GENERAL

- *Clostridium difficile* (*C. difficile*) is a bacterium that initiates a sporulation process when conditions are unfavourable for its survival. *C. difficile*-associated diarrhea is caused by toxigenic strains.
- Its sporulated form, which is highly resistant to dryness and various biological and chemical agents, enables it to spread and persist.
- In favourable conditions, the spore germinates, assumes a vegetative form and multiplies, producing toxins that cause inflammation of the colonic mucosa and severe diarrhea.
- In certain individuals, *C. difficile* is part of the intestinal microbial flora but without causing any clinical symptoms, as evidenced by the prevalence of asymptomatic carriers.

Prevalence rates in asymptomatic carriers by age group:
- 15 to 63% in newborns
- 3 to 33% in infants and children under 2 years of age
- 8% of children aged 2 years and older
- 2 to 5% of healthy adults
- 10 to 20% of the elderly

PEDIATRIC CONSIDERATIONS

- Diarrhea is a common adverse effect associated with antibiotic use. Therefore, most cases of post-antibiotic diarrhea in children are not caused by *C. difficile*.
- There has been a slight increase in pediatric *C. difficile* infections in recent years.
- In children, the most common clinical manifestation of *C. difficile* infection is profuse diarrhea.
- Diagnostic tests should not be ordered in children less than 1 year of age.

PREVENTIVE MEASURES

In hospitals:
- Place the patient in isolation and apply the hospital’s infection prevention measures.
- Wash your hands with soap and water, vigorously rubbing them to eliminate any spores. Remind the patient of the importance of handwashing.
  - Alcohol-based gels are ineffective against *C. difficile* spores.
- Disinfect the patient’s surroundings.
  - Unlike alcohol, sodium hypochlorite (e.g., bleach) is effective in destroying the spores.
PROBIOTICS

- Although there is a low level of scientific evidence that certain probiotic formulations may confer benefits in terms of preventing *C. difficile*-associated diarrhea (CDAD), no favourable recommendation can be made with the current state of knowledge because of the significant methodological limitations of the clinical trials. For further information, consult the report entitled: **Usage des probiotiques en prévention des diarrhées associées à *Clostridium difficile* chez les patients hospitalisés sous antibiothérapie, au Québec**.

RISK FACTORS

When a patient has diarrhea, check if he/she has taken any antibiotics in the past 2 months, as they increase the risk of contracting *C. difficile* infection, especially if the patient has taken any of the following antibiotics (in the order of risk):

- Clindamycin;
- A cephalosporin, especially a 2nd or 3rd generation one;
- A fluoroquinolone.

The risk is higher in patients who, in addition:

- Have a history of such an infection;
- Are taking a proton pump inhibitor (PPI);
- Have been hospitalized in the past 2 months;
- Have an inflammatory bowel disease;
- Are elderly, especially if they live in a long-term care setting;
- Are immunocompromised.

DIAGNOSIS

- If a patient has important diarrhea, check if he/she has used any antibiotics in the past 2 months, especially those listed above.

- Confirm the clinical diagnosis with a toxin screen (a bacterial stool culture is not the appropriate test).
  - Check that the diarrhea is well established (3 liquid stools in more or less 24 hours) before obtaining a sample for a diagnostic test.

- Determine the severity of the infection using the table below.

- A test of cure after treatment is not recommended.

- Do not perform tests in asymptomatic patients.
### INFECTION SEVERITY

<table>
<thead>
<tr>
<th></th>
<th>Adult</th>
<th>Child</th>
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</thead>
<tbody>
<tr>
<td><strong>Mild</strong></td>
<td>A mild infection is any infection that does not meet the criteria for a severe infection.</td>
<td>Watery diarrhea with no systemic toxicity; 3 or 4 abnormal stools per day.</td>
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<tr>
<td><strong>Severe</strong></td>
<td>Look for the following severity criteria:</td>
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<td></td>
<td>• A white blood cell count ≥ 15 x 10⁹ cells/l</td>
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<td></td>
<td>• A 50 % or greater increase in the serum creatinine level above the person's usual baseline level</td>
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<td>• Documented temperature &gt; 38.5 °C</td>
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<td></td>
<td>• Albumin &lt; 30 g/l</td>
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<tr>
<td><strong>Child</strong></td>
<td>Signs of systemic toxicity (e.g., high fever or chills)</td>
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<tr>
<td><strong>Complicated</strong></td>
<td>Look for signs of complication:</td>
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<tr>
<td></td>
<td>• Hypotension, whether or not vasopressors are required, or septic shock</td>
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<tr>
<td></td>
<td>• Ileus² or toxic megacolon</td>
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<tr>
<td></td>
<td>• Bowel perforation</td>
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<td></td>
<td>• Septicemia</td>
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<td></td>
<td>• Changes in mental status</td>
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<tr>
<td></td>
<td>• White blood cell count ≥ 35 x 10⁹ cells/l or &lt; 2 x 10⁹ cells/l</td>
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<tr>
<td></td>
<td>• Serum lactate &gt; 2.2 mmol/l</td>
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<tr>
<td></td>
<td>• Any evidence of organ failure</td>
<td></td>
</tr>
<tr>
<td><strong>Child</strong></td>
<td>Signs of systemic toxicity or severe colitis, including hypotension, septic shock, ileus, peritonitis or megacolon</td>
<td></td>
</tr>
<tr>
<td><strong>Recurrence</strong></td>
<td>Reappearance of the symptoms of <em>C. difficile</em> infection occurring after symptom resolution within 8 weeks of the previous infection.</td>
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</tr>
</tbody>
</table>

1 The clinical signs listed below are based on expert opinion, since the infection severity criteria have not been validated.

2 The signs and symptoms of ileus include acute nausea, vomiting, the sudden cessation of diarrhea, abdominal distention and radiological signs consistent with ileus (distension, fluid-air levels).

### TREATMENT PRINCIPLES

#### GENERAL MEASURES

- **Discontinue all treatments involving:**
  - Antiperistaltic agents, such as loperamide or diphenoxylate;
  - Laxatives.

- **Reevaluate and discontinue, if possible:**
  - Antibiotics;
  - PPIs;
  - Opioids (because of the risk of bowel perforation).

Do not treat asymptomatic carriers.
It is reasonable to initiate empirical treatment in certain situations while awaiting the diagnosis. Discontinue the empirical treatment if the toxin screen turns out to be negative.

**Mild infection**
- Metronidazole 500 mg PO TID x 10 days
  - if pregnancy
  - if breastfeeding
  - if intolerance, allergy or contraindication to metronidazole
  - if patient is at high risk for complications*
  - if deterioration or no response to treatment with metronidazole after 3 to 5 days
- Vancomycin** 125 mg PO QID x 10 days
  - if deterioration
- Refer patient to a specialist

**Severe infection**
- Vancomycin* 125 mg PO QID x 14 days
  - if deterioration
- Refer patient to a specialist

**Complicated infection**
- Vancomycin* 125 to 500 mg PO QID AND metronidazole 500 mg IV TID
  - if deterioration
- If patient cannot be treated orally
- Refer patient to a specialist

**Severe infection**
- Vancomycin* 125 mg PO QID x 14 days
  - if deterioration
- Vancomycin* 125 to 500 mg PO QID AND metronidazole 500 mg IV TID
  - if deterioration
- Refer patient to a specialist

**Recurrent infection**
- 1st recurrence
  - Repeat initial treatment
  - 42-day treatment, as follows:
    - Vancomycin*: 125 mg PO QID x 7 days
    - 125 mg PO BID x 7 days
    - 125 mg PO OD x 7 days
    - 125 mg every 2 days x 7 days
    - 125 mg every 3 days x 14 days
  - If additional recurrence, refer patient to a specialist

**> 1 recurrence**
- If the patient is taking an antibiotic for another indication, it is not advisable to administer antibiotics against *C. difficile* as prophylaxis. However, in certain specific situations, for example, for treating patients with a history of multiple recurrences of *C. difficile* infection, it may be acceptable to do so. If applicable, treatment with 125 mg of vancomycin PO QID would be indicated, this up to one week after the patient stops taking the antibiotic for the first indication.
If the child cannot be treated orally, refer him/her to a specialist.

* In the event of a complete ileus, consider adding rectal instillation of vancomycin (maximum: 2 g/day).


It should be noted that other references were consulted.