

UC Davis Health Antimicrobial Stewardship Program - Vol 2 Issue 3

Rhodotorula mucilaginosa (formerly Rhodotorula rubra) growing on Sabouraud agar. Colonies may vary from orange to pink to a vibrant coral. It is not particularly virulent and is rarely associated with clinical disease, but case reports of opportunistic infection have been reported. From: http://thunderhouse4-yuri.blogspot.com/2015/

Volume 2, Issue 3

July 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.

In This Issue

- Hospital Acquired Pneumonia: What You Need to Know
 - CAP for Kids
 - ASP Website Launched
- Extended Infusion Beta-Lactams: Better Pharmacokinetics
 - Test Your Knowledge
 - ASP Gold Star Recognition
 - Meet the Stewardship Team

Hospital-Acquired Pneumonia (HAP)

HAP Diagnosis

- Clinical symptoms of pneumonia (e.g., fever, cough, dyspnea, pleuritic chest pain) **PLUS** hypoxia **PLUS** a new radiographic infiltrate that develops at least 48 hours after hospitalization
- Microbiology: either community-associated (e.g., Streptococcus pneumoniae, Haemophilus influenzae) or healthcare-associated pathogens (e.g., Enterobacteriaceae spp., Pseudomonas aeruginosa, Staphylococcus aureus); Legionella is an uncommon cause

- Enterococcus spp. and Candida spp. that grow in sputum cultures are highly likely to be colonizers and do not require treatment
- Obtain sputum Gram-stain and culture whenever possible
- Obtain blood cultures for severely ill patients
- Consider obtaining Legionella urine antigen in patients with immunocompromise or severely ill
- Consider obtaining viral respiratory testing during respiratory virus season
- Consider non-infectious causes such as pulmonary embolism, volume overload, at electasis

HAP Treatment

Empiric therapy

- Coverage for Enterobacteriaceae spp., P. aeruginosa, streptococci, and S. aureus with an antipseudomonal β-lactam; consider combination therapy with an aminoglycoside or fluoroquinolone 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 HAP-targeted therapy
- Use sputum culture results to narrow therapy
 - Discontinue antibiotics directed at MRSA and Pseudomonas spp. if not recovered
- If cultures have not been obtained, base the decision to de-escalate therapy on clinical judgement and individual patient risk factors
- After clinical improvement is observed and oral medications can be tolerated, consider conversion from intravenous to oral therapy
 - Levofloxacin 750 mg PO q24hrs

HAP Treatment Duration

• 7 days if clinical response by day 3

References

- 1. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61-e111. PMID: 27418577.
- 2. Wooten DA, Winston LG. Risk factors for methicillin-resistant *Staphylococcus aureus* in patients with community-onset and hospital-onset pneumonia. Respir Med. 2013 Aug;107(8):1266-70. PMID: 23756035.
- 3. Robicsek A, Suseno M, Beaumont JL, et al. Prediction of methicillin-resistant *Staphylococcus aureus* involvement in disease sites by concomitant nasal sampling. J Clin Microbiol. 2008 Feb;46(2):588-92. PMID: 18057132.
- 4. Dangerfield B, Chung A, Webb B, et al. Predictive value of methicillin-resistant *Staphylococcus aureus* (MRSA) nasal swab PCR assay for MRSA pneumonia. Antimicrob Agents Chemother. 2014;58(2):859-64. PMID: 24277023.
- 5. Klompas M, Li L, Menchaca JT, et al. Ultra-short-course antibiotics for patients with suspected ventilator-associated pneumonia but minimal and stable ventilator settings. Clin Infect Dis. 2017 Apr 1;64(7):870-876. PMID: 28034888.
- 6. Safdar N, Handelsman J, Maki DG. Does combination antimicrobial therapy reduce mortality in Gram-negative bacteraemia? A meta-analysis. Lancet Infect Dis. 2004 Aug;4(8):519-27. PMID: 15288826.
- 7. Paul M, Soares-Weiser K, Grozinsky S, et al. Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropaenia. Cochrane Database Syst Rev. 2002;(2):CD003038. PMID: 12076467.
- 8. Paul M, Soares-Weiser K, Leibovici L. Beta lactam monotherapy versus beta lactamaminoglycoside combination therapy for fever with neutropenia: systematic review and meta-analysis. BMJ. 2003 May 24;326(7399):1111. PMID: 12763980.
- 9. Paul M, Benuri-Silbiger I, Soares-Weiser K, et al. Beta lactam monotherapy versus beta lactamaminoglycoside combination therapy for sepsis in immunocompetent patients: systematic review and meta-analysis of randomised trials. BMJ. 2004 Mar 20;328(7441):668. PMID: 14996699.
- 10. Paul M, Silbiger I, Grozinsky S, et al. Beta lactam antibiotic monotherapy versus beta lactamaminoglycoside antibiotic combination therapy for sepsis. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003344. PMID: 16437452.
- 11. Marcus R, Paul M, Elphick H, et al. Clinical implications of β-lactam-aminoglycoside synergism: systematic review of randomised trials. Int J Antimicrob Agents. 2011 Jun;37(6):491-503. PMID: 21292449.

- 12. Paul M, Leibovici L. Combination antibiotic therapy for *Pseudomonas aeruginosa* bacteraemia. Lancet Infect Dis. 2005 Apr;5(4):192-3; discussion 193-4. PMID: 15792730.
- 13. Chastre J, Wolff M, Fagon JY, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. JAMA. 2003 Nov 19;290(19):2588-98. PMID: 14625336.
- 14. Vardakas KZ, Mavros MN, Roussos N, et al. Meta-analysis of randomized controlled trials of vancomycin for the treatment of patients with gram-positive infections: focus on the study design. Mayo Clin Proc. 2012 Apr;87(4):349-63. PMID: 22469348.
- 15. Walkey AJ, O'Donnell MR, Wiener RS. Linezolid vs glycopeptide antibiotics for the treatment of suspected methicillin-resistant *Staphylococcus aureus* nosocomial pneumonia: a meta-analysis of randomized controlled trials. Chest. 2011 May;139(5):1148-1155. PMID: 20864609.
- 16. Kalil AC, Klompas M, Haynatzki G, et al. Treatment of hospital-acquired pneumonia with linezolid or vancomycin: a systematic review and meta-analysis. BMJ Open. 2013 Oct 14;3(10):e003912. PMID: 24127058.
- 17. Kalil AC, Murthy MH, Hermsen ED, et al. Linezolid versus vancomycin or teicoplanin for nosocomial pneumonia: a systematic review and meta-analysis. Crit Care Med. 2010 Sep;38(9):1802-8. PMID: 20639754.

CAP for Kids

Treatment of Pediatric Community Acquired Pneumonia (CAP)

Most pediatric respiratory infections, especially in young children <5 years of age, are due to viral pathogens. If a patient clinically or by radiologic evaluation is deemed to have community-acquired bacterial pneumonia (CAP), here are a few things to keep in mind:

1) Streptococcus pneumoniae is the most common etiology of CAP in children.

Despite the success of routine childhood vaccination in decreasing invasive pneumococcal disease, *Strep pneumoniae* remains the most common etiology of CAP in children. Other common causes of CAP in children include Group A streptococcus, *Staphylococcus aureus*, and in children >age 5 years, *Mycoplasma pneumoniae*.

2) High dose amoxicillin (or ampicillin) remains the most appropriate empiric choice for treatment of CAP.

The introduction of PCV-13 has led to a significant decrease in resistant circulating pneumococcal strains (including 19A); thus, the majority of CAP in children will be due to penicillin-susceptible strains. Even in pneumococcal strains with penicillin-binding protein (PBP) mutations, using high-dose amoxicillin (90-100mg/kg/day) can usually overcome resistance.

3) TID dosing of amoxicillin is more effective than BID dosing.

Beta lactam drugs, including amoxicillin, result in more bacterial killing when levels are maintained throughout a 24-hour period. More frequent dosing can improve bacterial killing and is preferred for treatment of CAP.

4) Oral cephalosporins are inferior to amoxicillin treatment for treatment of CAP.

Oral cephalosporins (such as cefdinir) have short half-lives, are poorly absorbed, and highly protein bound, leading to low serum concentrations and decreased effectiveness. They are not equivalent to IV ceftriaxone. If used for penicillin allergic patients, more frequent dosing is recommended to increase serum concentrations. Other options for penicillin allergic patients include clindamycin and doxycycline (if age>7 years).

5) Appropriate length of therapy for mild-moderate CAP is 5-7 days.

There is evidence that shorter courses of antibiotics for CAP (5-7 days) are as effective as longer courses of antibiotics. In general, shorter duration is preferred to minimize possible side effects to an individual patient and decrease overall antimicrobial resistance.

- For a healthy outpatient -> consider 5 days
- For an inpatient with rapid response -> consider 5 days
- For an inpatient with underlying comorbidities -> consider 7 days

References:

- 1. Bradley et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: Clinical practice guidelines by PIDS and IDSA. *CID* October 2011.
- 2. Messinger AI, et al. Management of pediatric community-acuired bacterial pneumonia. *Peds in Review* Sept 2017.
- 3. Klugman et al. Impact of existing vaccines in reducing antibiotic resistance: Primary and secondary effects. *PNAS* Dec 2018.

ASP Website Launched



UC Davis Medical Center's ASP has launched its own antimicrobial stewardship homepage accessible at work and at home. With links to current national and local guidelines, quick topic reviews, infection prevention material, and convenient email access to an ASP team member, it's a one stop antimicrobial stewardship shop.

The website can be found at: https://health.ucdavis.edu/antibiotic-stewardship/

Or type "antibiotics" into your Internet Explorer address bar from a work computer to be linked directly!

santimicrobial stewardship tip

EXTENDED INFUSION BETA-LACTAMS

BACKGROUND

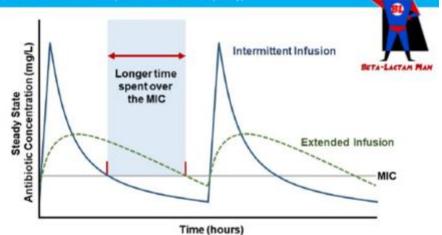
- Beta-lactam antibiotics exhibit time-dependent bactericidal activity, meaning that bacterial killing is enhanced when serum drug concentrations are maintained above the MIC for longer periods of time.
- Extended infusion dosing is a strategy of prolonging the infusion time to maximize the time over MIC

WHY USE EXTENDED INFUSION?

Taking advantage of this time-dependent property, extended infusion beta lactams are associated with:

- · Increased efficacy!
- · Reduced adverse drug reactions! (often peak-dependent)
- . Decreased cost! (can be dosed less frequently)

Extended infusion is the preferred way to administer beta-lactams!



WHEN TO DO EXTENDED INFUSION?

Intermittent-Infusion

Duration: 30-60 min

Candidates:

- Multiple concurrent IV medications
- Limited IV access
- ESRD

Extended-Infusion

Duration: 3-4 hours Candidates:

- Critically ill
- Hyperdynamic state
- Fluctuating renal function

EXTENDED INFUSION ORDERSETS AT DAVIS

-	Name		
P	CeFAZolin IV 4-Hour Extended Infusion	4	Nafcillin IV 4-Hour Extended Infusion
P	Celepime IV 4-Hour Extended Infusion	2	Piperacillin/Tazobactam IV 4-Hour Extended Infusion
2	Ceftazidime IV 4-Hour Extended Infusion	2	Nafcillin IV Extended Infusion
2	Meropenem IV Extended Infusion	2	Penicillin G Potassium IV Extended Infusion

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 <a href="https://doi.org/10.2016/nc.2016/

A 50 year old man with morbid obesity and diabetes presents to the ED from home with chest pain and and is found to have a STEMI. He is admitted for further treatment. Nearing the end of his admission he develops fevers, chills, and cough for which he undergoes CXR. A 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 2g 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 be treated with vancomycin as well given the pneumonia's hospital onset. Given the patient's stability, 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 and he is ready for discharge by the next hospital day. 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 hospital acquired pneumonia (HAP)?
- a. Linezolid 600 mg PO q12hrs x 14 day total antibiotic course
- b. Cefpodoxime 200 mg PO q12hrs x 14 day total antibiotic course
- c. Trimethoprim-sulfamethoxazole 1 DS tab PO q12hrs x 7 day total antibiotic course
- d. Levofloxacin 750 mg PO q24hrs x 7 day total antibiotic course

- 4. A 5 year old male with no major past medical history but none of the routine childhood vaccinations presents to the ER with fever and productive cough progressively worsening for a few days. His chest x-ray shows lower lobe consolidation. Sputum gram stain show diplococci suggestive of *Streptococcus pneumoniae*. He is started on empiric antibiotics. What is the optimal antibiotic regimen?
- a. High dose amoxicillin (90-100 mg/kg/day) divided into q12h dosing
- b. Cefdinir 300 mg q12h
- c. High dose amoxicillin (90-100 mg/kg/day) divided into q8h dosing
- d. Clindamycin 30-40 mg/kg/day divided into q8h dosing

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

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:

- Kristin Hoffman (Peds)
- Costa Demiriades (Peds)
- Chris Adams (ED)

Meet the Stewardship Team

After getting her bachelor's degree in Community Health at Brown University and medical degree at UC San Francisco, **Sarah Waldman** started at UC Davis in 2011 as an internal medicine resident. Since joining the faculty after completing her Infectious Disease fellowship at UCD, she has been involved in all aspects of clinical infectious diseases. She serves as the Director of the Outpatient Parenteral Antimicrobial Therapy program where she manages patients who are discharged on intravenous antimicrobials from the hospital. In her free time, she enjoys traveling, reading, and spending time with her two toddlers.

Fun Microbe Fact

Exactly which bacteria choose to take up residence in your gut is determined, in part, by your genes. In 2014, scientists examined more than 1,000 fecal samples from 416 pairs of twins. Identical twins, who share 100 percent of their DNA, had more similar populations of gut microbes than did non-identical twins. Moreover, some types of bacteria seemed to be especially susceptible to the genetics of their human host. One of the most heritable types was a family of bacteria called *Christensenellaceae*, which are more abundant in lean people than in obese people. When the scientists inoculated mice with these bacteria, they gained less weight and put on less fat than mice without the bacteria. The researchers suggested that one way your genes influence your chances of becoming obese is by shaping your microbiome.

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, MD
- Christian Sandrock, MD
- Larissa May, MD

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"