CREUTZFELDT-JAKOB DISEASE (CJD) PROTOCOL

1. Cause/Epidemiology

Creutzfeldt-Jakob disease (CJD) is a rare, fatal degenerative disorder. CJD belongs to a family of human and animal diseases known as the transmissible spongiform encephalopathies (TSEs). TSEs, also known as prion diseases, are a group of rare degenerative brain disorders characterized by tiny holes, giving the brain a "spongy" appearance. These holes are caused by pathological changes in the brain involving a specific protein called Prion Protein, or PrP.

Some researchers believe an unusually slow-growing virus causes CJD. However, a virus or other organism has never been isolated from people with the disease. Furthermore, the agent that causes CJD has several unusual characteristics, is difficult to eliminate, and usually has a long incubation period before symptoms appear.

CJD is the most common of the known human TSEs. Other human TSEs include Kuru, Fatal Familial Insomnia (FFI), and Gerstmann-Sträussler-Scheinker disease (GSS). There is no evidence CJD is contagious through casual contact with a CJD patient.

There are two types of CJD: Classic and Variant.

2. Classic CJD

Sporadic: the disease appears even though the person has no known risk factors for the disease. This is by far the most common type of CJD and accounts for at least 85% of cases.

Hereditary (familial): the person has a family history of the disease and/or tests positive for a genetic mutation associated with CJD.

Acquired (iatrogenic): person-to-person transmission has occurred via transfer of tissue from an affected donor (corneal transplant and dura mater grafts), through peripheral injection of pooled cadaveric pituitary gland extract (growth hormone injection and human gonadotropin injection), and by use of contaminated neurosurgical instruments. Since CJD was first described in 1920, fewer than 1% of cases have been acquired CJD.

Globally 80% of cases of CJD occur as sporadic disease. Most sporadic CJD (sCJD) occurs in persons between the ages of 60 and 80 years with an average age at death of approximately 67 years [20.6].

3. Variant CJD (vCJD)

Was first described in 1996, and has been found in Great Britain and several other European countries. Variant CJD should not be confused with the classic form of CJD endemic throughout the world. The initial symptoms of vCJD are different from those of classic forms of CJD and the disorder typically occurs in younger patients. Research suggests vCJD may have resulted from human consumption of beef from cattle with a TSE disease called bovine spongiform encephalopathy (BSE), also known as "mad cow disease".

The reported incidence is generally between one and two cases per million persons per year. [20.4]

4. Clinical Presentation

Clinical presentation includes rapidly progressive dementia; myoclonus; impaired vision; progressive motor dysfunction; and behavioural changes, including impaired memory, judgment, and thinking. People with the disease also may experience insomnia, depression, or unusual sensations. They eventually lose the ability to move and speak, and enter a coma. Pneumonia and other infections often occur in these patients and can lead to death. Death usually occurs within one year of symptom onset. CJD causes unique changes in brain tissue that can be seen at autopsy.

Classic CJD usually appears in later life and runs a rapid course. Some CJD symptoms can be similar to symptoms of other progressive neurological disorders such as Alzheimer's or Huntington's disease, though a more rapid deterioration is noted.

Variant CJD affects younger patients than other types of CJD (i.e., 30-70 years of age versus 50-70 years of age in classic CJD). It begins primarily with psychiatric symptoms and has a longer than usual duration from onset of symptoms to death (i.e., median 14 month clinical course versus 4 months for sCJD).

Clinical and Pathologic Characteristics Distinguishing Classic CJD from Variant CJD

Characteristic	Classic CJD	Variant CJD
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/behavioural symptoms; painful dyesthesiasis; 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

*An abnormal signal in the posterior thalami on T2- and diffusion-weighted images and fluid-attenuated inversion recovery sequences on brain magnetic resonance imaging (MRI); in the appropriate clinical context, this signal is highly specific for vCJD. [20.3]

5. Incubation Period

Classic CJD usually has a long incubation period before symptoms appear. In some cases, this may be as long as 40 years. The incubation period for vCJD is unknown but is likely measured in terms of many years or decades.

6. Transmission

CJD is not known to spread person-to-person though droplet, contact or airborne routes [20.1]. Spouses and other household members of CJD patients do not have a higher risk of contracting the disease than the general population.
There is no firm evidence that sCJD is an exogenously acquired disease. Sporadic CJD has no recognized pattern of transmission; it is believed to originate spontaneously [20.5].

Iatrogenic transmission of CJD has occurred following the use of contaminated cadaver-derived human pituitary hormone, dura mater and corneal grafts, EEG depth electrodes, and neurosurgical instruments [20.5].

Transmission of vCJD is not well understood. The mechanism of transmission of BSE from cattle to humans has not been established, but the favoured hypothesis is that humans are infected through dietary consumption of the BSE agent. Studies have found infectious prions from BSE and vCJD may accumulate in the lymph nodes, the spleen, and the tonsils. These findings suggest blood transfusions from people with vCJD might transmit the disease. There has been concern it may be possible to transmit CJD through blood and related products such as plasma; however this has never been shown in humans.

7. Diagnosis

There is currently no single diagnostic test for CJD. All forms of CJD are initially diagnosed based on clinical features, EEG and MRI findings [20.5].

The only way to confirm a diagnosis of CJD is by brain biopsy or autopsy. Brain biopsy may be dangerous for the patient, and the procedure does not always obtain tissue from the affected part of the brain. Brain biopsy is discouraged unless needed to rule out a treatable disorder.

Imaging techniques are useful in excluding other causes of sub-acute dementia. A lumbar puncture is often done to exclude other disease processes. A diagnostic test for detection of 14-3-3 protein in CSF has a high sensitivity and specificity for diagnosis of sporadic CJD during clinical illness.

Standard diagnostic tests include:

- A spinal tap to rule out more common causes of dementia
- An EEG to record the brain's electrical pattern (which can show a specific abnormality in CJD)
- Computed Tomography (CT) of the brain to help rule out alternative diagnoses such as stroke or a brain tumor
- Magnetic Resonance Imaging (MRI) brain scans to reveal characteristic patterns of brain degeneration that can help diagnose CJD.

Label "suspect CJD" on the requisition for all specimens containing high or low infectivity tissue from high-risk patients, or high infectivity tissue and CSF from at risk patients.

Refer to **Appendix A: National Surveillance Case Definition for Classic CJD** (page 7.4.15).

8. Risk Assessment for CJD

Determining potential for CJD transmission requires consideration of multiple factors. Assessments of patient, tissue, and instrument risks are necessary. The following sections present information helpful in the determination of risk associated with each factor.

8.1. Patient Risk for CJD

8.1.1. High-risk patients

Patients considered to be at high risk of transmitting CJD are those diagnosed, prospectively or retrospectively, with:

CJD	Either confirmed, probable, or possible CJD, familial CJD, GSS, or FFI depending on pathological, laboratory, and clinical evidence and following Surveillance Definitions for Classic CJD. Refer to **Appendix A: National Surveillance Case Definition for Classic CJD** (page 7.4.15).
Suspected CJD	Undiagnosed, rapidly progressive dementia and CJD not ruled out
Asymptomatic Carrier of Genetic	Person without signs or symptoms of TSE, but meets one or more of the following:

TSE	– Confirmed by genetic testing to carry a genetic mutation causative of TSE – At least one first-degree relative confirmed by genetic testing to carry such a mutation, with or without pathologic TSE confirmation – Two or more first-degree relatives diagnosed with either confirmed or probable TSE, with or without confirmation by genetic testing

To minimize the risk of transmitting CJD, elective procedures in high-risk patients (involving high-risk or low-risk tissues) should be well justified and carefully planned in advance. Refer to Tissue Risk for CJD, Section B below.

9. At-risk patients

The following patients are at risk of iatrogenic CJD:

- Recipients of a dura mater graft (until 1992 for Lyodura grafts, until 1997 for Tutoplast Dura grafts)
- Recipients of human tissue derived pituitary hormone treatment (either growth hormone or gonadotrophin)
- Recipients of a corneal graft originating in a jurisdiction that does not require graft donors to be screened for neurological disease
- Patients who have been exposed, via contact with instruments, to high-infectivity tissue of a confirmed CJD patient.

The risk of transmission via instruments used on at-risk, asymptomatic patients is negligibly low, and therefore such instruments may be routinely decontaminated and then reused.

Screening procedures should be performed to identify high-risk patients, and not to identify at-risk patients.

A patient who self-identifies as being at-risk should be evaluated clinically for evidence of CJD.

9.1. Tissue Risk for CJD

The procedures recommended for managing instruments used on **high-risk** patients depend on the potential infectivity of the tissue contacted. Human tissue is classified into three categories, according to its risk of transmitting CJD.

1. High Infectivity		**2. Low Infectivity**	
Brain	Dura Mater	Cornea	Spleen
Pituitary Gland	Trigeminal ganglia	Kidney	Placenta
Posterior eye (optic nerve and retina)	Spinal cord and spinal ganglia	Liver	Lymph nodes

Cerebrospinal fluid (CSF)[2]	Lung	
3. No Detected Infectivity		
Adipose tissue	Ileum	Seminal vesicle
Adrenal gland	Jejunum	Skeletal muscle
Appendix	Large intestine	Skin
Blood (including cord blood)	Nasal mucosa	Sweat
Blood vessels	Nasal mucous	Tears
Bone marrow	Ovary	Testis
Breast milk (including colostrum)	Pancreas	Thymus
Dental pulp	Pericardium	Thyroid gland
Epididymis	Peripheral nerves	Tongue
Esophagus	Placental fluids	Tonsil
Feces	Prostate	Trachea
Gingival tissue	Saliva	Urine
Heart	Semen	Uterus (non-gravid)

[2] Note: While CSF is a low-infectivity tissue, contact with CSF necessarily implies contact with high-infectivity tissue and should be managed as a high infectivity tissue/fluid for infection prevention and control purposes

9.2. Instrument Risk for CJD

To minimize the risk posed by instruments, the following strategies are needed:

- Limit the number of instruments used for any procedure
- Use disposable rather than reusable instruments whenever possible and especially when contacting high-infectivity tissue
- When using reusable instruments, choose, whenever possible, those that can tolerate the rigors of CJD decontamination
- Track the use of reusable instruments.

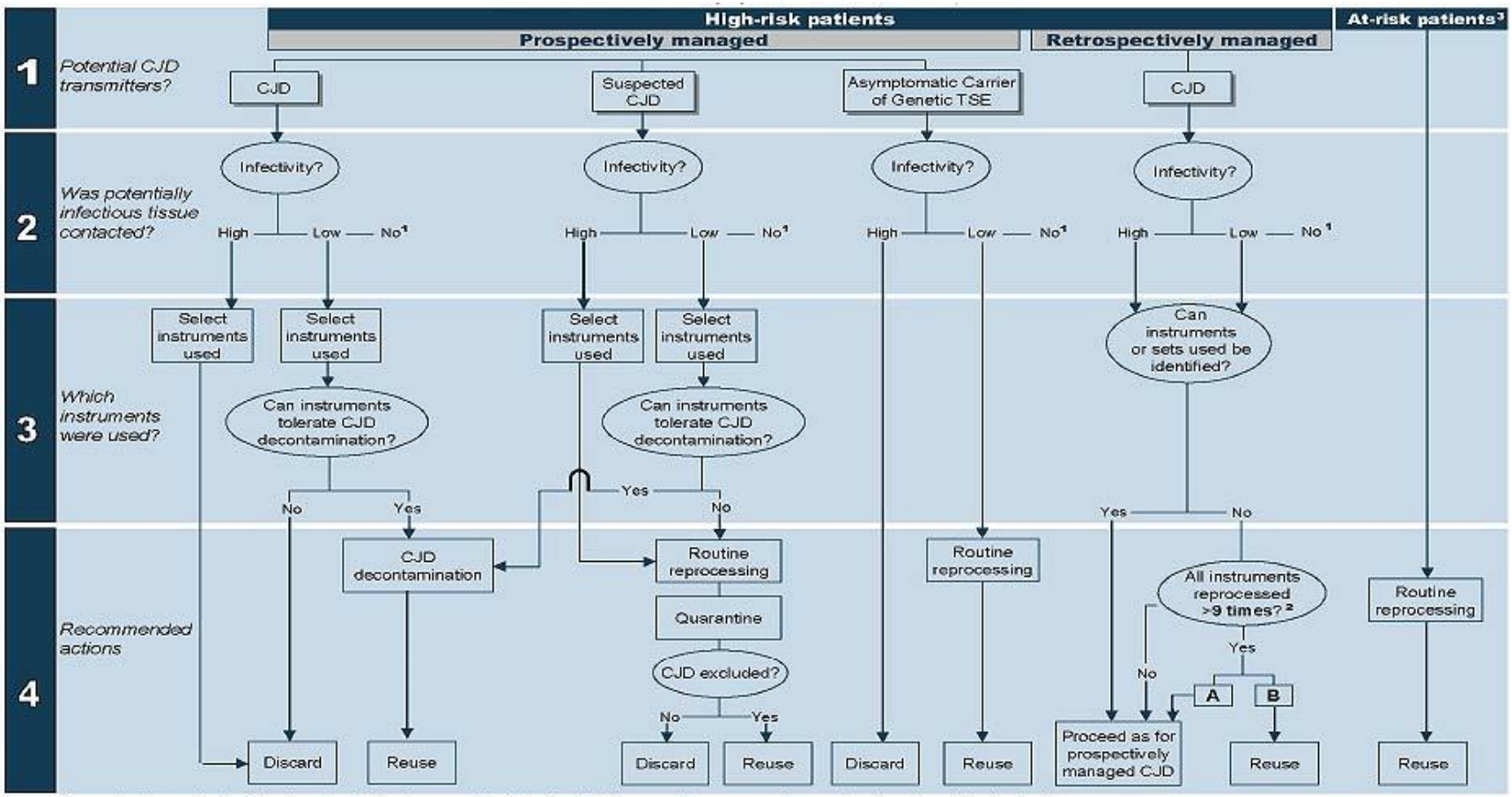
It is recommended instruments are managed prospectively, as retrospectively managed instruments have cost hospitals millions of dollars due to disposal of instruments.

9.2.1. Instrument identification

Without detailed information as to which reusable instruments were in contact with potentially infectious tissue, the only way to eliminate all risk of iatrogenic transmission is to discard all potentially contaminated instruments, creating considerable waste. Without such information, the opportunity to reduce the risk of transmission by instruments already in circulation – risk to which some patients have already been exposed – is lost.
NOTE: To reduce or eliminate such risk without waste, it is strongly recommended all reusable instruments be tracked.

Once an evaluation of the patient, tissue, and instrument risks has occurred, utilize the **Risk Assessment Tool Recommendations for Managing Instruments Used on CJD Patients** (page 7.4.8) to identify recommended actions for instrument management.

10. Risk Assessment Tool Recommendations for Managing Instruments used on CJD Patients



For explanations of each of the four steps in the above graphic, including definitions, see the corresponding numbered sections in the text below.
1 No detected infectivity tissue: No CJD precautions, reprocess as usual.
2 >9 times: no evidence that it removes all risk.
3 Recipients of human tissue derived pituitary hormone treatment, dura mater graft, corneal graft and patients exposed via contact with instruments to high-infectivity tissue in a confirmed CJD patient.

11. Risk Assessment Tool Recommendations for Managing Instruments Used on CJD Patients continued

11.1. High-risk CJD Patients Managed Prospectively

CJD	
*Instruments in contact with: ****	*Action to be taken:*
High-infectivity tissue**	Discard
Low-infectivity tissue**	Can the instruments tolerate CJD decontamination? • Yes → CJD decontaminate and reuse • No → Discard
No detected infectivity tissue**	Routine reprocessing & reuse
Suspected CJD	
*Instruments in contact with: ****	*Action to be taken:*
High-infectivity tissue**	Routine reprocessing separately and quarantine Is diagnosis of CJD excluded? • Yes → Reuse • No → Discard
Low-infectivity tissue**	Can the instruments tolerate CJD decontamination? • Yes → CJD decontaminate & reuse • No → Routine reprocessing separately and quarantine Is diagnosis of CJD excluded? • Yes → Reuse • No → Discard
No detected infectivity tissue**	Routine reprocessing & reuse
Asymptomatic Carrier of Genetic TSE*	
*Instruments in contact with: ****	*Action to be taken:*
High-infectivity tissue**	Discard
Low/No detected infectivity tissue**	Routine reprocessing and reuse

* Refer to: Is the patient a potential CJD transmitter?
** Refer to: Was infectious tissue contacted?
*** Refer to: Which instruments were used?

11.2. High-risk CJD Patients Managed Retrospectively

CJD	
*Instruments in contact with: ****	*Action to be taken:*
High/Low infectivity tissue**	Can specific instruments or sets be identified? • Yes → Proceed as for prospectively managed CJD • No → Were instruments reprocessed more than 9 times? • Yes → Proceed as for prospectively managed CJD (option A) or reuse (option B) • No → Proceed as for prospectively managed CJD (option A)
No detected infectivity tissue**	Continue to reuse

* Refer to: Is the patient a potential CJD transmitter?
** Refer to: Was infectious tissue contacted?
*** Refer to: Which instruments were used?

11.3. At-risk CJD Patients for CJD

Recipients of human tissue derived pituitary hormone treatment, dura mater graft, corneal graft, and patients exposed via contact with instruments to high infectivity tissue in a confirmed CJD patient*	
Instruments in contact with: ***	Action to be taken:
Any tissue**	Routine reprocessing & reuse.

* Refer to: Is the patient a potential CJD transmitter?
** Refer to: Was infectious tissue contacted?
*** Refer to: Which instruments were used?

12. Infection Prevention and Control

Notify site Infection Prevention and Control of positive or suspect cases.

CJD is a reportable disease. Refer to **Reporting of a Communicable Disease to Manitoba Health by Infection Prevention & Control in Hospitals Operational Directives** for additional information.

Health care workers must employ **Routine Practices** when caring for patients with CJD.

Consult Infection Prevention and Control regarding autopsy and handling deceased patients. When performing medical/surgical procedures and post-mortem examinations, the most important safety rule is to avoid self-induced injury from instruments used in the course of removing and processing tissues for pathological examination. In particular, avoid contact between contaminated material and skin with cuts or abrasions.

13. Personal Protective Equipment (PPE)

Put on PPE according to the Point of Care Risk Assessment.

14. Laboratory Specimens

Label “suspect CJD” on the requisition for all specimens containing high or low infectivity tissue from high-risk patients, or high infectivity tissue and CSF from at risk patients.

15. Spills

Spills of fluids containing high or low infectivity tissue from high risk patients or high infectivity tissue and CSF from at risk patients should be flooded with full strength sodium hypochlorite for 1 hour before the absorbent material is applied. After the absorbent material has been used to remove the fluid it should then be sealed in a leak proof, puncture-resistant container, labeled ‘biohazardous’, and incinerated. The surface should then be disinfected using the hard surface decontamination process [20.1].

16. Solid Waste

All solid waste exposed to high or low infectivity tissues from a high risk patient or high infectivity tissues and CSF from an at risk patient should be sealed in a leak proof, puncture-resistant container, labelled ‘biohazardous’, and incinerated. Employees should use personal protective equipment and engineering controls (e.g., splash guards) to prevent exposure from splashing and aerosols during the emptying of waste containers. Liquids used for cleaning can be flushed down the drain [20.1].

Consult Infection Prevention and Control and Waste Management for management and pick-up of instruments.

17. Medical Devices

Normal sterilization procedures do not prevent transmission of CJD. Re-used instruments and materials should be kept moist until they can be appropriately decontaminated and cleaned. Neurosurgical and ophthalmic instruments used on a suspect patient with CJD should be quarantined until diagnosis of CJD is confirmed.

17.1. Quarantine

After routinely reprocessing separately from other instruments, store instruments in dry conditions. Do not reuse unless a diagnosis is made eliminating the possibility the patient on whom the instruments were used

had CJD. A confirmed diagnosis other than CJD, either clinical or pathological, or a postmortem examination excluding CJD, is required to take instruments out of quarantine. A brain biopsy that is negative for CJD, in the absence of a confirmed alternate diagnosis, does not suffice to take instruments out of quarantine.

A combination of the following measures is necessary to manage or reduce the risk of transmitting CJD infection through reused instruments. It is important to separate instruments used on known cases from those used on suspect cases.

17.2. Discard

- To discard means to ensure an instrument cannot possibly transmit infection to another patient. Incineration is the most unambiguous means of doing so.
- Whenever possible, contaminated instruments and other materials should be discarded as medical pathological waste or destroyed by incineration.
- When this is not possible, special decontamination methods may be employed as described below, followed by disposal in landfill.

17.3. CJD decontamination

Where appropriate, four step method of CJD decontamination should be followed:

17.3.1. Clean thoroughly: removal of adherent particles through mechanical or manual cleaning must be completed prior to any chemical/sterilizer decontamination of instruments. Instruments and other materials to be decontaminated should be kept moist between the time of exposure to infectious materials and subsequent decontamination.

- Clean and decontaminate reusable instruments that have been exposed to high or low infectivity tissues separately from those reusable instruments that have been exposed to no detected infectivity tissues
- Reusable instruments should be manually cleaned using an enzymatic cleaner prior to CJD decontamination. Reusable instruments to be cleaned in an automatic mechanical processor must be manually cleaned before they are put in the processor. After the instruments have been through the processor, the mechanical washer/disinfector should be run through a complete empty cycle before any further use.

17.3.2. Soak in 1N sodium hydroxide (NaOH) (0.4gm NaoH in 10 ml of water) for 1 hour (acceptable to substitute 2% sodium hypochlorite (NaOCl) [20,000 ppm available chlorine] for NaOH) [20.1].

17.3.3. Thoroughly rinse

17.3.4. Sterilize in a pre-vacuum-method autoclave at 134˚C for 60 minutes

- Instruments made of high-quality stainless steel can tolerate CJD decontamination using NaOH
- Instruments containing plastic or electronic devices, such as bronchoscopes, cannot tolerate CJD decontamination and must be discarded
- Instruments containing both steel and other metals, and particularly aluminum, should never be exposed to NaOH and must be discarded.

18. Environmental Surfaces

Surfaces (e.g., floors, counter-tops) exposed to high or low infectivity tissues from a high risk patient or high infectivity tissues and CSF from an at risk patient should be cleaned and decontaminated thoroughly following guidelines for hard surface decontamination. When possible, efforts should be made to prevent contamination to surfaces (i.e., through the use of temporary covers, shields, or guards made of disposable, liquid-resistant materials that can then be removed, sealed in a leak proof, puncture-resistant container, labeled 'biohazardous', and incinerated).

18.1. Hard Surface Decontamination

- Remove visible soil
- Flood with 2N NaOH (0.8gm NaoH in 10 ml of water) or undiluted NaOCl; let stand for 1 hour; then mop up and rinse with water; [20.1]
  Or

- If surfaces cannot tolerate NaOH or undiluted sodium hypochlorite, thorough cleaning will remove most infectivity by dilution. [20.1]

19. Occupational and Environmental Safety and Health

Contact Occupational and Environmental Safety and Health (OESH) for staff assessment and/or concerns.

20. References

20.1. Classic Creutzfeldt-Jakob Disease in Canada. An infection control guideline. (2002). Health Canada. CCDR2002;28S5:1-84. Accessed January 18, 2019.

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20.5. Heymann David L. Prion Diseases. In: Control of Communicable Diseases Manual 20th Ed, pp 484-490. (2014). American Public Health Association, Washington.

20.6. WHO Guidelines on Tissue Infectivity Distribution in Transmissible Spongiform Encephalopathies. (2006). World Health Organization. Accessed January 18, 2019.

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Appendix A: National Surveillance Case Definition for Classic CJD Sporadic Case

Confirmed CJD

	Spongiform encephalopathy in cerebral and/or cerebellar cortex and/or sub-cortical grey matter
AND/OR	Encephalopathy with prion protein (PrP) immunoreactivity (plaque and/or diffuse synaptic and/or patchy/perivacuolar types)
AND/OR	Scrapie associated fibrils (SAF)

Probable CJD

	Rapidly progressive dementia
AND	Typical EEG
AND	At least two of the following four clinical features: myoclonus, visual or cerebellar disturbances (ataxia), pyramidal/extrapyramidal dysfunction, akinetic mutism
OR	
	Rapidly progressive dementia
AND	Two of the four clinical features listed above
AND	Duration of illness < 2 years
AND	14-3-3 positivity (in CSF)

Possible CJD

	Rapidly progressive dementia
AND	Two of the four clinical features listed above
AND	Duration of illness < 2 years

Iatrogenic CJD

	Progressive cerebellar syndrome in a pituitary hormone recipient
	Sporadic CJD with a recognized exposure risk (e.g., dura mater transplant)

Familial CJD

	Confirmed or probable sporadic CJD plus confirmed or probable CJD in a first degree relative
AND/OR	Neuropsychiatric disorder plus disease-specific PrP mutation

Gerstmann-Sträussler-Scheinker (GSS)

	GSS in a family with dominantly inherited progressive ataxia
AND/OR	Dementia and one of a variety of PrP gene mutations • Encephalo(myelo)pathy with multicentric PrP plaques

Familial Fatal Insomnia (FFI)

	FFI in a member of a family with PrP178 mutation • Thalamic degeneration, variable spongiform change in cerebrum

Kuru

	Kuru in the Fore population of Papua New Guinea: • Although most neurologic features correspond to those of CJD with plaques, kuru should be diagnosed only in members of the Fore population in Papua New Guinea