

## **Creutzfeldt-Jakob Disease: A Resource for Health Professionals**

- Cases of suspect or probable Creutzfeldt-Jakob Disease (CJD) should be reported to the Creutzfeldt-Jakob Disease Surveillance System (CJDSS) at the Public Health Agency of Canada, who will assist with DNA sequencing, autopsy and case confirmation.
- Probable and confirmed cases of CJD are reportable in British Columbia and must be reported to your local Medical Health Officer (MHO) or public health office. This is especially important when probable or confirmed cases of CJD have had invasive procedures or have donated any tissues or organs for transplantation.

**NB: A confirmed diagnosis of sCJD can only be made with brain tissue obtained upon autopsy**

### **Overview:**

This resource document provides information on Creutzfeldt-Jakob Disease (CJD) for health and public health professionals. It also outlines reporting procedures and provides links to resources and information for health professionals and patients.

### **Background:**

CJD is a rare, degenerative and fatal neurological disease which typically presents with confusion, depression, changes to behaviour, sleep or concentration, abnormal vision, physical sensation or balance. Patients rapidly progress to akinetic mutism (the inability to move or speak), dementia and eventually, death. The underlying cause of CJD and several related animal diseases is the prion, a novel and potentially infectious protein. The vast majority (85-95%) of “classic” CJD cases are sporadic (sCJD), while 5-15% are genetic (*PRNP* gene encoding the PrP protein is implicated), and less than 1% are iatrogenic CJD (iCJD), acquired through tissue transplantation or contaminated instruments.<sup>1</sup>

Among “classic” forms of CJD the most common subtype, sporadic CJD (sCJD), is defined by characteristic prion neuropathology (particularly spongiform degeneration and deposition of pathologic PrP in brain tissue) in the absence of a discernible genetic or infectious cause. Sporadic CJD appears to occur endemically in all populations with an average mortality rate of one to two million per year, and generally constitutes 85% to 95% of all CJD cases identified through epidemiologic surveillance.

Iatrogenic cases of classic CJD (iCJD) have occurred through accidental prion transmission in the health care setting, particularly with therapeutic use of cadaveric tissues or tissue extracts presumably contaminated by donations from individuals with unrecognized sCJD.

Further information for patients and their families about CJD can be found through Healthlink BC:

<http://www.healthlinkbc.ca/healthfiles/pdf/hfile55a.pdf>

Variant CJD (vCJD), or human bovine spongiform encephalopathy (BSE), is a similar but distinct prion disease transmitted to animals through infected animal feed material and to humans through consumption of contaminated livestock. It usually affects a younger population (less than 30 years old), and begins with mood and memory disturbances, progressing to movement disorders, cognitive decline and death within 2 years. As of February 2017, there have only been 2 documented cases of vCJD in Canada, both of whom were likely exposed to BSE outside of Canada.<sup>2</sup>

Further information on vCJD for patients and their families can be found through Healthlink BC:

<http://www.healthlinkbc.ca/healthfiles/pdf/hfile55b.pdf>

### **Diagnosis and Laboratory Testing:**

As per guidelines from the US Centres of Disease Control,<sup>3</sup> a confirmed diagnosis of sCJD can only be made with brain tissue obtained upon autopsy, with neuropathological examination, immunocytochemical methods, or Western blot detection of disease-specific PrP.

Cases can be designated as “**probable CJD**” if they conform to the following 3 criteria<sup>4</sup>:

1. Progressive Dementia
2. At least two of the following:
  - myoclonus
  - visual or cerebellar disturbance
  - pyramidal or extra-pyramidal dysfunction
  - akinetic mutism
3. At least 1 of the following:
  - periodic sharp wave complexes on EEG
  - positive 14-3-3 assay on CSF
  - MRI imaging showing high abnormal signal in the caudate nucleus and putamen on fluid attenuated inversion recovery (FLAIR) or Diffusion weighted imaging (DWI)

Cases can be entered in Panorama as “**suspect CJD**” if they conform to the criteria 1 and 2 for **probable CJD** as above, but do not have any of EEG, CSF or MRI imaging results indicative of CJD.

Immunoassays of specific brain-derived proteins in the CSF, such as 14-3-3, tau and S100B, are used as diagnostic tools for sCJD. These proteins appear in the CSF as a result of the degeneration of neurons, and perhaps other processes such as neuroinflammation. Results from 1000 Canadian patients and a review of published studies showed that diagnostic sensitivities and specificities of these proteins in sCJD typically fall in the range of 80–90%,<sup>4-5</sup> as some CJD patients have negative results and other patients with non-CJD conditions have positive results. Thus, none of these tests can confirm or exclude

a diagnosis of CJD. Of note, testing for these proteins have only been well characterized for sCJD, not for genetic or vCJD. The National Microbiology Lab (NML) currently performs testing for 14-3-3 and tau proteins.

A novel laboratory test, the Real-Time Quaking –Induced Conversion (RT-QuIC) assay, has recently been developed, with improved diagnostic accuracy for sCJD. This test is based on the ability of the diseased form of PrP in patient samples to induce misfolding and aggregation of normal PrP in vitro after being subject to agitation. This test can detect low levels of diseased PrP, and thus distinguish between patients with and without CJD.<sup>6-7</sup> This method been shown to have 80–90% sensitivity and close to 100% specificity when applied to CSF, and 97% sensitivity (95% CI 82-100) and 100% specificity (95% CI 90-100) when tested on olfactory epithelium brushings (the latter is not a routinely available sample type for testing).<sup>8</sup> The NML began offering the RT-QuIC assay in February 2016 for CSF samples only. Future revisions of CJD categorizations (confirmed and probable) will likely incorporate the RT-QuIC test as a criterion, once the significance of this test is determined.

For genetic CJD, a diagnosis can be made with the presence of a neuropsychiatric illness in the context of a positive genetic test for disease-specific PrP, or the presence of confirmed or probable CJD in both the patient and a first degree relative.<sup>3</sup>

### **Surveillance:**

Since 2000, all forms of CJD have been nationally notifiable in Canada and are now reportable in all provinces and territories. CJD became reportable in BC in 2006. Diagnostic investigations of CJD and other subacute encephalopathies in a living patient is challenging, hence, the need for high-quality epidemiologic surveillance with a variety of supporting information, as well as follow-up on individual cases in real time.

Canadian CJD statistics are collected and reported by the Creutzfeldt-Jakob Disease Surveillance System (CJDSS) at the Public Health Agency of Canada (PHAC).<sup>1</sup> From 1997 to August 31, 2017, the CJDSS opened 1817 case-referral files on patients suspected of having CJD, or being at risk for CJD from across Canada.

From 1994 to August 31, 2017 the CJDSS recorded 889 deaths from definite and probable cases of CJD, of which 818 were classified as sCJD (92%), 34 were classified as Familial prion disease (3.8%), 5 were classified as iCJD (0.6%), and 2 were classified as vCJD (0.2%). In BC a total of 116 CJD cases have been identified, 13% of all cases in Canada and based on population size is similar to predicted (99.6%).

For more information on the CJDSS, including national surveillance statistics by province, and newsletters to families and physicians, see the PHAC website:

<http://www.phac-aspc.gc.ca/hcai-iamss/cjd-mcj/index-eng.php>

**Characteristics Distinguishing Classic CJD from variant CJD**

<b>Characteristic</b>	<b>Classic CJD</b>	<b>Variant CJD</b>
Median age at death	68 years	28 years
Median duration of illness	4-5 months	13-14 months
Clinical signs and symptoms	Dementia; early neurologic signs	Prominent psychiatric/behavioral symptoms; painful dyesthesia; delayed neurologic signs
Periodic sharp waves on electroencephalogram	Often present	Often absent
"Pulvinar sign" on MRI*	Not reported	Present in >75% of cases
Presence of "florid plaques" on neuropathology	Rare or absent	Present in large numbers
Immunohistochemical analysis of brain tissue	Variable accumulation	Marked accumulation of protease-resistance prion protein
Presence of agent in lymphoid tissue	Not readily detected	Readily detected
Increased glycoform ratio on immunoblot analysis of protease-resistance prion protein	Not reported	Marked accumulation of protease-resistance prion protein

Source: Centers for Disease Control and Prevention. Clinical and Pathologic Characteristics Distinguishing Classic CJD from variant CJD. Accessed June 14, 2017. <http://www.cdc.gov/prions/vcid/clinical-pathologic-characteristics.html>

**Reporting:**

Upon suspecting a case of CJD, the case details should be reported to the CJDSS by the attending physician by calling their toll free number (1-888-489-2999). The case should also be reported to the appropriate local Medical Health Officer, who can be contacted by the appropriate phone number on page 2 of the **BCCDC CJD reporting form**:

[http://www.bccdc.ca/NR/rdonlyres/B0EB1754-B897-4F31-AB45-86DECD90050/0/EPI\\_Form\\_CJD\\_Sep08\\_20091202.pdf](http://www.bccdc.ca/NR/rdonlyres/B0EB1754-B897-4F31-AB45-86DECD90050/0/EPI_Form_CJD_Sep08_20091202.pdf)

The CJDSS arranges appropriate steps for DNA sequencing and autopsy in order to confirm cases. DNA sequencing is important to distinguish sCJD from genetic CJD. Diagnosis of non-genetic forms may offer some reassurance to families of cases, while families of genetic CJD cases should be referred for genetic counselling.

Upon completion of investigation by the CJDSS, the CJDSS will enter case details, with the updated disease status (confirmed or probable) into the **BCCDC CJD reporting form** and send the form to the attending physician. The physician is requested to fax the form to the appropriate local MHO or public health office as outlined on page 2 of the reporting form.

Public health authorities can enter case details into Panorama with drop-down menu options for suspect, probable and confirmed cases available. Upon receiving updated information at the end of case investigations, public health authorities should update information in Panorama, or enter cases into Panorama, if not done previously. Confirmed or probable cases should be classified as “Confirmed” or as “Probable” respectively, while the appropriate stage should be selected from the choices of: “Sporadic”, “Genetic”, “Iatrogenic”, or “Variant”.

If you have any concerns or questions, please contact the CJDSS toll free at 1-888-489-2999 or by email at [CJDSS@phac-aspc.gc.ca](mailto:CJDSS@phac-aspc.gc.ca), or your local MHO/public health office.

**Infection Control:**

Person-to-person contact is not thought to contribute to transmission of CJD. However, corneal or dural tissue transplantation, neurosurgical instruments and growth hormone or gonadotropin injection have all been implicated in acquired cases.<sup>9-10</sup> Variant CJD has been transmitted through transfusion of blood products in the UK.<sup>11</sup>

The local MHO/public health authority should be informed of cases of CJD that have had any invasive procedure or donated any tissue specimen for transplantation.

The PHAC has established the following guidelines to minimize risk of transmission in both prospective and retrospective cases. This guide outlines an assessment of transmission risk, appropriate procedures

for managing instruments, handling tissue samples, and decontamination. It also includes a decision algorithm for disinfection of instruments potentially or definitely contaminated with CJD.

Infection Control Guidelines: quick reference guide, 2007:

<http://www.phac-aspc.gc.ca/nois-sinp/pdf/cjd-eng.pdf>

Infection Control Guidelines: Classic Creutzfeldt-Jakob Disease in Canada

<http://www.phac-aspc.gc.ca/nois-sinp/cjd/cjd-eng.php>

### **Funeral and crematory practitioners**

Centre for Disease Control has published Information for funeral and Crematory Practitioners  
Funeral service workers can safely remove the body of a CJD patient from the place of death and transport it to the funeral home preparation room for mortuary procedures using appropriate standard infection control measures, which includes wearing personal protective gear. The World Health Organization (WHO) recommends placing the body in a leak proof pouch prior to moving. The bag should be lined with absorbent material to prevent leakage of body fluids. Embalming an autopsied of traumatized body is not recommended by WHO.

Creutzfeldt-Jacob disease, Classic (CJD). Information for funeral and crematory practitioners.

<https://www.cdc.gov/prions/cjd/funeral-directors.html>

WHO infection control guidelines for transmissible spongiform encephalopathies. Report of a WHO consultation, Geneva, Switzerland, 23-26 March 1999 available at

[http://www.who.int/csr/resources/publications/bse/WHO\\_CDS\\_CSRAPH\\_2000\\_3/en/](http://www.who.int/csr/resources/publications/bse/WHO_CDS_CSRAPH_2000_3/en/)

### **Patient Resources:**

CJD and Human Prion Disease Information:

<http://www.phac-aspc.gc.ca/hcai-iamss/cjd-mcj/cjd-eng.php>

Alzheimer Society of Canada (support group for CJD and other neurological diseases)

<http://www.alzheimer.ca/en>

CJD Support Network: Charity established in 1995 for relatives of people who have died of CJD

<http://www.cjdsupport.net/>

CJD in Canada; Family Edition Newsletter:

<http://www.phac-aspc.gc.ca/hcai-iamss/cjd-mcj/sub-abo-eng.php>

### **Laboratory worker perception of disease transmission**

BCCDC has conducted studies into risk perceptions of disease transmission in various contexts including laboratory workers handling suspected specimens. See appendix for abstracts of published manuscripts.<sup>11-12</sup>

### **Additional Resources:**

Further Links published by PHAC-CJDSS (organized by country/organization)

<http://www.phac-aspc.gc.ca/hcai-iamss/cjd-mcj/links-eng.php>

The UK National Creutzfeldt-Jakob Disease Research & Surveillance Unit (NCJDRSU)

<http://www.cjd.ed.ac.uk/>

CJD: public health action following report of new case or person at increased risk Public Health England  
Published 30 January 2014

<https://www.gov.uk/government/publications/cjd-public-health-action-following-report-of-new-case-or-person-at-increased-risk>

Centres for Disease Control and Prevention: References and Resources

<http://www.cdc.gov/prions/cjd/resources.html>

WHO resource including CJD/vCJD definition, classification criteria, infection control recommendations and epidemic management guidelines:

<http://www.who.int/zoonoses/diseases/Creutzfeldt.pdf>

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## Appendix

### **Abstract 1**

Buxton JA, Henry B, Crabtree A, Waheed A. Prion disease risk perception in Canadian medical laboratories. *Can J Infect Dis Med Microbiol.* 2012; 23 (2) e31-35

**Background:** There are no national guidelines specific for handling prion-associated specimens in Canadian medical laboratories. Medical laboratory workers may perceive themselves at risk of prion transmission and, on occasion, decline to process such specimens.

**Objective:** To examine the knowledge, attitudes and reported behaviours of medical laboratory workers in relation to prion disease to understand their risk perception and the need for national laboratory guidelines on prion infection control.

**Design:** Survey development and cross-sectional web-based administration

**Methods:** The survey was developed through key informant interviews and a modified Delphi process. Medical laboratory workers across Canada were invited by laboratory managers and national organizations to complete the web-based survey.

**Results:** Twelve key informant interviews were performed. Consensus for questionnaire content was reached through two rounds of the Delphi process. Responses were received from 426 Canadian medical laboratory workers; 37% of medical laboratory staff reported processing prion-associated specimens. Different protocols for specimen processing were followed, and 18% believed they were at risk when processing these specimens. Less than one-third of those receiving specimens believed they were adequately trained. The mean ( $\pm$ SD) knowledge score was  $9.25 \pm 4.5/24$ ; individuals who had received training scored significantly higher than those who were untrained ( $P < 0.01$ ). Eighty-one per cent of respondents would be more comfortable processing specimens if national guidelines existed and were used in their laboratory.

**Conclusion:** There is a high perception of risk and few perceived benefits of processing prion-associated specimens. National guidelines for prion infection control in medical laboratories and adequate training would enable medical laboratory workers to process these specimens efficiently and confidently.

### **Abstract 2**

Buxton JA, Henry B, Crabtree A, Waheed A, Coulthart M. Using qualitative methods to investigate risk perception of Canadian medical laboratory workers in relation to current prion disease infection control policies. *J Toxicol Environ Health A.* 2011;74(2-4):241-7.

The aim of this study was to determine the rationale, methodology, and progress of risk perceptions of laboratory workers in relation to existing prion disease infection control policies in Canadian medical laboratories. This study developed a Web survey that investigated the knowledge, behavior, and attitudes of laboratory staff in order to (1) identify strengths, weaknesses, and gaps of current prion infection prevention and control guidelines and (2) inform the development of national medical lab specific guidelines. The use of qualitative methods to develop a relevant survey is described and future research activities are outlined. Preliminary, qualitative data indicate that, among laboratory staff, there is a high degree of perceived susceptibility toward prion transmission in medical laboratories. Significant barriers to following existing prion infection control guidelines are reported with few benefits of following these guidelines. As a result, laboratories take precautions above those that are required when processing suspect prion-infected specimens, which may result in testing delays. A focused survey for laboratory staff that addresses these issues will provide insight on the necessary steps that will ensure safe and efficient diagnostic testing for suspect prion specimens.