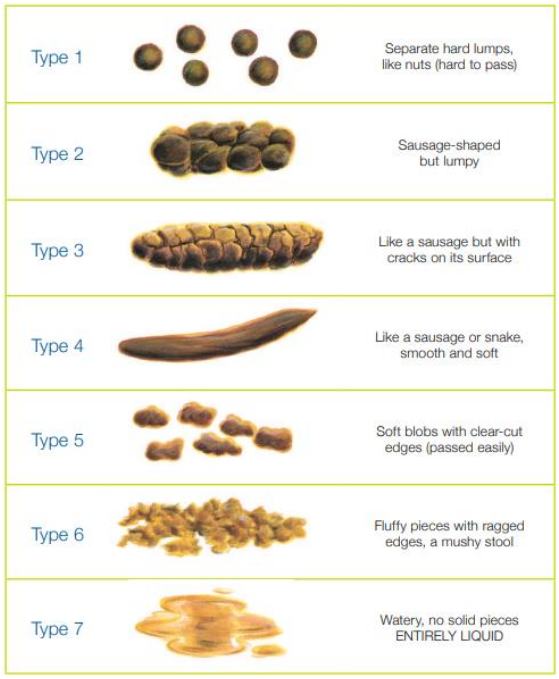
Stony Brook University Hospital Treatment Guidelines:

Guideline for the Diagnosis and Treatment of *Clostridioides difficile* Infection

1. *Clostridioides difficile* infection (CDI) Diagnosis

- General CDI Testing Recommendations
  - **Do not test all patients with loose stool for CDI**
    - CDI is responsible for < 10% of nosocomial diarrhea
    - Consider other causes of diarrhea first (i.e. tube feeds, laxative use, oral contrast, medication side effects) unless symptoms strongly suggest CDI
  - Patients with mild-moderate diarrhea without CDI features (see below) should have non-CDI causes treated and be monitored for response before CDI testing is considered
  - **Do not test formed stool, asymptomatic patients, or as a "test for cure"**
  - **Do not routinely test infants < 2 years old as they are likely to be colonized**
  - **Reserve testing for patients with CDI features:**
    - Significant diarrhea (> 3 watery bowel movements in < 24 hours) and at least one feature suggestive of CDI such as:
      - Unexplained elevation in WBC or fever
        - Isolated leukocytosis in the absence of diarrhea is not an indication for CDI testing
      - New onset abdominal pain and/or distention with diarrhea
    - Severe diarrhea (> 7 watery bowel movements or > 1.5 L over 24 hours)
    - Persistent diarrhea for > 24 hours which is not resolved with conservative treatment and does not have another explanation
  - Two-step testing protocol
    - 1. *C. difficile* toxin PCR (*note: this is not available in the GI/diarrhea PCR panel*)
    - 2. Positive PCR results are reflexed to a *C. difficile* toxin EIA
      - CDI testing is limited to attending physicians if the patient has any of the following:
        - < 3 bowel movements documented in the EMR
        - Recent laxative use in the past 48 hours
        - Prior CDI testing within the past 7 days
      - Stool specimens that are not liquid (Bristol Stool Form Scale 6 or 7, see **Figure 1** below) will be rejected by the laboratory
      - If patient has an ileus, rectal swab should be used for stool sample collection
        - **For this specimen type please consult with the Molecular Diagnostics Laboratory at x4-3747**

Figure 1. Bristol Stool Form Scale



- *C. difficile* two-step testing interpretation

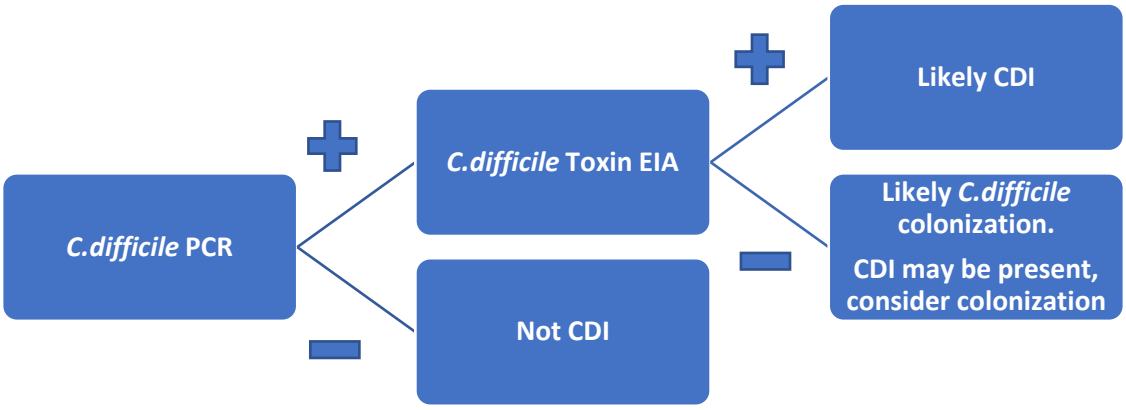


Table 1. *C. difficile* Two-Step Testing Interpretation

C. difficile PCR	*C. difficile* EIA	Interpretation	Recommendations
Positive	Positive	Likely CDI	• Initiate severity-based treatment (see Table 2) • Stop concomitant acid suppressants and antibiotics if possible • Enteric contact isolation
Negative	Negative	Not CDI	• Discontinue CDI treatment and isolation • Stop concomitant acid suppressants and antibiotics if possible • Evaluate for other possible causes of diarrhea
Positive	Negative	May be CDI	• Enteric contact isolation • Stop concomitant acid suppressants and antibiotics if possible • Treatment decisions should be individualized (see section 3)

2. *Clostridioides difficile* infection (CDI) General Treatment and Management

- **Risk factor mitigation recommendations**
  - Stop concomitant gastric acid suppressant medications and antibiotics if possible
  - If systemic antibiotics are needed, de-escalate away from high risk medications (i.e. clindamycin, ciprofloxacin, levofloxacin, cefepime, meropenem, ertapenem) if possible
- Treatment recommendations detailed in **Table 2**

Table 2. Treatment Recommendations (preferred regimens highlighted in yellow)

	Recommended Treatment	Additional Notes
Initial episode	Vancomycin 125 mg PO Q6 x 10 days Fidaxomicin 200 mg PO Q12 x 10 days‡	**Fidaxomicin requires ID or GI approval for use**
Severe, complicated CDI (ICU patient, toxic megacolon, ileus)	Vancomycin 500 mg PO Q6 + metronidazole 500 mg IV Q8 **+/-** Vancomycin 500 mg retention enema (if ileus present)	ID and GI consultations strongly recommended Colorectal surgery consultation recommended for possible colectomy
First CDI recurrence	Vancomycin 125 mg PO Q6 x 10 days Vancomycin pulse taper‡‡ 125 mg PO Q6 x 10-14 days 125 mg PO Q12 x 7 days 125 mg PO Q24 x 7 days 125 mg PO Q72 x 14 days Fidaxomicin 200 mg PO Q12 x 10 days	**Fidaxomicin requires ID or GI approval for use**
Second or subsequent CDI recurrence	Vancomycin pulse taper 125 mg PO Q6 x 10-14 days 125 mg PO Q12 x 7 days 125 mg PO Q24 x 7 days 125 mg PO Q72 x 14 days‡‡ Fidaxomicin 200 mg PO Q12 x 10 days	**Fidaxomicin requires ID or GI approval for use** Consider outpatient referral to ID or GI for additional adjunctive therapy on discharge*: • Fecal microbiota transplantation (rectal): Rebyota™ • Fecal microbiota transplantation (oral): Vowst™

* Rebyota and Vowst are not on the hospital formulary and are not available for inpatient use.

‡Note that fidaxomicin use for the initial episode of CDI has been associated with a 16% relative risk reduction in recurrent CDI. However, this needs to be balanced with the high cost expense of fidaxomicin therapy compared to oral vancomycin, which may ultimately impact on patient adherence.

‡‡The duration of vancomycin pulse taper regimens may vary depending on clinical factors. Consultation with ID or GI is recommended.

3. CDI Discordant Test Result Interpretation

- PCR Positive, EIA negative test results are most suggestive of *C.difficile* colonization. Most patients with PCR positive, EIA negative tests **do not need CDI treatment.**
  - Initial management should focus on stopping unnecessary antibiotics and unnecessary gastric acid suppressant medications, if possible
  - Stop unnecessary laxative use
- The decision to treat should be individualized. It may be considered in persons with severe immunosuppression and in cases of severe, non-resolving, or otherwise unexplained diarrhea strongly suggestive of CDI (i.e. leukocytosis *with* diarrhea, no recent laxative use, clinical workup without alternative diagnosis)

4. CDI Prevention and Prophylaxis

- Strategies for preventing CDI include the following:
  - Minimize antibiotic use
  - Avoid unnecessary gastric acid suppression
- Probiotics
  - The role of probiotics (i.e. *Lactobacillus, Acidophilus*) remains unclear. Results from clinical trials have been inconsistent. An increased risk of bacteremia has been noted in severely immunocompromised patients. National clinical guidelines from the IDSA and ACG do not support the use of probiotics.
- Vancomycin
  - Use of vancomycin as prophylaxis against CDI is controversial. Clinical data is limited to small studies that suggest a potential benefit in preventing CDI. However, this must be balanced with the known risk of disrupting the natural microbiome and driving microbial resistance (i.e. vancomycin-resistant *Enterococci* and multidrug resistant *Enterobacteriaceae*).
  - Vancomycin prophylaxis may be considered in the following high-risk groups with histories of severe CDI *with* at least two recurrent episodes of CDI:
    - Age 65+ years of age
    - Severely immunocompromised

5. References

1. Johnson S, Lavergne V, Skinner AM, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of Clostridioides difficile Infection in Adults. Clin Infect Dis. 2021;73(5):755-757. doi: 10.1093/cid/ciab718. PMID: 34492699.
2. Kelly CR, Fischer M, Allegretti JR, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of Clostridioides difficile Infections. Am J Gastroenterol. 2021;116(6):1124-1147. doi: 10.14309/ajg.0000000000001278. Erratum in: Am J Gastroenterol. 2022 Feb 1;117(2):358. PMID: 34003176.
3. Kociolek L, Gerding D, Carrico R, et al. Strategies to prevent Clostridioides difficile infections in acute-care hospitals: 2022 Update. Infection Control & Hospital Epidemiology. 2023; 44(4), 527-549. doi:10.1017/ice.2023.18