Center for Antimicrobial Utilization, Stewardship and Epidemiology
Wake Forest Baptist Medical Center

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.[2,4]
- 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.[2]
- A history of antimicrobial or antineoplastic agents within the previous 8-12 weeks is present in the majority of patients.[2,4]
- Virtually every antibiotic has been associated with *C difficile* infection[1,2]
- 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.[4,5]
- 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.[1] 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[1]. **Hand washing** with antimicrobial soap and water is preferred over alcohol-based products to prevent the spread of *C difficile*.[1,2]

Diagnosis

- Required diagnostic components include symptoms ***plus*** either a positive stool test for the organism/toxin *or* direct visualization of pseudomembranous colitis.[2]
- 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.[3]
- 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.[3]
  - 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[2].
- When severe *C difficile* infection is suspected, initiate empirical treatment as soon as the diagnosis is suspected[2]. 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.[2] 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.[2]
- 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.[1,2]
- Prophylactic therapy directed at preventing colonization or clinical disease from *C difficile* is of unproven value and not recommended.[1,2]

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.
5. Severe *Clostridium difficile*–associated disease in populations previously at low risk. MMWR Morb Mortal Wkly Rep 2005;54:1201-5.
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Antibiotic therapy for *Clostridium difficile* infection[2,6]

Clinical Definition	Supportive data	Recommended treatment
Initial episode, mild or moderate	Leukocytosis with a WBC count <15,000 cells/mL ***AND*** 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 ≥15,000 cells/mL ***OR*** a serum creatinine level ≥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 ≥ 15,000 cells/mL -- serum creatinine level ≥1.5 times the premorbid level in a non-dialysis patient -- mean arterial pressure <60mmHg -- temperature ≥100.4°F -- age >60 years -- albumin <2.5g/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	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 ≥100.4°F; serum albumin < 2.5 g/dL; admission to an intensive care unit; and colonoscopic evidence of pseudomembranes