

## ***Clostridium difficile* Infection**

### Diagnosis and Management Guidelines

11/2013  
v 3.0

#### **Important Points regarding *Clostridium difficile* infection**

- Infection with toxin producing strains of *C difficile* may result in clinical scenarios ranging from symptomless carriage to mild to moderate diarrhea, to fulminant and sometimes fatal pseudomembranous colitis.<sup>2,4</sup>
- Diarrhea is the key clinical feature of disease. Rarely (<1%), a symptomatic patient with ileus and colonic distention will present with minimal or no diarrhea.<sup>2</sup>
- A history of antimicrobial or antineoplastic agents within the previous 8-12 weeks is present in the majority of patients.<sup>2,4</sup>
- Virtually every antibiotic has been associated with *C difficile* infection<sup>1,2</sup>
- Typically affected have been elderly or severely ill patients in health care systems. However, recent reports of severe infection in patients without usual risk factors prompt consideration of *C difficile* infection in all patients with a compatible clinical syndrome.<sup>4,5</sup>
- Gastric acid suppression, especially with proton pump inhibitors, has been recognized as a risk factor for *C difficile* infection, in both hospitalized and ambulatory patients.<sup>1</sup> Re-evaluation of the need for such therapies should take place at regular intervals.
- *C difficile* colonization is frequently acquired through health system care, emphasizing the importance of infection control measures, including “Special Enteric” contact isolation<sup>1</sup>. **Hand washing** with antimicrobial soap and water is preferred over alcohol-based products to prevent the spread of *C difficile*.<sup>1,2</sup>

#### **Diagnosis**

- Required diagnostic components include symptoms **plus** either a positive stool test for the organism/toxin **or** direct visualization of pseudomembranous colitis.<sup>2</sup>
- The WFBMC laboratory detects *C. difficile* toxin in stool samples using a Real-Time PCR assay. PCR methodology is highly sensitive compared to traditional assays (see next bullet).
- **Multiple tests for *C difficile* are unnecessary.** The real-time PCR assay detects *C difficile* toxin gene sequences. Samples are processed daily with results usually available within hours. Both specificity and sensitivity are higher than previously employed methods (>97%, >90%, respectively), obviating the need of sending serial samples to increase negative predictive value.<sup>3</sup>
- Recommendation for testing:
  - The PCR test should generally be ordered only for patients experiencing 3 or more loose stools per day for 1-2 days.<sup>3</sup>
  - Submit soft or liquid stool samples. **Formed stool specimens will be rejected**, as this test is not approved for testing formed stools.
  - If the first test is negative, do not send a second specimen for at least 3 days.
  - In patients treated for *C difficile* infection, **retesting to document clearance of the toxin is not recommended.**

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#### **Treatment principles**

- Discontinue concurrent antibiotics or de-escalate concurrent antibiotics as soon as possible, as this may interfere with resolution of *C difficile* disease may increase the risk of *C difficile* infection recurrence<sup>2</sup>.
- When severe *C difficile* infection is suspected, initiate empirical treatment as soon as the diagnosis is suspected<sup>2</sup>. For patients with mild to moderate disease, the accuracy and rapid turnaround of the PCR toxin assay permits holding therapy until the test result is available.
- If possible, **avoid use of anti-peristaltic agents**, e.g. loperamide, as they may obscure symptoms and precipitate toxic megacolon.<sup>2</sup> Use of cholestyramine also is not recommended as it may bind anti-*C difficile* therapies.
- Consider early surgical consultation for critically ill patients or those with severe, complicated disease to assess need for colectomy.<sup>2</sup>
- The use of probiotic products, e.g. those containing Lactobacillus, to prevent or treat *C difficile* infection is not recommended. Data are limited and there is potential risk of blood stream infection due to the probiotic agent.<sup>1,2</sup>
- Prophylactic therapy directed at preventing colonization or clinical disease from *C difficile* is of unproven value and not recommended.<sup>1,2</sup>

#### **References**

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3. Peterson, LR, Robicsek A. Does my patient have *Clostridium difficile* infection? *Ann Intern Med* 2009; 151:176-179.
4. Kelly CP, LaMonth JT. *Clostridium difficile* – More difficult than ever. *N Engl J Med* 2008;359:1932-40.
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**Antibiotic therapy for *Clostridium difficile* infection<sup>2,6</sup>**

Clinical Definition	Supportive data	Recommended treatment
Initial episode, mild or moderate	Leukocytosis with a WBC count $\leq 15,000$ cells/mL <b>AND</b> a serum creatinine level $< 1.5$ times the premorbid level in a non-dialysis patient	Metronidazole 500mg 3 times per day by mouth for 10–14 days
Initial episode, severe*	Leukocytosis with a WBC count $\geq 15,000$ cells/mL <b>OR</b> a serum creatinine level $\geq 1.5$ times the premorbid level in a non-dialysis patient	Vancomycin 125mg 4 times per day by mouth for 10–14 days
Initial episode, severe, critically ill patient	Patients bedded in an ICU who have at least 3 of the following clinical features: -- leukocytosis with a WBC count $\geq 15,000$ cells/mL -- serum creatinine level $\geq 1.5$ times the premorbid level in a non-dialysis patient -- mean arterial pressure $< 60$ mmHg -- temperature $\geq 100.4^\circ\text{F}$ -- age $> 60$ years -- albumin $< 2.5$ g/dL -- heart rate $> 90$ bpm	Vancomycin, 125mg 4 times per day by mouth or by nasogastric tube PLUS metronidazole 500mg every 8 hours intravenously
Initial episode, severe, complicated	Severe sepsis, septic shock, ileus, or megacolon	Vancomycin, 500mg 4 times per day by mouth or by nasogastric tube PLUS metronidazole 500mg every 8 hours intravenously. If complete ileus, consider adding rectal instillation of vancomycin
First recurrence		Same as for initial episode
Second recurrence		Oral vancomycin in a tapered and/or pulsed regimen

\*Other features of severe disease include: age  $> 60$  years; fever  $\geq 100.4^\circ\text{F}$ ; serum albumin  $< 2.5$  g/dL; admission to an intensive care unit; and colonoscopic evidence of pseudomembranes