



UC Davis Health Antimicrobial Stewardship Program - Vol 2 Issue 5

Vancomycin dependent Enterococcus faecium's response to a Vancomycin E-test (Mueller-Hinton Agar - 24+hours, 37°C). Vancomycin dependence may develop from the loss of a functional D-Ala:D-Ala ligase in the VRE strain, which is then unable to survive unless vancomycin induces the production of D-Ala: D-Lac ligase to compensate. This dependence involves mutations to the dll gene which encodes the enterococcal D-Ala:D-Ala ligase protein. From: <http://thunderhouse4-yuri.blogspot.com/2014/01/vancomycin-dependant-enterococcus-vde.html>

Volume 2, Issue 5

November 2020

The UC Davis Antimicrobial Stewardship Program (ASP) was first established in 1986 and then expanded in pediatrics in 2011 and hospital wide in 2013 in response to the growing challenge of antibiotic resistance. Due to increasing antibiotic resistance, patients are at a higher risk for adverse effects and poor outcomes and treatment strategies become more complex.

Antibiotics are life-saving drugs and their use has important implications for patient care and public health. With this in mind, the UC Davis Health ASP strives to ensure all patients receive optimal

antibiotic therapy when indicated. We thank you for your support in putting this very important program into action.

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Ventilator-Associated Pneumonia (VAP)



VAP Diagnosis

- Pneumonia occurring greater than 48 hours after endotracheal intubation
 - Clinical symptoms include purulent tracheal secretions, new infiltrate on chest imaging, worsening oxygenation (usually in association with leukocytosis and/or fever/hypothermia)
- Microbiology: *Staphylococcus aureus*, *Enterobacteriaceae* spp., *Pseudomonas aeruginosa*
 - *Enterococcus* spp. and *Candida* spp. that grow in sputum cultures are highly likely to be colonizers and do not require treatment
- If pneumonia develops within 48 hours of intubation, common organisms are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *S. aureus*; treat as community-acquired pneumonia
- Obtain endotracheal aspirate and send for Gram-stain and culture
- VAP is unlikely with bacterial burdens below the following thresholds:
 - Protected specimen brush <1,000 CFU/mL
 - Bronchoscopic alveolar lavage fluid <10,000 CFU/mL
 - Endotracheal aspirate <100,000 CFU/mL

- Obtain blood cultures; may be positive in up to 15% of patients
- Consider obtaining *Legionella* urine antigen in patients with immunocompromise

VAP Treatment

Empiric therapy

- Coverage for *Enterobacteriaceae* spp., *P. aeruginosa*, streptococci, and *S. aureus* with an anti-pseudomonal β -lactam; consider combination therapy with an aminoglycoside with pseudomonal activity if severely ill
- Coverage for methicillin-resistant *S. aureus* (MRSA) should be considered if the patient has known history of MRSA colonization or infection, intravenous drug use, necrotizing pneumonia, a recent stay in a nursing home or skilled nursing facility, or prolonged hospitalization with unknown MRSA colonization status
- For all: Cefepime 2g IV q8hrs
- Add MRSA coverage if indicated or critically ill: Vancomycin per pharmacy
- Add a 2nd empiric gram negative antibiotic if critically ill: Amikacin 10-15 mg/kg IV x 1

Narrowing and oral therapy

- If an alternate diagnosis is identified, stop VAP-targeted therapy
- If patient is able to be weaned from a ventilator within 1-2 days, VAP is less likely; consider stopping therapy
- Use respiratory culture results to narrow therapy
 - Discontinue antibiotics directed at MRSA and *Pseudomonas* spp. if not recovered
 - If a second agent directed at Gram-negative organisms was started empirically, discontinue if an appropriate β -lactam is available for treatment
- After clinical improvement is observed and oral medications can be tolerated, consider conversion from intravenous to oral therapy:
- Levofloxacin 750 mg PO q24hrs

Duration

- 7 days if clinical response by day 3

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Would You Like Some Salt With That? Sodium in IV Antibiotics.

IV antibiotics often come with more than just the antibiotic. Sodium is a significant portion of the carrier fluid in many IV ready to use (RTU) formulations or in the IV fluid diluent necessary for the administration of many intravenous antibiotics. In some cases, the amount of sodium infused can exceed 2g per a day making the treatment of many conditions, congestive heart failure to name just one, significantly more difficult to manage. Yet another reason to switch from IV to PO when it's safe to do so.

Table 1. Sodium Content of Intravenous Antibiotic Preparations

Antibiotic	Usual Dose (mg)	Available Dosages	Intrinsic Sodium Content in RTU (mg)	Intrinsic Sodium per Vial (or in 100 mL) (mg)*	Total Sodium Content in 10 mL vial, mg†	Total Sodium Content in 100 mL, mg	Total Sodium Content (mg) in Other Volume of NS	Total Sodium (mg) per Day of Therapy (No. of Doses)‡
Beta-lactams								
Penicillin G Potassium	4 MU	RTU, DSW, NS	84	212	213.2	380.3	-	2343 (6)
Penicillin G Sodium	4 MU	DSW, NS	-	388.8	242.1	531.1	-	3183 (6)
Zaprinol	2300	NS	-	131.8	-	488.8	-	2818 (6)
Ampicillin-sulbactam	1600	NS	-	115	232	488	-	3888 (6)
	3000	NS	-	230	-	582	-	2541 (6)
Oxacillin	3000	RTU, DSW, NS	188.8	128	376.8	352.8	-	3129 (6)
	3700	RTU, DSW, NS	183.2	133.2	416.4	362.4	-	3581 (6)
Piperacillin-tazobactam	3375	RTU, DSW, NS	182	102	302.1	503.1	-	2781 (6)
	4500	RTU, DSW, NS	282	218	482.8	842.8	-	2943 (6)
Cefazolin	1000	RTU, DSW, NS	48	48	225	402	-	1593 (3)
	2000	RTU, DSW, NS	96	96	-	492	-	1593 (3)
Ceftriaxone	1000	RTU, DSW, NS	83	83	234	431	-	431 (1)
	2000	RTU, DSW, NS	166	166	418.8	817.8	-	1181 (2)
Cefepime	1000	RTU, DSW, NS	54	54	231	408	-	1233 (3)
	2000	RTU, DSW, NS	108	108	295	492	-	1233 (3)
Cefepime	1000	RTU, DSW, NS	0	0	212.4	389.4	-	1173 (3)
	2000	RTU, DSW, NS	0	0	212.4	389.4	-	1173 (3)
Aztreonam	2000	RTU, DSW, NS	0	0	-	368	-	1062 (3)
Ertapenem	1000	NS	-	137	340.4	526.4	-	531 (1)
Meropenem	1000	RTU, NS	230.2	96.2	287.2	444.2	-	1330 (3)
	2000	NS	-	192.4	-	534.4	-	889 (3)
Imipenem	500	DSW, NS	-	375	-	426.9	-	1713 (6)
Fluoroquinolones/Macrolides								
Ciprofloxacin	400	RTU	0	-	-	-	-	0 (2)
Glebecefloxacin	800	RTU, DSW, NS	0	0	-	280.8 (60 mL)	280.8 (60 mL)	280.8 (1)
Azithromycin	500	DSW, NS	-	114	-	-	599 (250 mL)	1663 (1)
Anti-MRSA Agents								
Vancomycin	1000	RTU, DSW, NS	788	0	-	885 (250 mL)	885 (250 mL)	2541 (6)
	2000	DSW, NS	-	0	-	-	1770 (500 mL)	3582 (3)
Linezolid	600	NS	-	0	212.4	388.4	-	388.4 (1)
	1200	RTU	118.1186*	-	-	-	1186 (300 mL)	2282 (3)
Ceftazidime	600	DSW, NS	-	0	247.8	424.8	-	1272 (3)
Doxycycline	100	DSW, NS	-	0	-	388.4	-	180 (3)
Clindamycin	600	RTU, DSW, NS	0	0	177	324	-	1425 (6)
	800	RTU, DSW, NS	2	0	177	354	-	1480 (6)
Sulfamethoxazole-trimethoprim	1675-375	DSW	-	0	-	-	-	17 (6)
Mitrofurantoin								
Mitrofurantoin	500	RTU	226	-	-	-	-	1230 (6)

Abbreviations: RTU, room temperature; DSW, distilled water; NS, normal saline; DS, normal saline at 0.9% (0.9%); RTU, room temperature.
 *Values derived from immediate single-dose vial (single sodium content may vary slightly between manufacturers).
 †Intrinsic sodium content of antibiotic plus sodium content in NS, 177 mg sodium per 100 mL NS. 204 mg sodium per 100 mL NS, 0.16% is a recommended volume for reconstitution per manufacturer; sodium content from the solvent is also included.
 ‡Sodium (mg) per liter in 100 mL NS or other volume of 100% sterile diluent with appropriate drug concentration per manufacturer; values are rounded to the nearest 0.1 mg.
 †††Solutions available in both 100 and 200 mg sodium per DSW (14 mg sodium).
 ††††Based on 5-mg/kg trimethoprim component; weight of 75 kg.
 †††††Sodium content from excipients negligible.

From Wang, P, Nguyen, C, Pham, et al. Sodium Content of Intravenous Antibiotic Preparations. *Open Forum Infectious Diseases*, Volume 6, Issue 12, December 2018. <https://doi.org/10.1093/ofid/ofy308>

Test Your Knowledge

Would you like to win a \$10 gift certificate to the sunshine café? Complete the following post-newsletter quiz and submit to hs-ASP@ucdavis.edu to be entered into a raffle for a free lunch.

A 50 year old man with morbid obesity and diabetes presents to the ED from home with chest pain and SOB is found to have a STEMI with new onset heart failure. He is intubated for respiratory failure, undergoes cardiac catheterization with stent placement, and is admitted to the cardiac ICU where he responds to diuresis and medical therapy over the following days. On HD5 he develops fevers, chills, and increased respiratory secretion production for which he undergoes CXR. A new right-sided infiltrate is noted. He is otherwise stable and non-toxic appearing though his WBC count trended up from 8.5 to 10 this morning. He has no history of prior infections or drug use. His MRSA nasal swab was negative 5 days prior. He is started on intravenous antibiotics.

1. Which antibiotic regimen would be most appropriate?
 - a. Meropenem 1 g IV q8hrs
 - b. Cefadroxil 500 mg IV q12hrs
 - c. Ceftriaxone 2 g IV q24hrs + Azithromycin 500 mg IV x 1

d. Cefepime 2g IV q8hrs

2. True or False: The patient's nurse asks whether the patient needed to have been treated with vancomycin as well given the pneumonia's hospital onset. Given the patient's stability, relatively mild illness, and absence of MRSA risk factors or colonization within the prior 7 days vancomycin was not necessary as the probability of MRSA infection was very low.

3. The patient rapidly improves, he is extubated a few days later, and he is ready for discharge by HD9. He has tolerated his antibiotics and is now tolerating a full cardiac diet without event. His most recent QTc on EKG is 410. Which regimen would be best to complete his antibiotic treatment for his ventilator acquired pneumonia (VAP)?

a. Trimethoprim-Sulfamethoxazole 1 DS tab PO daily

b. Azithromycin 250 mg PO daily

c. Levofloxacin 500 mg PO daily

d. Amoxicillin 500 mg PO twice daily

4. Which IV antibiotics come with more than the daily recommended allowance of sodium (>2.3 g) in a typical daily dosing?

a. Penicillin G, Ampicillin, Nafcillin, Piperacillin-Tazobactam, Linezolid

b. Piperacillin-Tazobactam, Vancomycin, Trimethoprim-Sulfamethoxazole

c. Ciprofloxacin, Levofloxacin, Piperacillin-Tazobactam

d. None of the above

Answers to last newsletter's quiz: 1. A, 2. True, 3. B, 4. C

ASP Gold Star Recognition



The following staff have been recognized by the Antimicrobial Stewardship team for their dedication to combating antimicrobial resistance and commitment to the principles of antimicrobial stewardship:

- Blair Colwell (Peds)
- Swati Patki (IM)

Meet the Stewardship Team



Alan Koff is an Infectious Diseases physician working with the Antimicrobial Stewardship team. After completing medical school in Australia, he moved to Connecticut where he did Internal Medicine residency and Infectious Diseases fellowship. He has an interest in clinical ID and treatment of infections in patients who are immunosuppressed. In his free time, he enjoys hiking and spending time with his family and dogs.

Fun Microbe Fact

Pseudomonas natriegens, an ocean-dwelling bacterium, has one of the shortest generation times known. It can go from birth to reproduction in 10 minutes flat. In five hours a single cell could theoretically give rise to more than 1 billion offspring.

Read more: <https://www.discovermagazine.com/health/20-things-you-didnt-know-about-bacteria>

Contact Us

The Antimicrobial Stewardship Program Team Members

Adult ASP Physicians:

- Stuart Cohen, MD
- Archana Maniar, MD
- Sarah Waldman, MD
- Scott Crabtree, MD
- Natascha Tuznik, DO
- Christian Sandrock, MD
- Larissa May, MD
- Angel Desai, MD
- Naomi Hauser, MD
- Alan Koff, MBBS

Pediatric ASP Physicians:

- Natasha Nakra, MD
- Jean Wiedeman, MD
- Ritu Cheema, MD
- Elizabeth Partridge, MD

ASP Pharmacists:

- Monica Donnelley, PharmD, BCIDP

- Nicola Clayton, PharmD, BCIDP
- Jen Curello, PharmD, BCIDP
- James Go, PharmD

Antibiotic questions? Contact us.

See the On-Call Schedule for the ASP attending/fellow of the day

Contact the ASP Pharmacist at 916-703-4099 or Vocera "Infectious Disease Pharmacist"