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 infection¹,²
- 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 isolation¹. 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.
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. 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.\(^2\)
- If possible, avoid use of anti-peristaltic agents, e.g. loperamide, as they may obscure symptoms and precipitate toxic megacolon. Use of cholestyramine also is not recommended as it may bind anti-*C difficile* therapies.\(^2\)
- 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

### Antibiotic therapy for *Clostridium difficile* infection

<table>
<thead>
<tr>
<th>Clinical Definition</th>
<th>Supportive data</th>
<th>Recommended treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial episode, mild or moderate</strong></td>
<td>Leukocytosis with a WBC count &lt;15,000 cells/mL <em>AND</em> a serum creatinine level &lt; 1.5 times the premorbid level in a non-dialysis patient</td>
<td>Metronidazole 500mg 3 times per day by mouth for 10–14 days</td>
</tr>
<tr>
<td><strong>Initial episode, severe</strong>*</td>
<td>Leukocytosis with a WBC count ≥15,000 cells/mL <em>OR</em> a serum creatinine level ≥1.5 times the premorbid level in a non-dialysis patient</td>
<td>Vancomycin 125mg 4 times per day by mouth for 10–14 days</td>
</tr>
</tbody>
</table>
| **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 colonoscopically evidence of pseudomembranes*