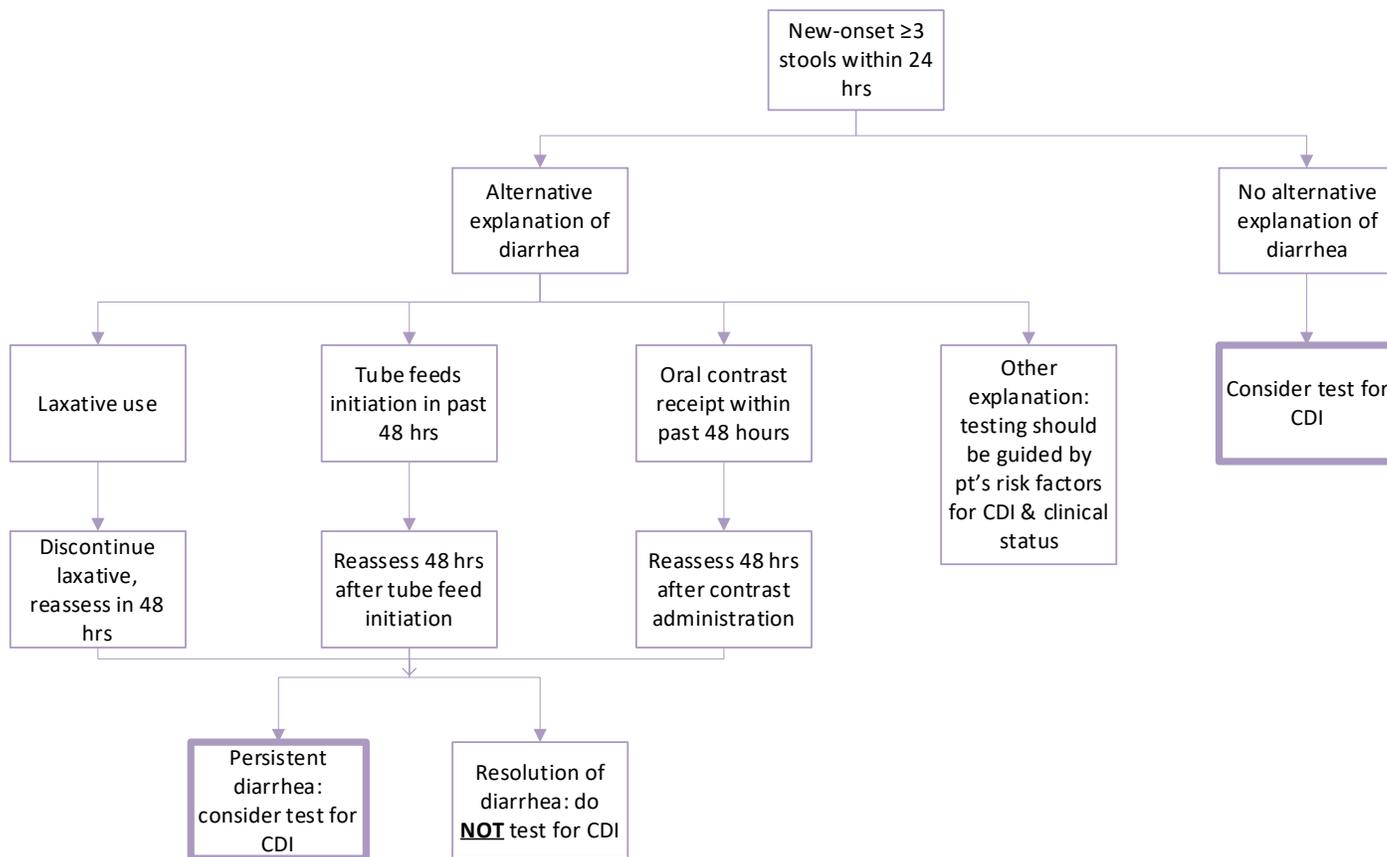




GUIDELINES FOR TREATMENT OF CLOSTRIDIUM DIFFICILE COLITIS IN ADULTS

Prior studies show that 3-26% of hospitalized patients are asymptotically colonized with *C. difficile*. Available assays are not able to distinguish between *C. difficile* infection and colonization, and treatment of asymptomatic colonization is not recommended.

Patients with new-onset diarrhea without an alternative explanation should be considered for CDI testing. Diarrhea is defined as ≥ 3 unformed stools in 24 hours. A large percentage of hospitalized patients have other reasons for diarrhea, such as laxatives, chemotherapy, and enteral tube feeds. When possible, one should consider first stopping therapies to which diarrhea may otherwise be attributed (e.g., laxatives), and then reassess prior to testing for CDI.



1. The “*Clostridium difficile* by PCR” assay is the preferred test for CDI. The “Gastrointestinal Pathogen Panel” is a multiplex PCR assay that, in addition to CDI, tests for 21 other primarily community-acquired gastrointestinal pathogens and costs ~3x more than the dedicated *C. difficile* by PCR” assay. The GI Panel is intended for use in patients with diarrhea that began prior to or within three days of hospitalization and there is concern for other etiologies aside from *C. difficile*. Both tests provide the same diagnostic information regarding *C. difficile*: a PCR and a toxin result. There is no role for performing both tests simultaneously or performing a *C. diff* PCR after a positive GI Panel result. These practices do not change management, lead to overutilization of testing resources, and should be avoided. Either assay may remain positive for up to 30 days after successful treatment; tests of cure should not be performed. As such, orders for repeat testing within 14 days of positive will be rejected by Microbiology Lab. In addition, repeat testing within 7 days of a negative test will also be rejected by Microbiology Lab due to low likelihood of acute infection within this time frame. The ordering provider will be notified by pager, and in situations with a significant change in clinical status accompanied with high clinical suspicion, may contact the lab to request that testing proceed.

PCR Result	EIA Toxin Result	Interpretation
Negative	--	No <i>C. difficile</i> present. The negative predictive value of this test for ruling-out <i>C. difficile</i> -associated diarrhea approaches 99%
Positive	Positive	Toxigenic <i>C. difficile</i> present.
Positive	Negative	The gene that produces <i>C. difficile</i> toxin is detected, but toxin is not detected.

This may represent either colonization or active clinical infection. Clinically correlate to determine if treatment is warranted.

Treatment of *Clostridium difficile* colitis

For all patients:

- Discontinue/change antibiotics if possible.
- Avoid PPI/H2 blockers without an appropriate indication.
- [Implement infection control measures](#)

Clinical Setting	Initial Episode ^{1,2}	First Recurrence ^{1,2,3}	Second Recurrence ^{1,3}
<p>Non-Fulminant Disease</p>	<p><u>Consider Infectious Diseases and Surgery consultation in patients with severe disease (defined as WBC ≥15,000, absolute neutrophil count ≤500, or SCr ≥1.5 times premorbid level):</u> Vancomycin 125 mg PO QID x10 days</p> <p><u>True vancomycin allergy (not vancomycin infusion reaction):</u> Fidaxomicin 200 mg PO BID X 10 days</p>	<p><u>Infectious Diseases consultation is recommended</u></p> <p>If metronidazole was used for the initial episode: Vancomycin 125 mg PO QID x10 days</p> <p>If vancomycin was used for the initial episode: Vancomycin 125 mg PO QID x14 days then taper⁷ over 5-11 weeks.</p> <p>Alternative if vancomycin taper cannot be performed: Fidaxomicin 200 mg PO BID x10 days</p>	<p><u>Infectious Diseases consultation is strongly recommended</u></p> <p>If vancomycin taper was NOT used for the first recurrence: Vancomycin 125 mg PO QID x14 days then taper⁷ over 5-11 weeks</p> <p>If vancomycin taper was used for the first recurrence, the following options may be considered in consultation with Infectious Diseases⁷:</p> <ul style="list-style-type: none"> - Repeat Vancomycin taper - Fidaxomicin 200 mg PO BID x10 days - Fecal microbiota transplant - Repeat Vancomycin taper followed by Rifaximin ‘chaser’ - Kefir staggered protocol
<p>Fulminant Disease (Hypotension or septic shock, ileus, bowel obstruction, toxic megacolon, bowel perforation or peritonitis)</p>	<p><u>Surgery and Infectious Diseases Consultation are strongly recommended</u></p> <p>Vancomycin 500 mg PO QID + Metronidazole 500 mg IV q8h⁴</p> <p>If ileus, bowel obstruction, or fecal diversion, add Vancomycin by enema q6h⁵</p> <p>See footnote 11 for diverting loop ileostomy protocol.</p> <p>Duration: Minimum of 14 days of therapy, depending on clinical response.</p>	<p><u>Surgery and Infectious Diseases Consultation are strongly recommended</u></p> <p>Repeat primary therapy then taper vancomycin over 5-11 weeks⁷</p> <p>Alternative if vancomycin taper cannot be performed: Fidaxomicin 200 mg PO BID x10 days</p> <p>See footnote 11 for diverting loop ileostomy protocol.</p>	<p><u>Surgery and Infectious Diseases Consultation are strongly recommended</u></p> <p>If vancomycin taper was NOT used for the first recurrence: Repeat primary therapy then taper⁷ vancomycin over 5-11 weeks.</p> <p>If vancomycin taper was used for the first recurrence, the following options may be considered in consultation with Infectious Diseases⁷:</p> <ul style="list-style-type: none"> - Repeat Vancomycin taper - Fidaxomicin 200 mg PO BID x10 days - Fecal microbiota transplant - Repeat Vancomycin taper followed by Rifaximin ‘chaser’ - Kefir staggered protocol <p>See footnote 11 for diverting loop ileostomy protocol.</p>

1. Failure is defined as no improvement or worsening symptoms after 48-96 hours of primary therapy. In failing patients, look for alternative explanations diagnoses, continue *C. difficile* treatment doses until resolution, and consider infectious diseases and surgery consultation.
2. Randomized trials have all utilized 10-day durations of therapy. Extension of course to 14 days may be considered in patients who have not had symptom resolution by day 10.
3. *C. difficile* colitis recurrence is defined as recurrent symptoms and positive testing (after initial resolution) ≤ 8 weeks from the start of the original episode
4. Parenteral administration of metronidazole has poor intraluminal penetration and should not be used alone for treatment. Parenteral vancomycin has no significant luminal accumulation and should not be used for *C. difficile* treatment.
5. Intracolonic vancomycin 500 mg in 500 mL of normal saline every 6 hours given as retention enema using the following procedure: 18-inch Foley catheter with a 30-ml balloon inserted into rectum, balloon inflated, vancomycin instilled, catheter clamped for 60 minutes, deflate and remove. In patients who do not have the entire colon in place (i.e., a colorectal stump due to Hartman’s procedure), a smaller volume of enema (100 mL) is acceptable.
6. Avoid multiple or prolonged courses of metronidazole in recurrent disease due to the risk for cumulative neurotoxicity.
7. Alternative and/or adjunctive agents:
 - a. Vancomycin tapers should begin after the treatment course is completed. Example of PO **vancomycin** taper: 125 mg PO BID x7 days, then 125 mg PO daily x7 days, then 125 mg PO every other day x7 days, then 125 mg PO every 3 days x2-8 weeks. Patients on tapered doses of PO vancomycin should continue to be monitored for signs and symptoms of *C. difficile* disease.
 - b. Rifaximin ‘chaser’: **Vancomycin** 125 mg PO QID x10 days followed by **Rifaximin** 400 mg TID x20 days
 - c. Kefir staggered protocol: **Vancomycin** 125 mg QID x2 weeks, 375 mg q72h x2 weeks, 250 mg q72h x2 weeks, and 125 mg q72h x2 weeks PLUS kefir (5-oz glass with each meal (at least 3 glasses per day)) for 15 weeks.
 - d. Fecal microbiota transplantation (FMT) is a highly effective option for patients with recurrent CDI. Michigan Medicine uses stool preparations obtained from OpenBiome to perform FMTs in both the inpatient and outpatient settings. Patients with recurrent CDI (defined as having two or more episodes) or CDI not responsive to standard pharmacologic therapies by day 5 may be considered for FMT. Patients with hypotension or shock, ileus, megacolon, severe sepsis, peritonitis, or bowel perforation attributed to CDI are generally not candidates for FMT. For inpatient use, infectious diseases and gastroenterology consultation are required. For outpatient use, patients should be referred to the infectious diseases clinic. For more information [CLICK HERE](#). For additional [OpenBiome resources](#)
 - e. The role of probiotics in prevention and treatment of *C. difficile* colitis is unclear, and their use is not currently recommended for inpatients. Avoid the use of probiotics in immunocompromised patients (transplant recipients, unintact gut mucosa, neutropenic patients, HIV/AIDS patients, etc) and patients with severe *C. difficile* colitis.
 - f. Cholestyramine binds PO vancomycin and may decrease its efficacy. Avoid concomitant use.
8. Oral vancomycin capsules are available in generic form but may still be cost-prohibitive for patients. Discharge planners should be made aware of this issue prior to discharge so coverage may be assessed. In patients for whom oral capsules are not feasible, some options are:
 - a. Metronidazole is an option for patients with non-severe primary (i.e., not recurrent) disease
 - b. Taubmann outpatient pharmacy compounds oral vancomycin (from the intravenous formulation) that may be less expensive for some patients.
 - c. A patient assistance program is available for Fidaxomicin (<https://www.merckconnect.com/dificid/patient-assistance.html?hcpUser=yes>), which is often an option (see above) in patients who cannot afford or tolerate vancomycin.
9. In patients being treated for CDI who require concomitant antibiotic therapy beyond the 10-14 day of CDI treatment, continuation of vancomycin can be considered for the duration of the concomitant antibiotic course. The dose of vancomycin in this scenario should be 125 mg daily to BID.
10. Consider the use of vancomycin prophylaxis in patients that had a first or greater recurrence of CDI or fulminant disease in the past 90 days and require antimicrobials for a different infection. Other patients may be considered candidates for prophylaxis on a case-by-case basis in consultation with Infectious Diseases. The dose of prophylactic vancomycin is 125 mg daily to BID and the duration should be at least 50% of the expected duration of antibiotic therapy for the other infection.
11. Postoperative diverting loop ileostomy regimen consists of antegrade vancomycin flushes (500 mg in 500 mL of Lactated Ringers; q8 hours for a duration of 10 days) via a 24 French Malecot catheter in the efferent limb of the ileostomy and intravenous (IV) metronidazole (500 mg q8 hours) for 10 days. See Reference Neal MD, et al. [Ann Surg 2011;254:423-7](#).

Reference:

Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Available at: <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/cix1085/4855916>

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Neal MD et al. Diverting Loop Ileostomy and Colonic Lavage: An Alternative to Total Abdominal Colectomy for the Treatment of Severe, Complicated Clostridium Difficile Associated Disease. [Ann Surg 2011;254 \(3\), 423-7.](#)

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The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider’s professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.

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