**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 3) **Modify risk factors** 4) Start Empiric Treatment

<table>
<thead>
<tr>
<th>Mild to Severe CDI (first Occurrence)</th>
<th>Complete ileus, Toxic megacolon, Severe complicated CDI</th>
<th>Fidaxomicin: Restricted Abx—Must meet 1 of the criteria below</th>
</tr>
</thead>
</table>
| Vancomycin[^3^] 125 mg PO QID x14d | - Colonic ileus or toxic dilatation with abdominal pain and distension (minimal or no diarrhea)  
- Hypotension requiring vasopressors  
- Toxic megacolon/shock  
- Bowel perforation  
- Hypoalbuminemia | 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 |
| Consider ID Consultation | Vancomycin 500 mg PO QID **PLUS** Metronidazole 500 mg IV Q8H x14d | 2. Documented recurrence of CDI after a vanco taper |
| If complete ileus:  
- Add vancomycin 500 mg/100 mL PR Q6H  
Consider GI consultation for colonic tube placement for intercolonic vanco administration | 3. Patients with a documented allergy to vancomycin  
4. Therapeutic failure (lack of improvement or worsening) after 72 hours of vanco +/- metronidazole |

[^3^] **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

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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)

<table>
<thead>
<tr>
<th>Recurrence</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Recurrence</strong></td>
<td>Same regimen as the initial episode</td>
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<tr>
<td><strong>Second Recurrence</strong></td>
<td>Vancomycin Taper</td>
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<td></td>
<td>- Initial 2wk therapy, followed by</td>
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<tr>
<td></td>
<td>- 125mg BID x 7 days, followed by</td>
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<tr>
<td></td>
<td>- 125mg daily x 7 days, followed by</td>
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<td></td>
<td>- 125mg Q48h x 7 days, followed by</td>
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<tr>
<td></td>
<td>- 125mg q72h x 14 days</td>
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<td></td>
<td><strong>Alternative 1: (Rifaximin Chaser)</strong></td>
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<tr>
<td></td>
<td>- Rifaximin 400mg BID or 200mg Q8H x 14 days following a vancomycin taper</td>
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<tr>
<td></td>
<td><strong>Alternative 2: (Fidaxomicin)</strong></td>
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<tr>
<td></td>
<td>- Fidaxomicin 200 mg PO BID x 10 days (see criteria)</td>
</tr>
<tr>
<td><strong>≥3 Recurrences</strong></td>
<td>Consider ID consultation</td>
</tr>
<tr>
<td></td>
<td>Evaluation for fecal microbiota transplant (FMT)</td>
</tr>
</tbody>
</table>

#### 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. 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.

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 Microbiota Transplant (FMT) in the treatment of CDI?
A: 1- Recurrent CDI (> 3 episodes 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.

References:


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