Infectious Disease
PG17: Surgical Critical Care Board Review

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2012 Clinical Congress
Presenter Disclosure Slide

American College of Surgeons ♦ Division of Education

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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

ABUTI

- 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 U\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.

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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

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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

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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

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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)

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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)

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Prophylactic vs. Empiric vs. Preemptive anti-fungal use in the ICU

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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

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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

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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)

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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)

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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)

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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)

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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

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High Yield ID Facts: Necrotizing soft tissue infections

- The right answer is almost always surgical debridement
- Broad spectrum antibiotic coverage
  - Empiric MRSA coverage dues to high rates of community acquired MSRA
  - Add clindamycin
    - mostly bacteriostatic
    - also prevents toxin production by staphylococci
- Can consider hyperbaric oxygen

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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)

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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 endocarddidits
- Use Duke criteria to diagnose endocarditis

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High Yield ID Facts: Open fractures

- 1st 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).

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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, levofloxacin

Some Antibiotic Classes (with examples)

- Cyclic peptides
  - Vancomycin, Streptogramins, Polymyxins
- Lincosamides (clindamycin)
- Oxazolidinoes - 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 interations
  - Caspofungin, Micafungin, Anidulafungin

High Yield Drug Facts

- Common drugs that cause Thromobocytopenia
  - 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 flouroquinolones (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

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- Good Luck

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