Ministry of Health

Ontario Public Health Standards:
Requirements for Programs, Services and Accountability

Infectious Disease Protocol

Appendix 1: Case Definitions and Disease-Specific Information

Disease: *Clostridium difficile* Infection (CDI) outbreaks in public hospitals

Effective: May 2022

Ontario

Clostridium difficile Infection (CDI) outbreaks in public hospitals

☒ Communicable
☐ Virulent

Health Protection and Promotion Act **(HPPA)**
Ontario Regulation (O. Reg.) 135/18 (Designation of Diseases)

Provincial Reporting Requirements

☒ Confirmed outbreaks and outbreak-associated cases occurring in hospitals under the *Public Hospitals Act*.
☐ Probable case

As per Requirement #3 of the "Reporting of Infectious Diseases" section of the *Infectious Diseases Protocol, 2018* (or as current), the minimum data elements to be reported for each case are specified in the following:

- O. Reg. 569 (Reports) under the HPPA;[8]
- The iPHIS User Guides published by Public Health Ontario (PHO); and
- Bulletins and directives issued by PHO.

Type of Surveillance

Outbreak and case level data

Outbreak Classification

Clostridium difficile infection (CDI) outbreak definitions incorporate the concept of notification thresholds that optimally trigger action and dialogue between the local public health unit and the facility to determine if an outbreak is occurring.

Facilities should use the following CDI notification thresholds to assist them in

determining the need for consultation with their local public health unit. Facilities with limited experience in managing CDI should consult with the local public health unit and/or with the local regional infection control network. These thresholds were developed by the Ministry of Health ('ministry').

Notification Thresholds are defined as:

- For wards/units with ≥20 beds, three (3) new cases of nosocomial CDI identified on one ward/unit within a seven-day period OR five (5) new cases of nosocomial CDI within a four-week period,

OR

- For wards/units with <20 beds, two (2) new cases of nosocomial CDI identified on one ward/unit within a seven-day period OR four (4) new cases of nosocomial CDI within a four-week period,

OR

- Facilities that have a facility nosocomial CDI rate that exceeds their annual nosocomial baseline rate for a period of two consecutive months. **Note:** This is not valid for a small community hospital, where a single case of nosocomial CDI can artificially elevate the facility rate.

It should be noted that exceeding a threshold does not necessarily imply that an outbreak will be declared. Following consultation between the facility and the local public health unit, decisions on the declaration of an outbreak will be made based on the following criteria:

- There has been a significant* (as determined by the facility and the local

---

* Significance may be determined by reviewing:

- number of new nosocomial cases associated with the reporting ward/unit or facility;
- historic level of CDI activity of the ward/unit or facility;
- current trend in ward/unit CDI activity or facility rate; and
- location of current cases and possible epidemiologic links between cases.

public health unit) increase in CDI numbers or rate compared to own baseline and/or that of comparator facilities.

- Recognized control measures are in place and are being used.
- There is epidemiologic evidence of ongoing nosocomial transmission on the ward/unit or facility.

Confirmed Case Definition

- Diarrhea[ǂ] with laboratory confirmation of toxin A or B for *Clostridium difficile* (*C. difficile)* (e.g., Enzyme immunoassay (EIA) for toxin A or B, nucleic acid amplification testing (NAAT) for *C. difficile* toxin genes A or B, or *C. difficile* cytotoxicity assay);

OR

- Visualization of pseudomembranes on sigmoidoscopy or colonoscopy;

OR

- Histological/pathological diagnosis of pseudomembranous colitis;

OR

- Diagnosis of toxic megacolon.

For the purpose of defining a case of CDI, there should be three or more episodes of diarrhea within a 24-hour period.

The following definitions are from Ontario's mandatory patient safety reporting program and can be used to determine whether the case is nosocomial:

[ǂ] Diarrhea is defined as:

- loose/watery bowel movements (conform to the shape of the container), and
- the bowel movements are unusual or different for the patient, and
- there is no other recognized etiology for the diarrhea (for example, laxative use).

CDI Attributable to Your Facility

- The symptoms of CDI were not present on admission (i.e., onset of symptoms > 72 hours after admission) or the infection is present at the time of admission but is related to a previous admission to your facility within the last four weeks.

CDI Not Attributable to Your Facility

- The symptoms of CDI were present on admission or < 72 hours after admission and there was no admission to your facility within the last four weeks.

OR

- The symptoms of CDI recur within two months of the last infection (relapse).

Outbreak Case Definition

The outbreak case definition varies with the outbreak under investigation. Please refer to the *Infectious Diseases Protocol, 2018* (or as current) for guidance in developing an outbreak case definition as needed.

The outbreak case definitions are established to reflect the disease and circumstances of the outbreak under investigation. The outbreak case definitions should be developed for each individual outbreak based on its characteristics, reviewed during the course of the outbreak, and modified if necessary, to ensure that the majority of cases are captured by the definition. The case definitions should be created in consideration of the outbreak definitions.

Outbreak cases may be classified by levels of probability (*i.e.* confirmed and/or probable).

Please also see the Provincial Infectious Diseases Advisory Committee (PIDAC)'s Annex C of Routine Practices and Additional Precautions in All Health Care Settings.[1]

Clinical Information

Clinical Evidence

Clinically compatible signs and symptoms are characterized by the following:

- Diarrhea (as defined above);
- Fever;
- Loss of appetite;
- Nausea; and
- Abdominal pain or tenderness.

C. difficile infection can lead to diseases ranging from mild diarrhea to toxic megacolon and death.

Clinical Presentation

Symptoms of *C. difficile* infection are listed under Clinical Evidence above.

Complications include dehydration and colitis, and may also lead to life threatening systemic toxicity requiring surgical intervention and may also lead to death.[1,2]

Recurrence of CDI is common and occurs in about 30% of cases.[1]

Laboratory Evidence

Laboratory Confirmation

Any of the following will constitute a confirmed case of CDI:

- Laboratory confirmation by validated methods;
- Visualization of pseudomembranes on sigmoidoscopy or colonoscopy;
- Histological/pathological diagnosis of pseudomembranous colitis;
- Diagnosis of toxic megacolon.

Approved/Validated Tests

- *C. difficile* enzyme immunoassay (EIA) for toxin (A and/or B);
- Molecular testing (NAAT) for *C. difficile* toxin genes (A and/or B);
- *C. difficile* cytotoxicity assay.

Indications and Limitations

- Laboratory testing for CDI requires the identification of toxin A or B, or the genes related to cytotoxin production. Cultures for *C. difficile* are not routinely performed and require confirmation of toxin A and/or B or the related genes.
- Stool specimen collection should occur as soon as possible after the onset of symptoms.
- Specimens are not recommended from patients who are less than 12 months old.
- Quick turnaround time for *C. difficile* testing is essential and should be pre-arranged with the microbiology laboratory serving the facility.
- A single negative EIA should not be relied on to rule out *C. difficile*. If a single EIA is negative, a second specimen should be sent.
- Testing by molecular methods such as PCR is more sensitive and if the first test is negative, a second test is not necessary. Some laboratories employ a two-step method, with detection of *C. difficile* glutamate dehydrogenase antigen (GDH) followed by a molecular test if GDH is positive. Molecular testing is now considered the testing method of choice.
- Testing can detect *C. difficile* colonization or disease. Results of laboratory testing must be correlated with the clinical condition of the patient. If the patient does not meet the case definition for CDI, he/she should not be counted as a case of CDI.
- *C. difficile* toxin testing is not recommended as a test of cure. Toxin and toxin genes may be detected long after clinical symptoms have resolved.
- Formed stool specimens will be rejected. If CDI is still suspected, contact the

testing laboratory to arrange testing.

For additional information, please consult Public Health Ontario's (PHO) testing information on *Clostridium (Clostridioides) difficile*.[3]

For further information about human diagnostic testing, contact the Public Health Ontario Laboratories

Case Management

In addition to the requirements set out in the Requirement #2 of the "Management of Infectious Diseases – Sporadic Cases" and "Investigation and Management of Infectious Diseases Outbreaks" sections of the *Infectious Diseases Protocol, 2018* (or as current), the board of health may be requested to provide guidance to manage cases. Individual cases should be managed as per individual facility protocols. Facilities developing protocols may refer to the Roles and Responsibilities of Hospitals and Public Health Units in CDI Reporting and Outbreak Management, 2014 (or as current) and the PIDAC's Annex C: Testing, Surveillance and Management of *Clostridium difficile*.[1,9]

Contact Management

Not applicable.

Outbreak Management

Provide public health support to health care facilities in the management of outbreaks or clusters in order to identify the source of illness and manage the outbreak as per the *Infectious Diseases Protocol, 2018* (or as current) and Roles and Responsibilities of Hospitals and Public Health Units in CDI Reporting and Outbreak Management, 2014 (or as current).[9]

PHO's can provide Infection Control expertise and support in the event of an outbreak.

The criteria for declaring an outbreak over should be determined collaboratively by

the facility and the local public health unit as part of the outbreak management team process.

Factors to consider in declaring an outbreak over should include:

- Control measures have been implemented and validated through an audit process.
- There has been a return to unit/ ward or facility baseline for nosocomial CDI. For a facility-wide outbreak, this should be a minimum period of one month.
- Reservoir of colonized patients/ residents in the facility has been discharged.
- Facility's past experience with CDI outbreaks demonstrates ability to bring them under control.

Prevention and Control Measures

Personal Prevention Measures

Effective hand hygiene is essential to limit the spread of *C. difficile*. Other infection prevention and control strategies, including, but not limited to, education for staff, patients, visitors/families may be used.[1]

Messaging to visitors should be written in clear language and include the following:

- What is CDI and what the visitor's risk of acquiring it is;
- How to properly clean their hands (and its importance);
- When personal protective equipment is needed and how to put on and take off;
- Measures to take when providing direct care to the patient/or having significant contact with the patient's environment (i.e., wear gown and gloves);
- Instructions to only use visitor washrooms and where these are located; and
- Instructions to visit their significant other in isolation last if they are visiting more than one person in the hospital.

Infection Prevention and Control Strategies

Prevention Strategies in institutions include:[1]

- early identification and testing of patients with symptoms;
- empowering front-line staff to institute additional precautions at onset of symptoms; and
- daily surveillance reporting to Infection Prevention and Control program staff.

In addition to Routine Practices, Contact Precautions should be initiated by any regulated health care provider (e.g., physician, nurse) at onset of diarrhea and prior to receipt of *C. difficile* test results.

More detailed information is available in PIDAC's Annex C: Testing, Surveillance and Management of Clostridium difficile.[1]

Disease Characteristics

Aetiologic Agent - *Clostridium difficile* (*C. difficile)* is a gram-positive, spore-forming, anaerobic bacillus. It is widely distributed in the environment and colonizes up to 3-5% of adults without causing symptoms. Some strains can produce two toxins that are responsible for diarrhea: toxin A and toxin B.[1]

Outbreaks in Canada, the United States, and Europe have been associated with a hypervirulent epidemic strain referred to as the NAP1/BI/027 strain. Characteristics of this strain include the presence of a binary toxin; increased resistance to clindamycin and the fluoroquinolone class of antibiotics; and an increased likelihood of a serious illness.[1]

Modes of Transmission - *C. difficile* is widely distributed in the environment. It produces spores that survive for longer periods of time and are resistant to destruction by environmental factors (e.g. temperature, humidity), including standard cleaning agents.[5] In an effort to protect itself from undesirable environmental conditions, it assumes its spore form.

C. difficile is spread through the fecal-oral route of transmission.[4] *C. difficile* can be

acquired in both hospital and community settings.[5] *C. difficile* can be transmitted and/or acquired by patients through contact with contaminated surfaces (including both vegetative cells and spores).

CDI may occur when antibiotics kill normal bowel bacteria and allow the *C. difficile* to grow. When *C. difficile* grows, it may produce toxins, which can damage the bowel and may cause diarrhea.[4]

Incubation Period – The incubation period of *C. difficile* following acquisition has not been clearly defined. Studies have determined that onset of infection can occur within 48 hours after exposure and up to 3 months post exposure.[6,7]

Period of Communicability - Precise period of communicability is unknown; it may vary depending on the amount of toxin in the stool, which can vary from very small to large spores and are very difficult to eliminate from surfaces and objects. Cytotoxins may persist in stool for weeks.[1]

Reservoir - *C. difficile* bacteria are found in feces of humans.[4]

Risk Factors for Acquisition of CDI - Risk factors include:[1]

- a history of antibiotic usage, particularly broad-spectrum antibiotics that affect the normal gut bacterial flora, such as fluoroquinolones;
- immunosuppressive therapy post-transplant;
- proton pump inhibitors;
- bowel disease and bowel surgery;
- chemotherapy; and/or
- hospitalization.

Additional risk factors that predispose some people to develop more severe disease include:[1]

- history of CDI;
- increased age;
- immunosuppressive therapy;

- recent surgery; and/or
- CDI with the hypervirulent strain of *C. difficile*.

Please refer to PHO's Reportable Disease Trends in Ontario reporting tool for the most up-to-date information on infectious disease trends in Ontario.

For additional national and international epidemiological information, please refer to the Public Health Agency of Canada and the World Health Organization.

Comments

- It should be noted that exceeding a threshold does not necessarily imply that an outbreak will be declared. Declaration of an outbreak can be made by either the institution or the Medical Officer of Health (MOH).
- In the event of a disagreement between the institution and the MOH, the MOH has the authority to determine if an outbreak of a communicable disease exists, for purposes of exercising statutory powers under the HPPA. Once an outbreak is declared it is reported to the ministry through integrated Public Health Information System (iPHIS).
- The hospital may declare an outbreak over and shall consult with the MOH in doing so. Rationale for declaring or not declaring an outbreak, and declaring an outbreak over should be documented.

References

1. Ontario Agency for Health Protection and Promotion, Provincial Infectious Diseases Advisory Committee. Annex C – Testing, Surveillance and Management of Clostridium difficile. Annexed to: Routine Practices and Additional Precautions in All Health Care Settings. Toronto, ON: Queen's Printer for Ontario; 2013. Available from: https://www.publichealthontario.ca/-/media/Documents/C/2013/cdiff-testing-surveillance-management.pdf?sc_lang=en

2. Government of Canada. C. difficile (Clostridium difficile) [Internet]. Ottawa, ON: Her Majesty the Queen in Right of Canada; 2012 [updated October 9, 2012; cited May 31, 2018]. Available from: https://www.canada.ca/en/public-health/services/diseases/c-difficile.html
3. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Testing Information: Clostridium difficile [Internet]. Toronto, ON: Queen's Printer for Ontario; 2016 [updated September 30, 2016; cited June 11, 2018]. Available from: https://www.publichealthontario.ca/en/laboratory-services/test-information-index/clostridium-difficile
4. Government of Canada. Fact Sheet - Clostridium difficile (C. difficile) [Internet]. 2014 [updated May 2, 2014. Available from: https://www.canada.ca/en/public-health/services/infectious-diseases/fact-sheet-clostridium-difficile-difficile.html
5. McFarland LV, Beneda HW, Clarridge JE, Raugi GJ. Implications of the changing face of Clostridium difficile disease for health care practitioners. American Journal of Infection Control. 2007;35(4):237-53.
6. Muto CA, Pokrywka M, Shutt K, Mendelsohn AB, Nouri K, Posey K, et al. A large outbreak of Clostridium difficile–associated disease with an unexpected proportion of deaths and colectomies at a teaching hospital following increased fluoroquinolone use. Infection Control & Hospital Epidemiology. 2005;26(3):273-80.
7. Wilkins TD, Lyerly DM. Clostridium difficile testing: after 20 years, still challenging. Journal of clinical microbiology. 2003;41(2):531-4.
8. Health Protection and Promotion Act, R.S.O. 1990, Reg. 569, Reports, (2018). Available from: https://www.ontario.ca/laws/regulation/900569

9. Ontario. Ministry of Health and Long-Term Care. Roles and Responsibilities of Hospitals and Public Health Units in CDI Reporting and Outbreak Management, 2014. Toronto, ON: Queen's Printer of Ontario; 2014. Available from: http://www.health.gov.on.ca/en/pro/programs/publichealth/oph_standards/reference.aspx

Case Definition Sources

Dallal RM, Harbrecht BG, Boujoukas AJ, Sirio CA, Farkas LM, Lee KK, et al. Fulminant Clostridium difficile: an underappreciated and increasing cause of death and complications. Annals of Surgery. 2002;235(3):363.

Government of Canada. Fact Sheet - Clostridium difficile (C. difficile) [Internet]. 2014 [updated May 2, 2014. Available from: https://www.canada.ca/en/public-health/services/infectious-diseases/fact-sheet-clostridium-difficile-difficile.html

Ontario Agency for Health Protection and Promotion, Provincial Infectious Diseases Advisory Committee. *Annex C – Testing, Surveillance and Management of Clostridium difficile.* Annexed to: Routine Practices and Additional Precautions in All Health Care Settings. Toronto, ON: Queen's Printer for Ontario; 2013. Available from: https://www.publichealthontario.ca/-/media/Documents/C/2013/cdiff-testing-surveillance-management.pdf?sc_lang=en

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Testing Information: Clostridium difficile [Internet]. Toronto, ON: Queen's Printer for Ontario; 2016 [updated September 30, 2016; cited June 11, 2018]. Available from: https://www.publichealthontario.ca/en/laboratory-services/test-information-index/clostridium-difficile

Document History

Revision Date	Document Section	Description of Revisions
April 2022	Entire Document	New template. Appendix A and B merged. No material content changes.
April 2022	Epidemiology: Occurrence section	Removed, except for paragraph, "Outbreaks in Canada, the United States, and Europe have been associated with a hypervirulent epidemic strain referred to as the NAP1/BI/027 strain. Characteristics of this strain include the presence of a binary toxin; increased resistance to clindamycin and the fluoroquinolone class of antibiotics; and an increased likelihood of a serious illness.[1]" This paragraph was moved to Aetiologic Agent.
April 2022	ICD Codes	Removed.