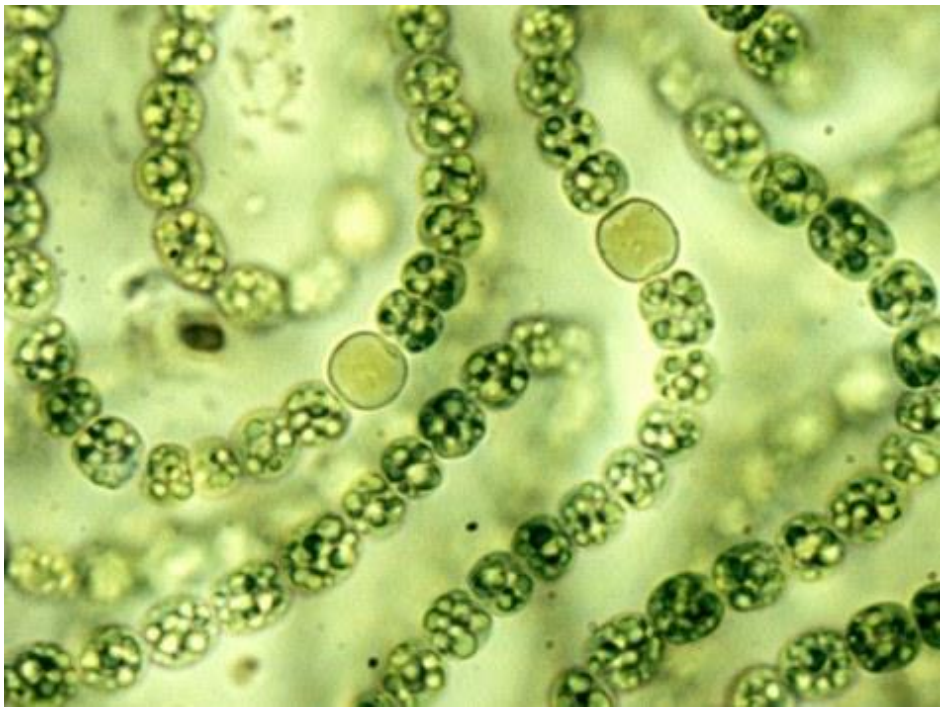

UC Davis Health Antimicrobial Stewardship Program

Cyanobacteria are aquatic and photosynthetic and can grow in colonies large enough to see. They have the distinction of being the oldest known fossils, more than 3.5 billion years old, in fact!

Cyanobacteria are important providers of nitrogen fertilizer in the cultivation of rice and beans. The cyanobacteria have also been tremendously important in shaping the course of evolution and ecological change throughout earth's history. The oxygen atmosphere that we depend on was generated by numerous cyanobacteria during the Archaean and Proterozoic Eras.

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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

Management of *Clostridium difficile* Infection (CDI)

CDI Diagnosis

Clinical spectrum of infection ranges from watery diarrhea with lower abdominal pain, cramping, and nausea (with or without low-grade fevers and leukocytosis) to severe or fulminant colitis.

Case definition: ≥ 3 unformed stools in a 24-hour period without an alternative explanation and positive stool toxin test for *C. difficile.*

Patients with severe disease may have ileus without stool output; these patients generally have colitis on imaging, abdominal pain/distention, and systemic illness.

About 30% of patients have recurrent CDI within 30 days of treatment (retest to confirm the diagnosis).

***C. difficile* testing recommendations -**

- Appropriate test at UC Davis Medical Center is "C diff stool toxin EIA"
- Do not test formed stool samples as this will detect colonization
- Confirm patient has not received a laxative or new tube feeds in the previous 48 hours
- Do not test infants <1 year of age
- Do not repeat testing within 7 days due to very low yield
- Do not obtain "tests of cure" due to false positive risk

CDI Treatment

Discontinue antibiotics not used for CDI treatment whenever possible.

If antibiotic therapy is still needed, select the narrowest agent possible and avoid agents with a strong association with CDI (i.e., fluoroquinolones, clindamycin, and third- and fourth-generation cephalosporins).

Discontinue gastric acid suppression medications whenever possible.

Do not prescribe anti-motility agents.

Non-severe CDI -

- Adults: vancomycin (125 mg PO 4 times a day) for 10 days
- Children: metronidazole (7.5 mg/kg/dose (max dose: 500 mg) PO 4 times a day) or vancomycin (10 mg/kg (max dose: 125 mg) PO 4 times a day) for 10 days

Severe (WBC ≥ 15,000 cells/mL and/or serum creatinine ≥1.5 mg/dL) or fulminant CDI (hypotension, intestinal perforation, toxic megacolon) -

- Obtain abdominal imaging and prompt surgical consultation
- Adults: vancomycin 125 mg PO/NG 4 times a day for severe colitis; vancomycin 500 mg PO/NG 4 times per day for fulminant colitis for 10 days
- Children: vancomycin 10 mg/kg/dose PO/NG 4 times a day for severe or fulminant colitis for 10 days
- If ileus present, vancomycin can also be administered via rectum as a retention enema, along with metronidazole intravenously for 10 days

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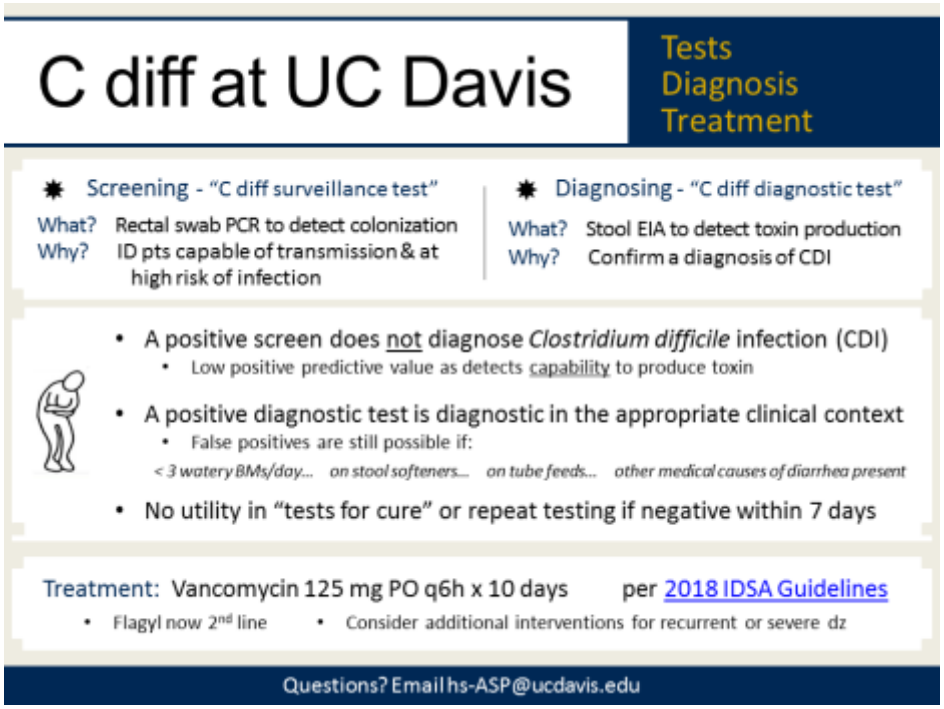
C diff Screening at UC Davis Medical Center



Think Twice When Prescribing Vancomycin with Piperacillin-Tazobactam (Zosyn)

Health care providers often reach for the combination of vancomycin and piperacillin-tazobactam (Zosyn) when they would like to provide broad spectrum coverage. This combination provides both broad gram positive and gram negative, as well as anaerobic coverage. Recent literature has brought to light the concern for increased risk of acute kidney injury (AKI) due to the combination of vancomycin and piperacillin-tazobactam. Vancomycin alone is known to cause nephrotoxicity, however the addition of piperacillin-tazobactam increased the risk of AKI by 250% in 1 study [1].

A recent prospective multicenter study [2] additionally examined patients >18 years old (n=242) receiving vancomycin and piperacillin-tazobactam (V+PT), and compared this to patients receiving vancomycin and cefepime (VC), or vancomycin and meropenem (VM). The incidence of AKI in the patients receiving V+PT was 29.8%, as opposed to 14.9% in the VM group, and 5.9% in the VC group. AKI was more likely in patients receiving V+PT if they were concomitantly receiving loop diuretics or vasopressors, or had a vancomycin trough of >30mg/L.

This phenomenon has been observed in pediatrics as well. A recently published retrospective study [3] demonstrated that AKI developed in 28.9% of pediatric patients who received V+PT, as opposed to 7.9% in patients who received VC. The median time to development of AKI was also earlier (7 days) in the

V+PT group as compared to the VC group (15 days), although this was not statistically significant. The mechanism of this nephrotoxicity is still unclear.

Overall, providers should be cognizant of the increased risk of AKI when prescribing vancomycin with piperacillin-tazobactam, especially in patients with pre-existing renal dysfunction or who are receiving other nephrotoxic agents. More frequent monitoring of renal function should be considered in patients who are on this combination.

References

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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 with chest pain, and is found to have a NSTEMI. He is admitted for further treatment. Upon admission his C diff rectal swab PCR returns positive and he is placed on Contact Enteric isolation. For reasons that are not entirely clear a urinalysis is obtained on hospital day 2, returns positive for leukocyte esterase, and the patient is started on ceftriaxone for UTI. He had not reported any urinary symptoms. By hospital day 5 he is ready for discharge, but develops new diarrhea having 6 watery BMs overnight. He is otherwise stable and well. A C diff stool toxin EIA is obtained which returns positive. What antibiotic regimen should he be started on? This is his first episode of CDI.

1.

a. Metronidazole 500 mg PO q8hrs x 10 days

b. Vancomycin 125 mg PO q6hrs x 10 days

c. Vancomycin 125 mg PO q6hrs + Metronidazole 500 mg PO q8hrs x 10 days

d. Metronidazole 500 mg IV & PO q8hrs x 10 days

2. True or False: The patient's nurse asks whether the patient should have been treated upon admission because his screening C diff rectal swab was positive. Because the patient was not having any symptoms consistent with CDI at the time, however, the patient is only colonized with *Clostridioides difficile* and treatment is not indicated.

3. While reviewing the patient's chart you see that in addition to his new cardiac medications he is also on insulin and pantoprazole from prior to the hospitalization. It appears he started taking the pantoprazole a few years ago for heartburn and has taken it ever since. The overnight resident had also started him on PRN loperamide after his diarrhea started. He remains on his ceftriaxone with no end date ordered. What additional interventions can be made which may improve outcomes?

a. Stop the patient's loperamide

b. Stop the patient's PPI

c. Stop the patient's ceftriaxone

d. Stop all of the above

4. A 59 year old male with CKD stage III, paroxysmal atrial fibrillation, and chronic alcohol dependence with prior withdrawal symptoms presents to the ER with palpitations, dizziness and tremors. After a long detox and 10 days after admission he develops a fever, cough, hypotension, leukocytosis, and his chest x-ray shows lower lobe consolidation. Procalcitonin is 1.51 and he is requiring intermittent fluid boluses with pending transfer to the MICU. He is he is started on empiric antibiotics. What combination of antibiotics would provide adequate coverage while posing the least risk for AKI?

a. Vancomycin alone

b. Vancomycin + Piperacillin-Tazobactam

c. Vancomycin + Cefepime

d. Cefepime alone

Answers to last newsletter's quiz: 1. B, 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:

Brittany Chatterton (IM)

Tameka Coy (IM)

Maria Galkin (IM)

Maricela Rangel-Garcia (IM)

Meet the Stewardship Team

Larissa May is a passionate advocate for antimicrobial stewardship and patient safety in general. After obtaining all her training at the George Washington University in Washington DC (BS in Chemistry, MD, Emergency Medicine Residency, followed by an MS in public health microbiology, and a second one in clinical and translational research) and completing nine years on faculty there, she was recruited to start one of the first emergency department antibiotic stewardship programs in the country in 2015. This work expanded to include all of outpatient antibiotic stewardship at UC Davis Health in 2017. In addition to leading ambulatory antibiotic stewardship efforts for the ASP team, she chairs the Infection Prevention Committee and is involved in mentoring junior faculty in career development and scholarly activities. She enjoys collaborating with other universities, health departments, and others in developing and implementing outpatient antibiotic stewardship programs and using implementation science methods. When she is not here at UC Davis or on the road lecturing, she enjoys spending time with her husband, three children (one grown), exploring California's outdoor beauty and food and wine and reading.

Fun Microbe Fact

In the Home Microbiome Project published in Science in 2014, scientists detailed the longitudinal microbiome evolution of 7 families and their living environment over the course of 6 weeks. Each family

had a signature microbiome that was readily identifiable even by tests performed of samples in their living environment (doorknobs, light switches, etc). Whenever a family member left the home for a few days their microbiome fingerprints began to fade. When 3 of the families moved houses their signature microbiome became detectable in the new home almost immediately.

Contact Us

The Antimicrobial Stewardship Program Team Members

Adult ASP Physicians:

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ASP Pharmacists:

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- 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"