

Clostridioides difficile Infection

About the Guideline

This guideline provides an overview of *Clostridioides difficile* infection (CDI) along with the diagnosis and treatment options. Recommendations for the control and prevention of outbreaks of CDI remain unchanged from previous publications.

Key Clinical Considerations

Become familiar with the recommendations and best-practice statements in this guideline. Although the greatest risk for CDI remains highest in hospitals and long-term care facilities, the number of community-associated CDI cases is increasing.

Diagnosis

- Only patients with signs and symptoms consistent with active CDI should have their stool tested for *Clostridioides difficile*.
 - Defined as unexplained and new-onset diarrhea with 3 or more unformed stools in a 24-hour period
- A testing algorithm should involve a two-step process that includes both a highly sensitive test and a highly specific test to assist in differentiating between colonization (presence of *C. difficile* in stool without clinical symptoms) and active infection.
 - Sensitive:
 - Nucleic acid amplification test (NAAT) detects the presence of *C. difficile* toxin genes (for example, via polymerase chain reaction).
 - Glutamate dehydrogenase (GDH) detects the presence of *C. difficile* bacterium but doesn't distinguish between toxic and nontoxic strains; GDH can be used in a two- or three-step screening process with subsequent toxin A and B testing; however, GDH testing is less sensitive than NAAT testing.
 - Specific:
 - Enzyme immunoassay (EIA) detects the presence of free *C. difficile* toxin.
- Repeat testing and testing for a cure is not recommended because individuals may have persistent shedding of *C. difficile* for as long as 4 weeks after completion of treatment and resolution of symptoms.

Treatment and Management

- If there is a strong suspicion of CDI before testing, empiric therapy should be considered regardless of the laboratory testing result.
- If oral antibiotics cannot reach a segment of a colon (for example, the ileus), vancomycin therapy delivered via enema should be added until patient improvement is noted.
- Avoid antiperistaltic agents to control diarrhea in untreated CDI and in patients with fulminant infection because these agents may obscure symptoms and precipitate complicated disease.
- Because of limited evidence supporting the use of probiotics to prevent CDI and some case reports of bloodstream infections with probiotic organisms in critically ill patients, probiotics are not recommended for primary prevention of CDI in patients being treated with antibiotics or for prevention of CDI recurrence (secondary prevention).

- Assess the appropriateness of antisecretory therapy in patients with CDI; if the indication for an antisecretory agent is appropriate, continue therapy.
- Patients with an initial episode of nonsevere CDI:
 - Criteria: Three or more new-onset, unexplained unformed stools in 24-hours plus any additional signs or symptoms not meeting severe or fulminant criteria
 - Treatment recommendations may be one of the following:
 - Oral vancomycin 125 mg four times daily for 10 days
 - Oral fidaxomicin 200 mg twice daily for 10 days
 - Oral metronidazole 500 mg three times daily for 10 days for initial nonsevere CDI in low-risk patients (for example, younger patients without hospital admission)
- Patients with severe CDI:
 - Criteria: Nonsevere symptoms plus one of the following:
 - White blood cell count greater than or equal to 15,000 cells/mm³
 - Serum creatinine greater than 1.5 mg/dL
 - Treatment recommendations for initial therapy of severe CDI include one of the following:
 - Vancomycin 125 mg orally four times per day for 10 days
 - Fidaxomicin 200 mg twice daily for 10 days
 - *Note:* Metronidazole should not be used for treatment of severe CDI.
- Patients with fulminant CDI:
 - Criteria: Severe CDI plus any of the following:
 - Hypotension or shock
 - Ileus
 - Megacolon
 - Treatment recommendations:
 - Supportive care, including volume resuscitation
 - Oral vancomycin 500 mg orally every 6 hours per day for the first 48 to 72 hours; if clinical improvement occurs, dose may be changed to 125 mg every 6 hours for 10 more days
 - Metronidazole IV 500 mg every 8 hours per day may be considered as combination therapy with oral vancomycin.
 - If the patient has ileus, rectal instillation of vancomycin (500 mg in 500 mL saline as enema) every 6 hours.
 - If surgical intervention is required, either total colectomy with an end ileostomy and stapled rectal stump or diverting loop ileostomy with colonic lavage and intraluminal vancomycin based on patient's projected response to surgery and surgeon's best judgment.
 - Fecal microbiota transplantation (FMT) should be considered for severe and fulminant CDI that is refractory to antibiotic therapy, especially for patients who are considered poor surgical risks.
- Patients with recurrent CDI (rCDI):

- Defined as recurrence of diarrhea and a confirmatory positive test (NAAT or EIA) within 8 weeks following the completion of initial therapy
- Antibiotic selection for a first recurrence rCDI is based on the initial course of therapy
- First episode of rCDI can be treated with one of the following:
 - Tapering/pulsed dose oral vancomycin regimen after initial course of fidaxomicin, vancomycin, or metronidazole
 - Oral fidaxomicin 200 mg twice daily for 10 days after initial course of vancomycin or metronidazole
 - Metronidazole is not recommended for treatment of rCDI.
- For second or more episodes of rCDI, FMT should be considered.
 - FMT is recommended for patients with three or more episodes of CDI (for example, initial CDI episode and rCDI two or more times).
 - Method of delivery for FMT is through colonoscopy (preferred) or capsules; delivery via enema may be an alternative if other methods are unavailable.
 - Repeat FMT is recommended for rCDI within 8 weeks of initial FMT.
 - Patients undergoing FMT should have follow-up at 4 to 8 weeks after FMT.
- Suppressive and prophylactic vancomycin for rCDI:
 - Long-term suppressive oral vancomycin may be used to prevent further rCDI in patients who are not candidates for FMT, who relapsed after FMT, or who require ongoing or frequent antimicrobial therapy
 - Oral vancomycin prophylaxis may be considered for patients at high risk for recurrence while receiving subsequent antibiotic therapy.
- Bezlotoxumab, a human monoclonal antibody that binds to *C. difficile* toxin B, should be considered for prevention of rCDI in patients at high risk for recurrence.
 - Patients 65 years or older with at least one of the following: second episode of CDI within past 6 months, immunocompromised, or severe CDI
 - Bezlotoxumab should be used with caution in patients with history of heart failure or severe underlying cardiovascular comorbidities.
- Patients with CDI and comorbid conditions:
 - Inflammatory bowel disease (IBD)
 - All patients should be tested for CDI if they experience an acute flare-up associated with diarrhea.
 - All patients should be treated with oral vancomycin 125 mg four times daily for a minimum of 14 days.
 - Immunosuppressive IBD therapy should not be held during treatment for CDI; IBD immunosuppressive may need to be optimized or increased if clinical symptoms do not lessen after initiation of CDI therapy.
 - FMT should be considered for rCDI in patients with IBD.
 - Pregnant, peripartum, and lactating patients
 - Patients should be treated with oral vancomycin.
 - Metronidazole is secreted in breast milk and therefore not recommended for breastfeeding mothers.
 - FMT should be delayed while patient is pregnant.

- Immunocompromised patients
 - Vancomycin or fidaxomicin are recommended for treatment of initial CDI episode.
 - If FMT is being considered for rCDI, immunocompromised patients should be tested for cytomegalovirus and Epstein-Barr virus before FMT and if seronegative, discussion about risk, benefits, alternatives to FMT.

Reference

Kelly, C. R., Fischer, M., Allegretti, J. R., LaPlante, K., Stewart, D. B., Limketkai, B. N., & Stollman, N. H. (2021). ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of Clostridioides difficile Infections. *The American journal of gastroenterology*, 116(6), 1124–1147. <https://doi.org/10.14309/ajg.000000000001278>