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Session Title: 'Vanc and Zosyn' is NOT the Answer for Everything
Session Type: 6 Minute 40 Second PK Presentation

Educational Goals and Objectives

- Given a well-appearing Emergency Department patient with healthcare-associated pneumonia, design an appropriate antimicrobial regimen that includes atypical coverage.
- Define which patients with diabetic foot infections need broad antimicrobial coverage.
- Interpret the data linking piperacillin/tazobactam with increased risk of acute kidney injury when prescribed with vancomycin.

It's almost reflexive to start vancomycin + piperacillin/tazobactam in many ED patients. But, do all of these patients really need the broad spectrum gram-positive, gram-negative, and anaerobic coverage this antibiotic combination provides?

1. The Hospital-Acquired Pneumonia Guidelines date all the way back to 2005 (*Am J Respir Crit Care Med* 2005;171(4):388-416). We know what to do with the sick HCAP patient; give broad-spectrum antibiotics including coverage for MRSA and Pseudomonas. But, what about the not-so-sick HCAP patient? Do they really need vancomycin and piperacillin/tazobactam?
    a. A 2013 study says probably not (Maruyama T, et al. *Clin Infect Dis* 2013;57(10):1373-83).
    b. In this potentially ground breaking study, HCAP patients with non-severe illness (not requiring intubation or ICU admission) AND < 2 risk factors for multi-drug resistant (MDR) pathogens received the equivalent of ceftriaxone and azithromycin (or a respiratory fluoroquinolone).
    c. Risk factors for MDR pathogens in this study were: antimicrobial therapy in preceding 90 days, recent hospitalization of 5 days or more, poor functional status, and immunosuppresive disease and/or therapy.
    d. Only 50% of patients ended up receiving broad-spectrum coverage, yet 93% of regimens were appropriate for the identified pathogen. Atypical pathogens were identified in 10% of cases.
    e. **Bottom line**: In the not-so-sick HCAP patient, treating with CAP antibiotics is generally sufficient. Don't forget the atypical coverage with a macrolide or fluoroquinolone for HCAP patients who have been in the community for any length of time.
    f. Further reading: http://www.aliem.com/new-treatment-strategy-not-so-sick-health-care-associated-pneumonia/
2. Do all diabetic foot infections need vancomycin and piperacillin/tazobactam?
    a. Here is what the 2012 Diabetic Foot Infection Guidelines (Lipsky BA, et al. *Clin Infect Dis* 2012;54(12):132-73) say:
        i. For mild to moderate infections in patients who have not recently received antibiotic treatment, we suggest that therapy just targeting aerobic GPC is sufficient.

   ii. For most severe infections, we recommend starting broad-spectrum empiric antibiotic therapy, pending culture results and antibiotic susceptibility data.
   iii. Empiric therapy directed at Pseudomonas aeruginosa is usually unnecessary except for patients with risk factors for true infection with this organism.
   iv. Consider providing empiric therapy directed against MRSA in a patient with a prior history of MRSA infection; when the local prevalence of MRSA colonization or infection is high; or if the infection is clinically severe.

b. **Bottom line**: Mild and most moderate diabetic foot infections generally do not need coverage for anaerobes and pseudomonas. Vancomycin and piperacillin/tazobactam is perfectly appropriate for severe cases (those accompanied by systemic signs or metabolic perturbations).

3. Several studies in the past few years, in both internal medicine and critical care patient populations, have linked the combination of vancomycin + piperacillin/tazobactam with a higher risk of acute kidney injury vs. vancomycin alone or vancomycin + cefepime.
   a. Further reading with references: http://www.aliem.com/piperacillin-tazobactam-acute-kidney-injury/
4. Pulmonary penetration
   a. A recent study investigated the pulmonary penetration of piperacillin/tazobactam in critically ill patients and found that intrapulmonary exposure is highly variable and unrelated to plasma exposure and pulmonary permeability (Felton TW, et al. *Clin Pharmacol Ther* 2014;96:438-48). Current dosing may be inadequate.
   b. Further reading: https://umem.org/educational_pearls/2528/
5. Sodium load
   a. Each 4.5 gm dose of piperacillin/tazobactam contains 250 mEq of sodium (http://labeling.pfizer.com/showlabeling.aspx?id=416). Use caution in heart failure patients receiving q 6 hour dosing. It will add 1 gram of sodium per day.
6. Empiric susceptibilities
   a. Make sure you know them for your institution. For pseudomonas, my institution has 12% better empiric coverage with cefepime compared to piperacillin/tazobactam.
7. Frequent dosing
   a. The need for q 6 hour dosing with piperacillin/tazobactam can be problematic in the ED. With long boarding times, subsequent doses get missed. The opposite problem also occurs where admitted patients receive two doses with an hour or two of each other.