



CREUTZFELDT-JAKOB DISEASE (CJD)

Cause/Epidemiology

The agent causing CJD and other human transmissible spongiform encephalopathy (TSE) has not yet been definitively identified. It was originally thought the infectious agent was a slow virus or virus-like particle. However, increasing evidence suggests the unconventional agents, termed prion proteins (PrP), are central in the etiology of these diseases. The prion is theorized to contain only protein, has no DNA or RNA and replicates by converting the structure of the normal cellular prion protein into an abnormal one. Prions are remarkably resistant to sterilization.

CJD was first described in the 1920's and is the most common TSE. It has been identified in all developed countries, and the incidence worldwide is between 0.5 and 1 case per million population, per year. The Canadian epidemiologic pattern is similar to that found elsewhere.

CJD has 4 different categories: sporadic (sCJD) accounting for 80-90% of cases, iatrogenic CJD associated with medical use of infected pituitary-derived hormones and dura mater, familial CJD and the recently described variant CJD (vCJD).

Variant CJD was first recognized in the United Kingdom in 1996. As of April 2002 the worldwide reported definite and probable cases of variant CJD include 117 cases in the UK, 6 in France, 1 in the Republic of Ireland, 1 in Hong Kong, and 1 in Italy. Epidemiologic and scientific evidence indicates that the agent responsible for BSE in cattle is the same agent responsible for variant CJD. The outbreak of variant CJD most probably is the result of consumption of beef products from BSE - infected cattle.

Clinical Presentation

The typical clinical presentation is a progressive dementia that soon becomes associated with progressive unsteadiness and clumsiness (cerebella ataxia), visual deterioration, muscle twitching (myoclonus), and a variety of other neurological signs and symptoms. The affected person is usually mute and immobile in the terminal stages, and in most cases death occurs within a few months of onset of symptoms (mean 5 months). CJD is invariably fatal, and there is no treatment.

Variant CJD differs in several ways from sporadic CJD. The individuals affected are younger with a median age of 29 years. The presenting features are often psychiatric disturbances (e.g., anxiety, depression, withdrawal) and



sensory symptoms (e.g., persistent parasthesia or dysesthesia), followed by other neurological symptoms and progressive cognitive impairment. Variant CJD has a marginally longer duration of illness (median 14 months, range 8 - 38 months) than classic CJD. The electroencephalograms, though not normal, do not show the typical triphasic wave complexes found in sporadic CJD. Magnetic resonance (MRI) brain scans show bilateral pulvinar high signal in over 70% of cases. The neuropathology in variant CJD differs in key aspects from other human TSE's. It is characterized by the presence of prominent spongiform change and extensive PrP deposition with florid plaques throughout the cerebrum and cerebellum.

Public Health Agency of Canada 2002 Guidelines national case definitions include

Sporadic Case (Confirmed)

- Spongiform encephalopathy in cerebral and/cerebellar cortex and/or subcortical grey matter, and/or
- Encephalopathy with prion protein (PrP) immunoreactivity (plaque and/or diffuse synaptic and/or patchy/perivascular types, and/or
- Scrapie associated fibrils (SAF)

Sporadic Case (Probable)

- Rapidly progressive dementia, and
- Typical EEG, and
- At least 2 of the following four clinical features
 - Myoclonus
 - Visual or cerebellar disturbances (ataxia)
 - Pyramidal/extrapyramidal dysfunction
 - Akinetic mutism, or
- Rapidly progressive dementia, and
- 2 out of the four clinical features listed above, and
- Duration of illness <2 years, and
- 14-3-3 positivity (in cerebrospinal fluid)

Sporadic Case (Possible)

- Rapidly progressive dementia, and
- Two out of the 4 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

Humans are the only proven reservoir of classical CJD, but new variant CJD may be transmitted to humans from ingestion of contaminated beef.

CJD must be differentiated from other forms of dementia, especially Alzheimer disease, from other slow infections, from toxic and metabolic encephalopathies, and occasionally, from tumors and other space occupying lesions.

Incubation Period

The incubation period can extend up to 30 years.

Transmission

Unknown in most cases; *de novo* spontaneous generation of the self-replicating protein has been hypothesized. Iatrogenic cases have been recognized from corneal transplants, cortical electrodes that had been used on known CJD residents, human dura mater grafts, and injections of growth or gonadotropic hormones prepared from human pituitary glands. Some cases have had a history of brain surgery within two years of onset. As indicated above, new variant CJD may be acquired by ingestion of beef from cows with BSE.

There has never been a documented case of variant CJD transmitted through blood transfusion. However, evidence from experimental work in animals suggests that transmission of variant CJD by blood is theoretically possible. As a precaution, since 1999, Public Health Agency of Canada has implemented policies to protect Canadians from the theoretical risk of transmission of variant CJD through blood.

Public Health Agency of Canada 2002 Guidelines indicate it is important to assess the resident and tissue risk for CJD. The assessment is dependent upon two factors

- The probability that a resident has or will develop CJD, and
- The level of infectivity on the resident tissues



Resident Risk Assessment for CJD

Residents with diagnosed or suspected CJD (as well as GSS and FFI) pose the highest risk for transmission of prion disease.

Resident Risk for CJD

High Risk Resident	At Risk Resident*
<p>Diagnosed CJD**</p> <p>Suspected CJD** undiagnosed, unusual, progressive neurological disease consistent with CJD** (e.g., dementia, myoclonus, ataxia)</p>	<p>Only under conditions in which there could be exposure to their high infectivity tissues, including CSF.</p> <p>Recipients of human dura mater grafts †, Corneal grafts §, and human pituitary hormones</p> <p>Members of families with familial CJD, Gerstmann-Straussler-Scheinker (GSS) and Familial Fatal Insomnia (FFI) ¶</p>

- * The incidence of CJD in Canada does not justify classifying people who have undergone neurosurgical procedures as at risk residents
- ** All forms of classic CJD (sporadic, familial and iatrogenic), GSS and FFI, excluding variant CJD
- † Recipients of dura mater grafts are frequently unaware of having received the graft
- § Corneal grafts, originating in a jurisdiction requiring the graft donor to be evaluated for neurological disease, are not considered a risk for CJD
- ¶ Familial CJD, Gerstmann- Straussler- Scheinker (GSS) and Familial Fatal Insomnia (FFI) can be determined by genetic testing or may be indicated by the occurrence of two or more cases of CJD, GSS, or FFI in the family (parent, child, sibling)



Tissue Risk for CJD

Level of Infectivity	Tissues, Secretions and Excretions
High Infectivity	Brain, spinal cord, dura mater, pituitary, eye* (including optic nerve and retina)
Low Infectivity	CSF**, kidney, liver, lung, lymph nodes, spleen, placenta
No Detected Infectivity	Adipose issue, skin, adrenal gland, heart muscle, intestine, peripheral nerve, prostate, skeletal muscle, testis, thyroid gland, feces, milk, nasal mucus, saliva, serous exudate, sweat, tears, urine, blood, bone marrow, semen

- * The highest levels of infectivity in the eye are associated with the optic nerve and retina and, to a much lower level, the cornea. It is expected levels of infectivity for other parts of the eye are low or nonexistent. There is no infectivity associated with tears
- ** Although CSF is classified as low infectivity and is less infectious than high infectivity tissues, it was felt instruments contaminated by CSF should be handled in the same manner as those contacting high infectivity tissues in high risk and at risk residents

Infection Prevention and Control

Contact Infection Prevention and Control and Sterile Processing Department for management of these instruments and protocols for autopsy and handling of deceased resident.

Follow Routine Practices for a resident with CJD, although special precautions are required for specific instruments, during autopsy and handling of deceased body.

Precautions for instruments

- Special precautions are required for
 - Instruments used on a high-risk resident when there has been exposure to high or low risk infectivity tissues. Refer to the above tables
 - Autopsy of a suspect or confirmed CJD resident
 - Handling of a suspect or confirmed deceased CJD resident

Neurosurgical and ophthalmic instruments used on a suspect resident with CJD shall be quarantined until diagnosis of CJD is confirmed



Implement Additional Precautions immediately when a resident has a communicable infection (e.g., pulmonary tuberculosis). Refer to the Management of Communicable Diseases in Personal Care Homes table for specific disease/microorganism information.

Refer to the Routine Practices section 4 and/or the Routine Practices for Reducing the Risk of Infection Transmission policy # 90.00.060 for specific information.

Occupational Health

Definition of Occupational Exposure

A healthcare worker who has had a percutaneous exposure or direct contact with high or low infectivity tissues of a person with suspect CJD.

Refer to the above table for tissue risk for CJD.

Non-invasive contact does not transmit CJD.

A Healthcare Worker Exposed to CJD

Unbroken Skin Exposure

- Wash skin with detergent and copious amounts of warm water (avoid scrubbing). Rinse and dry or, for maximum safety, one minute soak with 0.1 Sodium Hydroxide (NaOH) or a 1:10 dilution of bleach
 - Refer to Materials Safety Data Sheets (MSDS)
- Exposed healthcare workers shall contact Occupational Health/designate for clinical management

Percutaneous Exposure

- Gently encourage bleeding. Immediately wash the wound with copious amounts of warm soapy water (avoid scrubbing). Rinse, dry, and cover with a waterproof dressing
- Exposed healthcare workers shall contact Occupational Health/designate for clinical management

Mucous Membrane Exposure

- Immediately irrigate with either saline (eye) or tap water (mouth)
- Exposed healthcare workers shall contact Occupational Health/designate for clinical management

Health Care Worker is Symptomatic or Infected with CJD

- Physician confirmed diagnosis
- Healthcare workers shall be referred to Occupational Health/designate for clinical management