

Background

Prion diseases, also referred to as transmissible spongiform encephalopathies (TSE), are rare and fatal neurodegenerative diseases of animals and humans. “Prion” stands for *proteinaceous infectious particles*. The causative agent of prion diseases is thought to be a misfolded infectious isoform, called PrP^{Sc}, of a normally occurring cellular protein, PrP^C. This abnormal folding process can occur spontaneously (sporadic), by genetic mutations (familial), or by the uptake of prions from an external source (iatrogenic, variant). The resulting accumulation of abnormal protein in the central nervous system causes progressive neurodegenerative spongiform changes.

Creutzfeldt-Jakob disease (CJD) is the most common human prion disease with an incidence of 1-2 cases per million population per year. Sporadic CJD (sCJD) occurs for unknown reasons and accounts for approximately 85-90% of cases. Familial CJD (fCJD) results from an inherited mutation in the prion protein gene and accounts for about 10-15% of cases. Less common inherited forms include Fatal Familial Insomnia (FFI) and Gerstmann-Straussler-Scheinker Syndrome (GSS).

Historically, iatrogenic cases (iCJD) have been associated with human-derived pituitary hormone, dura mater grafts, corneal grafts, and contaminated neurosurgical equipment. All of the equipment-related cases occurred before routine implementation of the sterilization procedures currently used in health care facilities. No equipment-related cases have been reported since 1976. In the United States, 29 iCJD cases have been linked to the use of pituitary human growth hormone (hGH) in patients treated before 1977. The growth hormone now used for treatment poses no threat of infection with CJD.

Variant CJD (vCJD) is associated with consumption of cattle products contaminated with the prion agent causing bovine spongiform encephalopathy (“mad cow disease”). To date, no case of variant CJD acquired in the United States has been documented.

Clinical Features of Human Prion Disease

Sporadic CJD is most frequently characterized by a rapidly progressive dementia. Other observed manifestations include movement abnormalities (gait imbalance, myoclonus, ataxia, tremor, rigidity) visual deficits (diplopia, hallucinations, cortical blindness), cerebellar signs (nystagmus, truncal ataxia, opsoclonus), pyramidal signs (spastic paralysis, hyperreflexia, Babinsky’s sign, spasticity, clonus), extrapyramidal signs (bradykinesia, hypomimia, chorea, shuffling gait), behavioral and psychiatric symptoms (mood disturbance, anxiety, depression, personality changes, disinhibition), dystonia, sleep disturbances, and akinetic mutism.

Given the wide variety of clinical manifestations, the most important and consistent characteristic is the rapid progression of these manifestations in the context of no other clear etiology.

Variant CJD usually presents at younger ages with prominent behavioral and psychiatric symptoms in the initial stages, and dementia and neurological symptoms developing later in the illness.

For case classification criteria please see:

<https://www.cdc.gov/prions/cjd/diagnostic-criteria.html>

<https://www.cdc.gov/prions/vcjd/diagnostic-criteria.html>

Epidemiology

For updated information of prion disease epidemiology in Washington State, please see our [Annual](#) and [Decennial](#) Prion Disease Surveillance data.

Diagnostic Testing for Prion Diseases

Confirmatory testing for prion disease requires pathologic examination of brain tissue usually obtained at autopsy. *Ante mortem* tests, such as CSF 14-3-3, MRI, and EEG are not confirmatory, but can suggest probable prion disease as the etiology for the patient's symptoms.

Post mortem Testing:

- **Brain Autopsy:** In suspected cases of prion disease, the Department of Health **strongly** encourages physicians to recommend an autopsy to the patient's family in order to confirm prion disease and determine its type. Arrangements for autopsy and laboratory testing **free of charge** can be made through the National Prion Disease Pathology Surveillance Center (NPDPSC; see below). This national reference center provides comprehensive state-of-the-art prion disease diagnostics, including histopathology, immunohistochemistry, Western blot, and genetic analysis.

Ante mortem Indicators:

- **Brain biopsy:** In rare cases of dementia for which a reliable diagnosis cannot be established on the basis of clinical symptoms and ancillary testing, biopsy may be a helpful diagnostic approach. Although a brain biopsy result positive for prion disease confirms the diagnosis, a negative result cannot rule it out.
- **Cerebral spinal fluid and protein markers:** Cerebral spinal fluid (CSF) findings in a patient with sCJD are generally unremarkable, although mild protein elevation is not uncommon. Testing CSF for the protein markers 14-3-3 and Tau may be helpful in patients exhibiting rapidly progressive dementia; however these markers are not specific for sCJD and sensitivity decreases as the illness progresses.

In April 2015, the NPDPSC began offering CSF Real Time Quaking Induced Conversion (RT-QuIC) testing which detects prions by amplifying them into amyloid fibrils. . *This test has a sensitivity >85% and specificity is close to 100%.*

- **Electroencephalogram (EEG):** Obtaining *serial* EEGs in suspected cases of sCJD can assist in the diagnosis. In early sCJD, the EEG may be normal or show non-specific slowing. As disease progresses, patient with certain subtypes of sCJD develop biphasic or triphasic synchronous complexes on a slow background evolving into *periodic sharp wave complexes* occurring at about 1 per second. Importantly, this EEG pattern is transient in many patients, so its absence in a single test does not rule out CJD. However, when this pattern is observed, it does increase diagnostic likelihood.
- **Magnetic Resonance Imaging (MRI):** Frequently, hyperintense signal in the basal ganglia, thalamus, and cortex, which is non-enhancing, may be seen on T2- and FLAIR-weighted sequences in cases of sCJD. Diffusion-weighted imaging (DWI) is particularly sensitive, and will often show signal abnormality at the cortical gray-white junction ("cortical ribboning"). While these findings are not specific for CJD, they are helpful in supporting the diagnosis in a clinically suspicious case. If CJD is suspected (any form) the interpreting radiologist should be informed of this possibility.

Reporting a Suspect Case of Prion Disease to a Public Health Agency in Washington

Prion diseases in humans are notifiable per Washington Administrative Code 246-101-101.

All confirmed or suspected cases should be reported to the local health jurisdiction where the patient resides within 3 business days. Contact information for local health jurisdictions is available at:

<https://www.doh.wa.gov/AboutUs/PublicHealthSystem/LocalHealthJurisdictions>

Arranging Autopsy and Post Mortem Testing

All expenses for brain only autopsy, including collection of brain tissue and laboratory testing of brain tissue are covered if arrangements are made through the NPDPSC (see below). Patients or families interested in autopsy should complete the autopsy consent form available at:

<https://case.edu/medicine/pathology/sites/case.edu.pathology/files/2018-06/NPDPSC-Autopsy-Consent-%282018%29.pdf>

Additional information about NPDPSC autopsy is available at:

<https://case.edu/medicine/pathology/divisions/prion-center/resources-for-families/>

Infection Control Considerations

- Prion diseases are not known to spread from person to person, but transmission can occur during invasive medical procedures. The abnormally folded prion proteins are regarded as being highly resistant to the routine decontamination and sterilization methods currently used in medical facilities.
- If a patient with suspected or confirmed prion disease requires an invasive procedure, healthcare providers should contact the facility's infection control division and implement appropriate infection control measures. No single method is considered to be 100% effective against prions but instruments in contact with certain high risk tissues (i.e. brain, spinal cord, and eye) can be decontaminated by a combination of specific chemical and autoclaving methods before subjecting them to routine sterilization.

A guideline for disinfection and sterilization of prion-contaminated medical instruments is available at: <https://pdfs.semanticscholar.org/1fd4/8ad48c5d88f0552184bf6dbe48ab7d820c76.pdf>

- World Health Organization (WHO) Infection Control Guidelines for Transmissible Spongiform Encephalopathies should be followed during autopsy of a patient with suspected or confirmed human prion disease: <http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf>
- Tissues and organs from patients confirmed, suspected, or at risk for prion disease should not be donated for transplantation or teaching purposes.

Additional information about infection control measures related to CJD is available from the Centers for Disease Control and Prevention (<https://www.cdc.gov/prions/cjd/infection-control.html>).

Obtaining Clinical History to Determine Potential Risk Factors

History of travel or residence abroad, game meat consumption, and family history of prion disease or known PrP gene mutation should be assessed on every patient with suspected prion disease when obtaining the medical history. Though rare, cases of human prion disease have been iatrogenically-acquired from human-derived pituitary hormones, dura mater grafts, corneal grafts, and contaminated neurosurgical equipment, so it is important to ask about these exposures as well.

Also rarely, blood transfusion-associated vCJD transmission has occurred. Investigations of suspected vCJD cases should also include a history of transfusion products received and blood donations made by the patient.

Resource for Patients and Families

The CJD Foundation operates a national toll-free line at (800) 659-1991 and a web site:

<https://www.cjdfoundation.org/> offering support, information and practical advice for patients and families.

Contact Information

- Local health departments:
<https://www.doh.wa.gov/AboutUs/PublicHealthSystem/LocalHealthJurisdictions>
- Washington State Department of Health, Office of Communicable Disease Epidemiology:
(206) 418-5500 or (877) 539-4344 or
<https://www.doh.wa.gov/AboutUs/ProgramsandServices/DiseaseControlandHealthStatistics/CommunicableDiseaseEpidemiology>
- National Prion Disease Pathology Surveillance Center (NPDPSC), Case Western Reserve University: (216) 368-0587, cidsurveillance@uhhospitals.org or
<https://case.edu/medicine/pathology/divisions/prion-center>

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