Clostridioides difficile Infection (CDI) Testing and Treatment Guideline

C. difficile is an important nosocomial pathogen causing diarrhea, particularly in patients who have received antibiotics. *C. difficile* infection may result in a variety of clinical syndromes ranging from asymptomatic colonization to mild, self-resolving diarrhea, to severe diarrhea and even complications such as toxic megacolon and death. CDI is generally classified as Community-Onset (CO-CDI) or Hospital-Onset (HO-CDI). HO-CDI is defined as symptom onset ≥4 days after admission to a healthcare facility with testing date being the surrogate marker for symptom onset. HO-CDI is a nationally reported quality metric and high rates of HO-CDI may result in financial penalties. The currently available tests for CDI, particularly the molecular tests (C diff PCR and GI Panel) are highly sensitive and may detect levels of the bacteria which are not clinically meaningful. Thus, current guidelines recommend using restricting testing to those patients who have a clinical syndrome suggestive of CDI. Below we have included guidance on clinical criteria for testing patients and test interpretation.

General Testing Recommendations:

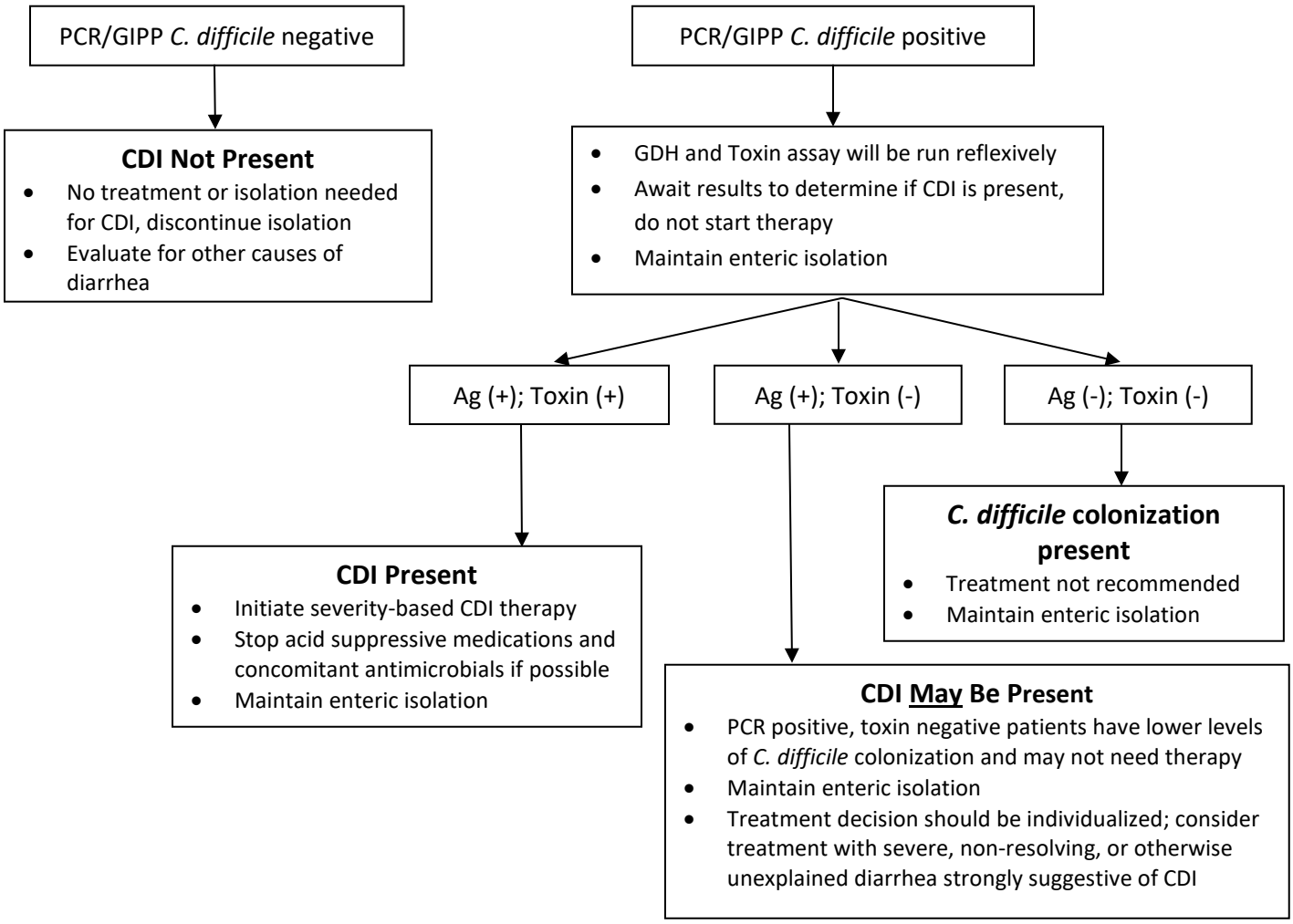
- **Do not test all patients with loose or watery stools for CDI**
    - CDI is responsible for <10% of nosocomial diarrhea
    - Consider other causes of diarrhea first (e.g. tube feeds, oral contrast, bowel regimens, antibiotic side effects, etc.) unless symptoms strongly suggest CDI
    - Utilize clinical criteria below to direct testing
- Patients with mild-moderate nosocomial diarrhea without CDI features (see below) should have non-CDI causes treated (stop inciting meds especially laxatives, add fiber to tube feeds, etc.) and be monitored for resolution before CDI testing is considered
- Infants <12 mo. are often colonized with *C. difficile* and should not be tested as it does not produce clinically significant disease
- **Patients who are admitted with diarrhea should be tested in the first 2 days of their hospital stay**
- **Never** test formed stool, asymptomatic patients, or perform a "test of cure"
- Unformed stool is the only acceptable specimen (i.e., stool conforms to the shape of the container)
    - Non-liquid stool will not be processed by the microbiology lab
        - Order only one CDI test and await results before initiating therapy (exception: If severe disease with typical symptoms, reasonable to initiate therapy before results)

Criteria for CDI testing:

- Patients should meet one of the three criteria before being tested for CDI. These criteria are built into the CDI test order and clinicians should document which of the criteria are met before testing.
    - **Significant diarrhea:** >3 watery bowel movements in <24 hours AND at least one feature suggestive of CDI including:
        - Unexplained elevation in WBC count or fever
            - Isolated leukocytosis without diarrhea is NOT an indication for CDI testing
        - New onset abdominal pain and/or distention with diarrhea
    - **Severe diarrhea**: >7 bowel movements or >1.5L of stool over 24 hours
    - **Persistent diarrhea**: >3 watery bowel movements per day without CDI features for >24 hours which has not resolved with conservative treatment and does not have another explanation

Clostridium difficile **Test Interpretation Algorithm:**

Initial testing for CDI begins with the PCR test or GI Pathogen panel (GIPP). If negative, CDI is ruled out and no additional testing will occur. If positive the *C. difficile* antigen and toxin will be reflexively processed with results generally back in hours. Treatment decisions should await the antigen/toxin results.



CDI Test Interpretation

PCR/GIP Result	Antigen Result	Toxin Result	Interpretation	Recommendations
Negative	NA	NA	No *C. difficile* present	No further action. Repeat testing strongly discouraged.
Positive	Negative	Negative	*C. difficile* colonization is present. Very low levels of organism present and unlikely to be cause of symptoms	Treatment not indicated but should remain in isolation
Positive	Positive	Positive	Toxigenic *C. difficile* infection is present	Begin therapy according to management algorithm.
Positive	Positive	Negative	*C. difficile* infection may be present. Negative toxin due to non-functioning toxin gene, low level of *C. difficile*, or false negative toxin assay	Determine need for treatment based on risk for CDI and clinical presentation; not all patients need treatment. Consider other causes of diarrhea.
Positive	Negative	Positive	Indeterminate	Repeat test

C. difficile Tests Available at NM

- ***C. difficile* PCR** = Detected via GI pathogen panel or *C difficile* PCR test. Molecular assays are exceedingly sensitive and the detection of *C. difficile* via PCR alone has not been associated with outcomes different than those who test negative for *C difficile*. Patients with a positive PCR test for CDI will reflexively be tested for the *C. difficile* antigen and toxin.
    - Patients who test negative for both antigen and toxin should be considered to have *C. difficile* colonization without clinically meaningful CDI and should NOT be treated but should be placed in enteric isolation as they may shed *C. difficile* spores into the environment.
    - Interpretation of the PCR test should always be made in relation to the antigen and toxin assay (see algorithm below).
- ***C. difficile* antigen** = this test detects vegetative *C. difficile* bacteria but does not detect toxin which is the disease-causing component of CDI. The CDI antigen has a very high negative predictive value (98-99%) for meaningful CDI. A negative antigen test strongly suggests clinically meaningful CDI is absent.
- ***C. difficile* toxin** = Detection of toxin in the stool is associated with worsened outcomes including increased mortality and morbidity compared to molecular tests (PCR/GIPP) and in the setting of diarrhea is strongly suggestive of CDI and the need for treatment.

Treatment Recommendations for CDI

Do not start empiric therapy, await testing results to determine if CDI is present. Base treatment choice for CDI on an assessment of infection severity. It is reasonable in very mild infections to discontinue the inciting antibiotics and monitor for diarrhea resolution over the next 24-48 hours without initiating antibiotic therapy. A CDI management order set is available in OneChart to assist with severity-based treatment.

Treatment Recommendations for All Patients with CDI:

- Replace fluids and electrolytes as needed
- Discontinue acid suppressive medications (ASM) if possible. Continued use is associated with increased risk of CDI and recurrence
- Discontinue concomitant antibiotics if possible. Continued antibiotic use is associated with prolonged time to CDI symptom resolution and CDI recurrence. Narrow antibiotic spectrum as much as possible and discontinue necessary antibiotics as early as medically safe.
- Discontinue both anti-motility and pro-motility medications
- Monitor for clinical worsening and adjust therapy as needed

Mild-Moderate Infection: Diarrhea that does not meet criteria for severe or complicated

- Vancomycin 125mg PO q6h x 10 days (preferred)
- Fidaxomicin 200mg PO BID x 10 days (non-formulary, consider use in high-risk outpatients including age >65, stem cell transplant, solid organ transplant)
- For mild cases only and if unable to obtain preferred alternatives
    - Metronidazole 500 mg PO q8h x 10 days
    - Avoid IV metronidazole as data suggests inferior to PO
    - If no improvement by day 3-5, change to PO vancomycin

Severe Infection: CDI associated with the development of any of the following: WBC > 15,000, SCr ≥ 1.5 X baseline, acute decrease in albumin <3.0 g/dl, severe abdominal tenderness/pain, or requires ICU care for CDI

- Vancomycin 125 mg PO q6h x 10 days (DO NOT treat with IV vancomycin)

Severe, Complicated Infection: associated hypotension or shock, ileus, toxic megacolon, and/or fulminant colitis

- Consult ID Service to assist with therapy management
- Consult GI and General Surgery for evaluation for possible colectomy
- Vancomycin 500 mg PO q6h + metronidazole 500 mg IV q8h +/- vancomycin enema 500 mg in 100 mL of 0.9% NaCl; instill rectally via Foley catheter q6h and retain for 1h

Recurrent CDI: CDI recurrence defined as the re-appearance of signs/symptoms of CDI with a positive *C. difficile* test within 8 weeks of a previous CDI episode for which signs/symptoms had resolved. Recurrence of diarrhea is frequent in patients with previous CDI and is often not due to CDI. Reserve testing for those meeting previously described testing thresholds. In early, mild diarrhea, it is reasonable to hydrate and monitor symptoms for 24-48 hours to determine if they resolve spontaneously. If symptoms worsen or do not resolve, initiate CDI testing. Do not start empiric therapy.

- All Patients with recurrence:
    - Stop acid-suppressive medications and concomitant antibiotics if possible
    - Consider ID or GI consultation to assist with therapy choices
- First Recurrence:
    - Fidaxomicin 200mg BID X 10 days (**expensive**)
    - If unable to acquire fidaxomicin, use Vancomycin taper
        - Vancomycin 125 mg PO q6h x 10 days followed by, vancomycin taper of 125 mg PO q12h x 7 days, 125 mg PO q24h x 7 days, then 125 mg PO every 3 days x 14 days
    - Consider Bezlotoxumab 10 mg/kg IV once as additional therapy (decreases recurrence 40%)
        - No benefit in resolution of acute symptoms. Outpatient only.
- Second Recurrence:
    - If patient has not received vancomycin taper, attempt this first (cure rate 60-70%); if CDI recurs after vancomycin taper, proceed to Fecal Microbiota Therapy (FMT)
    - **Referral to ID or GI for evaluation for potential FMT.** Options include:
        i. Bezlotoxumab 10 mg/kg IV once if not previously given
            1. Strongly consider where FMT is not an option (unsafe/unwilling) or likely to receive additional courses of antibiotics in near future
        1. Rebyota (Fecal microbiota, live-jslm) via single rectal installation (AWP ~$9000)
            - Maintain CDI treatment until FMT arranged and stop at least 48 hours before installation
            - Avoid antibiotics during and after FMT
        2. Vowst (Fecal microbiota spores, live-brpk) oral capsules 4 capsules once per day for 3 days (AWP ~$16500)
            - Stop CDI therapy at least 48 hours before starting Vowst and drink 10 oz Magnesium citrate 1-3 days after finishing oral CDI therapy and before starting capsules
            - Do not eat or drink for 8 hours before starting capsules
            - Avoid antibiotics during and after FMT
        3. Biobank derived FMT via colonoscopy is no longer available at NM/UNMC

CDI Isolation/Infection Control

- When testing for CDI is ordered place patient in enteric isolation until results available
- PCR test negative (C diff PCR or GI Panel) = discontinue enteric isolation unless another pathogen is detected
- PCR test positive with any result on antigen and toxin = continue enteric isolation
- Enteric isolation includes:
    - Glove and gown use upon room entry and soap and water hand hygiene preferred after patient and/or environment contact
    - Environmental Services will perform routine bleach cleaning of rooms of all patients with *C. difficile* infection (CDI) weekly and at patient discharge along with terminal UV disinfection if available
    - Patients will remain in isolation for 1 week after treatment is completed and they are asymptomatic (no diarrhea), whichever is longer

Updated November 2023