

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

Infectious Disease Protocol

Appendix 1:

Case Definitions and Disease-Specific Information

Disease: Creutzfeldt-Jakob Disease, all types

Effective: May 2022

Creutzfeldt-Jakob Disease, all types

Communicable

Virulent

[Health Protection and Promotion Act \(HPPA\)](#)

[Ontario Regulation \(O. Reg.\) 135/18 \(Designation of Diseases\)](#)

Provincial Reporting Requirements

Confirmed case

Probable case

Suspect 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;⁴
- The iPHIS User Guides published by Public Health Ontario (PHO); and
- Bulletins and directives issued by PHO.

Type of Surveillance

Case-by-case

Case Definition

Confirmed Case

Neuropathologically confirmed, with confirmation of protease-resistant prion protein (immunohistochemistry, PET blot, or Western Blot).

Probable Case

- Rapidly progressive dementia

AND

- At least two additional neurological manifestations (See Clinical Evidence section)

AND

- One of three clinical tests:
 - Typical electroencephalography (EEG): generalized bilateral or unilateral triphasic periodic complexes at approximately one per second, lasting continuously for at least 10 seconds.
 - MRI with caudate nucleus and/or (anterior) putamen attenuation (preferred sequence DWI or FLAIR).
 - Positive assay for 14-3-3 protein in cerebrospinal fluid (CSF) **AND** total disease duration less than 24 months.

Suspect Case

- Rapidly progressive dementia

AND

- At least two additional neurological manifestations (See Clinical Evidence section)

AND

- Duration of illness less than 2 years in the absence of a conclusive MRI and 14-3-3 protein assay.

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

Additional neurological manifestations include:

- Myoclonus
- Visual or cerebellar disturbances such as ataxia
- Pyramidal or extrapyramidal symptoms
- Akinetic mutism

Clinical Presentation

CJD is a prion disease and part of a group of rare, rapidly progressive, universally fatal neuro-degenerative syndromes that are characterized by neuronal degeneration, spongiform vacuolation in the cerebral gray matter, reactive proliferation of astrocytes and microglia, and accumulation of abnormal misfolded protease-resistant prion protein.¹

Clinical presentation most commonly manifests as a rapidly progressive syndrome with confusion, behavioural and cognitive abnormalities, dementia, and variable other symptoms such as ataxia and myoclonus.¹

Classic CJD can be sporadic (sCJD), familial or iatrogenic. It typically presents as a subacute illness in the middle-aged and elderly.

Variant CJD (vCJD) is another category, first described in 1996 and associated with ingesting meat from bovine spongiform encephalopathy (BSE) infected cattle.¹ vCJD has a longer clinical course than sCJD and usually presents with psychiatric or behavioural abnormalities, followed by signs of neurologic dysfunction, usually delayed by several months after the onset of illness.²

Laboratory Evidence

Laboratory Confirmation

The following will constitute a confirmed case of sporadic Creutzfeldt-Jakob Disease:

- Confirmation of protease-resistant prion protein (immunohistochemistry, PET blot, or Western Blot), and when available, combined with routine neuropathological evidence of CJD (typical spongiosis). See also Indications and Limitations.

Approved/Validated Tests

- Immunohistochemistry (or PET blot) demonstrating prion protein immunoreactivity (plaque and/or diffuse synaptic and/or perivacuolar): confirmatory (if positive)
- Prion Protein (PrP) Western blot: confirmatory (if positive)
- Histopathology to demonstrate spongiform encephalopathy in cerebral and/or cerebellar cortex and/or subcortical grey matter: supportive (if positive)
- *PRNP* gene sequencing: supportive (if negative)
- CSF 14-3-3 Western blot: supportive (if positive).

The CJD Surveillance System (phone 1-888-489-2999) provides support for pathological evaluation (autopsies and biopsies), CSF testing, and genetic testing.

Indications and Limitations

- Histopathologic evidence of spongiform change is no longer considered sufficient in itself for diagnostic confirmation of CJD. However, the diagnostics in CJD/prion diseases on both a clinical and laboratory level are complex.
- Demonstration of scrapie-associated fibrils (SAF) by electron microscopy historically was part of the diagnostic criteria. Although historically important, this technique is no longer used for diagnostic purposes.
- Absence of a known pathogenic mutation causative for genetic CJD supports a diagnosis of sCJD.
- Because of limited diagnostic specificity, the CSF 14-3-3 assay is restricted to a supporting role in the diagnosis of probable sCJD.

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.

The following disease-specific information should also be obtained during case management:

- History of invasive neurological or neuro-surgical procedures, corneal transplants;
- Any possible exposure to human growth hormone or transplacental tissue; and
- A family history of dementia.

Investigation of cases occurs in collaboration with the Ministry of Health, PHO and

the Public Health Agency of Canada (PHAC).

There is no specific treatment available.¹

For further information please refer to *Classic Creutzfeldt-Jakob Disease in Canada: Quick Reference Guide 2007*.³

Contact Management

No public health action required.

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. Review case for potential IPC issues for follow up in institutional settings.

Prevention and Control Measures

Personal Prevention Measures

Preventive measures include:²

- Excluding infected persons as well as their family members from donating blood, organs, and other body tissues;
- Avoiding iatrogenic exposures; and
- Avoiding exposures to the BSE-causing agent in food of bovine origin.

For further information regarding preventing iatrogenic transmission please refer to [Classic Creutzfeldt-Jakob Disease in Canada: Quick Reference Guide 2007](#).³

Infection Prevention and Control Strategies

Surgical instruments that have been in contact with high-risk tissue from infected persons, such as the brain, spinal cord, cornea, retina, pituitary gland, *dura mater*, and CSF should be considered contaminated and must be discarded or decontaminated and quarantined until the diagnosis is confirmed. Any surgical instruments that have contacted high risk tissue in a confirmed case of CJD should be discarded.³

Single use cardiac catheters, pacemakers, and other single use devices should not be re-used after being used on an infected person.

For further information regarding infection prevention and control please refer to [Classic Creutzfeldt-Jakob Disease in Canada: Quick Reference Guide 2007](#).³

Disease Characteristics

Aetiologic Agent - The infectious agents associated with Creutzfeldt-Jakob Disease (CJD) are abnormally folded, unique proteins called prions which potentially become a template causing the further conversion of normal proteins.¹

Modes of Transmission - The mode of transmission for sporadic disease is unknown; some cases of CJD have occurred iatrogenically and some have a genetic component. vCJD is believed to be transmitted by consumption of specific risk materials from BSE-infected cattle.² Three cases of vCJD have also been transmitted by blood transfusion.²

Incubation Period – Incubation periods in prion diseases can be extremely long and are not applicable to naturally occurring sporadic and genetic cases, since these do not involve exposure to an external source of infection. In iatrogenic cases, the route of exposure influences the length of the incubation period: direct CNS exposure results in an incubation period from 1.3 to 30 years, while peripheral exposure results in an incubation period of 5 to 42 years.² It is estimated that the incubation period for vCJD cases related to exposure of BSE-infected cattle is from 10 to 20 years.² vCJD contracted via a transfusion of red cells has an incubation period estimated to be from 6.6 to 8.5 years.²

Period of Communicability - Transmissibility and period of communicability varies with disease, tissue involved and stage of disease. CNS and other tissues are infectious throughout symptomatic illness; lymphoid and other organs are probably infectious before signs of illness appear. Blood has been proven infectious in the preclinical phase of vCJD.²

For further information regarding the infectivity of various tissues please refer to Classic Creutzfeldt-Jakob Disease in Canada: Quick Reference Guide 2007.³

Reservoir - Human cases constitute the only known reservoir for classic CJD. BSE-infected cattle were the original main reservoir for vCJD. However, changes made in the management of livestock feeding and the introduction of specific risk material management processes during slaughter since the early 2000s have reduced the number of BSE-infected cattle significantly. Currently, subclinical (ongoing) infections in humans are considered to be a potential reservoir for secondary, human-to-human transmission of vCJD by blood transfusion, organ transplantation or surgery.²

Host Susceptibility and Resistance - Genetic differences in susceptibility, resembling those of autosomal dominant traits, have been shown to explain patterns of occurrence of the disease in families.^{1,2}

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.

References

1. Committee on Infectious Diseases, American Academy of Pediatrics. Section 3: Summaries of Infectious Diseases: Prion Diseases - Transmissible Spongiform Encephalopathies. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. Red Book: 2018 Report of the Committee on Infectious Diseases. 31 ed. Itasca, IL: American Academy of Pediatrics; 2018.

2. Heymann DL, editor. Control of Communicable Diseases Manual. 20 ed. Washington, D.C: American Public Health Association; 2015.
3. Public Health Agency of Canada. Classic Creutzfeldt-Jakob Disease in Canada: Quick Reference Guide 2007. Ottawa, ON: Her Majesty the Queen in Right of Canada; 2007. Available from: <https://www.canada.ca/en/public-health/services/infectious-diseases/nosocomial-occupational-infections/creutzfeldt-jakob-disease/infection-control-guidelines.html>
4. Health Protection and Promotion Act, R.S.O. 1990, Reg. 569, Reports, (2018). Available from: <https://www.ontario.ca/laws/regulation/900569>

Case Definition Sources

Heymann DL, editor. Control of Communicable Diseases Manual. 20 ed. Washington, D.C: American Public Health Association; 2015.

National Creutzfeldt-Jakob Disease Research & Surveillance Unit. Surveillance: Diagnostic Criteria. Edinburgh, UK: The University of Edinburgh; 2017. Available from: <http://www.cjd.ed.ac.uk/surveillance>

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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.

