Outline

- What do I need to know about microbiology to:
  - Pass the POS
  - Be a safe and efficient clinician

- What do I need to know about antibiotics to:
  - Pass the POS
  - Be a Safe and efficient clinician
Introduction to Microbiology

Micro-organisms

Bacteria  Virus  Fungi  Parasite
Bacteriology

Bacteria

Gram Positive  Gram Negative  Other
Gram Stain

Diagram showing the structure of Gram-negative and Gram-positive bacteria, highlighting their cell walls, membranes, flagella, peptidoglycan, cytoplasm, DNA, and ribosomes. The process of Gram staining is illustrated with steps:

(a) Application of crystal violet
(b) Application of iodine
(c) Alcohol wash
(d) Application of safranin

The figure also includes an image of actual Gram-stained bacteria cells.
Cellular Morphology

Color and shape of the cells help classify which type of bacteria are present.

Used with permission of AAFP-PT.
You are on call for the orthopedic surgery service at the JHCC. You get called at 2 am by a nurse on F5 with a positive blood culture result, gram positive cocci.

- What are the possible organisms?
- How do you decide if you need to treat?
- What do you treat with?
Gram Positive Cocci

Staphylococcus
  - Coagulase
  - S. aureus CNSt

Streptococcus
  - Catalase
  - Strep. pneumo
  - Viridan’s group strep
  - Lancefield groupable strep

Enterococcus
Glycopeptides

- The glycopeptide available to you is vancomycin
- Also teicoplanin, televancin, bleomycin, dalvabancin
- Bind to the cell wall to prevent peptidoglycan synthesis
- Bacterostatic (except against enterococci)
Glycopeptides

- **Toxicities** –
  - Renal – probably overstated
  - Hypotension/red man syndrome
  - Hematologic – eosinophilia, thrombocytopenia
- Monitoring – only in patients with blood stream/bone infections, renal disease/changing renal function, large BMI
Beta-lactams

Similarity in structure of cell wall peptide and penicillin

D-alanine-alanine

Penicillin

Trace red oxygen and blue nitrogen backbone

C. Ophardt, c. 2003
Beta-lactam Antibiotics

• Includes:
  • Penicillins
  • Cephalosporins
  • Cephahmycin
  • Carbapenems
  • Monobactams

• Generally regarded as bacteriocidal
Beta-lactam Antibiotics

- Adverse reactions:
  - Allergy – IgE mediated
  - Other rash
  - Neurologic
  - Renal
  - Gastrointestinal
  - Pulmonary
  - Hematologic
Pen G

- **Active against:**
  - Gram positive cocci (exception – penicillinase producing Staphylococci, penicillin resistant pneumococci, enterococci, MRSA)
  - Gram positive bacilli
  - Gram negative cocci (exception penicillinase producing Nisseria gonnorhea)
  - Most anaerobes (exception Bacteroides)

- **For susceptible GPC there is NO BETTER ANTIBIOTIC CHOICE**
Anti-staphylococcal Penicillins

- Active against penicillinase producing strains of *S. aureus*, but not against MRSA
- For susceptible strains of *S. aureus* these antibiotics are ALWAYS the drug of choice
- Use limited by side effects and toxicities, less active than pen G against non-penicillinase producers; not active against GPB or GNC
Broad Spectrum Penicillins

- Distinguished by activity against GNB

- None are active against penicillinase producing S. aureus

- 2<sup>nd</sup> generation (amox/amp) – active against most strains of E. coli, P. mirabilis, Salmonella, Shigella, H. flu

- 3<sup>rd</sup> generation (carbenicillin) – more stable to chromosomal beta lactamases, useful in Pseudomonal infections

- 4<sup>th</sup> generation (Piperacillin) – similar to 3<sup>rd</sup> generation, more active against Pseudomonas
Penicillins

- All have relatively short half-lives and achieve good levels in pericardium, pleural fluid, urine, peritoneal and synovial cavities

- All achieve higher levels in bile than serum, especially true for amp and piperacillin

- Dose adjustments in renal dysfunction in all but clox
Cephalosporins

1\textsuperscript{st} generation (Cefazolin/ Cephelexin)

2\textsuperscript{nd} generation

Activity against \textit{H. flu} (cefuroxime)

Activity against \textit{Bacteroides} (cefoxitin)

3\textsuperscript{rd} generation

No pseudomonas (Ceftriaxone)

Anti-psuedomonal (Ceftaz)

4\textsuperscript{th} generation
Cephalosporins

- **First generation (Cephelexin, Cefazolin):**
  - Active against most GPC (not MRSA, penicillin resistant pneumococcus, enterococci)
  - Active against most E. coli, P. mirabilis, K. pneumoniae
  - Not active against SPICE organisms, non-fermenters, H. flu (generally)
  - Active against many anaerobes, not Bacteroides
Cephalosporins

- 2nd generation (Cefuroxime)
  - Less active against GPC, enhanced activity against some gram negatives
  - Highly active against H. flu and betalactamase producing M. catarrhalis

- Cefamycins (cefoxitin, cefotetan)
  - Good activity against Enterobacteriaceae (not SPICE) and against anaerobes including Bacteroides (variable resistance)
  - Useful for interabdominal infections
Cephalosporins

3\textsuperscript{rd} generation:

- Poor pseudomonal coverage (Cefotaxime, Ceftriaxone, Cefipime) – excellent gram negative coverage (not SPICE), no activity against Acinitobacter or Pseudomonas, less effective than first generation ceph against GPC
- Anti-pseudomonal group (Cefoparazone, Ceftaxadime) – similar gram negative coverage with addition of Pseudomonas; poor activity against GP organisms
Cephalosporins

- **4th generation (Cefepime)**
  - Excellent gram negative coverage (equivalent to 3rd generation), pseudomonas coverage equivalent to Ceftaz, active against SPICE organisms,

- **5th generation (Ceftobiprole)**
  - Broad spectrum – active against MRSA, enterococci, penicillin resistant S. pneumo, gram negatives
Pop quiz # 2

• Another night on call, this time on urology rotation at St Joes

• Called from ward with regards to post-op patient with positive blood culture – gram negative bacilli
  • What are the possible bugs?
  • What will help you decide if you need to treat?
  • What antibiotics will you use?
Gram Negative Bacilli
Gram Negative

**coccobacilli**
- H. influenzae: X & V factors required
- B. pertussis: growth on Bordet-Gengou medium, oxidase +
- Brucella spp.: aerobic
- F. tularensis: requires cystein for growth
- P. multocida: oxidase +, catalase +
- L. pneumophila: growth on charcoal yeast agar with iron and cysteine

**cocci=N. Neisseria spp.**
- N. meningitidis: glucose and maltose +
- N. gonorrhoeae: Lactose +

**bacilli**
- Lactose -
  - Oxidase +
    - V. cholerae: glucose +
    - P. aeruginosa
  - Oxidase -
    - Fast fermenter
      - Klebsiella urease +
      - E. coli, indole +
      - Enterobacter
    - Slow fermenter
      - Citrobacter
      - Serratia
      - Others

**Strict anaerobe**
- B. fragilis

Urease +
- P. mirabilis
- Y. pestis, bipolar staining
- H. pylori: grows on campy agar

Urease -
- Y. enterolitica, motile at 25C, non-motile at 37C
- C. jejuni, grows on campy agar
- S. dysenteriae, non-motile campy agar
- Salmonella spp.: motile & produces H₂S
Fluoroquinolones

- Direct inhibitors of DNA gyrase and topoisomerase IV (bactericidal)
- Excellent gram negative coverage (enterobacteriaciae, pseudomonas, GNC)
- Respiratory fluoroquinolones have added coverage against GPC and agents of atypical pneumonia
- Moxifloxacin has enhanced anaerobic coverage
Aminoglycosides

- Bind to ribosomal RNA to inhibit protein synthesis
- Main uses include treatment of serious infections due to gram negative bacilli and synergistic treatment of some staphylococcal and enterococcal infections
Aminoglycosides

- Once daily dosing is sufficient (preferred) for all but a few indications

- Toxicity:
  - Renal
  - Ototoxicity
  - Neuromuscular blockade (myasthenia gravis)
Pop Quiz #3

Several months later you are on call as the in-house junior on your ICU-E rotation at the HGH. You are called at 2 am regarding a patient post-op day 1 after laparotomy for penetrating trauma. The patient has become suddenly hypotensive, tachycardic and has a fever of 39.5 Celsius
Pop quiz 3

- What are the potential organisms
- What factors will lead you to treat empirically
- What antibiotics
THE BIG GUNS
Piperacillin - Tazobactam

- Broad spectrum antibiotic with excellent gram positive, gram negative, anaerobic coverage

- Does not:
  - Reliably cover SPICE organisms
  - Cover MRSA
  - Cover amp-resistant Enterococcus
  - Cover (generally) pip resistant strains of Pseudomonas
CARBAPENEMS

- Generally stable to most beta-lactamase enzymes
- Excellent gram positive, gram negative, anaerobic coverage
- **DOES NOT cover**
  - Burkholderia, Stenotrophomonas, Enterococcus faecium, MRSA
  - Ertapenem does not cover pseudomonas
AMOX/CLAV

- Similar spectrum of activity to pip/taz, no pseudomonas coverage
- Available as oral preparation
- Main side effect is gastrointestinal upset/diarrhea
MOXIFLOXACIN

- Available as po or IV
- Similar coverage to levofloxacin with enhanced anaerobic coverage
- No MRSA, rapid resistance develops with S. aureus, not reliable for serious enterococcal infections
The Big Guns - Principles

• Try to tailor antibiotic choice to clinical presentation

• When source of infection is unclear and patient is seriously ill, cover broadly

• ALWAYS reassess antibiotics in patients on broad spectrum agents at least daily; narrow spectrum if source becomes clear

• Become familiar with what is being missed, if patient not improving, broaden (or stop?)
Questions?