Overview of Antimicrobials
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I. *Natural Penicillins*
- A. MOA: interfere with cell wall synthesis by acting on PBP
- B. Spectrum of activity: **gm + coverage (mostly strep,** enterococcus**)**; some Neisseria, and anaerobes (not bacteroides); mouth anaerobes (peptostreptococcus, clostridia); *Treponema pallidum* (syphilis - DOC)
- C. MSBI: PCN G, PCN V
- D. SE: N/D, **hypersensitivity** (anaphylaxis up to 0.5%, fatal 5-10%); interstitial nephritis (rare)

II. *Aminopenicillins*
- A. MOA: same as above
- **B.** Spectrum of activity: similar to Natural PCNs**; gm + (enterococcus, listeria, streptococcus)**; also **add'l coverage for gm – (H.influenzae, E.coli, Proteus, Salmonella, Shigella)**
- C. MSBI: amoxicillin (PO), ampicillin (IV/PO)
- D. SE: N/D, rash with infectious mono (ampicillin)-this is not a true pcn allergy

III. *Antistaphylococcal PCNS/Penicillinase Resistant PCS*
- A. Spectrum of activity: **STAPH and streptococcus**
  No enterococcus!!
- B. MSBI: Dicloxacillin (PO), Nafcillin (IV)
- C. SE: Neutropenia (nafcillin) similar to other B lactams; Interstitial nephritis (methicillin)
- D. Nafcillin may decrease warfarin's anticoagulant effect

IV. *Antipseudomonal PCNS (piperacillin, ticarcillin)*
- A. Spectrum of activity: strep, additional gm – coverage, including enterobacter and pseudomonas. Piperacillin (some enterococcus)

V. *B lactamase Inhibitor Combination*
- A. MOA: Clavulanate, sulbactam, tazobactam blocks B lactamases
- B. Spectrum of activity: Same as PCNS, and bacteria that produces **B lactamase**;

S. aureus
H. influenzae
Moraxella catarrhalis
Klebsiella
Bacteroides
N. gonorrhea

Also, N. meningitidis, E.coli, Proteus, **PSEUDOMONAS, serratia, enterobacter (ticar/clav, pip/tazo);** anaerobes (**Bacteroides**, clostridia)

C. MSBI: Piperacillin/tazobactam (Zosyn IV-restricted) ; Ampicillin/sulbactam (Unasyn IV); Amoxicillin/clavulanate (Augmentin po)
D. SE: DIARRHEA (augmentin); hypernatremia (ticar), hyperkalemia (ticar), platelet dysfxn esp in renal failure
E. Sodium Content:
Pip/Tazo (Zosyn) 2.79 meq (64 mg) sodium per g

VI. *Cephalosporins*

	1st Generation Cefazolin, cephalexin	**2nd Generation** Cefuroxime (IV/PO), Cefoxitin (IV)	**3rd Generation** Ceftriaxone (IV), Cefpodoxime (PO), Ceftazidime (IV)*	**4th Generation** Cefepime (IV, IM)	**5th Generation** Ceftaroline (IV/IM)
Gm + cocci (NOT ENTEROCOCCUS) Staph aureus Streptococcus	+++	++	+	+	MRSA
Gm – E. coli, K. pneumoniae, P. mirabilis, H. flu, M. catarrhalis	+	+++	++++ (P.aeruginosa -ceftaz)	+++++ (P.aeruginosa, Enterobacter)	Similar to CTX
Anaerobes Bacteroides	None	Cefoxitin, cefotetan	Cefotaxime/ Cefpodoxime (PO anaerobes only)	None	

*Cross reactivity with PCNS is 5-10%
*SE: N/V/D

NOTE: **Cefepime** must be renally dosed; great broad spectrum. NO ATYPICALs, POOR ANAEROBIC COVERAGE, indications: Healthcare assoc pneumonia, complicated intraabdominal infxn (+metronid), diabetic foot (+metronid)

VII. *Macrolides*
A. MOA: Bacteriostatic; binds to 50S ribosomal subunit and inhibits protein synthesis
B. Spectrum of activity: similar to PCNS (staph, strep, Listeria, H.influenzae, N. gonorrhoeae, M. catarrhalis) but also, **Mycoplasma pneumoniae, Legionella pneumophila, Chlamydia, MAI, Toxoplasma gondii**

C. MSBI: Azithromycin*, Clarithromycin, Erythromycin
D. Cyt P-450 Inhibition: Emycin > Clarithromycin > Azithromycin (none)
E. SE: GI distress (emycin); IM emycin very painful!; ↑ LFTS; high dose iv erythro, po clarithro-ototoxicity
F. DRUG INTERACTIONS! Major concern-prolonged QTc

VIII. *Clindamycin (Cleocin)*
A. MOA: Bactericidal/bacteriostatic; inhibit bacterial protein synthesis by binding to 50S ribosomal subunit
B. Spectrum of activity: **Great gm + coverage (staph,** strep**)** , NOT ENTEROCOCCUS, **anaerobes** (some B. frag, actinomyces, prevotella, peptostreptococcus)
C. SE: anorexia, N/V/D, pseudomembranous colitis 2/2 C.difficile (DO NOT USE ANTIDIARRHEALS!)

Comment [MF1]: Around 30% of B. frag are resistant to clindamycin per CID2010;50:S26-33

IX. *Metronidazole (Flagyl)*
A. MOA: Synthetic nitroimidazole; bactericidal; requires microbial reduction by a nitroreductase enzyme to form highly reactive intermediates that disrupt bacterial DNA and inhibit nucleic acid synthesis, leading to cell death.
B. Spectrum of activity: Trichomonas vaginalis, Entamoeba histolytica, Giardia lamblia, B. fragilis, Fusobacterium, Prevotella, Clostridium
C. SE: metallic taste, GI complaints; dizziness, vertigo, paresthesias in high doses; mild, reversible neutropenia (rare), disulfiram reaction with ETOH!

X. *Trimethoprim and Sulfamethoxazole (Bactrim)*
A. MOA: SMX is a synthetic analog of PABA which competitively inhibits the synthesis of dihydropteric acid from PABA in microorganisms; TMP inhibits the enzymatic reduction of DHF to THF acid; bacteriostatic
B. Spectrum of activity: Gm -, Gm +, good staph coverage (esp CA-MRSA), NO ANAEROBES, NO PSEUDOMONAS, **NO GROUP A STREP**
C. SE: N/V/D; hypersensitivity, allergic skin rxns, bone marrow suppression (leukopenia, neutropenia, thrombocytopenia), reversible hyperK, pseudo elevation in Cr, fever; TEN; SJS; EM

XI. *Fluoroquinolones*
A. MOA: Inhibits bacterial DNA gyrase
B. Spectrum of activity: Good staph, not so good for strep and anaerobes (except moxiflox), **Good gm –,** enterobactericiae, **Pseudomonas sp. (cipro is best), anaerobes (moxi, levoflox)**
C. MSBI: Ciprofloxacin, Levofloxacin* (restricted!)
D. Comments: Levofloxacin covers CAP microorganisms including S.pneumo, S.aureus, HENPEK, M. catarrhalis, M.pneumoniae, C.pneumoniae, Legionella, Citrobacter, Serratia; NO ANAEROBIC Coverage, as compared to moxi: no anaerobic coverage, slightly less gm + coverage; as compared to cipro: less pseudomonas coverage, otherwise similar gm – coverage.

E. Moxifloxacin-400mg po /iv qd, no renal dose adjustment nec.; 4th gen-so more **anaerobic** coverage; can prolong QTc interval!; DI-take 4 hrs B4 or 8 hrs AFTER antacids
F. SE: GI intolerance; HA, restlessness, dizziness, insomnia, skin rashes, photosensitivity

XII. *Aminoglycosides*
A. MOA: concentration dependant bactericidal activity; binds to 30S and 50S ribosomal subunits;
B. Spectrum of activity: **mainly gm - coverage**; **pseudomonas**; used together for **synergy with B-lactams for enterococcus**; B-lactams punch holes in cell membrane that allow for greater AG penetration; PAE can be exploited to decrease dosing frequency; Nephrotoxicity (troughs); Ototoxicity (peaks)
C. MSBI: Gentamicin, Tobramycin, Amikacin* (restricted, amikacin level is send out lab TAT of 3-5 day)
D. SE: nephrotoxicity; ototoxicity, neuromuscular blockade

XIII. *Chloramphenicol*
A. MOA: Bacteriostatic; inhibits protein synthesis by binding to 50S ribosomal unit
B. Spectrum of activity: resembles macrolides; **2nd line for Rocky Mtn Spotted Fever**; use in PCN allergic pts; meningococci; VRE; good for amp resistant H. influenza, Salmonella spp., typhoid
C. SE: Reversible bone marrow suppression (dose-related), aplastic anemia, gray baby syndrome (fatal cardiovascular respiratory collapse), optic neuritis
D. NOT currently available due to shortage

XIV. *Tetracyclines*
A. MOA: Bacteriostatic; inhibits protein synthesis by binding to 30S ribosomal unit
B. Spectrum of activity: Gm +, Gm -, aerobic, anaerobic bacteria, spirochetes, Strep, H.influenza, Mycoplasma (2nd line), **DOC for Chlamydia, Rocky Mtn Spotted Fever**; lyme disease; not so much for staph (except **CA-MRSA)**, **no activity against Group A strep**
C. MSBI: Doxycycline, Tetracycline
D. SE: N/D, discoloration of teeth in children; phototoxic skin rxns; Fanconi syndrome; hepatotox-rare
E. DI: forms chelating complex with cations-↓absorption of TCN; so separate from antacids, iron, sucralfate; milk/dairy also ↓absorption of TCN; warfarin, OCPs, enzyme inducers

XV. *Vancomycin*
A. MOA: binds irreversibly to cell wall; concentration independent-so, **clinical cure rates ARE NOT associated with peak concentrations! Trough concentrations ARE related to therapeutic outcome! Trough: at least 10**

ug/ml; 15-20mg/L (endocarditis, osteomyelitis, meningitis, HAP caused by S.aureus)*

B. Spectrum of activity: **MRSA** and Enterococcus; **PO for C.difficile**
C. SE: Chills, fever, nausea, phlebitis, Red man syndrome; ototoxicity (rare! 53 cases over 30 yrs, only 17 were using monotherapy); nephrotoxicity (rare! 5% incidence, few trials show association); eosinophilia; neutropenia
D. Dose: **15-20 mg/kg** (actual body weight) given Q8-12 H with normal renal Function*

Comment [MF2]: My thought is that the true incidence of vancomycin associated nephrotoxicity is controversial. Usually occurs in patient with concomitant nephrotoxins and other host factors (sepsis, de-hydration)

XVI. *Aztreonam (Azactam®)*
A. MOA: monobactam
B. Spectrum of activity: **Only covers gm -** including pseudomonas; last line; coverage similar to 3rd gen cephalosporins
C. SE: minimal, ok to use in PCN, ceph allergic pts, cross allergenicity is low

XVII. *Carbapenems: Imipenem/cilastatin (Primaxin®), Ertapenem (Invanz), Meropenem (Merrem)*
A. MOA: cilastatin is a renal dehydropeptidase inhibitor that has no antimicrobial activity but inhibits imipenem's metabolism by prox tubular kidney cells, thus ↑ urinary ccns and ↓ nephrotoxicity
B. Spectrum of activity: Everything!
(except: Stenotrophomonas maltophilia, Pseudomonas cepacia, MRSA, MRSE, Enterococcus faecium, Corynebacterium jeikeium, Nocardia)
C. SE: **Seizures**; N/V sometimes assoc with hypotension, diaphoresis, rashes; some cross allergenicity with PCNS; dose adjust in renal impairment; use when all else fails
D. Comments: Ertapenem-all anaerobes and Gm – **except P.aeruginosa**, Acinetobacter; Meropenem-similar coverage to imipenem including **P.aeruginosa; Enterococcus: imipenem>meropenem>ertapenem (no coverage)**

XVIII. *Quinupristin/dalfopristin (Synercid®)*
A. MOA: Streptogramin that inhibits protein synthesis
B. Spectrum of activity: VREF (**Vanco resistant Enteroccoccus faecium**) Staph aureus, MRSA, Strep pyogenes
C. SE: Pain, inflammation, edema at infusion site
D. Dose: VREF 7.5mg/kg IV Q8H
Skin infections: 7.5mg/kg IV Q12H
E. Other: Do not need to dose adjust in renal/hepatic dz

XIX. *Linezolid (Zyvox®)*
A. MOA: Inhibits protein synthesis
B. Spectrum of activity: Staph aureus, Staph epi, MRSA, **E.faecium, E.faecalis**
C. SE: Diarrhea, N/V, ↑ LFTs, reversible **thrombocytopenia, leukopenia, (>2 weeks). optic/peripheral neuropathy (use>28d)**
D. Dose: Uncomplicated skin infxn: 600mg PO q12h

Other: 600mg PO/IV q12h

E. DI: Non-selective reversible inhibitor of MAO; avoid tyramine rich foods
F. Other: Avoid in pts with phenylketonuria
G. Restricted at MSBI

XX. *Ketolide- Telithromycin (Ketek)*

A. MOA: inhibits bacterial protein synthesis by binding to 50-S ribosomal subunit. Similar to azithro/clarithro against atypicals.
B. Spectrum: atypicals, also group a B-hemolytic strep, emycin susceptible strains of S.aureus, H.pylori and some anaerobes
C. SE: Diarrhea, vomiting, blurry vision, diplopia (visual symptoms can occur after any dose, but most common after 1st or 2nd dose); can prolong QT, exacerbation of myasthenia gravis, including life threatening respiratory failure
D. Dose: 800mg po qd x 7-10 days for CAP; 5 days for acute bacterial sinusitis or acute exacerbations of chronic bronchitis
E. DI: CYP3A4 inhibitor-can increase levels of simvastatin, lovastatin, atorvastatin, midazolam and others
F. Other: $$$$$$$; for pneumoccocal resp infxns resistant to macrolides

XXI. *Daptomycin (Cubicin)*

A. MOA: binds to bacterial membranes causing rapid depolarization of membrane potential which inhibits DNA, RNA, protein synthesis.
B. Spectrum: almost all Gm + including S.aureus, MRSA, E.faecalis, E.faecium, VRE; don't use in pneumoniae (high failure rate)
C. SE: Gen well tolerated; LFTs ,alk phos, LDH, dose dep CPK elevation (reversible) with or without myopathy (higher risk with 4mg/kg q12h dosing)
D. Dose: 4mg/kg/ IV once daily (SSTI), 6mg/kg IV once daily (endocarditis/bacteremia); must renally, hepatic dose
E. DI: no cyp 450 issues; d/c statin during dapto therapy
F. Restricted at MSBI

XXII. *Ceftaroline (5th generation cephalosporin)*

A. Spectrum: Similar to Ceftriaxone but **first cephalosporin to have MRSA coverage.** Might be useful in areas with high S.pneumoniae resistance. Also VISA. No enterococcus, No pseudomonas, No acinetobacter, No anaerobes. For SSTI, CAP.
B. SE: N/D (4-5%), HA, insomnia, allergic reactions, Positive Coombs test w/o hemolytic anemia, phelbitis
C. Dose: 600mg IV q12 infuse over 1 hr; must renal dose adjust
D. DI: none likely
E. Role in therapy: Alt agent for VISA, alternative for CAP (or HAP) or other invasive MRSA infxn in pts intolerant to other agents (such as linezolid and concomitant SSRI, or CK increase due to dapto) or with strains with reduced susceptibility to other agents.
F. Restricted at MSBI

Classification of Bacteria Based on Gram's Stain and Morphology

Gram + Cocci	Gram – Diplococci	Gram – Rods	Gram + Rods
Staphylococci Streptococci Enterococcus	Meningococci Neisseria gonococci Moraxella	Salmonella Shigella Pseudomonas H.influenzae Bordetella E.coli Campylobacter H.pylori Klebsiella Proteus Serratia Legionella	Listeria monocytogenes Clostridia Bacteroides

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