

'Vanc & Zosyn' is Not the Answer to Everything

Session Overview

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, & anaerobic coverage this antibiotic combination provides? Learn how to better select antibiotics for your patients!

Objectives

- 1) Design an appropriate antimicrobial regimen for community-acquired pneumonia based on the 2019 guidelines
- 2) Define which patients with diabetic foot infections need broad antimicrobial coverage
- 3) Interpret the data linking piperacillin/tazobactam with increased risk of acute kidney injury when prescribed with vancomycin

Virtual ACEP Questions

1. Which of the following agents does not provide coverage for atypical organisms?
 - a. Levofloxacin
 - b. Ceftriaxone**
 - c. Azithromycin
 - d. Doxycycline
2. Which classification of diabetic foot infection generally requires broad spectrum antibiotic coverage including anaerobes?
 - a. Uninfected
 - b. Mild
 - c. Moderate
 - d. Severe**

PNEUMONIA

After 12 years, the Infectious Diseases Society of America (IDSA) and American Thoracic Society (ATS) finally published an update to the Adult [Community-Acquired Pneumonia \(CAP\) guidelines](#)! It is set up as 16 questions, and for each they provide a recommendation, summary of evidence, rationale, and research needed in that area. Below is a summary of the half of recommendations regarding medication therapy. I share their recommendations and add my thoughts, when applicable [my comments are in brackets]. Of note, there are additional antibiotics mentioned for some of the indications below. The ones listed are preferred based on side effect profile, drug interaction risk, local susceptibility patterns, dosing schedule, and cost. These guidelines, for the most part, do not address the prevalence of atypical bacteria in CAP and how much CAP is attributable to non-bacterial causes.

Empiric Treatment in Outpatients (Question 8)

1. No comorbidities or risk factors for antibiotic resistant pathogens: Amoxicillin 1 gm TID **OR** Doxycycline 100 mg BID [Azithromycin is listed, but resistance is too high in all of the continental U.S. to use it as monotherapy]
2. Comorbidities (chronic heart/lung/liver/renal disease; diabetes; malignancy; asplenia)
 1. Combination: Amoxicillin/Clavulanate 875/125 mg BID **OR** Cefpodoxime 200 mg BID **OR** Cefuroxime 500 mg BID **PLUS** azithromycin 500 mg X 1, then 250 mg QDAY **OR** Doxycycline 100 mg BID
 2. Monotherapy: Levofloxacin 750 mg QDAY **OR** Moxifloxacin 400 mg QDAY [FQs have several black box warnings, other serious adverse reactions, and drug interactions – use combination therapy above unless patient absolutely can't tolerate]

Empiric Treatment in Inpatients (Questions 9 and 11)

1. Non-severe without MRSA or *P. aeruginosa* risk factors: Ceftriaxone 1-2 gm QDAY **PLUS** Azithromycin 500 mg QDAY [FQs are listed for monotherapy, but should be avoided whenever possible] [Doxycycline can be substituted for macrolides]
2. Severe without MRSA or *P. aeruginosa* risk factors: Same as non-severe. If using a FQ, add beta-lactam as well. [Avoid FQs whenever possible]
3. With MRSA or *P. aeruginosa* risk factors: As was alluded to in the [2016 Hospital-Acquired and Ventilator-Associated Guidelines](#), there is no more HCAP. The new guidelines recommend only covering empirically for MRSA or *P. aeruginosa* “if locally validated risk factors for either pathogen are present.” Vancomycin or Linezolid for MRSA, when indicated. Cefepime or Piperacillin/Tazobactam for *P. aeruginosa*, when indicated. Consider adding atypical coverage as well ([Eljaaly 2017](#), [Maruyama 2013](#)).

Table 1. 2007 Infectious Diseases Society of America/American Thoracic Society Criteria for Defining Severe Community-acquired Pneumonia

Validated definition includes either one major criterion or three or more minor criteria

Minor criteria

Respiratory rate \geq 30 breaths/min
 P_{aO_2}/F_{iO_2} ratio \leq 250
Multilobar infiltrates
Confusion/disorientation
Uremia (blood urea nitrogen level \geq 20 mg/dl)
Leukopenia* (white blood cell count $<$ 4,000 cells/ μ l)
Thrombocytopenia (platelet count $<$ 100,000/ μ l)
Hypothermia (core temperature $<$ 36°C)
Hypotension requiring aggressive fluid resuscitation

Major criteria

Septic shock with need for vasopressors
Respiratory failure requiring mechanical ventilation

*Due to infection alone (i.e., not chemotherapy induced).

Aspiration in Inpatients (Question 10)

Do not routinely add anaerobic coverage unless lung abscess or empyema is suspected. Standard inpatient CAP therapy above is sufficient.

Corticosteroids (Question 12)

Do not routinely use steroids in CAP (non-severe or severe) or severe influenza pneumonia. Follow Surviving Sepsis Campaign recommendations in refractory septic shock.

Concomitant Influenza (Questions 13 and 14)

1. Guidelines recommend anti-influenza treatment in CAP patients testing positive for influenza, in inpatients and outpatients, independent of duration of illness before diagnosis. [Data on antivirals is controversial, but IDSA and CDC both support their use]
2. Guidelines recommend antibacterial treatment be initially prescribed for adults with clinical and radiographic evidence of CAP who test positive for influenza in the inpatient and outpatient settings.

Duration of Treatment (Question 15)

At least 5 days with discontinuation guided by a validated measure of clinical stability.

What About HCAP?

- No more health-care associated pneumonia ([Kalil 2016](#), [Metlay 2019](#))
 - Risk of multidrug-resistant organisms (MDR) is low
 - Most patients who previously would have been designated as HCAP can be treated similar to the community-acquired pneumonia (CAP) pathway ([Ewig 2019](#))
 - Empiric treatment in the ED for MDR organisms should be individualized
 - Biggest risk factor = IV antibiotics within the last 90 days
 - Other risk factors include comorbidities, functional status, and severity of illness ([Shorr 2012](#), [Webb 2016](#)); and in the critically ill: acid suppression therapy within the previous 90 days, mechanical ventilation, and history of MDRO infection ([Lat 2018](#))

What is so bad about fluoroquinolones? See handout from my ACEP 2020 talk '[Black Box Drugs We Use: What's the Risk?](#)'

IV vs. PO

Most ED patients with SSTI can be managed with oral antibiotics ([Stevens 2014](#)). Many of the antibiotics we use in the ED have good oral bioavailability ([MacGregor 1997](#)). In fact, even one dose of IV antibiotics in the ED can lead to an increased risk of antibiotic-associated diarrhea and *C. diff* ([Haran 2014](#), [Belforti](#)

[2016](#)). There are some clinical risk factors associated with oral antibiotic failure in SSTI which may be taken into account when developing a plan ([Peterson 2014](#), [Yadav 2019](#)).

DIABETIC FOOT INFECTIONS

IDSA guideline update published in 2012 ([Lipsky 2012](#))

- Severities: uninfected, mild, moderate, severe
- Microbiology
 - Superficial: aerobic gram-positive cocci (including *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus pyogenes*, and coagulase-negative staphylococci)
 - Ulcers that are deep, chronically infected, and/or previously treated with antibiotics are more likely to be polymicrobial: above organisms in addition to enterococci, Enterobacteriaceae, *Pseudomonas aeruginosa*, and anaerobes
 - Wounds with extensive local inflammation, necrosis, malodorous drainage, or gangrene with signs of systemic toxicity should be presumed to have anaerobic organisms in addition to the above pathogens
- Risk factors for resistant bugs
 - MRSA: previous MRSA infections or known colonization, prior antibiotic use, previous hospitalization, and residence in a long-term care facility
 - *Pseudomonas aeruginosa*: warm climates, macerated ulcers, foot soaking, and other exposure to water or moist environments
 - Resistant enteric gram-negative rods (ESBL): prolonged hospital stays, prolonged catheterization, prior antibiotic use, or residence in a long-term care facility
- Treatment
 - Mild and some moderate: target the same bugs as we do for non-diabetic SSTI
 - More serious moderate and severe cases: broad-spectrum antibiotics including vancomycin, gram-negative, and anaerobic coverage

WHAT DOES BRYAN HAVE AGAINST ZOSYN?

Really nothing; I just want to reserve it for the right patients and have it available in the future.

1. Susceptibility patterns for target gram-negative organisms (*Pseudomonas*, *Klebsiella*, *E. Coli*) in many hospitals are slightly inferior to cefepime
2. Do we really need anaerobic coverage in all situations where broad-spectrum antibiotics are given in the ED?
3. There is a signal of increased AKI risk when combined with vancomycin compared to cefepime or meropenem ([Hammond 2017](#), [Luther 2018](#), [Chen 2018](#))
 - a. [Is piperacillin-tazobactam nephrotoxic?](#) From PulmCrit blog
 - b. [Piperacillin/Tazobactam and Risk of Acute Kidney Injury with Vancomycin](#) from ALiEM blog

4. Particularly in critically ill patients with lung infections or obesity, standard dosing may not reach sufficient concentrations in the target organs ([Zander 2016](#), [Felton 2014](#), [Jung 2017](#), [Damen 2019](#)). Pediatric patients are often underdosed ([Sosnin 2019](#)).
5. Each 4.5 gm dose of piperacillin/tazobactam contains 250 mg of sodium. Use caution in heart failure patients receiving q6 hour dosing. It will add a gram of sodium per day.
6. The need for q6 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 within an hour or two of each other ([Leisman 2017](#))
 - a. [Importance of Second Antibiotic Doses in ED Sepsis Patients](#) from PharmERToxGuy blog