CLINICAL PEARLS

- 90+% of S. aureus are resistant to PCN!!!!!! d/t production of beta-lactamase
- MOA of resistance
  - Decreased penetration to the target site
  - Inactivation by a bacterial enzyme
  - Alternation of target site
    - Alteration of penicillin binding proteins → beta-lactamase inhibitors act on PCN-binding protein in cell membrane/wall
    - Ribosomal methylation → macrolides act on ribosomes
    - Atypicals like mycoplasma don’t have a cell wall, so cover with macrolides that can attack ribosomes of mycoplasma (giving good coverage for atypicals in pneumonia)
- There is about ~0-11% cross-allergenicity between PCNs and cephalosporins or carbapenems → if pt has a PCN allergy but ceph or carba is best abx, it may be ok to attempt trial if the allergy is not life-threatening (hives, angioedema, anaphylaxis, etc.)
- The rash occurring after mis-treating mono as strep with PCN is a “morbilliform” rash - this is not IgE mediated and is not a drug rxn - pt can still get PCN
- Listeria Monocytogenes = tx with Ampicillin
  - In normal hosts, can cause food borne gastroenteritis (Sabra), can cause pervasive outbreaks
  - Can cause serious illness in immunocompromised pts, extremes of age (neonates and elderly), and pregnant women → meningitis, meningoencephalitis
    - Tx Listeria meningitis with ampicillin
      - See monocytes in blood (thus “mono”cytogenes)
- Presentation of fever, pharyngitis, LAD - always consider HIV and beware of acute HIV seroconversion syndrome - window of no seroconversion for 3-4wks
- Mycoplasma pneumonia (no cell wall!) can cause cold agglutination and hemolysis
- OTc prolongation seen with macrolides, fluoroquinolones
## BETA-LACTAM ABX

### PCN G
- GAS (strept pyogenes → pharyngitis, cellulitis)
- Strep viridans (endocarditis)
- Treponema pallidum (syphilis → IM PCN)
- Susceptible enterococci (non-VRE)
- Borrelia burgdorferi → lyme
- N. meningitides (susceptible isolates)
- P. multocida (cat scratch)
- Actinomyces israelii

### AMPICILLIN (IV)
- AMOXICILLIN (PO)
  - added amino group to PCN
  - Very similar to PCN spectrum but somewhat better gram neg coverage
    - Listeria monocytogenes (amp!)
    - Susceptible enterococci (non-VRE)
    - H influenza if B-lactam negative
    - GBS
    - Proteus mirabilis
    - Elkenella corrodens (dog bite)

### EXTENDED SPECTRUM PCN = PIPERACILLIN
- In addition to above
  - Covers PSEUDOMONAS!
    - But do not use alone to avoid resistance → pip-tazo
    - Higher than usual dose required (~18g)

### ANTI-STAPH PCNs = Nafcillin, Oxacillin, Dicloxacillin (PO)
- Methicillin (pulled)
- In addition to above
  - Covers MSSA (not MRSA)
  - Nafcillin - MSSA meningitis, endocarditis x6wks
    - Excellent in renal impairment
  - S/E = 3+ weeks of neutropenia
  - Dicloxacillin can increase clearance of warfarin
  - “MRSA” and “MSSA” bacteria is actually tested against Oxacillin, so technically the are “ORSA” and “OSSA” bacteria

### CEPHALOSPORINS

#### 1st gen: Cefazolin (IV = Ancef), Cephalexin (Keflex)
- MSSA, community acquired GNRs, streptococci

#### 2nd gen: Cefuroxime and Cephalexin → Cefetetan, Cefoxitin
- Covers ANAEROBES except B. fragilis resistance

#### 3rd gen: Ceftriaxone (IV)
- CAP, UTI, meningitis (crosses BBB)
- Cefotaxime is preferred in neonates and SBP
- Ceftriaxone is metabolized by kidney AND liver (if one doesn’t work, the other takes over)
- Note: ceftriaxone can cause ceftriaxone crystal build up in biliary tree and cause pseudolithiasis

#### 4th gen: Cefepime, Ceftazidine
- Think of as ceftriaxone + PSEUDOMONAS
- Covers MSSA and most GNRs

#### 5th gen: Ceftaroline
- Think of as ceftriaxone + MRSA

#### 6th gen: Ceftolozane-tazo → ESBL producing GNB

#### 7th gen: Ceftazidime-avibactam → ESBL producing GNB
*NO COVERAGE for enterococci, listeria, MRSA
| CARBAPENEMS          | Most broad-spectrum antibiotic!  
|----------------------|----------------------------------  
| Meropenem            | Carbapenemase-producing bacteria big problem  
| Imipenem            | - Imipenem (not used commonly d/t cause of seizures)  
| Ertapenem           | - Meropenem*  
| Doripenem           |   - **ANAEROBES**  
|                     |   - **PSEUDOMONAS**  
|                     |   - Gram neg and positive  
|                     |   - NO coverage for MRSA  
|                     |   - Ertapenem - does NOT cover pseudomonas  

| MONOBACTAM = AZTREONAM | “Rule of one’s” -  
|------------------------|-------------------  
|                        | - Only covers **GRAM NEGATIVES**  
|                        | - One ring  
|                        | - Only beta lactam you can use if IgE anaphylactic response to other BLs  
|                        | - Can use for **PSEUDOMONAS**  

| B-LACTAMASE INHIBITORS | cover BETA-LACTAMASE producing bacteria (i.e. **MSSA**, **M. catarrhalis**, bacteriodes, **E. coli**, enterobacteria), most **GNRs**, increases activity against **ANAEROBES**  
|------------------------|---------------------------------------------------------------------  
|                        | - Zosyn (pip-tazo)  
|                        | - Unasyn (amp-sulbactam)  
|                        | - Augmentin (amox-clavulanate)  
|                        | - Avibactam (non-beta lactam)  
|                        | - Vaborbactam (non-beta lactam)  

| TRIMETHOPRIM / SULFAMETHOXAZOLE |  
|---------------------------------|-------------------------------------------------------------------  
| Aka BACTRI M                     | **Has antibiotic, antiprotozoal, and antifungal properties**  
|                                  | - **E. coli UTI** (if resistance levels <10%)  
|                                  | - **Community acquired MRSA**  
|                                  | - Pneumocystis jiroveci (fungus often seen in AIDS)  
|                                  | - Toxoplasmosis  
|                                  | - Coxiella (in pregnancy), Nocardi a, Strenotrophomas  
|                                  | - Used as alternative tx for:  
|                                  |   - Listeria meningitis, acute chronic bronchitis, aeromonas  
|                                  | - NOT good for group A strep infx  
|                                  | - Adverse effects & DDIs (this is not a benign drug!)  
|                                  |   - **Skin - SJS, EM, TEN**  
|                                  |   - CNS - aseptic meningitis  
|                                  |   - Heme - pancytopenia  
|                                  |   - Renal - incr. Scr  
|                                  |   - DDI w/ **ACEIs/ARBs** → hypokalemia  

| AMINOGLYCOSIDES |  
|-----------------|-------------------------------------------------------------------  
| GENTAMYCIN      | - ONLY **GRAM NEGATIVE** COVERAGE (like aztreonam)  
| TOBRAMYCIN      | - No anaerobic coverage  
| STREPTOMYCIN    | - Once daily dosing now standard (less side effects)  
| NEOMYCIN        | - Vestibular & renal side effects**  

**Skin - SJS, EM, TEN  
CNS - aseptic meningitis  
Heme - pancytopenia  
Renal - incr. Scr  
DDI w/ ACEIs/ARBs → hypokalemia**
### MACROLIDES

<table>
<thead>
<tr>
<th>MACROLIDES</th>
<th>Azithromycin offers significant anti-inflammatory effects!</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZITHROMYCIN</td>
<td>Community-acquired PNA→ covers ATYPICALS</td>
</tr>
<tr>
<td>CLARITHROMYCIN</td>
<td>Mycoplasma don’t have a cell wall, so macrolides attack ribosomes</td>
</tr>
<tr>
<td>ERYTHROMYCIN</td>
<td>Fidaxomicin for C. DIFF COLITIS</td>
</tr>
<tr>
<td>FIDAXOMICIN</td>
<td>Side effects: N/V/D (d/t motilin-binding), hepatotoxicity, QTC prolongation</td>
</tr>
</tbody>
</table>

### VANCOMYCIN FAMILY

<table>
<thead>
<tr>
<th>Glycopeptides:</th>
<th>VANCOMYCIN*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEICOPLANIN</td>
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<table>
<thead>
<tr>
<th>Lipopeptides:</th>
<th>DAPTOMYCIN*</th>
</tr>
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<table>
<thead>
<tr>
<th>Lipoglycopeptides:</th>
<th>DALBAVANCIN</th>
</tr>
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<tbody>
<tr>
<td>ORITAVANCIN</td>
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<tr>
<td>TELAVANCIN</td>
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</tbody>
</table>

- Indications for vanco (available IV and PO)
  - C. DIFF COLITIS → PO only (not bioavailable, just avail enterically)
  - MRSA (but not MSSA)
  - PCN-intolerant cellulitis
- Vanco side effects:
  - “red man syndrome” with rapid IV infusion, causes histamine release with flushing, erythema, palpitations → tx with anti-histamine and stop infusion (not a “drug rxn”)
  - Thrombocytopenia
  - Hypersensitivity rash
- Dapto → covers gram+ organisms including strep, s. aureus, & enterococci
  - Good for skin & soft tissue infx, covers MRSA & VRE
  - Cannot use against PNA (inactivated by surfactant)
  - Can cause muscle toxicity

### FLUOROQUINOLONES

<table>
<thead>
<tr>
<th>CIPROFLOXACIN</th>
<th>LEVOFLOXACIN</th>
<th>MOXIFLOXACIN</th>
</tr>
</thead>
</table>

Act at the DNA topoisomerase - can be used for typicals and atypicals
- PSEUDOMONAS
- ATYPICALS
- CA-PNA + atypicals and some gram negative coverage?
- CAP → levo
- UTI if resistance <10%
- Moxi does NOT get in urine, don’t use for UTI
- Cipro probably has best gram neg coverage
- PO and IV doses have equal bioavailability - extremely well absorbed!
- MUST TAKE 3hrs before/after EATING!!!!
  - Chelations of cations i.e. Ca, Mg, vitamins
- Adverse Effects
  - Tendon rupture (also related to cation chelation of calcium) - athletes and chronic steroid users at higher risk
  - QTC prolongation
  - Photosensitivity

### OXAZOLIDINONES

<table>
<thead>
<tr>
<th>LINEZOLID</th>
<th>TEDIZOLID</th>
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</thead>
</table>

Linezolid has excellent bioavailability (IV=PO)
- MRSA, MRSE (epidermitides), VISA, VRSE, enterococci including VRE
- Adverse Effects:
  - serotonin syndrome (initially developed as anti-depressant)
  - BM suppression and irreversible optic neuropathy when >2wks rx
Tedizolid is newer, less side effects, approved for skin & soft tissue infx
### Lincosamides

<table>
<thead>
<tr>
<th>CLINDAMYCIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Acts on the ribosomes</td>
</tr>
<tr>
<td>- Gram+ coverage - strep, OSSA, <strong>community-acquired MRSA</strong></td>
</tr>
<tr>
<td>- Anaerobic coverage - gram+ actinomycetes, gram neg B. fragilis (50%)</td>
</tr>
<tr>
<td>- Anaerobic lower respiratory infx</td>
</tr>
<tr>
<td>- No gram neg coverage</td>
</tr>
</tbody>
</table>

### Tetracyclines

<table>
<thead>
<tr>
<th>DOXYCYCLINE</th>
<th>TETRACYCLE</th>
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<tbody>
<tr>
<td>MINOCYCLINE</td>
<td></td>
</tr>
<tr>
<td>- Indications: (“the weird stuff”)</td>
<td></td>
</tr>
<tr>
<td>- Spirochetes - lyme, syphilis, lepto</td>
<td></td>
</tr>
<tr>
<td>- Rickettsiae, Ehrlichia</td>
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</tr>
<tr>
<td>- Atypical pneumonia (mycoplasma, coxiella)</td>
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<tr>
<td>- STDs - LGV, granuloma inguinale</td>
<td></td>
</tr>
<tr>
<td>- Brucella, Tularemia, Whipple’s, Malaria</td>
<td></td>
</tr>
<tr>
<td>- Actino, Nocardia, non-TB mycobacteria</td>
<td></td>
</tr>
<tr>
<td>- Adverse effects:</td>
<td></td>
</tr>
<tr>
<td>- Pill esophagitis, photosensitivity, tooth discoloration, hepatotoxicity during pregnancy, vertigo, pseudotumor cerebri</td>
<td></td>
</tr>
<tr>
<td>- Jarisch-Herxheimer rxn post tx of syphilis</td>
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</tbody>
</table>

### Nitroimidazoles

<table>
<thead>
<tr>
<th>METRONIDAZOLE</th>
<th>TINIDAZOLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flagyl = best anaerobic coverage!</td>
<td></td>
</tr>
<tr>
<td>- Antibacterial &amp; anti/protozoan activity requires a strict anaerobic environment</td>
<td></td>
</tr>
<tr>
<td>- Gold standard for tx of bacteriodes</td>
<td></td>
</tr>
<tr>
<td>- Indications: BV, giardia, trichomonas vaginalis, amebiasis</td>
<td></td>
</tr>
<tr>
<td>- Adverse effects: metallic taste, disuiffiram rxn (don’t drink with this abx!), neuropathy (optic, peripheral, autonomic), aseptic meningitis</td>
<td></td>
</tr>
<tr>
<td>- Resistance is rare</td>
<td></td>
</tr>
</tbody>
</table>

Tinidazole has same indications, longer half life, fewer adverse rxns, higher tissue concentration

### Polymyxin

<table>
<thead>
<tr>
<th>POLYMIXIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Susceptible: most carbapenemase+ enterobacteria, pseudomonas, acinetobacter baumannii</td>
</tr>
<tr>
<td>- Bacteriocidal</td>
</tr>
<tr>
<td>- Always use as part of combination therapy</td>
</tr>
</tbody>
</table>
| **PSEUDOMONAS**                  | - Piperacillin  
|                                 | - Ceftazidime  
|                                 | - Cefepime  
|                                 | - Aztreonam  
|                                 | - Meropenem  
|                                 | - Fluoroquinolones  
|                                 | - Aminoglycosides??  |
| **MSSA**                        | - **Nafcillin  
|                                 | - NOT covered by PCN, aminoglycosides, aztreonam, flagyl  |
| **MRSA**                        | - Community-Acquired: *Bactrim, *Tetracyclines, FQs, Clinda somewhat  
|                                 | - Ceftaroline  
|                                 | - Vancomycin  
|                                 | - Daptomycin  
|                                 | - Linezolid  
|                                 | - Synercid  
|                                 | - Tigecycline  |
| **ENTEROCOCCUS**                | - requires DUAL THERAPY  
|                                 | - RIH standard = PCN/AMP/VANC + GENT  |
| **VRE**                         | - Daptomycin  
|                                 | - Linezolid  
|                                 | - Synercid  
|                                 | - Tigecycline  |
| **ANAEROBES**                   | - Pip-tazo or other beta-lactamase inhibitors  
|                                 | - Carbapenems  
|                                 | - Metronidazole  
|                                 | - Tigecycline  
|                                 | - If gram positives → cephalosporins, clinda, vanco, linezolid  |
| **C. DIFF COLITIS**             | - Metronidazole PO (if mild)  
|                                 | - Vancomycin PO****  
|                                 | - Fidaxomicin PO  |
| **Meningitis**                  | - ceftriaxone + vanc  
|                                 | - Listeria meningitis → ampicillin + gent  |
| **UTI**                         | - Ciprofloxacin  
|                                 | - Ceftriaxone  
|                                 | - Bactrim  |
| **CA-PNA**                      | - Azithromycin  
|                                 | - Ceftriaxone  
|                                 | - Levofloxacin  |