloxacin, ciprofloxacin) •better Gram- coverage, p. aeruginosa •Gram+ s. aureus and b. anthracis **3rd generation** (levofloxacin) •improved Gram+ •Gram- enteric and pseudomonas •mycoplasma, legionella, anaerobes	•well absorbed orally andparenterally •excellent tissue distribution; bone and CSF < serum •high intracellular concentration (PMNs) •most eliminated by kidneys (trovofloxin 3rd gen. eliminated by liver) •decreased oral absorption following coadministration of metal cations (antacids)	•empiric therapy for community-acquired pneumonia •complicated UTI or respiratory tract infections •serious infections like osteomyelitis, pneumonia, soft tissue •STDs: gonorrhea, chancroid, chlamydial urethritis •empiric therapy for traveler's diarrhea (infectious diarrhea) •multi-drug resistant TB	•well-tolerated •GI symptoms •CNS symptoms •allergic rxns (rash, uticaria, drug fever) •photosensitivity (esp. with additional F or Cl at position 8 of drug structure) •liver function abnormalities – rare fatalities following trovafloxacin •joint arthralgias or swelling in kids

Drug	Mechanism of Action	Mechanism of Resistance	Spectrum of Activity	Pharmacology	Indications for Use	Toxicity
Trimethoprim-Sulfamethoxazole (TMP-SMZ) synergistic drug combo	•sequential interference with folic acid synthesis •Sulfa is a structural analog of PABA; competes for enzyme dihydropteroate synthetase •TMP is a competitive inhibitor of dihydropteroic acid	Sulfa •decreased permeability (plasmid) •increased PABA production TMP •synthesis of dihydrofolate reductase with decreased affinity for TMP •overproduction of dihydrofolate reductase	Broad spectrum bactericidal •Gram+ staphylococci, streptococci, listeria, NOT enterococci •Gram- e. coli, klebsiella, proteus, salmonella, shigella, vibrio, neisseria, h influenzae •misc. pneumocystis, nocardia, chlamydia	•combo antibiotic 1:5 ratio of TMP:Sulfa; serum ratio 1:20 •oral and parenteral •well distributed; good levels in lungs, kidneys, biliary tree, and CNS •partially metabolized in liver, excreted in urine	•UTIs •prostatitis •pneumocystis carinii infection (AIDS) •diarrheal illness due to salmonella, shigella, enterotoxigenic e. coli •upper and lower respiratory infections •infections caused by p. cepacia, nocardia	•hypersensitivity rxns (rash, fever), rare Stevens Johnson syndrome (mucosal and cutaneous illness seen in AIDS pts) •GI – nausea, vomiting, diarrhea •(rare) hepatitis, megoblastic anemia, increased serum creatinine