Ministry of Health and Long-Term Care

Infectious Diseases Protocol

Appendix A: Disease-Specific Chapters

Chapter: Carbapenemase-producing Enterobacteriaceae (CPE) infection or colonization

Effective: February 2019

Ontario

Carbapenemase-producing Enterobacteriaceae (CPE) infection or colonization

☒ Communicable

☐ Virulent

Health Protection and Promotion Act:
O. Reg. 135/18 (Designation of Diseases)

1.0 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.

2.0 Case Definition

2.1 Surveillance Case Definitions

Refer to Appendix B for Case Definitions.

2.2 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).

3.0 Identification

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

1. The early identification of cases, transmission events and outbreaks at any institution or health facility;
2. 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
3. The evaluation of implemented control measures.

3.1 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]

3.2 Diagnosis

CPE are identified by any Ontario microbiology laboratory. A case of CPE is any patient with a positive isolate of CPE, regardless of the presence of signs and symptoms or clinical findings.

See Appendix B for diagnostic criteria relevant to the Case Definitions.

For further information about diagnostic testing, contact the Public Health Ontario Laboratories or refer to the Public Health Ontario Laboratory Services webpage: http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/default.aspx

4.0 Epidemiology

4.1 Occurrence

CPE are a global problem and are endemic in healthcare facilities in many countries. In India, there is also evidence of CPE transmission in the community and CPE contamination of water.[7]

Until recently, CPE were rare in Canada. Though still uncommon, CPE have been identified with increasing frequency in Ontario and in other Provinces. Since the Public Health Ontario (PHO) CPE surveillance program was initiated in 2012, the number of positive isolates has increased 2.4-times, from 115 positive isolates in 2015 to 276 positive isolates in 2016.[8]

In 2016, 148 patients with CPE were reported to PHO. The median age of patients was 70 years and 58.1% were male. Most (63%) of the 134 patients where clinical information was provided were colonized, although 37% had evidence of clinical infection. Risk factors included hospitalization within the prior 12 months in 66% and travel outside of Canada in 57%. Importantly, of the 104 patients for which information in hospitalization and travel were provided, 30% had no travel or hospitalization outside of Canada, suggesting that transmission occurred in Canada.[8]

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.

Please refer to Public Health Ontario's (PHO) Reportable Disease Trends in Ontario reporting tool and other reports for the most up-to-date information on infectious disease trends in Ontario.

http://www.publichealthontario.ca/en/DataAndAnalytics/Pages/DataReports.aspx

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

4.2 Reservoir

Human and environmental reservoirs.[7,9,10] Colonized patients are the main reservoir for CPE and can only be detected by active screening for CPE.

4.3 Modes of Transmission

Transmission of CPE occurs via direct or indirect contact.[11]

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.[9,10]

4.4 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.[12]

4.5 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.[13] Patients can be intermittently positive on repeat screening and may be colonized for months to years.

4.6 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).[14]

5.0 Reporting Requirements

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:

- *Ontario Regulation 569* (Reports) under the *Health Protection and Promotion Act* (HPPA);[15]
- The iPHIS User Guides published by PHO; and
- Bulletins and directives issued by PHO.

6.0 Prevention and Control Measures

6.1 Personal Prevention Measures

Effective hand hygiene is essential to limit CPE transmission. Other infection prevention and control (IPAC) strategies are discussed below.

6.2 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.[14]

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

6.3 Management of Cases

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 Section 5: 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).[14]

6.4 Management of Contacts

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

6.5 Management of Outbreaks

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's Infection Control Resource Teams (ICRTs) 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).[14]

7.0 References

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8.0 Document History

Table 1: History of Revisions

Revision Date	Document Section	Description of Revisions
April 2018	Entire appendix developed.	CPE was designated as a disease of public health significance effective May 1, 2018.
February 2019	General	Common text included in all Disease Specific chapters: Surveillance Case Definition, Outbreak Case Definition, Diagnosis, Reporting Requirements, Management of Cases, and Management of Outbreaks.
February 2019	4.4 Incubation Period	Improved clarity of second sentence.


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