Public Health Ontario | Santé publique Ontario

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# FREQUENTLY ASKED QUESTIONS

# Carbapenemase-Producing *Enterobacteriaceae* (CPE)

## New Regulations for Reporting CPE

CPE is an emerging threat to global health which requires a coordinated approach to prevention and control among public health, infection control, clinical and laboratory professionals.

The Ministry of Health and Long-Term Care updated the *Health Protection and Promotion Act* and its regulations for reporting diseases of public health significance (DOPHS) to include carbapenemase-producing *Enterobacteriaceae* (CPE) colonization and infection, effective May 1, 2018.[1,2]

The Disease Specific Chapter (Appendix A) and Provincial Case Definition (Appendix B) for CPE are available on the ministry's website under the Infectious Diseases Protocol, 2018.[3,4]

These frequently asked questions have been created to provide background information and new reporting information for public health inspectors, public health nurses, and other relevant personnel who may be unfamiliar with CPE and will be conducting follow-up.

## Sections:

# Background

## What is carbapenemase-producing *Enterobacteriaceae* (CPE)?

***Enterobacteriaceae*** are a family of gram-negative bacteria found in our gastrointestinal tract. Commonly encountered *Enterobacteriaceae* include *Klebsiella* species, *Escherichia coli*, and *Enterobacter* species.

**Carbapenems** are a class of antibiotics that includes ertapenem, imipenem, and meropenem. They are among the strongest antibiotics and are used for treating infections that are difficult to treat.

**CPE** are *Enterobacteriaceae* that produce enzymes (i.e., carbapenemases) that inactivate carbapenems and several other classes of antibiotics. This causes infections that are difficult to treat, with mortality up to 50% of severely infected patients.

## How common are CPE in Ontario?

Until recently, CPE were rare in Ontario. The voluntary surveillance program conducted from 2012 to 2017 via hospital infection control and Public Health Ontario's laboratory, Toronto location found that the total number of isolates submitted for testing and the incidence of positive isolates have increased since CPE surveillance was initiated in 2012.[5] See PHO's previous surveillance reports for further information.

Overall, 526 unique patients who tested positive for CPE were captured in the voluntary surveillance program from 2012 to 2017 in Ontario; 57% patients were colonized, 36% were infected (with or without previous colonization), and 11% had an unknown colonization or infection status.

# CPE Colonization and Infection

## Who is at Risk for acquiring CPE?

The primary risk factor for acquiring CPE is exposure in health care facilities with prevalent CPE. In health care facilities, contacts at highest risk for CPE are those with increased duration of exposure (e.g., prolonged length of stay) and intensity of exposure (e.g., invasive medical procedures, intensive nursing).[6]

Recent travel and hospitalization abroad are also important risk factors of CPE acquisition. Specifically, India, Pakistan, and Bangladesh are considered endemic for certain CPEs—New Delhi metallo-β-lactamase (NDM) is the most widespread carbapenemase in south central Ontario (roughly 50% of all CPE identified in Ontario) given the high rate of travel to and from the Indian subcontinent.[5] *Klebsiella pneumoniae* carbapenemase (KPC) is the most widespread carbapenemase in the United States.

## Where are CPE found?

Colonized patients and residents are the main reservoir for CPE (mainly found in the lower gastrointestinal tract). Colonization or infection can only be detected by microbiological testing for CPE. Besides humans, CPE can be found in environmental reservoirs such as sinks, shower drains or endoscopes that have not been reprocessed properly.[7,8]

## What is the difference between CPE colonization and CPE infection?

All CPE colonizations or infections are reportable in Ontario, since both are communicable and require surveillance for prevention of spread and control. See Case Definition for details.

- **Colonization:** the presence and growth of a microorganism in or on a body without tissue invasion, cellular injury or symptoms.[9]

  Patients and residents colonized with CPE are asymptomatic and can only be identified by microbiological testing. Typically, health care facilities screen patients or residents with risk factors for CPE, or those who are considered high risk by a health care facility (risk factors include hospitalization outside Canada in the last 12 months or contact with a patients or residents known to have CPE).

- **Infection:** the entry and multiplication of an infectious agent in the tissues of the host. Asymptomatic or subclinical infection is an infectious process running a course similar to that of clinical disease but below the threshold of clinical symptoms. Symptomatic or clinical infection is one resulting in clinical signs and symptoms (disease).[9]

  CPE can cause infections in any part of the body (e.g., lungs, bloodstream, abdomen, urinary tract, and central venous catheters); these infections are particularly difficult to treat since CPE are resistant to almost all available antibiotics. Mortality in patients with CPE bloodstream infections may be as high as 50%.

## What is the difference between carbapenem-resistant *Enterobacteriaceae* (CRE) and carbapenemase-producing *Enterobacteriaceae* (CPE)?

Carbapenem resistance in organisms (i.e., *Enterobacteriaceae* as well as other families of bacteria) can occur in a number of ways; however the rapid spread in North America and globally has been due to the enzymatic activity of carbapenemase-producing *Enterobacteriaceae* (CPE) to inactivate antibiotics. The Centers for Disease Control and Prevention (CDC) use the term, CP-CRE, a subset of CRE; these are the organisms which are required to be reported to public health authorities in Ontario as of May 1, 2018.

*Enterobacteriaceae* that are resistant to antibiotics via other mechanisms without the production of carbapenemases, as well as non-*Enterobacteriaceae* organisms (e.g., *Pseudomonas, Acinetobacter*), are not required to be reported in Ontario. However, the Public Health Agency of Canada conducts sentinel surveillance on all infections caused by carbapenemase-producing organisms (CPO) through Canadian Nosocomial Infection Surveillance Program (CNISP).

# Transmission

## What is the incubation period for CPE?

The incubation period from exposure to illness onset is undefined. Individuals may remain colonized if they are in good health but are still a reservoir for transmission to others. Factors that impair the function of the immune system (e.g., hematologic malignancy) and interventions that permit colonizing bacteria to invade (e.g., indwelling devices) increase the probability of infection with CPE.

## For how long is CPE communicable?

The period of communicability of CPE persists as long as an individual is colonized or infected with the organism. Several studies have evaluated the duration of colonization of patient or resident populations in different countries with varying results.[10] Patients and residents can intermittently test positive on repeat microbiological testing[11] and may be colonized for months to over a year.[12,13]

## How do CPE spread?

Transmission of CPE occurs via direct or indirect contact. CPE are isolated predominantly from patients and residents with exposures in health care facilities and can spread from person to person by the hands of health care workers when hand hygiene is missed, or via shared medical equipment that is not properly cleaned and disinfected.

## Can family and friends visit a patient or resident with CPE?

Healthy family and visitors have a low risk of acquiring a CPE infection. In a hospital, long-term care home, or retirement home, visitors should be instructed by health care providers on how to use Contact Precautions. Children and infants should be closely supervised. Visitors should clean their hands before entering and when leaving the room of a patient or resident who test positive for CPE. Avoid using the patient's or resident's bathroom.

## Should health care providers be tested for CPE?

Testing of health care providers for CPE is not recommended unless the health care provider is epidemiologically implicated in transmission. There is no evidence that rectal colonization of health care providers contributes to transmission.

## How can CPE transmission be prevented?

The consistent use of Routine Practices is essential to reduce the risk of CPE transmission in all health care settings. Routine practices include hand hygiene, cleaning and disinfection of all equipment prior to reuse on another patient or resident, as well as regular auditing of these infection prevention and control practices.

Initiate Contact Precautions for patients and residents with CPE, including:

- Appropriate patient and resident placement.
- Wearing of gloves for all activities in the patient room or bed space in acute care, or for direct care of residents in long-term care and clients in retirement homes and ambulatory and clinic settings. Remove and discard gloves immediately after the activity for which they were used. Also, change or remove gloves if moving from a contaminated body site to a clean body site within the same individual or before touching the environment. Remember to clean hands after removing gloves.
- Wearing of long-sleeved gown for activities where skin or clothing will come in contact with the patient or their environment in acute care, or for direct care of residents in long-term care and retirement homes and clients in ambulatory and clinic settings.
- Dedicated equipment. If this is not feasible, effectively clean and disinfect shared equipment.
- In the event of an outbreak, absolute cohorting of patients and residents, staff assignments and equipment is essential to prevent further transmission.

Despite the fact that the health care environment can be contaminated by these bacteria from colonized or infected patients and residents, careful application of routine cleaning practices should be sufficient to remove this pathogen. See PIDAC: Best Practices for Environmental Cleaning for Infection Prevention and Control (page 110).[14]

Hand washing sinks should not be used for other purposes, such as disposal of body fluids and bath water or cleaning of equipment. Facilities may want to consider enhanced sink and shower cleaning on a regular basis, (twice weekly), and at the time of discharge or transfer cleaning for rooms occupied by patients or residents with CPE, and may consider testing sink and shower drains for CPE at the time of patient or resident discharge and transfer. If sinks remain colonized despite repeated attempts at cleaning, replacement of sinks and/or the related horizontal drainage system may be required.

Recommendations for cleaning sinks or shower drain can be found in PIDAC: Best Practices for Environmental Cleaning for Infection Prevention and Control.[14]

There is no specific recommendation at this point for the removal of plumbing fixtures if enhanced cleaning fails to eradicate CPE from the drains. However, removal and replacement of plumbing fixtures may be essential to prevent further transmission of CPE. Discarding of the plumbing fixtures would be done in a manner similar to discarding other construction waste. The waste would be placed in closed bags or covered containers for transport through the facility.

## What testing is required for contacts of a case of CPE?

Contacts of CPE patients and residents include roommates and those in close geographic proximity (e.g., area with shared staffing assignments) to source CPE patients or residents while admitted to a health care facility. Contacts of CPE cases should have a minimum of 3 sets of specimens taken on different days, with at least one taken 21 days after last exposure. Re-testing is recommended if ongoing transmission of CPE is reported. Testing of household contacts is not required unless they are admitted to a health care facility. For more information, see Annex A – Screening, testing and surveillance for antibiotic-resistant organisms (AROs).[15]

## When can Contact Precautions be lifted for patients and residents with CPE?

Because of the implications of CPE transmission in hospitals, current recommendations are that patients remain on Contact Precautions for the duration of hospitalization, preferably in a single room. Patients should be presumed to be colonized and managed on Contact Precautions if they are readmitted within the next year. There are currently no recommendations for when follow-up screening should occur or how often it should be repeated. This would be a decision made on a case-by-case basis by relevant stakeholders. CPE colonization can last for an extended period of time, so frequent screening may not be necessary.

Contact Precautions should only be discontinued after consultation with Infection Prevention and Control. Discontinue Contact Precautions for patients and residents with risk factors or contacts when at the minimum 3 sets of specimens taken on different days test negative, with at least one taken 21 days after the last exposure. If this is not feasible, discontinue precautions if a screening specimen taken at least 7 days after the last exposure tests negative; screening should continue until complete. Primary screening specimens for CPE are stool or rectal swabs. Urine specimens and swabs from open wounds may also be indicated.[16] In critical care settings, sputum or endotracheal tube specimens and swabs from exit sites may be indicated. See Annex A – Screening, testing and surveillance for antibiotic-resistant organisms (AROs).[15]

## What are the environmental cleaning recommendations for sinks and shower drains to reduce environmental reservoirs of CPE?

Sinks and shower drains may act as a reservoir for CPE and persistent colonization of sinks can result in CPE transmission to subsequent room occupants. Sinks (including the drain pipes) have been documented as source of several CPE and ESBL outbreaks.[17-22] As these bacteria form biofilm in moist environments such as the sink drainage system, their eradication has been challenging[18,23]and may require replacement of the implicated sinks[17] and/or the horizontal drainage system[21] when enhanced cleaning and disinfection measures fail to prevent transmission. See PIDAC: Best Practices for Environmental Cleaning for Infection Prevention and Control.[14]

# Treatment

## Can CPE infections be treated?

Options for antibiotics against CPE infections are limited and adverse-effect profiles and risk of toxicity are increased among the antibiotic options used to treat CPE infections. Patients and residents who are colonized with CPE do not require treatment and current evidence does not support decolonization. However, in an uncontrolled outbreak, decolonization may be considered to attempt to reduce the bioburden. See PIDAC's CPE Information Sheet for Patients and Visitors.[24]

# Reporting

## Case Definition

The Ontario Ministry of Health and Long-Term Care definition of a confirmed case of CPE (as of May 1, 2018) is based on laboratory confirmation of CPE by an Ontario microbiology laboratory.

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.**

> **Note**: Once colonized or infected with CPE, individuals may carry CPE indefinitely, therefore only the first positive isolate is reportable unless a different carbapenemase is identified.

- The *CPE Investigation Tool* has been developed to assist PHUs with standardized data collection for CPE cases.

See Appendix B: Provincial Case Definitions for Reportable Diseases for a description of the required laboratory evidence for CPE.[4]

### If a patient is colonized with an *Escherichia* coli NDM carbapenemase-producing isolate, and two months later by a *Klebsiella pneumoniae* carbapenemase-producing isolate identified as NDM, do both isolates have to be reported?

Both CPE isolates have the same carbapenemase, therefore, only the first isolate needs to be reported. Plasmids (i.e., genetic mobile elements) that code for the resistance to carbapenems can be transmitted among bacterial species (e.g., *Klebsiella pneumoniae* and *Escherichia* coli), creating resistance in another species, but not considered a different type of CPE. If the patient were to have a KPC and then an NDM, the second isolate would be considered a new carbapenemase, and would be reportable.

### What timeframe for hospitalization is considered for reporting case risk factors outside of Canada?

Risk factors for CPE acquisition are captured in iPHIS, Ontario's reportable diseases information system, as part of CPE surveillance and reporting requirements. Hospitalization outside of Canada within the last 12 months is one of several risk factors that are required to be reported. If the case was hospitalized outside of Canada > 12 months prior, you are encouraged to indicate this as "Other, specify" and indicate additional details about the timeframe and location of hospitalization in the comments as colonization with CPE can last an extended period of time, and therefore, the information is still relevant.

## Case Management

### What should hospitals, long-term care and retirement homes do if they receive a laboratory report on a colonization or infection of CPE?

- **Report to local Medical Officer of Health:** The isolation of CPE should be considered to be a critical laboratory result and reportable to the local Medical Officer of Health.
- **Notify infection prevention and control and senior management:** The health care facility's infection prevention and control professional(s) (or health care providers overseeing an infection prevention and control program) and senior management are to be notified whenever CPE is identified.
- **Take screening specimens from contacts:** Any patient or resident who is considered to be a CPE contact should have at least one set of screening specimens taken. If initial specimens are negative, it is prudent to repeat them. If a single patient or resident with CPE is identified, a full unit or ward prevalence screen should be conducted.

> **Note:** If screening of the full unit or ward is not feasible due to size, screening of patients or residents in close proximity to the identified patient or resident, such as an area with shared staffing assignments, is strongly considered.

At a minimum, roommates should be screened for CPE. If there is evidence of transmission of a single species (two or more patients or residents with the same CPE strain), or two or more CPE-positive patients or residents carrying two different bacterial species with the same carbapenemase (suspected plasmid transmission), outbreak measures should be put into place and expert advice should quickly be sought (academic health sciences centre, medical microbiologist, reference laboratory services, IPAC Regional Support Teams) to assist with determination of an outbreak.

For more information, see Annex A – Screening, testing and surveillance for antibiotic-resistant organisms (AROs).[15]

## What should health care facilities do if there is a CPE outbreak in one of their facilities?

If the outbreak meets the definition in Appendix B: Provincial Case Definitions for Reportable Diseases,[4] report it to the local Medical Officer of Health within one business day (as per **Bulletin 17 – Timely entry of cases and outbreaks for Diseases of Public Health Significance**).

Patients and residents who may have been exposed to CPE should be managed as per individual facility protocols. In the event of an outbreak, absolute cohorting of patients and residents, staff assignments and equipment is essential to prevent further transmission. Facilities that are developing protocols should review Annex A – Screening, testing and surveillance for antibiotic-resistant organisms (AROs).[15]

Patients and residents who have been transferred from an outbreak unit or ward should be placed on Contact Precautions pending microbiological testing results. For patients and residents who have been transferred to another facility, the new facility should be informed and the patient or resident should be tested.

Patients and residents with known history of CPE colonization or infection should have their records flagged, placed on Contact Precautions and be re-tested on readmission. See Annex A – Screening, testing and surveillance for antibiotic-resistant organisms (AROs).[15]

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