Human Prion Diseases

Transmissible spongiform encephalopathies (TSE) including Creutzfeldt - Jakob disease (CJD)

Illness	The causative agents of TSEs are thought to be prions, abnormally folded, pathogenic versions of the self-replicating, host-encoded prion protein. The abnormal folding can occur spontaneously (sporadic), by genetic mutations (familial), or by the uptake of prions from an external source (iatrogenic, variant). Tissue deposits of prions in the central nervous system causes progressive neurodegenerative spongiform changes. An average of 14 cases occur in Washington annually. *No cases of variant CJD have been reported in Washington state to date.*
Signs and Symptoms	In sporadic cases: rapidly progressive dementia, visual disturbances, cerebellar dysfunction, pyramidal and extra pyramidal dysfunction, and myoclonus. In variant cases: behavioral changes (psychosis, depression), painful sensory symptoms, and delayed neurologic signs. See Appendix A
Incubation	Variable, but very long; in the order of years to decades. Note that the for sporadic and genetic prion diseases the concept of an incubation period may not be applicable.
Case Classification	Please see https://www.cdc.gov/creutzfeldt-jakob/hcp/clinical-overview/diagnosis.html for sporadic, familial, and iatrogenic CJD and www.cdc.gov/prions/vcjd/diagnostic-criteria.html for variant CJD. **Report all definite, probable and possible cases to CDE**
Differential diagnosis	Alzheimer's disease, dementia with Lewy bodies, frontotemporal dementia, corticobasal degeneration, progressive supranuclear palsy, neoplasms, viral encephalitis, metal toxicity
Treatment	Always fatal; death usually occurs within a year after onset of illness. Treatment is supportive.
Laboratory/ Imaging	Confirmatory testing requires pathologic examination of brain tissue. Pathologic and CSF testing are performed only at the National Prion Disease Pathology Surveillance Center (NPDPSC). See NPDPSC website for collection and shipment details. Tests for prion diseases are not performed at Public Health Laboratories (PHL). **CSF:** Protein markers 14-3-3 and Tau helpful if rapidly progressive dementia is seen. RT-QuIC (sensitivity ~90%, specificity ~100%). **EEG:** Electroencephalograms may show biphasic or triphasic synchronous complexes on a slow background evolving into periodic sharp wave complexes. **MRI:** Hyperintense signal in the basal ganglia, thalamus, and cortex, which is non-enhancing, may be seen on T2- and FLAIR-weighted sequences in sCJD cases. Diffusion-weighted imaging (DWI) will often show signal abnormality at the cortical gray-white junction ("cortical ribboning").
Public Health Investigation	• Collect information on clinical presentation and test results (provider interview/records review) • Determine receipt of human-derived pituitary hormones, dura mater or corneal grafts, neurosurgery, if related to a person with inheritable prion disease, or travel in Europe. • If still alive, encourage provider to discuss autopsy for diagnosis confirmation with the patient's family. An autopsy consent form is available on the NPDPSC website. • All autopsy (not funeral) arrangements and expenses are covered by the NPDPSC. • CDE receives pathology results and forwards them to LHJ; case classification is based on results. Prion disease can only be confirmed via autopsy. • If the patient is deceased, determine date of death and whether postmortem samples of brain tissue were collected. Include pathology reports with the case report form. Determine if prion disease was included in the causes of death. • Standard precautions recommended for hospitalized patients; additional special precautions necessary during some procedures. See Key Points for Infection Control Prevention • Follow WHO Infection Control Guidelines during autopsy of a confirmed or suspected case • Embalming: Follow https://www.cdc.gov/creutzfeldt-jakob/hcp/funeral-directors/?CDC_AAref_Val=https://www.cdc.gov/prions/cjd/funeral-directors.html • Tissue/organs from confirmed or suspected cases should not be donated (transplant/teaching) • If iatrogenically-acquired CJD, variant CJD or other novel acquired prion disease is suspected, contact CDE immediately. A more extensive investigation, including an interview with the next of kin, will be required. • If the patient is under the age of 55, an additional form needs to be completed for CDE to submit to CDC

Human Prion Diseases

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To monitor trends in the epidemiology of human prion diseases in Washington State.
2. To maximize laboratory confirmation of suspected cases and facilitate testing.
3. To promote awareness of available resources for patients, providers, and families.
4. To detect the emergence of variant Creutzfeldt-Jakob Disease or novel prion diseases in the United States.
5. To prevent potential iatrogenic transmission.

B. Legal Reporting Requirements

1. Health care providers and Health care facilities: notifiable to **local health jurisdiction** within 3 business days.
2. Laboratories: notifiable to **local health jurisdiction** within 2 business days; submission on request – specimen associated with positive result, within 2 business days.
3. Local health jurisdictions: notifiable to the Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE) within 7 days of case investigation completion or summary information required within 21 days.

C. Local Health Jurisdiction Investigation Responsibilities

1. Inform providers of the autopsy and laboratory services provided by the National Prion Disease Pathology Surveillance Center (NPDPSC).
2. Encourage providers to discuss the role of autopsy in the diagnosis of prion disease with the patient's family.
3. Discuss the importance of appropriate infection control procedures if surgical procedures are being considered.
4. Report all *definite, probable, and possible* cases to CDE (see definitions below). Complete the case report form for Human Prion Disease (https://www.doh.wa.gov/Portals/1/Documents/5100/420-003-ReportForm-Prion.pdf and enter the data into the Washington Disease Reporting System (WDRS) as Prion disease, human.
5. Perform a more extensive investigation for any suspect variant CJD, iatrogenic CJD, a novel prion disease, and suspected disease clusters.

2. THE DISEASE AND ITS EPIDEMIOLOGY

Background

Prion diseases, also known as transmissible spongiform encephalopathies (TSEs), are a group of rare, fatal neurodegenerative diseases of animals and humans. These diseases have long incubation periods, and cause characteristic spongiform brain changes,

neuronal loss, and gliosis without provoking an inflammatory reaction. Death usually occurs within a year after onset of symptoms.

Sporadic Creutzfeldt-Jakob disease (CJD) occurs worldwide and is the most common human prion disease (estimated global incidence: 1–2 cases per million population per year). Variant CJD was recognized in the United Kingdom in the 1990s and is associated with consumption of cattle products contaminated with the agent causing bovine spongiform encephalopathy.

Animal prion diseases include bovine spongiform encephalopathy (BSE, "mad cow disease") in cattle, scrapie in sheep, chronic wasting disease (CWD) in deer and elk, and transmissible mink encephalopathy.

In 2003 a 6-year-old Holstein cow imported from Canada was diagnosed with BSE in Washington State. In 2005, enhanced human prion disease surveillance was initiated in the United States and has since been conducted in collaboration with the Centers for Disease Control and Prevention (CDC) and the National Prion Disease Pathology Surveillance Center (NPDPSC).

To date, no cases of variant CJD acquired in the United States have been documented.

A. Etiologic Agent

The causative agent of prion diseases is thought to be prions. The term "prions" refers to abnormal, pathogenic agents that are transmissible and are able to induce abnormal folding of specific normal cellular proteins called prion proteins that are found most abundantly in the brain.Prion diseases are unique in that this abnormal folding process can occur spontaneously (sporadic), by genetic mutations (familial), or by the uptake of prions from an external source (iatrogenic, variant). Once initiated, the transformation of prion protein is exponential and the resulting deposits of abnormal protein in the central nervous system has been considered the cause of the progressive neurodegenerative spongiform changes. The term prion is derived from the phrase "proteinaceous infectious particle".

B. Description of Illness

Sporadic CJD is a fatal neurodegenerative disease that primarily occurs in people over 55 years of age. CJD affects many areas of the brain; therefore the clinical presentations can be quite variable but typically with early neurologic signs. Common symptoms include rapidly progressive dementia, visual disturbances, cerebellar dysfunction, pyramidal and extrapyramidal dysfunction, and myoclonus. About one-third of patients with sCJD have early constitutional symptoms, that include vertigo/dizziness, fatigue, headache, altered sleep pattern, and unexplained weight loss. Death is often caused by aspiration or sepsis and usually occurs within one year of onset.

A new type of sporadic prion disease was identified in 2008, and it is known as variably protease-sensitive prionopathy (VPrSP). The clinical features are more varied than in sCJD and include movement abnormalities, cognitive decline and unsteadiness while walking. The clinical illness is longer than for sCJD; most patients survive for over a year before succumbing to the illness. One case of VPrSP was reported in a Washington resident in 2012.

Familial CJD results from inherited mutations in the prion protein gene. It is thought that mutations make the prion protein more susceptible to transformation into an abnormal configuration. Compared to sporadic CJD, patients with familial CJD are often younger and have a family history of prion disease. However, clinical, and neuroimaging features are most commonly indistinguishable from sporadic disease. Most common familial prion diseases include Gerstmann-Sträussler-Scheinker (GSS) syndrome and fatal familial insomnia (FFI).

Iatrogenic CJD: Iatrogenic CJD (iCJD) is an uncommon acquired form of prion disease. Iatrogenic transmission of the CJD agent has been reported in over 450 patients worldwide. These cases have been linked to the use of contaminated human growth hormone (hGH) extracted from cadavers prior to 1977 (29 cases in the U.S.), dura mater (4 cases in the United States) and corneal grafts (1 case in the United States), or neurosurgical equipment (no cases in the United States). Of the six cases linked to the use of contaminated equipment, four were associated with neurosurgical instruments, and two with stereotactic EEG depth electrodes. All known equipment-related cases occurred before implementation of the routine sterilization procedures currently used in health care facilities. No such cases have been reported since 1976. No iatrogenic CJD cases associated with exposure to the CJD agent from surfaces such as floors, walls, or countertops have been identified. The only case of iCJD that has been reported in Washington State (in 2013) was associated with hGH administration during childhood.

Variant CJD: In the 1990s, a new variant of CJD was recognized in the United Kingdom (UK). The pathology of variant CJD is strikingly similar to that of cattle with BSE. vCJD is the only form of human prion disease known to be transmitted directly from animals to humans. Consumption of BSE-infected cattle products is the likely mode of transmission. Three cases have been associated with blood transfusions. In contrast to sporadic CJD, variant CJD is characterized primarily by behavioral and psychiatric changes (e.g., psychosis, depression), painful sensory symptoms, a younger age of onset (teens, 20s), and a longer duration of illness with delayed neurologic signs (Table 1).

As of July2022, 233 cases of variant CJD have been reported worldwide, mostly in the United Kingdom and Europe*. Although four cases of variant CJD have been reported in the United States, all are thought to have been exposed to the disease outside of the United States.

* Data from the National CJD Research and Surveillance Unit at the University of Edinburgh: http://www.cjd.ed.ac.uk/sites/default/files/worldfigs.pdf

Table 1: Clinical and pathologic characteristics distinguishing sporadic and variant CJD

Characteristic	Sporadic CJD	Variant vCJD
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 dysesthesia; delayed neurologic signs
Periodic sharp waves on EEG	Often present	Absent
"Pulvinar sign" on MRI*	Not reported	Present in >75%
Presence of "florid plaques" on neuropathology	Rare or absent	Present in large numbers
Immunohistochemical analysis of brain tissue	Variable accumulation	Marked accumulation of PrP†
Presence of agent in lymphoid tissue	Not readily detected	Readily detected

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

† Protease-resistant prion protein

Source: Centers for Disease Control and Prevention. Creutzfeldt-Jakob disease not related to a common venue—New Jersey, 1995–2004. MMWR 2004;53(18):392–6. Adapted from Belay E, Schonberger L. Variant Creutzfeldt-Jakob disease and bovine spongiform encephalopathy. Clin Lab Med 2002;22:849.

C. Human Prion Diseases in Washington State

From 1997 through 2004, surveillance for human prion diseases in Washington was primarily conducted by death certificate review. This surveillance method detected 3–9 cases of CJD per year. Enhanced surveillance and outreach to healthcare began in 2005. In the last decade 5–19 cases have been reported per year (average 12 cases per year). In 2023, 15 cases of human prion disease were reported.

Annual and decennial surveillance data are available on the DOH website.

D. Reservoirs

It is unknown whether a reservoir exists for sporadic CJD.

E. Modes of Transmission

The mode of transmission of sporadic CJD is not known. Approximately 5–15% of human prion disease is familial (i.e., inherited) and <1% is acquired through iatrogenic transmission or consumption of BSE-infected animal tissues. Rare cases of human prion

disease have been acquired during medical procedures from contaminated human-derived pituitary hormones, dura mater grafts, corneal grafts or neurosurgical equipment.

Acquisition of variant CJD has been associated with consumption of tissue from cattle with BSE. Food protection measures have been implemented to prevent meat products from suspected or confirmed BSE-infected cattle from being sold for consumption. Recent cases of variant CJD in the United Kingdom show that transmission of this disease can occur through blood transfusion (only 3 cases described in the UK). However, other human prion diseases are not known to be transmitted by transfusions. Prion diseases of humans are not transmitted through casual or intimate person-to-person contact.

F. Incubation Period

The incubation period for the few prion diseases with known sources (i.e., variant CJD, iatrogenically-acquired prion disease) is variable and extremely long, on the order of years to decades. Note that the for sporadic and genetic prion diseases the concept of an incubation period may not be applicable.

G. Period of Communicability

There is no evidence that prion disease is transmitted through casual or intimate person-to-person contact. However, in very rare circumstances, CJD has been acquired by contaminated neurosurgical instruments, transplanted dura mater and corneas, human-derived pituitary hormones, and transfused blood (for variant CJD only). As a precaution, infection control measures are recommended for neurosurgery or autopsy (Section 5B).

H. Treatment

These diseases are invariably fatal. Supportive care is needed and medications may be used to control aggressive or agitated behaviors.

3. CASE DEFINITIONS

A. Sporadic CJD* (2019)

1. **Definite:**
   - Diagnosed by standard neuropathological techniques; **and/or** immunocytochemically; **and/or** Western blot confirmed protease-resistant PrP; **and/or** presence of scrapie-associated fibrils.

2. **Probable:**
   - Neuropsychiatric disorder **plus** positive RT-QuIC in cerebrospinal fluid (CSF) or other tissues

   OR

   - Rapidly progressive dementia; **and** at least two out of the following four clinical features:
     - myoclonus
     - visual or cerebellar signs
     - pyramidal/extrapyramidal signs

- akinetic mutism

AND

- A positive result on at least one of the following laboratory tests;
  - A typical EEG (periodic sharp wave complexes) during an illness of any duration
  - A positive 14-3-3 cerebrospinal fluid (CSF) assay in patients with a disease duration of less than 2 years
  - High spinal in caudate/putamen on magnetic resonance imaging (MRI) brain scan or at least two cortical regions (temporal, parietal, occipital) either on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR).

AND

- The absence of an alternative diagnosis after routine investigation.

3. **Possible:**

- Progressive dementia; **and** at least two out of the following four clinical features:
  - myoclonus
  - visual or cerebellar signs
  - pyramidal/extrapyramidal signs
  - akinetic mutism

AND

- The absence of a positive result for any of the three laboratory tests that would classify a case as "probable" (see tests above) **and**
- Duration of illness less than two years **and**
- The absence of an alternative diagnosis after routine investigation.

B. Iatrogenic CJD* (2011)

Progressive cerebellar syndrome in a recipient of human cadaveric-derived pituitary hormone; or sporadic CJD with a recognized exposure risk, e.g., antecedent neurosurgery with dura mater implantation.

C. Familial CJD* (2011)

Definite or probable CJD plus definite or probable CJD in a first degree relative; **and/or** neuropsychiatric disorder plus disease-specific PrP gene mutation.

D. Variant CJD (2003)

1. **Definite:** Neuropathologic examination of brain tissue is required to confirm a diagnosis of variant CJD. The following confirmatory features should be present.

   a. Numerous widespread kuru-type amyloid plaques surrounded by vacuoles in both the cerebellum and cerebrum – florid plaques.

   b. Spongiform change and extensive prion protein deposition shown by immunohistochemistry throughout the cerebellum and cerebrum.

2. **Suspected:**

a. Current age or age at death <55 years (a brain autopsy is recommended, however, for all physician-diagnosed CJD cases).

b. Psychiatric symptoms at illness onset and/or persistent painful sensory symptoms (frank pain and/or dysesthesia).

c. Dementia, and development ≥4 months after illness onset of at least two of the following five neurologic signs: poor coordination, myoclonus, chorea, hyperreflexia, or visual signs. (If persistent painful sensory symptoms exist, ≥4 months delay in the development of the neurologic signs is not required).

d. A normal or an abnormal EEG, but not the diagnostic EEG changes often seen in classic CJD.

e. Duration of illness of over 6 months.

f. Routine investigations of the patient do not suggest an alternative, non-CJD diagnosis.

g. Did not receive cadaveric human pituitary growth hormone or a dura mater graft.

h. No history of CJD in a first degree relative or prion protein gene mutation in the patient.

NOTE

1. If a patient has the typical bilateral pulvinar high signal on MRI scan, a suspected diagnosis of variant CJD requires the presence of a progressive neuropsychiatric disorder, d, e, f and g of the above criteria, and four of the following five criteria: 1) early psychiatric symptoms (anxiety, apathy, delusions, depression, withdrawal); 2) persistent painful sensory symptoms (frank pain and/or dysesthesia); 3) ataxia; 4) myoclonus or chorea or dystonia; and 5) dementia.
2. A history of possible exposure to bovine spongiform encephalopathy (BSE) such as residence or travel to a BSE-affected country after 1980 increases the index of suspicion for a variant CJD diagnosis.

*These CDC diagnostic criteria for Creutzfeldt-Jakob Disease (2010) have been adapted from: 1) Global Surveillance, diagnosis, and Therapy of Human Transmissible spongiform Encephalopathies: Report of a WHO consultation, February 9-11, 1998, Geneva, Switzerland; 2) Zerr I, Kallenberg K, Summers DM, et al. Brain 2009, 132; 2659-2668; and c) National CJD Research & Surveillance Unit. Protocol: Surveillance of CJD in the UK. https://www.cjd.ed.ac.uk/sites/default/files/NCJDRSU%20surveillance%20protocol-april%202017%20rev2.pdf. Accessed 15 Aug 2018]

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Confirmatory diagnosis of prion diseases requires laboratory examination of brain tissue. The importance of autopsy and laboratory testing should be discussed with the patient's family. Arrangements for autopsy and laboratory testing can be made through the National Prion Disease Pathology Surveillance Center (NPDPSC, see below). This national reference center provides state-of-the-art prion disease diagnostics, including histopathology, immunohistochemistry, Western blot, and genetic analysis to confirm and determine the type of prion disease. Brain tissue examination services are offered to patients and families free of charge.

Antemortem indicators are not confirmatory. Antemortem indicators that support but cannot confirm the diagnosis of CJD include certain findings on EEG and MRI and elevated levels of 14-3-3 or tau protein in cerebral spinal fluid (CSF). Testing CSF for the protein markers 14-3-3 or tau may be helpful in patients exhibiting rapidly progressive dementia. However, these markers cannot confirm sporadic CJD, 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. Until January 1, 2019, RT-QuIC was performed as a reflex test following a positive 14-3-3 protein or Tau with a value of 500 pg/mL or higher. After January 1, 2019 RT-QuIC is performed on every sample. This test has a sensitivity >85% and specificity is close to 100%.

B. Services Available at DOH Public Health Laboratories (PHL)

PHL does not perform diagnostic testing for prion diseases. All specimens should be sent directly to the NPDPSC.

C. Specimen Collection

For information regarding specimen collection, shipping and handling please see the NPDPSC webpage: https://case.edu/medicine/pathology/divisions/prion-center/resources-for-professionals/

5. ROUTINE CASE INVESTIGATION

Cases of possible, probable, and definite prion disease are primarily identified from three sources: 1) reports from health care providers; 2) National Prion Disease Pathology Surveillance Center (NPDPSC) lab reports; and 3) death certificates.

A. Evaluate the Diagnosis

1. Determine the status (alive or deceased) of the patient. There is no need to interview the next of kin unless variant CJD, iatrogenically-transmitted CJD, a novel prion disease, or a CJD cluster is suspected, this includes patients 55 and under.
2. Interview the provider and/or review medical records to collect information on the patient's clinical presentation and antemortem test results (see above) as well as any potential risk factors. See Appendix A for definitions of neurologic terms found on the case report form.
3. If CJD is suspected and the patient is still alive, strongly encourage the provider to discuss the essential role of autopsy for diagnosis with the patient's family when appropriate. If the family consents to having an autopsy performed, they should complete the NPDPSC autopsy consent form (available at https://case.edu/medicine/pathology/sites/case.edu.pathology/files/2022-03/NPDPSC%20Autopsy%20Consent%20Packet_0.pdf) and submit it to the NPDPSC. All arrangements and expenses including transport of the body to a facility that can perform a brain-only autopsy, collection of brain tissue, return of the body, and specimen shipping and testing are covered by the NPDPSC. NPDPSC is the national reference laboratory for human prion diseases. The Center can confirm the diagnosis of prion disease and distinguish the type (e.g., variant CJD vs. familial CJD vs. sporadic CJD).

Once pathology results are available, they will be sent to the patient's physician and to the Office of Communicable Disease Epidemiology which, in turn, will send the pathology results to the local health jurisdiction. Using these results, the case can be classified.

4. If the patient is deceased, determine the date of death and whether postmortem samples of brain tissue were collected. Ascertain which laboratory has the tissues and forward any pathology report with the case report form.

B. Manage the Case / Infection Control Recommendations

1. Standard precautions are recommended for hospitalized patients; additional special precautions are necessary during some surgical procedures, including surgery on the brain, spinal cord, and posterior eye.
2. Surgical procedures: Prions are resistant to routine physical and chemical sterilization measures used in medical facilities. As a result, surgical equipment, surfaces, and other objects in contact with certain tissues, including nervous tissue or posterior eye tissue, of a person with suspected or confirmed prion disease require special decontamination measures. The brain, spinal cord, and posterior eye of patients with prion disease are considered highly infectious.

   If a patient with confirmed or suspected prion disease requires or recently had a surgical procedure or invasive EEG monitoring, contact the facility's infection control division so that appropriate infection control measures can be implemented, if needed. Information about infection control measures related to prion disease is available from the Centers for Disease Control and Prevention (https://www.cdc.gov/creutzfeldt-jakob/hcp/infection-control/?CDC_AAref_Val=https://www.cdc.gov/prions/cjd/infection-control.html) and the World Health Organization (https://apps.who.int/iris/bitstream/handle/10665/43498/9789241547017-eng.pdf).

   Please see the Key Points for Infection Control Prevention document, available at: https://www.doh.wa.gov/Portals/1/Documents/5100/420-162-PrionInfectionControl.pdf
3. Autopsy: The World Health Organization (WHO) Infection Control Guidelines for Transmissible Spongiform Encephalopathies should be followed during autopsy of a patient with confirmed or suspected human prion disease. WHO infection control guidelines can be found at: https://apps.who.int/iris/bitstream/handle/10665/66707/WHO_CDS_CSR_APH_2000.3.pdf?sequence=1&isAllowed=y
4. Embalming: The Centers for Disease Control and Prevention guidelines 'Information on Creutzfeldt-Jakob Disease for Funeral Home, Cemetery and Crematory Practitioners' should be followed (see https://www.cdc.gov/creutzfeldt-jakob/hcp/funeral-directors/?CDC_AAref_Val=https://www.cdc.gov/prions/cjd/funeral-directors.html).
5. Tissue/Organ Donation: Tissues and organs from patients with confirmed or suspected prion disease should not be donated for transplantation or teaching purposes.

   Note: Additional infection control measures are recommended in some circumstances for persons 'at risk' for developing prion disease. These persons are defined as asymptomatic persons who meet any of the following criteria: 1) received dura mater ***or*** human-derived

pituitary hormones, especially human-derived growth hormone ***or*** cornea transplants, 2) have undergone neurosurgery, or 3) are members of families with heritable prion disease.

Source: World Health Organization Communicable Disease Surveillance and Response. WHO Manual for surveillance of human transmissible spongiform encephalopathies including variant Creutzfeldt-Jakob disease. Geneva, Switzerland: 2003.

C. Identify Potential Sources of Infection

Ask the provider and/or review records to determine if the patient ever received human-derived pituitary hormones (especially human-derived growth hormone), dura mater or corneal grafts, had neurosurgery, or is biologically related to a person with heritable prion disease.

If a patient is suspected to have iatrogenically acquired prion disease, variant CJD or another novel acquired prion disease, contact CDE. An extensive investigation including an interview with the next of kin will need to be initiated.

D. Identify Potentially Exposed Persons

Determine if the patient had surgery (surgery on the brain, spinal cord or posterior eye are high risk surgeries) during this illness or before becoming ill. If so, contact CDE. The hospital where the procedure was performed should be contacted to determine if equipment, surfaces, and other objects were properly decontaminated.

E. Manage Others Potentially Exposed

No follow-up is needed for close contacts of the patient since there is no evidence that any human prion disease is transmitted through casual or intimate person-to-person contact. If the patient had a surgical procedure when the hospital was unaware of the suspected disease status, contact CDE.

F. Environmental Evaluation

None.

7. ROUTINE PREVENTION

A. Immunization Recommendations

There is no vaccine to prevent human prion diseases.

B. Prevention Recommendations

There are no prevention measures for most human prion diseases. See the infection control section above for precautions in hospital and other special settings.

UPDATES

April 2010: The guideline was reviewed. No significant revisions were made.

January 2011: The legal reporting requirements were revised to reflect the 2011 Notifiable Conditions Rule revision. The case definitions were updated due to revisions to the CDC cases definitions.

June 2012: The guideline was reviewed. No significant changes were made.

July 2014: The guideline was reviewed. No significant changes were made.

August 2016: Information regarding RT-QuIC test was included. Epidemiology of the disease in WA State was updated.

March 2018: The guideline was reviewed and updated for WDRS.

September 2018: The case definitions were updated due to revisions to the CDC cases definitions. Epidemiology of the disease in Washington was updated.

May 2019: The case definitions were updated to reflect CDC case definition revisions; MRI criteria expanded.

August 2021: The guideline was reviewed. No significant changes were made.

December 2022: For 2023 WAC revision combined provider and facility reporting requirement, updated laboratory submission (Section 1B). Guideline reviewed. Links verified and language updated to match CDC webpages.

August 2024: CDC links updated and routine review.

APPENDIX A

The following terms and their definitions may assist with the questions on the prion disease case report form and terms that you may find during Creutzfeldt-Jakob Disease (CJD) chart reviews.

- **Akinetic mutism:** Akinetic mutism is the loss of the voluntary ability to speak and move. This term should be specifically stated. Unless it is clearly stated that the patient is awake and not comatose, do not substitute the term "unresponsive." It is also known as "apallic syndrome".
- **Cerebellar signs** of CJD may include:
    - Ataxia: failure of muscular coordination. Affected patients have coordination, postural and balance problems early in the disease process and as the disease progresses, severe ataxia leads to loss of ability to walk.
    - Opsoclonus (horizontal and vertical oscillations of the eyes)
    - Nystagmus (involuntary rapid rhythmic movement of the eyeball)
    - Truncal titubation / truncal ataxia (staggering, stumbling gait with shaking of the trunk)
    - Appendicular ataxia (lack of coordination in a limb)
    - Movement tremor (involuntary trembling/quivering)
    - Termination or terminal tremor would be included in CJD signs, however "tremor" alone is not necessarily a cerebellar or CJD sign.
- **Chorea:** Writhing movements of the body / extremities. Rapid, highly complex jerky movements that appear to be well coordinated but occur involuntarily.
- **Dementia:** Dementia refers to cognitive decline.
- **Dysesthesia and painful sensory symptoms:** New onset of pain or other uncomfortable sensations unrelated to injury or stimulus.
- **Dystonia:** Abnormal tonicity in muscles resulting in impairment of voluntary movement.
- **Hyperreflexia:** Exaggerated reflexes
- **Myoclonus:** Sudden, involuntary contractions or jerking of a muscle or group of muscles. Terms such as "myoclonic jerks", "myoclonic jerking", "myoclonic activity" are also acceptable. These variants of myoclonus may be mentioned:
    - Nocturnal myoclonus
    - Facial myoclonus
    - Action myoclonus
    - Startle myoclonus

  Terms such as "twitching", "tremulousness", or "shaking / shakiness" are not equivalent and the term "clonus" represents a separate neurologic sign.
- **Progressive Dementia:** Ongoing cognitive decline. The development of dementia in CJD patients is very pronounced over a short period of time (weeks) unlike dementia associated with Alzheimer's disease. Terms like "delirium", "altered mental status", or "unresponsiveness" should not be interpreted as representing progressive dementia, unless there is clear evidence in the chart that the condition has been ongoing for weeks / months and that the patient is progressively getting worse in terms of cognitive ability.

- **Progressive neuropsychiatric disorder**: Abnormalities in the nervous system and in mental processes. In the variant form of CJD, the first symptoms are psychiatric and patients experience a progressive neuropsychiatric disorder lasting at least 6 months. In the sporadic form, if neuropsychiatric disorders are present, they usually are concurrent with the physical manifestations of the disease.
- **Pyramidal signs** refer to disorders of the upper motor neuron pathway going from the motor cortex through the brainstem and down to the spinal cord. Pyramidal signs would include things such as:
    - Upper motor neuron weakness
    - Hemiplegia (paralysis of one side of the body)
    - Spastic (limb) paralysis / paresis
    - Hyperreflexia
    - Presence of Babinski's sign / "upgoing toes"
    - Spasticity
    - Clonus (alternate muscular contraction and relaxation in rapid succession)
- **Extrapyramidal signs** refer to disorders of brain structures controlling movement, mainly with reference to the basal ganglia and related structures. The most commonly recognized extrapyramidal signs are those associated with Parkinson's disease. Extrapyramidal signs of CJD may include:
    - Bradykinesia / hypokinesia (slowness of movement)
    - Rigidity (limb or neck)
    - Tremor
    - Hypomimia (flat facies, masked facies, lack of facial expression)
    - Postural instability
    - Shuffling gait
    - Ballismus/hemiballismus (sudden flinging movements of the extremities)
    - Chorea/choreoathetosis (writhing movements of the body/extremities)
- **Visual Deficits:** The visual abnormalities in CJD most commonly are complex visual disturbances, such as hallucinations or cortical blindness. Do not count terms such as "blurred vision" or "decreased visual acuity." Terms that may be to describe CJD-associated visual deficits include the following:
    - Visual hallucinations
    - Hemianopsia (defective vision or blindness in half of the visual field)
    - Visual field cut / visual field deficit
    - Blindness
    - Opsoclonus (horizontal and vertical oscillations of the eyes)
    - Diplopia / double vision