Bugs and Drugs: an approach to the management of infections

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Objectives

• revisit the basic principles of infectious diseases and antibacterial therapy
• re-familiarize yourselves with the different antibiotics
• discuss the approach to some common infections: etiology, investigations, treatment
Basic Bacteriology

- Gram positive
  - stains purple
- Gram negative
  - doesn’t stain purple (so counterstains pink)
- Bacilli
  - rods
- Cocci
  - spheres
- Coccobacilli
  - a rod-sphere hybrid, or small rods
Gram Positive Cocci

- **Clusters**
  - usually staphylococci
    - *S. aureus* vs “coagulase negative”

- **Chains**
  - streptococci (letter streps, viridans group), *Enterococcus*, others

- **Pairs**
  - *Streptococcus pneumoniae*
Gram positive bacilli

- Usually important: *Clostridium, Listeria*
- Usually not important: *Bacillus* species, Corynebacteria (Diptheroids), *Propionibacterium*
Gram Negative Organisms

- **Bacilli:**
  - enterobacteriaceae (*E coli*, *Klebsiella*, etc.)
  - non-fermenters (*Pseudomonas*, *Stenotrophomonas*, *Burkholderia*, many others)

- **Cocci:**
  - *Neisseria* (diplococci), *Moraxella catarrhalis*

- **Coccobacilli:**
  - *Haemophilus influenzae*
What bugs cause problems where in a typical healthy host?

- ear, sinus
- lung
- meninges
- skin
- bone, joint
- urine
- perforated intestine
Group A *Streptococcus*

- pharyngitis, cellulitis, bone/joint infection...
- universally susceptible to penicillin
- most susceptible to clindamycin
- macrolide resistance ~30%
Group B, C, G *Streptococcus*

- susceptibilities the same as GAS
**S. aureus**

- cellulitis, bone/joint infections, toxic shock, hospital-acquired pneumonia, empyaema, surgical site infections, device-associated infections...
- cloxacillin and 1\textsuperscript{st} gen ceph. best for MSSA
- vancomycin and Septra best for MRSA
- clindamycin resistance varies (25-50\% @ MUMC)
S. pneumoniae

- pneumonia, meningitis, sinusitis, otitis, fever without source...
- amoxicillin 75-100 mg/kg/day 1\textsuperscript{st} line
  - only 6-8% pen-nonsusceptible @ MUMC
- cefuroxime is maybe \textit{as good as} ampicillin
- ceftriaxone 2\textsuperscript{nd} line
- vancomycin, levofloxacin options
Why I don’t like the simple paradigm

• what has good ‘gram-positive coverage’?
Antibiotic Classes

- Penicillins
- Cephalosporins
- Carbapenems
- Quinolones
- Aminoglycosides
- Macrolides
- Glycopeptides
- Other

\[ \beta - \text{lactams} \]
# Penicillins

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Indications</th>
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<tbody>
<tr>
<td>Penicillin</td>
<td>All group A, B, C, G <em>Streptococcus</em> a lot of: pneumococcus, <em>Neisseria meningitidis</em>, and anaerobes</td>
</tr>
<tr>
<td>Ampicillin/Amoxicillin</td>
<td>Same as pen but better for <em>pneumococcus</em> and <em>Listeria</em> also a few gram negatives</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>Same as pen but many more gram negatives (including <em>Pseudomonas</em>)</td>
</tr>
<tr>
<td>Amox/Clav, Pip/Tazo</td>
<td><strong>very broad</strong>-spectrum: <em>S. aureus</em>, most gram negatives, anaerobes</td>
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Cloxacillin

• cloxacillin better than vancomycin for MSSA
## Cephalosporins

<table>
<thead>
<tr>
<th>Cefazolin (IV)</th>
<th>Cephalexin (PO)</th>
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<tbody>
<tr>
<td>Cefuroxime (IV or po)</td>
<td>Cefprozil</td>
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<tr>
<td>Cefotaxime/Ceftriaxone</td>
<td>Cefixime (PO)</td>
</tr>
<tr>
<td>Ceftazidime (IV)</td>
<td>Cefixime (PO)</td>
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</table>
Beta-lactam antibiotics

- dose FREQUENTLY for maximum benefit
- can treat almost any infection
- if “penicillin-allergic”...what to do?
  - severely limits antibiotic choice -- NEED DETAILS
  - often misdiagnosed
  - even if true very little cross-reactivity, ESPECIALLY with advanced-generation cephalosporins
Carbapenems -- also beta-lactam

• if you think you need meropenem...you need to be talking to ID

• main uses:
  – resistant pathogens, including *Enterobacter*, *Citrobacter*, *Serratia*, and ESBL (extended-spectrum beta-lactamase) producing organisms
  – polymicrobial infections (including anaerobes)
  – CSF infections with gram-negative infections resistant to ceftriaxone
Which beta-lactams would you choose?

- ear, sinus, lung
- meninges
- skin
- bone, joint
- urine
- perforated intestine
Common bacteria resistant to all penicillins and cephalosporins

- MRSA
- SPICE (Serratia, Providencia, Indole-positive Proteus, Citrobacter, Enterobacter, Morganella, Hafnia)
- atypicals (Mycoplasma, Chlamydophila)
- gram-negatives with extended-spectrum beta-lactamases (ESBL)
- often CFers have resistant Pseudomonas, Burkholderia, Stenotrophomonas
Aminoglycosides

- Gentamicin, Tobramycin, Amikacin

- excellent aerobic gram negative coverage with little community resistance
- some synergy for other organisms (GAS, GBS, enterococci, *Listeria*)
- IV or IM – not absorbed orally
- main limitation: toxicity
- dose once daily for optimal bacterial killing
Clindamycin

- good anaerobe coverage “above the diaphragm”
- good viridans strep and GAS coverage
- fading MSSA and MRSA coverage
  - MUMC 2011: ~25% MSSA resistance, ~50% MRSA resistance
- antitoxin effect (for toxic shock, nec fasc)
- good bioavailability, eg. for bone infections
Vancomycin

- gram positive coverage ONLY
- inferior to beta-lactams for GAS and sensitive *S. aureus*
- first line for coagulase-negative staphylococcus, MRSA, and ceftriaxone-resistant pneumococcus (extremely rare!)
- commonly used for line infections, neonatal sepsis
Trimethoprim-sulfamethoxazole

- only fair gram negative coverage because of significant resistance rates (+++ use)
- often used for UTI prophylaxis
- first line for *Stenotrophomonas maltophilia, Pneumocystis jiroveci, Nocardia*
- good choice for MRSA skin/soft tissue infections
- NOT good GAS or pneumocococcus coverage
Metronidazole

- drug of choice for anaerobic gram-negative infections
- first line for *C. difficile* colitis
- very little toxicity
- excellent bioavailability and tissue penetration
Macrolides

- Erythromycin, Clarithromycin, Azithromycin

- first line therapy for *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Bordetella pertussis*

- Clarithro/azithro have extended gram-negative spectra

- ~30% resistance among GAS/pneumocococcus
Fluoroquinolones

- Ciprofloxacin: excellent gram negative coverage (in paediatrics), often including *Pseudomonas* and SPICE
- Levofloxacin: fewer gram negatives than Cipro but excellent pneumococcus and *Stenotrophomonas* coverage
- For these antibiotics po = IV
- Not licensed in children (beagle cartilage studies)
Contraindications you should know

• Many of the antibiotics we use are not approved for use in children
• Don’t use:
  – Ceftriaxone, TMP-SMX in newborns (jaundice)
  – Tetracyclines < 8 years old (tooth staining)
  – Quinolones unless compelling reason
  – Septra or aminoglycosides in worsening RF
  – Aminoglycosides > 2 wks
Useful tidbits

• unreliable, little, or no CSF penetration:
  – oral antibiotics
  – beta-lactamase inhibitors
  – first/second generation cephalosporins
  – macrolides
  – clindamycin
Useful tidbits (II)

- clindamycin also is NOT excreted in urine
- aminoglycosides almost never used alone
- aminoglycosides have poor lung penetration and generally should not be used for CSF coverage
Basics of Infectious Disease Therapeutics
Principles

1. PATHOGENESIS MATTERS
2. You do not need to treat everything that you find
3. If you start with empiric therapy, narrow your spectrum once you have an organism
4. Beware the immunocompromised patient
Principles

5. There is no such thing as an antibiotic that covers everything
6. Hospital acquired infections can be different from community acquired infections
7. Keep up to date with resistance patterns in your hospital, region, and country
1. PATHOGENESIS MATTERS

• the pathogenesis of the infection influences:
  – organisms involved (and so choice of abx)
  – type of treatment needed
  – length of therapy

• examples:
  – osteo of foot with and without nail puncture
  – *E. coli* sepsis in a patient with *E. coli* UTI, in a patient with a central venous catheter, and in a patient with clinical appendicitis
  – lung abscess in patient post-bender vs in a patient after severe pneumonia vs in a patient with endocarditis
2. You do not need to treat everything that you find

- Differentiate colonization from true pathogens
  - eg: endotracheal tube culture results

- Organisms that are reported may just be “innocent bystanders” = colonization

- Some organisms should always be considered pathogens depending where they are from:
  - e.g. *S aureus* in blood – never ignore!
3. If you start with empiric therapy, narrow your spectrum once you have an organism

• If unsure, broader always better at outset

• but...
  – Some narrower spectrum abx have much better activity against certain organisms
  – Judicious use can minimize resistance
  – Minimize complications/adverse events
4. Beware the immunocompromised patient

• Immune compromise may be due to:
  – Steroids, immunosuppressant medications
  – Chemotherapy
  – Premature neonates
  – Congenital/primary immunodeficiency
  – advanced HIV
  – splenic disorders (eg sickle cell)
  – severe disease (eg. nephrotic syndrome)

• Presentation may differ and pathogens may differ in these patients!
5. There is no such thing as an antibiotic that covers everything

- even the broadest spectrum antibiotics have no activity against certain pathogens
- don’t forget: if the antibiotic doesn’t get to the infection, it won’t help!
- even appropriate antibiotic therapy will not eradicate the infection if...
  - abscess
  - necrotizing fasciitis
  - infected vascular catheter or hardware
6. Hospital-acquired infections can be very different from community-acquired ones (aka pathogenesis matters)

- Pneumonia that starts after 48 hrs in hospital is very different from pneumonia on admission – why?
  - more *S. aureus*, gram negatives (especially *Pseudomonas*), and resistant organisms
7. Keep up to date with resistance patterns

• In your community
  – e.g. *S. pneumoniae* resistance to penicillin

• In your hospital
  – e.g. methicillin-resistant *S. aureus*

• In your patient
  – e.g. based on previous culture results
Approach to Infectious Diseases

• IS it an infection?
• Where is the infection?
• What is the infection?
• Which antibiotics?
Where is the infection?

• systemic?

• particular organ system or location?
  – eg. surgical site
What is the infection?

• What are the most common pathogens causing this type of infection?

• Who is the host?
  – age
  – immune status
  – underlying illness
Which antibiotics to use?

• What are the pathogens we are worried about?

• Are there particular pharmacokinetic considerations?
  – CSF penetration
  – renal failure

• is the host on any other medications that will interact with the antibiotics?

• allergies?