Infectious Disease
PG17: Surgical Critical Care Board Review

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None
Introduction - Topics

- Gram Negative Infections and Double Coverage
- Clostridium Difficile Infections
- Abdominal Infections
- Urinary Tract Infections
Gram Negative Double Coverage

Why might this be useful?
- Resistant Organisms have become more prevalent in many intensive care units
- Good evidence that early appropriate antibiotic therapy reduces mortality
- Early double coverage more likely to cover resistant organism and reduce mortality
- By providing better coverage, theoretic benefit of reducing risk of creating resistance
Gram Negative Double Coverage

- Potential Risk of Double Coverage
  - More antibiotics leaves one at higher risk of antibiotic associated diarrhea (C. Diff)
  - Other complications of antibiotic use (renal failure)
  - Creating resistant bacteria by increasing antibiotic exposure
Gram Negative Double Coverage

- Community Acquired Infections
  - Low rate of resistant gram – infections in most communities
  - If low resistance rate among bacteria, there is little evidence that double coverage of gram – is beneficial
Gram Negative Double Coverage

- Health Care Associated Infections
- Mixed Evidence
- Pro Evidence
  - Mostly retrospective studies
  - Beta lactam with aminoglycoside may be better for those with shock and neutropenia, but not overall survival- Meta analysis of RCTs.
  - Comparison of combination therapies
Gram Negative Double Coverage

- Con Evidence
  - Meta-analysis of 64 RCT: B lactam with aminoglycoside not beneficial
  - Another Meta-analysis showed benefit only when Pseudomonas present, this review included retrospective studies
Gram Negative Double Coverage

- Evidence is clearly mixed, but favors no double coverage.
- What should you do?
  - Many have stopped routine double gram negative
  - Base decisions on unit specific antibiotic resistance and bacterial growth patterns
  - May consider if severe shock or immunosuppression
  - If any double coverage is needed, likely an aminoglycoside is the appropriate choice.
Clostridium Difficile

- Diagnosis
- Toxin Assay
  - Most tests are done with this
  - Different toxins A and B
    - Enzyme immunoassay
      - Rapid
      - Miss 30%
  - GDH detects antigen – Not specific and used in combination
Clostridium Difficile

- Tissue culture
  - Test effects of toxin on human cells
  - More specific but 24 to 48 hours for result
- PCR
  - Newer and becoming more rapid, but expensive
- Toxigenic stool culture
  - Growth of bacteria and search for toxins
  - Gold standard, but takes 2 to 3 days
  - Cannot tell between overgrowth and colonization
Clostridium Difficile

- Different tests used per each hospital routine.
- These may have different sensitivities.
- Multiple sequential tests are generally not recommended.
Clostridium Difficile

- Prevention
  - Hand washing with soap and water effective at killing spore
  - Alcohol does not kill the spores
Clostridium Difficile

- **Treatment**
  - **Standard regimens**
    - Flagyl: PO or IV – absorbed if taken PO and delivered through the bloodstream. May not be as good for recurrent infections
    - Vancomycin: PO or rectal
      - 7-14 days depending on severity and if recurrent
  - **New antibiotics**
    - Fidaxomicin
      - Use for treatment failure or recurrence
      - $2800 for 10 day therapy
Abdominal Infections

• Types
  • Primary
    • Associated with bacterial infection of abdominal fluid
    • Usually ascites or peritoneal dialysis
  • Secondary
    • Primary infection form perforated viscous
    • Appendicitis, perforated ulcer, diverticulitis
Abdominal Infections

• Tertiary
  • Recurrent infection in those already with surgery for secondary peritonitis

• Quaternary
  • Severe recurrent infections, fistula, intra-abdominal catastrophe
Location: Organism

- **Proximal:** If no acid suppression therapy, Gram + aerobic (streptococcus)
  - May be different in face of distal obstruction

- **Distal**
  - Coliforms (E. Coli, Klebsiella)
  - Anaerobes (Bacteroides, Clostridium)
Prophylaxis

- **Elective**
  - Single agent to cover expected organism, no more than 24 hours, prior to skin incision
- **Emergent**
  - Single agent to cover expected organism, duration dependent on findings, prior to skin incision
- **Trauma**
  - Give prior to skin incision, If less than 12 hours of contamination, no more than 24 hours of therapy
- **Necrotizing pancreatitis – not indicated**
Treatment

- **Community Acquired:** Mild – to – moderate
- Many regimens work, single agent and monotherapy. Cover enteric gram-negative aerobic and facultative bacilli and enteric gram-positive streptococci, anaerobic bacilli distally
- Avoid significant anti-Pseudomonal activity agents for these mild infections
- Avoid Ampicillin-Sulbactam- E. Coli resistance
- Avoid cefotetan and clindamycin due to B frag resistance
- No need for empiric enterococcus nor candida coverage
Treatment – Severe

- Broad spectrum gram negative coverage
- Avoid quinolones with higher resistance of E. Coli
- Empiric coverage of enterococcus
- No need for empiric MRSA nor yeast coverage
- Get cultures and sensitivities, check local antibiogram
Treatment

- Health Care Related
  - Empiric therapy based on local antibiogram
  - Broad expanded spectrum coverage
  - Tailor to culture results
- SIS Guidelines cover this well
Specific Organisms

- **Antifungal**
  - Use antifungal if Candida grows
  - If C. albicans – fluconazole
  - Echinocandin if resistant species
  - If critically ill, use echinocandin instead of triazole
  - Ampho B not recommended as initial therapy
Specific Organisms

- Enterococcus/ MRSA
  - Treat for faecalis not VREF unless immunocompromised
  - Empiric coverage in health care associated disease
  - Treat if it is isolated
  - MRSA coverage if known carrier and prior treatment failure
Duration

- In general no more than seven days
- If proximal may only need 24 hours
- Non complicated appendicitis, less than 24 hours
Urinary Tract Infections

- Definitions
  - Symptomatic Urinary Tract infection (SUTI)
    - At least 1 of the following signs or symptoms with no other recognized cause:
      - fever (>38°C), suprapubic tenderness, or costovertebral angle pain or tenderness and,
      - a positive urine culture of $\geq 10^5$ colony-forming units (CFU)/ml with no more than 2 species of microorganisms
Patient with or without an indwelling urinary catheter has no signs or symptoms (i.e., for any age patient, no fever (>38°C), urgency, frequency, dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness, OR for a patient ≤1 year of age, no fever (>38°C core), hypothermia (<36°C core), apnea, bradycardia, dysuria, lethargy, or vomiting) and

- A positive urine culture of >10^5 CFU/ml with no more than 2 species of uropathogen microorganisms and
- A positive blood culture with at least 1 matching uropathogen microorganism to the urine culture, or at least 2 matching blood cultures drawn on separate occasions if the matching pathogen is a common skin commensal.
CAUTI

- Catheter Associated Urinary Tract Infection

- CAUTI if catheter in place at time of symptoms or culture or taken out within 48 hours and the above definitions are true
UTI

- **Measures**
  - Reporting of CAUTI and ABUTI to the CDC
  - Treated as preventable (never event)

- **Prevention**
  - Remove catheters ASAP
  - Not always possible in SICU
What to do in your unit?

- Decrease number of indiscriminate urinary cultures sent by team members
- Forbid pan cultures
- Research previous cultures and plan timing of new UTI searches
- Establish protocols for when to obtain urinary screens
- Screen for UTI using UA
- Add Foley removal to daily checklist
UTI

www.CDC.gov
Thanks for your attention

- Will save questions until after Dr. Haut’s presentation.
Elliott R. Haut, MD, FACS

Lippincott, Williams, & Wilkins
Book Royalties as editor of
“Avoiding Common ICU Errors”
Topics to Cover

• Selective digestive decontamination (SDD)
• Anti-fungal use in the ICU
• Antibiotic resistance patterns & mechanism
• High Yield Infectious Disease Facts
• Antibiotic Classes
• Anti-Fungals
• High Yield Drug Facts
Selective digestive decontamination (SDD)

• Background
  – ICU acquired infections in are important cause of morbidity and mortality with pneumonia being a common infection
  – Some thought that this is causes by aspiration of oral flora and may be prevented by reducing the bacterial load
  – One approach is SDD

• Topical or Systemic antibiotics
Selective digestive decontamination (SDD)

- Cochrane Systematic Review
  - 36 studies involving 6914 ICU patients
  - Does administration of antibiotics prevent the development of respiratory infections?
- 2 routes- systemic and/or topical
- Outcome measures - respiratory tract infection (RTI) and mortality
Selective digestive decontamination (SDD)

• Topical vs. systemic antibiotics
  – significant reduction in RTIs
    • (OR 0.28, 95% CI 0.20 to 0.38)
  – significant reduction in total mortality
    • (OR 0.75, 95% CI 0.65 to 0.87)
Selective digestive decontamination (SDD)

- Topical antimicrobials alone (or comparing topical plus systemic versus systemic alone)
  - significant reduction in RTIs
    - (OR 0.44, 95% CI 0.31 to 0.63)
  - NO significant reduction in total mortality
    - (OR 0.97, 95% CI 0.82 to 1.16)
Prophylactic vs. Empiric vs. Preemptive anti-fungal use in the ICU
Prophylactic anti-fungal use in the ICU

• Goal to prevent disease
  – Endorsed for at-risk patients in ICUs with high rates of invasive candidiasis
  – Target patients with ICU LOS >48-72 hours
  – Mostly focuses on candida - most common
  – Most studied drug is Fluconazole
  – At least 15 studies
  – Consistent data - reduces invasive candida infections
  – Some data - reduces mortality
Empiric anti-fungal use in the ICU

- Idea to wait until patient develops signs/symptoms of infection
  - Then add anti-fungal therapy in cases where fungal infection a concern
  - Some suggest this route to avoid widespread exposure to azoles which may lead to resistance
  - Drawback is real since delaying appropriate therapy is associated with higher mortality
Preemptive anti-fungal use in the ICU

- Middle ground between prophylactic and empiric approaches
  - Use early screening tools to detect need for anti-fungal therapy before usual signs and symptoms (such as fever) which are notoriously absent or delayed in the ICU
  - Tests that can be considered
    - Blood tests (i.e. galactomannan)
    - New radiographic finding
    - Positive fungal culture
Antibiotic resistance patterns and mechanisms of resistance

• Factors that drive resistance (WHO)
  – Inadequate commitment to a comprehensive and coordinated response
  – ill defined accountability and engagement
  – Weak or absent surveillance and monitoring
  – Inappropriate and irrational use of antibiotics
  – Poor infection prevention and control practices
  – Depletion of resources and lack of R&D
Antibiotic resistance MRSA
Methicillin Resistant S. Aureus

• Now more common in community
• Treat community and healthcare associated differently
  – Community Acquired
    • can use easy cheap, oral drugs
    • Bactrim (trimethoprim sulfa), Clindamycin
• Healthcare Acquired
  – Different resistance pattern, Need “bigger guns”
  – Vancomycin, Linezolid, Daptomycin, Tigecycline, Dalfopristin/Quinupristin (Synercid)
Antibiotic resistance
VRE

• Vancomycin-Resistant Enterococci (VRE)
• Two main species E. faecium (most common) and E. faecalis
• Plasmids or transposons contain DNA that confer vancomycin resistance
• Treatment options
  – Daptomycin, Linezolid, Dalfopristin/Quinupristin (Synercid), Tigecycline, Nitrofurantoin (UTI only)
Antibiotic resistance
ESBL

- Extended-spectrum beta-lactamases (ESBL) enzymes
- confer resistance to most beta-lactam antibiotics, including penicillins, cephalosporins, and the monobactam aztreonam
- Associated with poor outcomes
- Treat with carbapenem (imipenem, meropenem, ertapenem)
Antibiotic resistance
KPC

• Klebsiella pneumoniae carbapenemase (KPC) producing enzyme
  – Enzymes reside on transmissible plasmids and confer resistance to all beta-lactams
  – KPC can be transmitted from Klebsiella to other bacteria (i.e. E. coli, Pseudomonas aeruginosa, Citrobacter, Salmonella, Serratia, and Enterobacter)

• Carbapenems will not treat the infection
• Drugs to consider- colistin, aztreonam, tigecycline, fosfomycin (for UTI)
High Yield ID Facts: Pneumonia

• Community acquired
  – Most common pathogen in adults is Streptococcus pneumoniae (pneumococcus)
  – Atypical pneumonia
    • Legionella, Mycoplasma, Chlamydia
    • Consider empiric coverage with macrolide or respiratory fluoroquinolone

• Pneumocystis jiroveci pneumonia- new name for PCP (Pneumocystis pneumonia)
High Yield ID Facts: Pneumonia

- If use vancomycin, need to dose to get trough levels of 15-20 µg/mL
- Ventilator associated pneumonia
  - 8-day course appropriate for most uncomplicated cases (except pseudomonas)
  - Don’t use Daptomycin - inactivated by pulmonary surfactants
  - Don’t use tigecycline - associated with increased risk of death
High Yield ID Facts:
Necrotizing soft tissue infections

• The right answer is almost always surgical debridement

• Broad spectrum antibiotic coverage
  – Empiric MRSA coverage due to high rates of community acquired MSRA
  – Add clindamycin
    • mostly bacteriostatic
    • also prevents toxin production by staphylococci

• Can consider hyperbaric oxygen
High Yield ID Facts: Meningitis

• Make sure drug crosses blood-brain barrier (BBB) into central nervous system (CNS)

• NEVER use Zosyn (Piperacillin and Tazobactam) does not cross BBB
  – Ampicillin does cross BBB
  – Vancomycin only crosses BBB with inflammation so OK to use for meningitis (has meningeal inflammation)
High Yield ID Facts: Bacteremia

• Always need to document clearance (negative blood cultures) for gram positives
• Most (if not all) patients with gram positive bacteremia should get echocardiogram to rule out endocarditis
• Use Duke criteria to diagnose endocarditis
High Yield ID Facts: Open fractures

- 1\textsuperscript{st} generation cephalosporin good for most Grade I and II fractures
- Aminoglycosides useful for Grade III and should be dosed daily
- Rarely need anaerobic coverage, but may consider with contamination from likely source (cow pasture).
Some Antibiotic Classes (with examples)

• β-Lactam antibiotics
  – penicillins (amoxicillin, methacillin, oxacillin)
  – cephalosporins (Cephalexin, cefazolin, cefotetan, ceftriaxone)
  – carbapenems (Imipenem, Meropenem, Ertapenem)
  – monobactam (Aztreonam)
Some Antibiotic Classes (with examples)

• Tetracyclines (tetracycline)
• Macrolides
  – Erythromycin, Azithromycin, Clarithromycin
• Aminoglycosides
  – Gentamicin, Tobramycin, Amikacin
• Fluoroquinolones
  – ciprofloxacin, levofloxacain
Some Antibiotic Classes (with examples)

- Cyclic peptides
  - Vancomycin, Streptogramins, Polymyxins
- Lincosamides (clindamycin)
- Oxazolidinones - Linezolid (Zyvox)
- Sulfa antibiotics
  - Sulfamethoxazole (usually combined with Trimethoprim)
  - SMX/TMP = Bactrim
Anti-Fungals

• Polyenes
  – Binds to ergosterol in cell membrane and alters permeability
    • Amphotericin B
    • AmBisome (liposomal formulation of amphotericin B)- less toxic form
Anti-Fungals

- **Azoles**
  - inhibits the fungal cytochrome P450 enzyme which leads to ergosterol synthesis
  - targets fungal cell wall
  - Ketoconazole, Voriconazole, Fluconazole, Itraconazole
Anti-Fungals

• Echinocandins
  – inhibit glucan synthase (another cell wall component)
  – not through P450 system- fewer drug interactions
  – Caspofungin, Micafungin, Anidulafungin
High Yield Drug Facts

- Common drugs that cause Thrombocytopenia
  - Linezolid, Vancomycin, β-lactams
- Common drugs that lower seizure threshold - β-lactams
- Cefotetan/Clindamycin
  - Both option for abdominal surgery prophylaxis
  - DO NOT use to treat abdominal infection due to high bacteroides fragilis resistance
High Yield Drug Facts

• Colistin (polymyxin E)
  – Bactericidal drug - disrupts outer cell membrane of gram-negative rods
  – Currently used for pan-resistant bacteria (i.e. Acenitobacter, Pseudomonas)
  – Major side effects – nephrotoxicity and neuotoxicity
High Yield Drug Facts

- Most fluoroquinolones (i.e. ciprofloxacin, levofloxacin) are a good choice for UTI since they concentrate in urine – EXCEPT moxifloxacin (does not concentrate in urine)

- DO NOT use echinodandins (i.e. Caspofungin, Micafungin) for fungal UTI since they do not concentrate in urine
• Good Luck