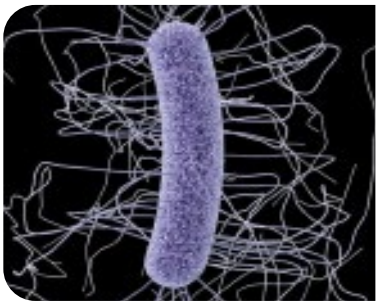

Diagnosis and Treatment of Adult 2024 update

Clostridioides difficile (C. diff) Infection

Intermountain Canyons and Desert Regions

This care process model (CPM) was developed by Intermountain Health's Antibiotic Stewardship and Gastroenterology groups to help prevent and more effectively manage *C. diff* infections (CDIs). It provides guidance for healthcare facilities on prevention strategies, diagnostic testing stewardship, and appropriate treatment of CDIs. The information is based on current literature, internal data, and guidelines of the American College of Gastroenterology (ACG), Infectious Disease Society of America (IDSA), and the Society for Healthcare Epidemiology of America (SHEA).

Key Points

Limiting the use of antibiotics and stringent infection-control measures can significantly decrease the number of *C. diff* infections.

- Use of antibiotics is the most common cause of *C. diff* infection. It is estimated that 50% of all antibiotic prescriptions are unnecessary.
- Because patients are often on antibiotics, appropriate infection-control measures (*contact/bleach precautions*) may also decrease spread of infections in healthcare facilities.

***C. diff.* testing should only be initiated if specific clinical criteria are met.[2]**

- Patients that are asymptomatic should *NOT* be tested for *C. diff.* False positives are common. *C. diff.* PCR is highly sensitive and can pick up common non-harmful *C. diff.* colonization.
- Consider testing for *C. diff.* in patients with ≥ 3 watery stools in 24 hours with one or more risk factors (see below) and no medications or diet changes that would promote diarrhea. See *Testing for C. diff* algorithm on pg 2.
- Risk factors for *C. diff.* infection include
  - Immunocompromised status
  - Underlying inflammatory bowel disease
  - Any of the following in past three months (antibiotics, proton pump inhibitors, prolonged contact with healthcare system)
  - Gastrointestinal procedure in the past 90 days
  - Greater than 7 days of tube feeding

Use guideline-directed medical therapy for treatment of initial and recurrent episodes of C. diff infection.

- The ACG as well as the IDSA in partnership with SHEA have in-depth guidelines for prevention, diagnosis, and treatment of *C. diff* infections (linked on right). See *Treatment tables* on pgs 3–4 for a summary of treatment recommendations.

What's new in this update?

- Diagnostic stewardship focus; see testing algorithm on *pg 2*
- Criteria for fidaxomicin use for recurrent CDI *pg 4*
- Guidance for use of adjunctive therapies bezlotoxumab and ursodiol *pg 4*

What's Inside?

Intermountain Measures

- Hospital-acquired *C. diff* infection rates
- Appropriate utilization of restricted agents (fidaxomicin)
- 14–day, 30–day and 90–day hospital readmission rates after *C. diff.* infection.

Supporting Guidelines

ACG Clinical Guidelines: Prevention, Diagnosis and Treatment of Clostridioides difficile Infections (2021)[1]

Clinical Practice Guidelines for CDI in Adults and Children : 2017 update by ISDA and SHEA[4]

Clinical Practice Guidelines-Focused update on Management of CDI in adults: 2021 update by IDSA and SHEA[5]

Intermountain Health

C. DIFF PREVENTION STRATEGIES

General

- **Minimize unnecessary antibiotic use.**
  - Treat infection, not colonization or contamination
  - Not every bacterial culture requires treatment
  - Review microbiology results after 48 hours to determine if modification is possible
  - Use the narrowest spectrum effective antimicrobial to treat
- **Short-term probiotics are safe and effective** in preventing *C. diff* infection when used with antibiotics in patients at high risk (exceptions: immune compromised or severely disabled)[3]
- Do not use acid-suppressing medications (H_2B/PPI) unless clinically indicated.

Hospital-specific

- **Isolate patients with:**
  - Any diarrhea suspected to be infectious
  - Suspected or confirmed *C. diff* infection
  - Recurrent diarrhea with recent *C. diff* infection
- **Confirmed *C. diff* infections require** contact/bleach precautions
  - Contact isolation (gown/glove/limit visitors/clean hands)
  - Disinfection of equipment with sodium hypochlorite (bleach) disinfectant. Use dedicated equipment.

*PCR testing should not be done more than once per 7 days. **Do not test-for-cure.** Molecular lab will only accept loose stool samples.

Testing for *C. diff* Infection (CDI)

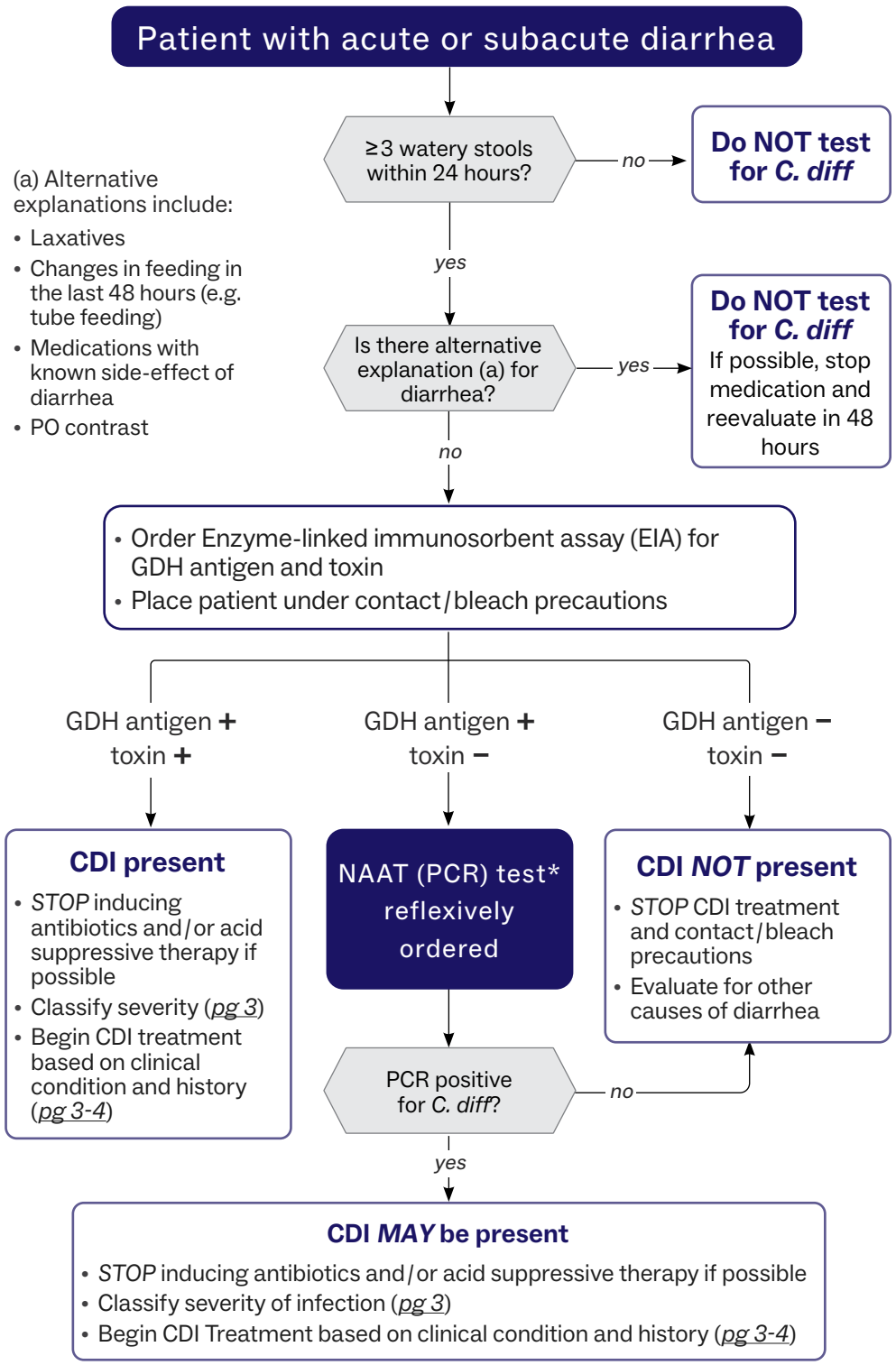

TABLE 1. Common *C. difficile* Tests

Test	Pros	Cons
EIA for toxin	Detects presence of toxin; Low cost; Fast	Variable sensitivity
EIA for Glutamate dehydrogenase (GDH)	Detects antigen	Antigen is produced by toxic and non-toxic strains
Nucleic Acid Amplification (NAAT): PCR	Detects gene	False positives, detects non-harmful colonization

CDI Severity Classification

TABLE 2. Severity Classification for *C. diff* Infection[4]	
Asymptomatic	Test positive but no diarrhea.
Non-severe	Diarrhea with leukocytosis (WBC ≤15,000 cells/mL) **AND** serum creatinine <1.5 mg/dL
Severe	Diarrhea with leukocytosis (WBC >15,000 cells/mL) **OR** serum creatinine >1.5 mg/dL
Fulminant	Diarrhea with any of the following: • Hypotension • Shock • Ileus • Megacolon

Treatment of Initial CDI Episodes

TABLE 3. Recommended Treatment of Initial Episodes of *C. diff* Infections by Clinical Condition [1,4]

Clinical condition	Drug/s	Route, Dosage, and Duration	Treatment notes
Asymptomatic	Do not treat *ANY* asymptomatic *C. diff* patient		
First episode, non-severe	Preferred: Vancomycin* **OR** Alternative: Metronidazole	125 mg PO, 4 times per day for 10 days 500 mg PO, 3 times per day for 10 days	• Metronidazole may be chosen in select patients with mild *C. diff* (especially if negative for toxin) • If no improvement in 3 days , consult ID and/or Gastroenterology
First episode, severe	Vancomycin	125 mg PO, 4 times per day for 10 days	• If no improvement in 3 days , consult ID and/or Gastroenterology
Fulminant, any episode	Vancomycin **PLUS** Metronidazole **PLUS** Vancomycin PR	500 mg PO, every 6 hours for 48–72 hours (if oral therapy is not possible, may be given by NG tube) 500 mg IV every 8 hours for 48–72 hours (can be considered if ileus is present) 500 mg PR enema, every 6 hours for 48–72 hours (can be considered if ileus is present)	• If no improvement in 48–72 hours: – Consult Colorectal Surgery for colectomy considerations for severely ill patients with refractory shock and serum lactate > 5 mmol/L and a peripheral WBC > 50,000 cells/mcL. – Consider ID and/or Gastroenterology consultation for evaluation for salvage fecal microbiota transplant (FMT). • Ensure patient is receiving proper volume resuscitation. • The volume of enema is patient specific (100 mL– 500 mL) instilled for at least 1 hour.

*Given the relatively hight NNT, low level of evidence for fidaxomicin as first-line therapy, and significant cost to patient, our recommendation departs slightly from national guidelines.

Treatment of Recurrent CDI Episodes

TABLE 4. Recommended Treatment of Recurrent *C. diff* Infection Episodes by History and Risk [1,4]

Clinical condition	Recommended drug/s	Route, Dosage, and Duration
First recurrence[c], low-risk	Vancomycin tapered/pulsed	125 mg (5mL) PO, every 6 hours for 14 days; → 125 mg PO, BID for 7 days; →125 mg PO, daily for 7 days; →125 mg PO, 1 time every other day for 14 days; →125 mg PO, 1 time every third day for 21 days
First recurrence[c], high-risk[a]	Vancomycin tapered/pulsed **OR** Fidaxomicin[d] **OR** Fidaxomicin[d] tapered/pulsed	125 mg (5mL) PO, every 6 hours for 14 days; → 125 mg PO, BID for 7 days; →125 mg PO, daily for 7 days; →125 mg PO, 1 time every other day for 14 days; →125 mg PO, 1 time every third day for 21 days 200 mg PO, 2 times per day for 10 days 200 mg PO, 2 times per day for 5 days; *THEN, if marked improvement* 200 mg PO, 1 time every 2 days for day 7 – 25.
Second recurrence or subsequent recurrences[c]	Fidaxomicin[d] **OR** Fidaxomicin[d] tapered/pulsed **OR** Vancomycin tapered/pulsed[b] **OR** Fecal Microbiota Transplant (FMT) (subsequent recurrences)	200 mg PO, 2 times per day for 10 days 200 mg PO, 2 times per day for 5 days; *THEN, if marked improvement* 200 mg PO, 1 time every 2 days for day 7 – 25. 125 mg (5mL) PO, every 6 hours for 14 days; → 125 mg PO, BID for 7 days; →125 mg PO, daily for 7 days; →125 mg PO, 1 time every other day for 14 days; →125 mg PO, 1 time every third day for 21 days Consultation with Infectious Disease and Gastroenterology required
Fulminant any recurrences	See fulminant disease treatment recommendations in *TABLE 3. Recommended Treatment of Initial Episodes of C. diff Infections by Clinical Condition (pg 3)*	
Adjunctive therapy for use in special populations. Consider ID consultation before use.		
Bezlotoxumab	• FDA-approved for adjunct treatment for vancomycin or fidaxomicin to decrease risk of recurrent CDI in high-risk patients. Particularly, for patients unlikely to mount an adequate antibody response to toxin B. • Non-formulary for Intermountain. • Best administered through an outpatient infusion center and requires prior authorization. • Caution using in patients with heart failure.	
Ursodiol	300 mg PO, 3 times per day for 30 – 90 days.	Although limited, basic and applied evidence indicate that ursodiol reduces the risk of recurrence. It is inexpensive, well tolerated, and doesn't cause ongoing damage to the GI microbiota like anti-*C. difficile* antibiotics. It has been successfully used as salvage treatment when FMT is not available.

a. Patients who have positive toxin antigen AND recurrent, symptomatic disease AND either fail to respond to initial therapy or have recurrent disease with one of the following risk factors: immunocompromised, advanced age (65 years or greater), concomitant antibiotics, and/or hospitalization in the last 90 days. Fidaxomicin is restricted to these high-risk patients only.

b. It is important to note that tapered/pulsed oral vancomycin and fidaxomicin have not been compared in a head-to-head randomized control trial, so all potential benefit of fidaxomicin is based on comparisons with non-tapered/pulsed oral vancomycin. Therefore, oral tapered/pulsed vancomycin remains a reasonable option for high-risk patients at a potentially lower cost to the patient.

c. In recurrent episodes, select a different agent than those used in previous episodes. If no improvement in 3 days , consult Infectious Disease and/or Gastroenterology.

d. Given the relatively hight NNT, low level of evidence for fidaxomicin as first-line therapy, and significant cost to patient, our recommendation departs slightly from national guidelines. If use fidaxomicin, confirm patient is able to pay out-of-pocket cost and contact retail pharmacies in advance to order drug.

TABLE 5. Clinical Considerations [1,4]

Special Populations (IBD)	• Patients with inflammatory bowel disease (IBD) and clinical presentations of an acute flare with diarrhea should have a *C. diff* test ordered. • Patients with both IBD and *C. diff* should have therapy extended to vancomycin 125 mg PO, 4 times per day for at least 14 days. • In patients with IBD and recurrent *C. diff*, take emerging therapies such as FMT into consideration.
Concomitant medications	• Prescribe and use antibiotics carefully; inquire about history of *C. diff* infection before prescribing. If patient is receiving systemic antimicrobials, stop systemic antibiotics when possible. If treating another infection, use narrow spectrum antimicrobial as much as possible. Consider ID consultation if continued systemic antibiotics are necessary. • Avoid antiperistaltic agents for patients with *C. diff.* They may obscure symptoms and precipitate toxic megacolon.[4] • Although cholestyramine is a *C. diff.* toxin binding agent, it interacts with vancomycin and should not be used concomitantly.
Recurrences	• Test of cure is unnecessary if symptoms improve, unless the clinical status of the patient changes. • Recurrences generally occur within 4 weeks of completing therapy. – Although bowel patterns should certainly improve with treatment, many patients may continue to experience some degree of irregularity following a successful treatment for several weeks. Not all patients with recurrent diarrhea after a *C. diff* infection have recurrent *C. diff*. – A repeat positive test in a patient with minimal or no symptoms should not prompt re-treatment. – If patients have a high risk for recurrent CDI, consider vancomycin prophylaxis twice daily during systematic antimicrobial treatment.
Fecal Microbiota Therapy (FMT)	• Indications for FMT: – Recurrent or relapsing *C. diff* infection (defined as at least 2 recurrences). – Moderate *C. diff* infection not responding to standard therapy for at least a week. – Severe or fulminant *C. diff i*nfection with no response to standard therapy after 48 hours. • FMT protocol. Intermountain's *Fecal Microbiota Therapy Protocol* provides indications, screening requirements, etc. • New microbiome-related therapies are changing the landscape of *C. diff.* At this time, OpenBiome (University of Minnesota) remains the preferred FMT agent. Commercial preparations such as Rebyota and Vowst are available on a case-by-case basis. • FMT education. Use Intermountain's fact sheets to educate the patient: – *FMT: Information for Recipients/ (Spanish)*

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This CPM presents a model of best care based on the best available scientific evidence at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative. Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base. Send feedback to Brandon Webb, MD; Associate Medical Director of Infectious Disease; Intermountain Health; *brandon.webb@imail.org*