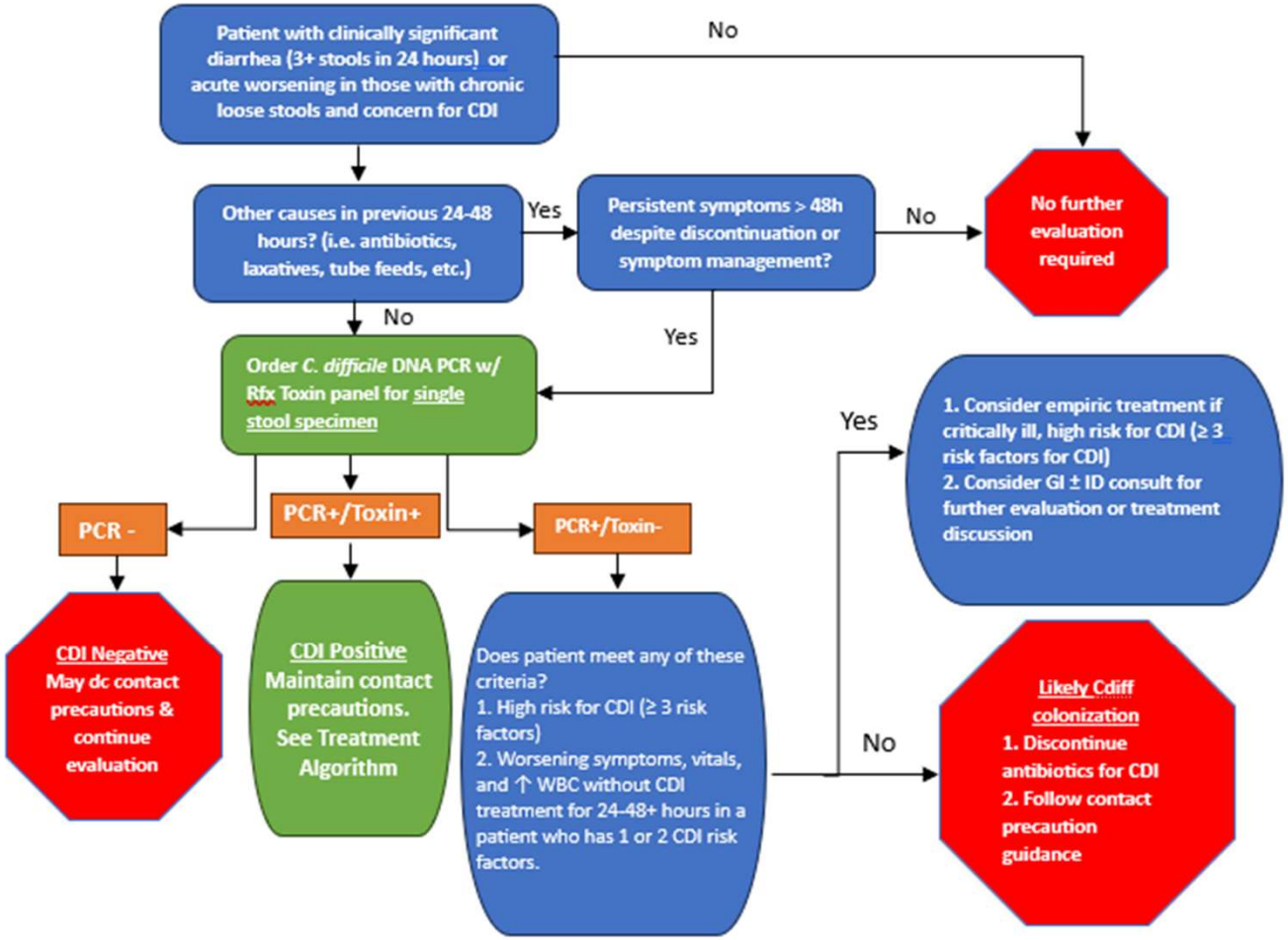
VASP *Clostridioides difficile Infection* (CDI) in Pediatric Patients
Inpatient Management
Clinical Practice Guideline

Monroe Carell Jr. Children's Hospital at Vanderbilt



Risk factors for CDI

- High-Risk Antibiotics in last 90 days (fluoroquinolones, clindamycin, carbapenems, 3rd/4th generation cephalosporins)
- Healthcare exposure in last 12 weeks or prolonged hospitalization
- Chronic Acid Suppression
- Solid Organ Transplant
- Hematopoietic Stem Cell Transplant
- Cancer chemotherapy
- Chronic Kidney Disease / End Stage Renal Disease
- Gastrointestinal procedure or GI motility disorder
- Inflammatory Bowel Disease
- History of definite CDI

Exclusion criteria

1. Infants ≤ 1 YO
   Asymptomatic intestinal colonization with *C difficile* (including toxin-producing strains) occurs in 50% of infants and is common in < 2 YO
   If concern for CDI in infant, please consult GI and/or ID
2. Children 1-2 YO without CDI risk factors

Note that this guideline does not consider individual patient situations and does not substitute for clinical judgment.

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Diagnostic Considerations:

- VUMC relies on a two-step algorithm for the diagnosis of *Clostridioides difficile* (C. *difficile*) infections (CDI).
    1. Molecular screen to test for the presence of toxigenic C. *difficile* via the toxin B gene (tcdB).
        - While *C. difficile* can produce both enterotoxin A and cytotoxin B, all toxigenic strains will produce toxin B indicating a better marker for detection.
        - Negative Predictive Value (NPV): 97.1% when compared against culture + toxin assay
    2. If molecular screen is positive, a rapid toxin antigen test is completed simultaneously looking for toxin A and B.
        - FDA package labeling for this test indicates: Sensitivity: 88%; NPV: 98.1% (n=1,126)
        - Other studies have found lower sensitivities for toxin enzyme immunoassays (EIA) at ~78.3%.[1]
            - Given the lower sensitivity for EIA tests, PCR +/Toxin – results should not be interpreted in isolation as the clinical context and risk factors of the patient could indicate a true infection.[2,3]
- Patients should be experiencing clinically significant diarrhea (≥3 liquid stools per day) or an acute change in stooling without any alternative causes identified in patients with chronic unformed stools. **Testing is only performed on loose or watery stool specimens.**
- Repeat testing to assess for C. *difficile* eradication (also known as a "test of cure") is not necessary. Many successfully treated patients will continue to test positive for weeks or months after resolution of symptoms.[1]
- When the C. *difficile* PCR with RFx toxin is ordered, place the patient on contact precautions and follow VUMC infection prevention guidance regarding discontinuation of isolation.
- The laboratory will not perform repeat testing for C. *difficile* sent within 7 days of a prior positive result. For negative results, the laboratory will perform a maximum of 2 C. *difficile* tests within 7 days.
- A negative test is NOT required for removal from isolation. Follow VUMC Infection Prevention guidance on isolation

Table 1. Interpreting C. *difficile* Panel Results[5,6,7]

Testing Result	Interpretation
C. *difficile* DNA PCR: Not detected	Toxigenic C. *difficile* is not present in this patient (97% NPV). Continue work-up for alternative causes.
C. *difficile* DNA PCR: Detected C. *difficile* Toxin Ag: Not detected	Likely represents colonization with toxigenic C. *difficile;* however, this can sometimes represent infection Interpret in clinical context of the patient (See inpatient management flowsheet): 1. Is the patient at high risk for CDI? 2. Have all alternative causes for diarrhea been ruled out? 3. Are the patient's symptoms, white blood cell count/labs, and vitals worsening off CDI therapy?
C. *difficile* DNA PCR: Detected C. *difficile* Toxin Ag: Detected	Patient is likely experiencing CDI; if meets clinical criteria for testing (3+ stools in 24 hours or acute change in diarrhea in patient with chronic loose stools), then follow treatment algorithm. Note: Recent data suggests that PCR+/toxin+ results can still reflect colonization. Therefore, patient may not need treatment if has had improvement in stool frequency or volume prior to or after test was sent[5]

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Table 2. Treatment Considerations[3,4,6,7]

C. difficile Classification	Treatment
Initial Episode: *mild-moderate*	PO Metronidazole or PO Vancomycin. (PO Vancomycin preferred in immunocompromised hosts). If PO antibiotics are unable to reach colon, add Vancomycin enema
Initial Episode: *severe* *Leukocytosis, leukopenia, or worsening renal function*	PO Vancomycin
Any Episode: severe & complicated (Fulminant CDI) *Hypotension, shock, pseudomembranous colitis, megacolon, or ileus due to CDI*	NO abdominal distention: PO Vancomycin and IV Metronidazole WITH abdominal distention: PO Vancomycin, IV Metronidazole, & Vancomycin enema for full course
First Recurrence: *mild-moderate*	Preferred: PO Vancomycin Alternatives: PO Metronidazole for mild infection; may consider PO Fidaxomicin* If enteral antibiotics are unable to reach colon, add Vancomycin enema until improvement
First Recurrence: *severe* *Leukocytosis, leukopenia, or worsening renal function*	PO Vancomycin Alternative: May consider PO Fidaxomicin* If enteral antibiotics are unable to reach colon, add Vancomycin enema until improvement
Second or Multiple Recurrence: *all severities*	Consult Infectious Diseases or GI and consider 1 of the following options: • PO Vancomycin pulse or PO Vancomycin prolonged taper • PO Vancomycin followed by Rifaximin ○ Pediatric Rifaxamin dosing not well described (avoid if recent Rifaxamin use) • Fidaxomicin* • Live biotherapeutic product or fecal microbiota transplantation (in eligible patients)- Consult Gastroenterology

*Fidaxomicin is restricted to GI and/or ID approval

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Table 3. Medication Doses and Duration[6,7]

Medication (Enteral)	Dose	Frequency	Duration
Metronidazole	30 mg/kg/day (max 500 mg/dose)	Q6	10 days
Vancomycin	40 mg/kg/day (max 125 mg/dose)	Q6	10 days
Vancomycin pulse	40 mg/kg/day (max 125 mg/dose)	Q6	7 days
	40 mg/kg/day (max 125 mg/dose)	TID	7 days
	40 mg/kg/day (max 125 mg/dose)	BID	7 days
	40 mg/kg/day (max 125 mg/dose)	Daily	7 days
	40 mg/kg/day (max 125 mg/dose)	Every other day	7 days
	40 mg/kg/day (max 125 mg/dose)	Q72h	7 days
Vancomycin taper	40 mg/kg/day (max 125 mg/dose)	Q6	14 days
	20 mg/kg/day (max 125 mg/dose)	BID	7 days
	10 mg/kg/day (max 125 mg/dose)	Daily	7 days
	10 mg/kg/dose (max 125 mg/dose)	Every other day	14 days
Vancomycin followed by Rifaximin	40 mg/kg/day (max 125 mg/dose)	Q6	14 days
	Rifaximin 400 mg	TID	14 days
Vancomycin enema	500 mg/100 mL normal saline (decide volume based patient weight and size)	daily	Until improvement and tolerating enteral
Fidaxomicin[4]	16 mg/kg/dose (max 200 mg/dose)	BID	10 days

References

1. Yepez Guevara EA, Aitken SL, Olvera AV, Carlin L, Fernandes KE, Bhatti MM, Garey KW, Adachi J, Okhuysen PC. *Clostridioides difficile* Infection in Cancer and Immunocompromised Patients: Relevance of a Two-step Diagnostic Algorithm and Infecting Ribotypes on Clinical Outcomes. Clin Infect Dis. 2021 May 18;72(10):e460-e465. doi: 10.1093/cid/ciaa1184. PMID: 32803229.
2. https://www.accessdata.fda.gov/cdrh_docs/pdf16/K163085.pdf
3. Louie TJ, Miller MA, Mullane KM, et al; OPT-80-003 Clinical Study Group. Fidaxomicin versus vancomycin for Clostridium difficile infection. N Engl J Med 2011; 364:422–31.
4. Cornely OA, Crook DW, Esposito R, et al; OPT-80-004 Clinical Study Group. Fidaxomicin versus vancomycin for infection with Clostridium difficile in Europe, Canada, and the USA: a double-blind, non-inferiority, randomised controlled trial. Lancet Infect Dis 2012; 12:281–9.
5. Parnell JM, Fazili I, Bloch SC, et al. Two-step Testing for *Clostridioides difficile* is Inadequate in Differentiating Infection from Colonization in Children. *J Pediatr Gastroenterol Nutr*. 2021;72(3):378-383. doi:10.1097/MPG.0000000000002944
6. Shirley DA, Tornel W, Warren CA, Moonah S. Clostridioides difficile Infection in Children: Recent Updates on Epidemiology, Diagnosis, Therapy. *Pediatrics*. 2023;152(3):e2023062307. doi:10.1542/peds.2023-062307
7. Committee on Infectious Diseases AA of P. *Red Book: 2024–2027 Report of the Committee on Infectious Diseases*. (Kimberlin DW, Banerjee R, Barnett ED, Lynfield R, Sawyer MH, eds.). American Academy of Pediatrics; 2024. doi:10.1542/9781610027373

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