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Atrium Health
Wake Forest Baptist

Center for Antimicrobial Utilization, Stewardship, and Epidemiology

Clostridioides difficile Infection (CDI)

Adult Diagnosis and Management Guidelines

Diagnosis and Presentation

- Common signs and symptoms: Fever, abdominal cramping and pain, elevated WBC count, and severe diarrhea. Diarrhea is the key clinical feature of disease and can range from mild to moderate, fulminant, and sometimes fatal pseudomembranous colitis. Rarely (<1%), a symptomatic patient with ileus and colonic distention will present with minimal or no diarrhea.
- Who should be tested?
    - Patients with unexplained and new onset of ≥3 loose stools in 24 hours along with other signs or symptoms of CDI. To adequately assess a patient's risk of having CDI, consideration should be given to iatrogenic causes of diarrhea, including medications and enteral feeds. The pre-test probability of a patient having CDI is much lower for these patients.
    - The pre-test probability of CDI is diminished if the patient has no recent history of antibiotic exposure, including surgical prophylaxis. Clinical judgment should be used in conjunction with laboratory data to determine patient's likelihood of CDI.
    - Formed stool specimens will be rejected by the lab, as CDI tests are not approved for testing formed stools.
    - Do not repeat testing within 7 days during the same episode of diarrhea. Other causes of diarrhea should be investigated if diarrhea is persistent after a negative *C. difficile* test.
    - *C. difficile* testing should not be performed as a test of cure. Tests may remain positive even after effective treatment.
- Diagnosis is best supported by presence of signs or symptoms of CDI plus a positive stool test for the organism/toxin *OR* colonoscopic or histopathologic findings of pseudomembranous colitis.
- A multi-step approach is recommended for *C. difficile* testing. At AHWFB, a *C. difficile* EIA test is used which simultaneously tests for the antigen and the toxin. Results of both the antigen and the toxin EIA tests are reported together.
- Polymerase chain reaction (PCR) testing for *C. difficile* is overly sensitive and is no longer recommended alone due to risk of false-positives. The PCR may be useful to adjudicate discrepant EIA results among patients with clinical features strongly suggestive of CDI. However, the decision to adjudicate should not delay initiation of therapy for such patients. PCR testing for *C. difficile* requires prior authorization from CAUSE or via formal ID consultation.
- Enteric Contact Precautions should be in place for patients with suspected CDI. *C. difficile* colonization is frequently acquired through health system exposure, emphasizing the importance of infection control measures. Handwashing with antimicrobial soap and water is preferred over alcohol-based products. Contact precautions should continue for at least 48 hours after cessation of diarrhea.

Risk factors

- Recent antimicrobial or antineoplastic agent use (in the previous 12 weeks)
- Advanced age (≥65 years)
- Duration of hospitalization
- Severity of illness
- Recent health care exposure (in the previous 12 weeks)
- Alteration in the gastrointestinal tract (e.g., diverticulosis, inflammatory bowel disease, GVHD, GI surgery)
- Immunocompromised (e.g., solid organ or stem cell transplant, hematologic malignancies, active chemotherapy)
- Chronic kidney disease

*Almost every antibiotic has been associated with *C. difficile* infection (high risk: 3rd/4th generation cephalosporins, fluoroquinolones, carbapenems, and clindamycin)

Treatment Principles

Key Points	Rationale
Discontinue offending antibiotics or de-escalate as soon as possible	Concurrent antibiotics may interfere with resolution of CDI and may increase the risk of infection recurrence.
Surgical consultation for critically ill patients	Should be considered early in patients with megacolon, colonic perforation, acute abdomen, or patients with septic shock and associated organ failure
Avoid gastric acid suppression if possible	Gastric acid suppression, especially with proton pump inhibitors, is a risk factor for CDI, in both hospitalized and ambulatory patients. Re-evaluation of the need for such therapies should take place at regular intervals.
Avoid anti-peristaltic agents (e.g., loperamide)	Use of anti-peristaltic agents may obscure symptoms and can theoretically precipitate toxic megacolon.
Probiotics and cholestyramine are likely of little to no value	There is insufficient data to recommend probiotics as adjunctive treatment of CDI. Cholestyramine has the potential to bind oral vancomycin and reduce its effectiveness.

Antibiotic therapy for *Clostridioides difficile* Infection

Clinical Definition	Supportive Data	Recommended Treatment
Initial episode, non-severe	Leukocytosis with WBC count <15,000 cells/mL ***AND*** serum creatinine <1.5 mg/dL	• Preferred: Vancomycin 125 mg orally 4 times daily for 10 days • Alternative if vancomycin unavailable or impractical: Metronidazole 500 mg orally 3 times daily for 10-14 days
Initial episode, severe	Leukocytosis with WBC count ≥ 15,000 cells/mL ***OR*** serum creatinine >1.5 mg/dL[a]	• Preferred: Vancomycin 125 mg 4 times daily for 10 days • Alternative for patients at high risk of CDI recurrence[b]: Fidaxomicin[c, d] 200mg orally 2 times daily for 10 days • If no improvement within 72-96 hours of medical management, consider EGS consultation.
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	• Vancomycin 500 mg orally 4 times daily. Metronidazole 500 mg IV every 8 hours should be administered together with vancomycin. If ileus, consider adding rectal instillation of vancomycin (500mg in 100mL 0.9% sodium chloride PR every 6 hours). • **Urgent EGS consultation should be obtained** • Consider ID and/or GI consultation for assistance with additional management
First recurrence (second episode)		• Vancomycin 125 mg orally 4 times daily for 10-14 days followed by a prolonged tapered vancomycin regimen (125 mg orally 2 times daily for 1 week, then once daily for 1 week, and then every 2-3 days for 2-8 weeks) • Alternative for patients at high risk of CDI recurrence[b]: Fidaxomicin[c, d] 200mg orally 2 times daily for 10 days
Second or subsequent recurrence		• Vancomycin 125 mg orally 4 times daily for 10-14 days followed by fecal microbiota transplantation if available • Alternative for patients at high risk of CDI recurrence[b]: Fidaxomicin[c, d] 200mg orally 2 times daily for 10 days • GI and/or ID consultation strongly recommended

a. For patients without pre-existing renal dysfunction

b. Patients at highest risk for recurrence are those severely immunocompromised and/or those with multiple CDI recurrence risk factors such as age ≥75 years, IBD, and surgical anatomical disruption.

c. Fidaxomicin requires prior authorization by CAUSE or formal ID consultation for inpatient use

d. Outpatient pharmacy benefit analysis should be performed to determine feasibility of continuing fidaxomicin in the outpatient setting before requesting prior authorization

Bezlotoxumab

- In a prospective, controlled clinical trial, the addition of bezlotoxumab to anti-C difficile therapy resulted in fewer cases of CDI recurrence. It had the greatest benefit among patients with the highest risk for CDI recurrence, including patients age ≥

65 years, immunocompromised, severe CDI or Zar score ≥2, and a history of one or more recurrences. However, the effect was relatively small (11% reduction in absolute percent of patients with recurrence versus placebo).

- Bezlotoxumab should be considered for patients with risk factors for CDI recurrence AND only after the patient has failed previous therapies, including fecal microbiota transplantation. Of note, bezlotoxumab is restricted to the Gastrointestinal (GI) and Infectious Diseases (ID) clinic settings.

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