

'Vanc & Zosyn' is NOT the Answer for Everything: Critical Knowledge in Antibiotic Selection

Session Overview

Antibiotics are among the most frequently ordered medications in the Emergency Department. The purpose of this talk is to provide key strategies for proper selection and dosing of antimicrobials in the ED. Management of common infections (SSTI, pneumonia, UTI), allergy and cross-reactivity assessment, and dosing will be discussed.

Objectives

- 1) Determine the true risk of cross-reactivity between penicillins and cephalosporins
- 2) Create an antibiotic plan for ED patients presenting with SSTI, pneumonia, or urinary tract infections.
- 3) Recommend a proper vancomycin dose for ED patients.

Act 1 - Allergies

Challenges

We're up against a difficult challenge when navigating patient allergy histories. We're still taught incorrect information regarding true rates of cross-reactivity in school, package inserts still list outdated statistics, and electronic medical record alerts will not be disabled due to perceived liability. So, education has to be the primary solution. ([Shenoy 2019](#))

Penicillin 'Allergy' in the Patient Chart

Simply having a penicillin allergy listed in a patient's chart (whether true hypersensitivity or not) leads to worse outcomes. They spend significantly more time in the hospital, are exposed to significantly more antibiotics previously associated with C difficile and VRE, and are associated with increased hospital use and increased C difficile, MRSA, and VRE prevalence. ([Macy 2014](#), [MacFadden 2016](#))

Anaphylaxis Risk

The actual anaphylaxis risk is low for both penicillins (0.004-0.015%) and cephalosporins (0.0001-0.1%). ([Idsoe 1968](#), [Kelkar 2001](#)) In fact, There are more reported cases of anaphylaxis to cephalosporins in patients without a known penicillin allergy compared with those with known penicillin allergy. ([Pichichero 2005](#), [Anne 1995](#))

Busting Common Myths

- 1) The true incidence of penicillin allergy in patients who report that they are allergic is less than 10%. ([Pichichero 2014](#))
- 2) Penicillin-cephalosporin cross-reactivity is largely unrelated to the beta-lactam ring.

Where did the 10% cross-reactivity between penicillins and cephalosporins originate?

The high cross reactivity found in the early studies probably was caused, at least in part, by contamination of the study drugs with penicillin during the manufacturing process. Before the 1980s,

pharmaceutical companies used Acremonium (formally called Cephalosporium) to create both penicillins and cephalosporins. ([Campagna 2012](#))

Furthermore, the authors of the early studies loosely defined “allergy” and did not account for the fact that penicillin-allergic patients have an increased risk of adverse reactions to any medication.

Where does the true cross-reactivity come from?

The cross-reactivity seems to come mostly from similar side chains. ([Campagna 2012](#), [Pichichero 2014](#)) **If a patient is allergic specifically to amoxicillin or ampicillin, avoid these cephalosporins: cephalexin, cefaclor, cefadroxil, cefprozil.**

Does the risk of cross-reactivity decrease with later generation cephalosporins?

Technically, yes. But, the real reason is that the side-chain issue only exists with first and second generation cephalosporins. Third, fourth, and fifth generation cephalosporins don't have a similar side chain to any penicillins.

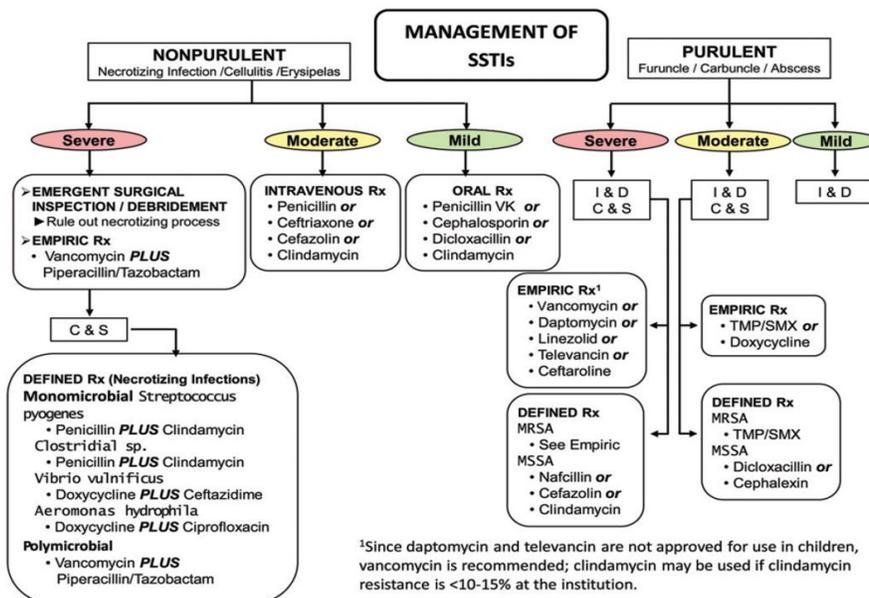
Solutions

- 1) Detailed patient history to determine extent of ‘allergy’
- 2) Possible test doses in the ED ([Blumenthal 2017](#))
- 3) Possible skin testing ([Bland 2019](#))

Act 2 - Infections

SSTI

The IDSA guideline is still the gold standard for managing Skin and Soft Tissue Infections in the ED ([Stevens 2014](#))



Generally, non-purulent infections should be managed with coverage against Strep species (eg, cephalosporins) and purulent infections should include coverage for Staph species including MRSA (eg, doxycycline, TMP-SMX, vancomycin).

Despite the increased incidence of community-acquired MRSA, cephalexin is still as effective as cephalexin + TMP-SMX for uncomplicated SSTI. ([Pallin 2013](#), [Moran 2017](#))

Most ED patients with SSTI can be managed with oral antibiotics. 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](#))

What about vancomycin? Don't give vancomycin as first-line or as a one-time dose. If IV antibiotics are truly indicated, choose the IV form of the antibiotics you plan to continue at home. ([Mueller 2015](#), [Belforti 2016](#))

What about diabetic foot infections? In most mild and mild-to-moderate diabetic foot infections, we can target the same bugs as we do for non-diabetic SSTI. ([Lipsky 2012](#)) More serious moderate and severe cases should be managed with broad-spectrum antibiotics including vancomycin, gram-negative, and anaerobic coverage.

Pneumonia

No more health-care associated pneumonia ([Kalil 2016](#))

Biggest risk factor for multi-drug resistant pathogens = IV antibiotics within the last 90 days. Other risk factors in critically-ill patients are acid suppression therapy within the previous 90 days, mechanical ventilation, and history of MDRO infection ([Lat 2018](#))

Strategy for patients who would have been considered HCAP under the old guidelines ([ATS 2005](#))

- Not-So Sick: Treat like Community-Acquired Pneumonia ([Maruyama 2013](#))
- Sick: Treat like old HCAP with broad-spectrum antibiotics PLUS atypical coverage

What about CAP? Beta-lactam PLUS macrolide for inpatients and most outpatients (no comorbidities can use doxycycline alone). ([Lee 2016](#), [Haran 2018](#), [Eljaaly 2017](#)) Fluoroquinolones can be considered, but there many drug interactions and adverse effects to consider. ([ALiEM 2014](#), [EMPharmD 2017](#), [PulmCrit 2016](#))

Urinary Tract Infections

Uncomplicated UTI in females: Nitrofurantoin first-line. ([Huttner 2018](#) w/ [PharmERToxGuy summary](#)) TMP-SMX and fosfomycin are other first-line options if resistance less than 20%. ([Gupta 2011](#))

E. Coli resistance in otherwise healthy female patients may be less than what the institutional or ED antibiogram reports ([Hines 2015](#))

What about pyelonephritis? Fluoroquinolones or TMP-SMX still first-line unless resistance rates > 20%. In that case, use cephalosporins (eg, cefuroxime, cefpodoxime). ([Gupta 2011](#))

What about male patients? Treat similar to complicated UTI in women; generally no nitrofurantoin; longer treatment course (7-14 days)

Act 3 - Dosing

Vancomycin

Changes are coming to vancomycin dosing ([Heil 2018](#)), but for now, two guidelines provide recommendations ([Rybak 2009](#), [Liu 2011](#)): In the ED, load with 15-20 mg/kg (actual body weight, max 2 gm) and consider 25-30 mg/kg in critically-ill patients. There is a strategy for loading if the patient requires more than 2 gm. ([Denetclaw 2015](#))

Even loading with 30 mg/kg in the ED only achieves therapeutic levels 34% of the time ([Rosini 2015](#))

Doses > 20 mg/kg in the ED do not increase risk of nephrotoxicity ([Rosini 2016](#))

When is vancomycin 1 gm ok? Patients < 50 kg or on dialysis (though HD pts can still get weight-based loading)

We only get dosing correct in about 20% of cases ([Rosini 2013](#), [Fuller 2013](#)), though incorporating weight-based dosing in electronic medical records helps ([Hall 2015](#), [Frankel 2013](#))

Dosing of other antibiotics in critically-ill obese ED patients ([Erstad 2004](#), [Medico 2010](#))

Class	Dose
<u>Penicillins</u>	High end of dosing range
<u>Cephalosporins</u>	High end of dosing range
<u>Carbapenems</u>	High end of dosing range
<u>Fluoroquinolones</u>	High end of dosing range
<u>Aminoglycosides</u>	Adjusted body weight*
<u>Vancomycin</u>	You know what to do!

*ABW (kg) = IBW + 0.4 X (actual body weight - IBW)