Infectious Disease
PG17: Surgical Critical Care Board Review
September 30, 2012
American College of Surgeons Annual Clinical Congress
McCormick Place, Chicago, IL

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1) Gram Negative Infections and Double Coverage
    a) Presumed need
        i) Resistant Organisms have become more prevalent in many intensive care units, especially in patients with recent prior hospitalization or treatment with antibiotics.
        ii) Good evidence that early appropriate antibiotic therapy reduces mortality
        iii) Early double coverage more likely to cover resistant organism and reduce mortality
        iv) By providing better coverage, theoretic benefit of reducing risk of creating resistance
    b) Potential risks of double coverage
        i) More antibiotics leaves one at higher risk of antibiotic associated diarrhea (C. Diff)
        ii) Other complications of antibiotic use (renal failure)
        iii) Creating resistant bacteria by increasing antibiotic exposure
    c) Community Acquired Infections
        i) Less likely to be resistant infections
        ii) No evidence of need for double gram negative coverage
    d) Health Care Associated Infections
        i) Much higher risk of resistant bacteria
        ii) Evidence is mixed
            (1) Pro
                (a) Beta lactam with aminoglycoside may be better for those with shock and neutropenia, but not overall survival
            (2) Con
                (a) Meta-analysis of 64 RCT: B lactam with aminoglycoside not beneficial
                (b) Another Meta-analysis showed benefit only when Pseudomonas present, this review included retrospective studies
            (3) Paul M, Benuri-Silbiger I, Soares-Weiser K, et al. Beta lactam monotherapy versus beta lactam-aminoglycoside combination therapy for sepsis in immunocompetent patients: systematic review and meta-analysis of randomised trials. BMJ. 2004; 328:668.
            (4) Safdar N, Handelsman J, Maki DG. Does combination antimicrobial therapy reduce mortality in gram-negative bacteraemia? A meta-analysis. Lancet Infect Dis. 2004; 4:519–27
            (5) Bliziotis IA, Michalopoulos A, Kasiakou SK, Samonis G, Christodoulou C, Chrysanthopoulou S, Falagas ME. Ciprofloxacin vs an aminoglycoside in combination with a beta-lactam for the treatment of febrile neutropenia: a meta-analysis of randomized controlled trials. Mayo Clin Proc. 2005 Sep;80(9):1146-56.
    e) How should you proceed?
        i) Many have stopped routine double gram negative
        ii) Base decisions on unit specific antibiotic resistance and bacterial growth patterns

iii) If any double coverage is needed, likely an aminoglycoside is the appropriate choice.

2) Clostridium Dificile infections
   a) Diagnosing Clostridium Difficile Associated Diarrhea (CDAD)
      i) Toxin Assay
         (1) Most test are done with this
         (2) Different toxins used per each hospital routine. These may have different sensitivities. Multiple sequential tests are generally not recommended.
      ii) Direct growth of bacteria
         (1) Difficult to grow
         (2) May be more useful in studying outbreaks
   b) Prevention
      i) Wash hands with soap and water- alcohol gels don't kill the spores
   c) Treatment
      i) Standard regimens
         (1) Flagyl: PO or IV – absorbed if taken PO and delivered through the bloodstream, May nor be as good for recurrent infections
         (2) Vancomycin: PO or rectal
         (3) 7-14 days depending on severity and if recurrent
      ii) New antibiotics
         (1) Fidaxomicin
            (a) Use for treatment failure or recurrence
            (b) $2800 for 10 day therapy

3) Abdominal Infections
   a) Types
      i) Primary
         (1) Associated with bacterial infection of abdominal fluid
         (2) Usually ascites or peritoneal dialysis
      ii) Secondary peritonitis
         (1) Primary infection form perforated viscous
         (2) Appendicitis, perforated ulcer, diverticulitis
      iii) Tertiary peritonitis
         (1) Recurrent infection in those already with surgery for secondary peritonitis
      iv) Quaternary peritonitis
         (1) Severe recurrent infections, fistula, intra-abdominal catastrophe
   b) Location – organism
      i) Proximal – If no acid suppression therapy – Gram + aerobic (streptococcus)
         (1) May be different in face of distal obstruction
      ii) Distal

(1) Coliforms (E. Coli, Klebsiella)
(2) Anaerobes (Bacteroides, Clostridium)

c) Prophylaxis (Mostly to prevent skin infections)
   i) Elective
      (1) Single agent to cover expected organism, no more than 24 hours, prior to skin incision
   ii) Emergent
      (1) Single agent to cover expected organism, duration dependent on findings, prior to skin incision
   iii) Trauma
      (1) Give prior to skin incision, If less than 12 hours of contamination, no more than 24 hours of therapy
   iv) Necrotizing pancreatitis – not indicated
d) Treatment
   i) Community Acquired
      (1) Mild – to – moderate
      (2) Many regimens work, single agent and monotherapy. Cover enteric gram-negative aerobic and facultative bacilli and enteric gram-positive streptococci, anaerobic bacilli distally
      (3) Avoid significant anti-Pseudomonal activity agents for these mild infections
      (4) Avoid Ampicillin-Sulbactam- E. Coli resistance
      (5) Avoid cefotetan and clindamycin due to B frag resistance
      (6) No need for empiric enterococcus nor candida coverage
   ii) Severe
      (1) Broad spectrum gram negative coverage
      (2) Avoid quinolones with higher resistance of E. Coli
      (3) Empiric coverage of enterococcus
      (4) No need for empiric MRSA nor yeast coverage
      (5) Get cultures and sensitivities, check local antibiogram
   iii) Health care Related
      (1) Empiric therapy based on local antibiogram
      (2) Broad expanded spectrum coverage
      (3) Tailor to culture results
   iv) Antifungal
      (1) Use antifungal if Candida grows
      (2) If C. albicans – fluconazole
      (3) Echinocandin if resistant species
      (4) If critically ill, use echinocandin instead of triazole
      (5) Ampho B not recommended as initial therapy
   v) Enterococcus/ MRSA

(1) Treat for faecalis not VREF unless immunocompromised
(2) Empiric coverage in health care associated disease
(3) Treat if it is isolated
(4) MRSA coverage if known carrier and prior treatment failure

e) Duration
   i) In general no more than seven days
   ii) If proximal may only need 24 hours
   iii) Non complicated appendicitis, less than 24 hours
f) Joseph S. Solomkin, John E. Mazuski, John S. Bradley, Keith A. Rodvold, Ellie J.C. Goldstein, Ellen J. Baron, Patrick J. O'Neill, Anthony W. Chow, E. Patchen Dellinger, Soumitra R. Eachempati, Sherwood Gorbach, Mary Hilfiker, Addison K. May, Avery B. Nathens, Robert G. Sawyer, and John G. Bartlett. Surgical Infections. February 2010, 11(1): 79-109.

4) Urinary Tract Infections (UTI)
   a) Definitions
      i) Symptomatic Urinary Tract infection (SUTI)
         (1) at least 1 of the following signs or symptoms with no other recognized cause:
            (a) fever (>38°C), suprapubic tenderness, or costovertebral angle pain or tenderness and,
            (b) a positive urine culture of ≥105 colony-forming units (CFU)/ml with no more than 2 species of microorganisms
      ii) Asymptomatic Bacteremic Urinary Tract Infection (ABUTI)
      iii) 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
         (1) a positive urine culture of >105 CFU/ml with no more than 2 species of uropathogen microorganisms** and
         (2) 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.
      iv) Catheter related (CAUTI) if catheter in place at time of symptoms or culture or taken out within 48 hours
   b) Measures
      i) Reporting of CAUTI and ABUTI to the CDC
      ii) Treated as preventable (never event)
   c) Prevention
      i) Remove catheters ASAP

ii) Not always possible in SICU

d) What do you do?
   i) Decrease number of indiscriminate urinary cultures sent by team members
   ii) Forbid pan cultures
   iii) Research previous cultures and plan timing of new UTI searches
   iv) Screen for UTI using UA
   v) Establish protocols for when to obtain Urinary screens
   vi) Add foley removal to dailychecklist

e) More data found at www.CDC.gov

5) Selective digestive decontamination (SDD)
   a) Background
      i) ICU acquired infections in are important cause of morbidity and mortality with pneumonia being a common infection
      ii) Some thought that this is causes by aspiration of oral flora and may be prevented by reducing the bacterial load
      iii) One approach is selective decontamination of the digestive tract (SDD)
         (1) Topical antibiotics
         (2) Systemic antibiotics
   b) Cochrane Systematic Review)D'Amico R, Pifferi S, Torri V, Brazzi L, Parmelli E, Liberati A. Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD000022.)
      i) 36 studies involving 6914 patients treated in ICUs
      ii) Does administration of antibiotics prevents the development of respiratory infections?
      iii) 2 routes- systemic and/or topical
      iv) Outcome measures - respiratory tract infection (RTI) and mortality
      v) In trials comparing a combination of topical and systemic antibiotics, there was a significant reduction in both RTIs (number of studies = 16, odds ratio (OR) 0.28, 95% confidence interval (CI) 0.20 to 0.38) and total mortality (number of studies = 17, OR 0.75, 95% CI 0.65 to 0.87) in the treated group.
      vi) In trials comparing topical antimicrobials alone (or comparing topical plus systemic versus systemic alone) there was a significant reduction in RTIs (number of studies = 17, OR 0.44, 95% CI 0.31 to 0.63) but not in total mortality (number of studies = 19, OR 0.97, 95% CI 0.82 to 1.16) in the treated group.

6) Prophylactic vs. Empiric vs. Preemptive anti-fungal use in the ICU
   a) Prophylactic anti-fungal therapy in ICU patients to prevent disease
      i) Endorsed for at-risk patients in ICUs with high rates of invasive candidiasis
      ii) Target at patients with expected length of stay of at least 48-72 hours

iii) Mostly focuses on candida- most common pathogen
iv) Most studied drug is Fluconazole (800mg load, then 200mg or 400mg/day)
v) At least 15 studies done on the topic
(1) Clear data that this reduces invasive candida infections
(2) Some data that this also reduces mortality (but less consistent)

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

c) Preemptive anti-fungal therapy
i) Middle ground between the two approaches (prophylactic and empiric) above
ii) 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
iii) Tests that can be considered
(1) Blood tests (i.e. galactomannan)
(2) New radiographic finding
(3) Positive fungal culture

7) Antibiotic resistance patterns and mechanisms of resistance
a) Factors that drive resistance (World Health Organization Antimicrobial Fact Sheet 2012)
i) Inadequate commitment to a comprehensive and coordinated response
ii) Ill defined accountability and engagement
iii) Weak or absent surveillance and monitoring
iv) Inappropriate and irrational use of antibiotics
v) Poor infection prevention and control practices
vi) Depletion of resources and lack of R&D

b) Methacillin Resistant Staph Aureus (MRSA)
i) Now more common in community
ii) Treat community and healthcare associated differently
(1) Community Acquired
(a) can use easy cheap, oral drugs
(b) Bactrim (trimethoprim sulfa), Clindamycin
(2) Healthcare Acquired
(a) Different resistance patterns
(b) Need “bigger guns”
(c) Vancomycin, Linezolid, Daptomycin, Dalfopristin/Quinupristin (Synercid), Tigecycline

c) Vancomycin-Resistant Enterococci (VRE)
    i) Two main species Enterococcus faecium (most common) and Enterococcus faecalis
    ii) Plasmids or transposons contain DNA that confer vancomycin resistance
    iii) Treatment options: Daptomycin, Linezolid, Dalfopristin/Quinupristin (Synercid), Tigecycline, Nitrofurantoin (UTI only)
d) ESBL
    i) Extended-spectrum beta-lactamases (ESBL) enzymes confer resistance to most beta-lactam antibiotics, including penicillins, cephalosporins, and the monobactam aztreonam
    ii) associated with poor outcomes
    iii) Treat with carbapenem (imipenem, meropenem, ertapenem)
e) KPC
    i) Klebsiella pneumoniae carbapenemase (KPC) producing enzyme
    ii) Enzymes reside on transmissible plasmids and confer resistance to all beta-lactams
    iii) KPC can be transmitted from Klebsiella to other bacteria (i.e. E. coli, Pseudomonas aeruginosa, Citrobacter, Salmonella, Serratia, and Enterobacter)
    iv) Carbapenems will not treat the infection
    v) Drugs to consider- colistin, aztreonam, tigecycline, fosfomycin (for UTI)

8) High Yield Infectious Disease Facts
a) Pneumonia
    i) Community acquired
        (1) Most common pathogen in adults is Streptococcus pneumoniae (pneumococcus)
        (2) Atypical pneumonia
            (a) Legionella, Mycoplasma, Chlamydia
            (b) Consider empiric coverage with
        (3) *Pneumocystis jiroveci* pneumonia- new name for PCP (*Pneumocystis* pneumonia)
        (4) If use vancomycin, need to dose to get trough levels of 15-20 μg/mL
    ii) Ventilator associated pneumonia
        (1) 8-day course appropriate for most uncomplicated cases (except pseudomonas)
        (2) Don't use Daptomycin - inactivated by pulmonary surfactants
        (3) Don't use tigecycline
            (a) associated with increased risk of death compared to other antibiotics
b) Necrotizing soft tissue infections
    i) The right answer is almost always surgical debridement
    ii) Broad spectrum antibiotic coverage
        (1) Empiric MRSA coverage dues to high rates of community acquired MSRA
        (2) Add clindamycin
            (a) mostly bacteriostatic

(b) also prevents toxin production by some staphylococci
iii) Can consider hyperbaric oxygen (although data still sparse)

c) Meningitis
  i) Make sure drug crosses blood-brain barrier (BBB) into central nervous system (CNS)
    (1) NEVER use Zosyn (Piperacillin and Tazobactam) does not cross BBB
    (2) Ampicillin does cross BBB
    (3) Vancomycin only crosses BBB with inflammation
      (a) OK to use for meningitis (has meningeal inflammation)
      (b) Does NOT otherwise penetrate CNS

d) Bacteremia
  i) Always need to document clearance (negative blood cultures) for gram positives
  ii) Most (if not all) patients with gram positive bacteremia should get echocardiogram to rule out endocardidits
  iii) Use Duke criteria to diagnose endocarditis
    (1) Clinical criteria for infective endocarditis requires:
      (a) (Two major) or (One major and three minor) or (Five minor)
      (b) Major
        (i) Positive blood culture for Infective Endocarditis (typical bug or persistent)
        (ii) Evidence of endocardial involvement (echo or new murmur)
      (c) Minor
        (i) Predisposition
        (ii) Fever
        (iii) Vascular phenomena
        (iv) Immunologic phenomena
        (v) Microbiological evidence:
        (vi) Echocardiographic findings

9) Some Antibiotic Classes (with examples)
  a) β-Lactam antibiotics
    i) penicillins (amoxicillin, methacillin, oxacillin)
    ii) cephalosporins (Cephalexin, cefazolin, cefotetan, ceftriaxone)
    iii) carbapenems (Imipenem, Meropenem, Ertapenem)
    iv) monobactams (Aztreonam)
  b) Tetracyclines
    i) tetracycline
  c) Macrolides
    i) erythromycin
  d) Aminoglycosides
    i) Gentamicin, Tobramycin, Amikacin
  e) Fluoroquinolones

i) ciprofloxacin, levofloxacin

f) Cyclic peptides
   i) Vancomycin, Streptogramins, Polymyxins
g) Lincosamides
   i) clindamycin
h) Oxazolidinoes
   i) Linezolid (Zyvox)
i) Sulfa antibiotics
   i) Sulfamethoxazole (usually combined with Trimethoprim) = SMX/TMP = Bactrim

10) Anti-Fungals
   a) Polyenes
      i) Binds to ergosterol in cell membrane and alters permeability
      ii) Amphotericin B
      iii) AmBisome (liposomal formulation of amphotericin B)- less toxic form
   b) Azoles
      i) inhibits the fungal cytochrome P450 enzyme which leads to ergosterol synthesis
      ii) targets fungal cell wall
      iii) Ketoconazole, Voriconazole, Fluconazole, Itraconazole
   c) Echinocandins
      i) inhibit glucan synthase (another cell wall component)
      ii) not through P450 system- fewer drug interations
      iii) Caspofungin, Micafungin, Anidulafungin

11) High Yield Drug Facts
   a) Common drugs that cause Thromobocytopenia
      i) Linezolid, Vancomycin, β-lactams
   b) Common drugs that lower seizure threshold
      i) β-lactams
   c) Cefotetan/Clindamycin
      i) Both can be option for abdominal surgery pre-op prophylaxis BUT
      ii) DO NOT use to treat abdominal infection due to high *bacteroides fragilis* resistance
   d) Colistin (polymyxin E)
      i) Bactericidal drug - disrupts outer cell membrane of gram-negative rods
      ii) Currently used for pan-resistant bacteria (i.e. Acenitobacter, Pseudomonas)
      iii) Major side effects – nephrotoxicity and neuotoxicity
   e) Most flouroquinolones (i.e. ciprofloxacin, levofloxacin) are a good choice for UTI since they concentrate in urine – EXCEPT moxifloxacin (does not concentrate in urine)
   f) DO NOT use echinodandins (i.e. Caspofungin, Micafungin) for fungal UTI since they do not concentrate in urine