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: Carbapenemase-producing Enterobacteriaceae (CPE) infection or colonization

Effective: May 2022

Ontario

Carbapenemase-producing Enterobacteriaceae (CPE) infection or colonization

☒ Communicable
☐ Virulent

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

Provincial Reporting Requirements

☒ Confirmed case
☐ 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;[14]
- The iPHIS User Guides published by Public Health Ontario (PHO); and
- Bulletins and directives issued by PHO.

Type of Surveillance

Case and outbreak level data (see Outbreak Definitions)

Case Definition

Confirmed Case

Laboratory confirmation of CPE by an Ontario microbiology laboratory.

Both colonization detected from active screening and clinical infections are considered confirmed cases of CPE. All confirmed cases of CPE require investigation to determine if nosocomial transmission of CPE has occurred, and to identify the source of transmission.

The first positive isolate from any individual identified as colonized or infected with CPE is reportable. Subsequent positive isolates from the same patient are reportable only if the patient tests positive for a different CPE (i.e., different carbapenemase).

Outbreak Definitions

Suspect Outbreak Definition

An outbreak may be suspected in a health care facility if:

- Two or more patients with CPE with the same carbapenemase (not known to be colonized or infected prior or upon admission) are reported on the same ward/unit(s) in a three-month period;

OR

- Three or more patients with CPE with the same carbapenemase (not known to be colonized or infected prior or upon admission) are reported at the same health care facility or institution in a three-month period.

Whenever an outbreak is suspected, point prevalence screening should be performed on the ward/unit(s) where the case originated.

Confirmed Outbreak Definition

An outbreak is confirmed in a health care facility if:

- Evidence of transmission between patients is identified;

OR

- An epidemiological link between patients is identified;

OR

- The health care facility/institution considers, based on their policies, transmission has occurred between suspected or confirmed cases, or if the incidence of CPE at the facility is higher than expected even without a clear link between patients.

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).

Clinical Information

Clinical Evidence

All CPE colonizations and infections are reportable. CPE are associated with a wide range of infections, including, but not limited to, pneumonia, bloodstream infections, intra-abdominal infections, urinary tract infections, and central venous catheter infections.

Clinical Presentation

Patients with CPE colonization are asymptomatic and can only be identified by active screening; however, colonizing CPE can cause infections if they gain access to sterile body sites (e.g., lungs, bladder, bloodstream).[4]

CPE are capable of causing difficult-to-treat infections in any part of the body, including pneumonia, bloodstream infections, intra-abdominal infections, urinary tract infections, and central venous catheter infections.[5] Mortality in patients with CPE bacteremia may be up to 50%.[6]

Laboratory Evidence

Laboratory Confirmation

- CPE isolated by culture from any human specimen (clinical or screening specimen) tested in an Ontario microbiology laboratory

OR

- Positive nucleic acid amplification technique (NAAT) results for CPE from any human specimen (clinical or screening) tested in an Ontario microbiology laboratory

Approved/Validated Tests

Any validated test approved for CPE culture or NAAT by an Ontario microbiology laboratory.

Note: The first isolate from any individual identified as colonized or infected with CPE should be forwarded to Public Health Ontario Laboratory (PHOL).

Indications and Limitations

- Not all carbapenem resistant organisms are due to a carbapenemase;
- In carbapenem resistant isolates, the presence of a carbapenemase must be confirmed by a laboratory before CPE is reported
- Carbapenemase genes may also be found in other gram-negative bacteria, including *Acinetobacter* and *Pseudomonas* spp.
- Most carbapenemase testing is limited to identification of known carbapenemases. Novel/currently unknown carbapenemases will not be detected by existing genotypic (e.g. PCR) laboratory testing methods.

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 shall investigate cases to determine the source of infection. Refer to Provincial Reporting Requirements above for relevant data to be collected during case investigation.

Individual cases should be managed as per individual facility protocols. Facilities developing protocols should review Annex A – Screening, testing and surveillance for antibiotic-resistant organisms (AROs) (2013, or as current) of the PIDAC document Routine Practices and Additional Precautions (2012, or as current).[13]

Contact Management

Not applicable. Contacts of patients with CPE must be assessed and may require screening and follow-up by the health care facility.

Outbreak Management

Please see the *Infectious Diseases Protocol, 2018* (or as current) for the public health management of outbreaks or clusters in order to identify the source of illness, manage the outbreak and limit secondary spread.

PHO can provide Infection Control expertise and support in the event of a CPE outbreak.

Further guidance on CPE outbreaks is also available Annex A – Screening, testing and surveillance for antibiotic-resistant organisms (AROs) (2013, or as current).[13]

Prevention and Control Measures

Personal Prevention Measures

Effective hand hygiene is essential to limit CPE transmission. Other Infection Prevention and Control (IPAC) strategies are discussed below.

Infection Prevention and Control Strategies

The consistent use of Routine Practices for all clinical care, including the use of hand hygiene and cleaning/disinfection of all shared equipment, are essential to reduce the risk of CPE transmission. Additional guidance of infection control practices that can reduce the risk of CPE transmission can be found in the PIDAC document Routine Practices and Additional Precautions (2012, or as current) with specific guidance on CPE located in Annex A – Screening, testing and surveillance for antibiotic-resistant organisms (AROs) (2013, or as current) of the same document.[13]

Refer to PHO's website to search for the most up-to-date information on IPAC.

Disease Characteristics

Aetiologic Agent - Carbapenemase-producing *Enterobactericeae* (CPE) refers to gram-negative bacteria belonging to the *Enterobactericeae* family harbouring carbapenemase-encoding genes.[1] Carbapenemases are beta-lactamases with ability to hydrolyze penicillins, cephalosporins, and carbapenems, rendering these antibiotics ineffective. As a result, there are limited antibiotic treatment options for patients with infection due to CPE and mortality is substantially increased.[2,3]

Globally, there are many different carbapenemase-encoding genes and many different resultant carbapenemases.[2] The carbapenemases that are most common in Ontario currently included NDM, KPC, OXA-48 and VIM.

Modes of Transmission - Transmission of CPE occurs via direct or indirect contact.[10]

CPE are isolated predominantly from patients with exposures in health care facilities and can spread from person to person on the hands of healthcare workers or via

shared medical equipment, particularly when hand hygiene is missed or equipment is not properly cleaned and disinfected. Transmission has also been associated with contaminated sink drains and outbreaks have occurred where CPE was transmitted between patients undergoing duodenoscopy, even when it appears that the duodenoscope was appropriately reprocessed between patients.[8,9]

Incubation Period – The incubation period for exposure-to-illness onset is undefined. Individuals colonized with CPE may remain asymptomatic if they are in good health and do not require medical interventions but can still act as a reservoir for transmission to others.

Factors that impair the function of the immune system (e.g., hematologic malignancy), and interventions which permit colonizing bacteria to invade (e.g., indwelling devices) increase the probability of infection with CPE.[11]

Period of Communicability - The period of communicability of CPE persists as long as the organism is present in the gastrointestinal tract of the patient. Several studies have evaluated duration of colonization of patient populations in different countries with varying results.[12] Patients can be intermittently positive on repeat screening and may be colonized for months to years.

Reservoir - Human and environmental reservoirs.[7,8,9] Colonized patients are the main reservoir for CPE and can only be detected by active screening for CPE.

Host Susceptibility and Resistance - *Enterobacteriaceae* are found in the lower gastrointestinal tract. The primary risk factor for acquiring CPE is exposure to patients in health care facilities with prevalent CPE. Because CPE are resistant to all penicillins, cephalosporins, and carbapenems, treatment of infections is difficult and involves the use of antibiotics with poor adverse event profiles and/or reduced efficacy (e.g., colistin, tigecycline).[13]

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

- Declaration of an outbreak can be made by either the institution/health facility or the medical officer of health (MOH).
- In the event of a disagreement between the institution/health facility 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 *Health Protection and Promotion Act*. Once an outbreak is declared, it is reported to the Ministry through the integrated Public Health Information System (iPHIS).
- The board of health shall declare whether an outbreak is over, in consultation with the institution/facility. Rationale for declaring or not declaring an outbreak, and declaring an outbreak over should be documented.
- Issuing a media release to the public is the responsibility of the institution or health facility. Should there be a public health risk to the general population, a joint media alert may be issued, or the board of health may issue an alert on behalf of the institution or health facility with their knowledge.

Preventing the emergence of CPE in Ontario will require comprehensive surveillance data to ensure:

- The early identification of cases, transmission events and outbreaks at any institution or health facility;
- The identification of risk factors for CPE carriage to allow health facilities to implement surveillance strategies based on an understanding of the incidence and risk factors for CPE in their region; and
- The evaluation of implemented control measures.

Although the prevalence of CPE in Ontario is low, the emergence of multidrug resistant organisms within Canadian health care facilities requires an integrated approach to surveillance and infection control between public health and primary care. With no or limited treatment options, even a single transmission event of CPE is of concern.

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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.
April 2022	ICD Codes	Removed.