Clostridium difficile Infection (CDI) Treatment Algorithm—Initial Episode

Signs and Symptoms:

- Unexplained diarrhea or ileus with other causes of diarrhea excluded (e.g. recent receipt of laxative or bowel stimulant ≤ 48 hours)
- Other signs/symptoms of CDI (e.g. fever, abd pain/cramping, nausea/vomiting, leukocytosis)

1) Initiate contact precautions 2) Send stool sample for GDH Ag/Toxin testing[1] **3) Modify risk factors[2]** 4) Start Empiric Treatment

Mild to Severe CDI (first Occurrence)

Vancomycin[3] 125 mg PO QID x14d

PO vancomycin is preferred for treatment of CDI.

Recent evidence shows that PO vancomycin was superior to PO metronidazole for producing clinical success in patients with mild to severe CDI.
OR 1.575 [1.035-2.396; P = 0.034]

Clin Infect Dis 2014; 59:345-354.

Complete ileus, Toxic megacolon, Severe complicated CDI [4]

- Colonic ileus or toxic dilatation with abdominal pain and distension (minimal or no diarrhea)
- Hypotension requiring vasopressors
- Toxic megacolon/shock
- Bowel perforation
- Hypoalbuminemia

Consider ID Consultation

Vancomycin 500 mg PO QID ***PLUS***
Metronidazole 500 mg IV Q8H x14d

If complete ileus:

- *Add* vancomycin 500 mg/100 mL PR Q6H

Consider GI consultation for colonic tube placement for intercolonic vanco administration

Fidaxomicin: Restricted Abx—Must meet 1 of the criteria below

1. Documented CDI in patients with ≥3 of the following risk factors present:
   - Age >65
   - Concomitant systemic antibiotics (e.g. beta-lactams, quinolones, clindamycin)
   - Immunocompromised (e.g. receiving chemotherapeutic or immunosuppressant agents, ANC <1500)
   - Hypotension requiring vasopressors
   - Laboratory abnormality
     - WBC > 15
     - SCr 1.5x > baseline
     - Serum albumin ≤ 3.2
2. Documented recurrence of CDI after a vanco taper
3. Patients with a documented allergy to vancomycin
4. Therapeutic failure (lack of improvement or worsening) after 72 hours of vanco +/- metronidazole

[1]**Testing**: The *C. difficile* GDH antigen/Toxin A/B assay is used for diagnosis of CDI at SHC. If discrepant results (GDH + / Toxin -) the sample will be forwarded for PCR testing. The assay has a high negative predictive value (97%) and therefore repeat testing is not recommended. If there is a strong suspicion of CDI and the screening antigen is negative, a PCR should be requested. Repeat testing should not be used to assess clinical response OR as test of cure as patients may continue to shed organism/toxin for several weeks after treatment.

[2]**General Management:** Provide hydration and supportive care and modify risk factors

- **Discontinue or de-escalate implicated antibiotics when possible**[3]
- Do NOT treat asymptomatic bacteriuria
- Discontinue acid suppressive therapy or de-escalate from PPI to H2RA when possible
- Discontinue all stool softeners/laxatives
- Avoid anti-peristaltic agents (e.g. loperamide, diphenoxylate/atropine, opiates)

[3]**If concurrent antibiotic therapy** is required, continue CDI treatment throughout treatment plus an additional week.

[4]**Consider de-escalation** of therapy after initial improvement

The above guidelines are recommendations based on the available literature and are not intended to replace clinical judgment.

Clostridium difficile Infection (CDI) Treatment Algorithm — Recurrent Infection

Recurrent CDI—Recurrence within 8 weeks of successful completed treatment

Risk Factors:
- Age ≥65 years
- Need for concurrent antimicrobials during initial CDI treatment
- Severe underlying medical disorders (e.g. defective immune response to toxin)

First Recurrence

- Same regimen as the initial episode

Second Recurrence

Vancomycin Taper

- Initial 2wk therapy, followed by
- 125mg BID x 7 days, followed by
- 125mg daily x 7 days, followed by
- 125mg Q48h x 7 days, followed by
- 125mg q72h x 14 days

Alternative 1: (Rifaximin Chaser)

- Rifaximin 400mg BID or 200mg Q8H x 14 days following a vancomycin taper

  Note: should not be used concurrently, potential to develop increased MIC during treatment, non-FDA approved for CDI

Alternative 2: (Fidaxomicin)

- Fidaxomicin 200 mg PO BID x 10 days (see criteria)

≥3 Recurrences

- Consider ID consultation
- Evaluation for fecal microbiota transplant (FMT)

Frequently Asked Questions :

Q: Should I give probiotics to prevent recurrent CDI?

A: There is moderate quality evidence on the effectiveness of probiotics to prevent primary CDI, but there are few data to support use in secondary prevention of recurrent infection.

Q: Can cholestyramine be administered as adjunctive therapy?

A: There is limited evidence to support the use of cholestyramine as an adjunctive agent. While it is thought to bind *C. difficile* toxins, there is risk it may bind CDI antibiotics as well. Use is not recommended.

Q: Should I consider using CDI prophylaxis in patients receiving antibiotics with a history of recurrent or prior severe infection?

A: CDI prophylaxis is not routinely recommended. There may be a benefit in high risk patients with a recent history of severe or prior history of life-threatening infection. Secondary prophylaxis should be evaluated on a case by case basis in consultation with Infection Diseases.

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Frequently Asked Questions Continued:

Q: When should I consider using fidaxomicin?

A: Studies have shown fidaxomicin to be non-inferior to vancomycin for the initial clinical cure of CDI. Treatment with fidaxomicin resulted in fewer recurrences in non-NAP1/BI/027 (hypervirulent) strains[1]. Fidaxomicin should be considered for patients with severe CDI at high risk for recurrence, severe CDI not responding after 72 hours of vancomycin +/-metronidazole, or for recurrence after a vancomycin taper. Refer to the criteria for use for additional information.

[1]SHC does not provide *C. difficile* strain specific typing

Q: Should fidaxomicin be continued beyond 10 days in patients on concurrent broad spectrum antimicrobials?

A: Continuation of fidaxomicin beyond 10 days should be evaluated on a case by case basis in consultation with Infectious Diseases.

Q: Should IVIG be used as adjunctive treatment in patients with CDI?

A: IVIG is not routinely recommended due to limited data supporting use. Evaluation in consultation with Infectious Diseases is recommended.

Q: What are indications for Fecal MicrobiotaTransplant (FMT) in the treatment of CDI?

A: 1-Recurrent CDI ($\geq$ 3 epidoses of mild to moderate severity) and failure of a 6-8 week taper with vancomycin; 2– At least 2 episodes of severe CDI resulting in hospitalization and associated with significant comorbidity; 3-Mild to moderate CDI not responding to standard therapy for at least 1 week; 4-Severe or fulminant *C. difficile* colitis that has not responded to standard therapy after 48 hours.

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