*epi*TRENDS

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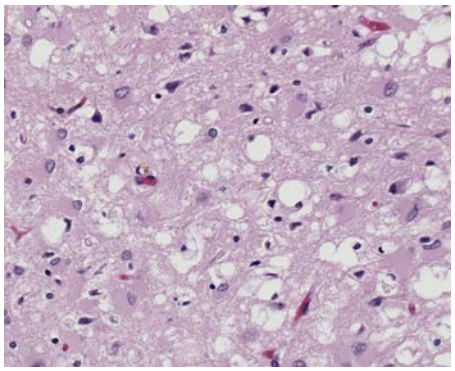
Human Prion Disease

Prion diseases, also called transmissible spongiform encephalopathies (TSE), are rare and fatal neurodegenerative diseases of animals and humans. “Prion” stands for proteinaceous infectious particles. The cause of prion diseases is thought to be a misfolded form, called PrPSc, of a normally occurring cellular protein, PrPC. This abnormal folding 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 brain causes progressive damage with a sponge-like appearance microscopically.

CJD

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



Variant CJD
www.cdc.gov

Historically, iatrogenic cases (iCJD) were associated with human-derived pituitary hormone, dura mater grafts, corneal grafts, and contaminated neurosurgical equipment. All the equipment-related cases occurred before routine implementation of the sterilization practices currently used in healthcare facilities. No equipment-related cases have been reported in this country since 1976. In the United States, 29 iCJD cases were linked to pituitary human growth hormone (hGH) used in patients before 1977.

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The current growth hormone used for treatment poses no threat of CJD.

CJD is characterized by rapidly progressing dementia, poor balance, visual changes, and/or muscle jerks. Other symptoms may include personality changes, anxiety, depression, and insomnia. In vCJD cases, psychiatric symptoms are usually more prominent at the onset, with dementia developing later in the illness. Prion diseases are invariably fatal, with a median duration of four months between onset of symptoms and death. Most patients die within a year of diagnosis.

Confirmatory testing for prion diseases requires pathologic examination of frozen brain tissue (biopsy or autopsy). Testing can distinguish the type of CJD, including the main forms as well as less common inherited forms such as fatal familial insomnia (FFI) and Gerstmann-Straussler-Scheinker syndrome (GSS) and rare sporadic forms such as variably protease-sensitive prionopathy (VPSPr).

To provide effective surveillance for CJD and other prion diseases, it is strongly recommended that clinicians make an effort to have an autopsy performed in all suspected cases of prion disease. Autopsy can be arranged through the National Prion Disease Pathology Surveillance Center (NPDPSC). Currently, NPDPSC covers all autopsy related costs, including the autopsy itself, any transportation or use-of-facility fees associated with the autopsy, and testing for prion diseases.

Ante mortem tests are not confirmatory but can help in establishing a clinical diagnosis:

- The NPDPSC offers cerebrospinal fluid (CSF) testing for 14-3-3 and Tau proteins, indirect markers of neural degeneration. Since April 2015, the NPDPSC offers CSF Real Time Quaking Induced Conversion (RT-QuIC) testing which detects prions by amplifying them into amyloid fibrils. It is performed as a reflex test following a positive 14-3-3 protein or Tau value of 500 pg/mL or higher. RT-QuIC sensitivity is over 85% and specificity is close to 100%.
- Serial electroencephalograms (EEGs) showing periodic sharp wave complexes increase the diagnostic likelihood.
- Brain magnetic resonance imaging (MRI) shows hyper-intense signal in the basal ganglia, thalamus, and cortex, which is non-enhancing and may be seen on T2- and FLAIR-weighted sequences. Diffusion-weighted imaging (DWI) is particularly sensitive, and will often show signal abnormality at the cortical gray-white junction (“cortical ribboning”).

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http://listserv.wa.gov/cgi-bin/wa?SUBED1=epitrends&A=1

Choose the option to join the listserve. Enter your name and email address.

CDC case classification criteria (Definite, Probable, and Possible cases) can be found at: http://www.cdc.gov/prions/cjd/diagnostic-criteria.html and

http://www.cdc.gov/prions/vcjd/diagnostic-criteria.html

Healthcare and Public Health Interventions

Normal social or routine contact with a CJD patient carries no risk for household members, healthcare workers, or others. Standard precautions should be used for all patients with known or suspected CJD; isolation is unnecessary. Body secretions and body fluids have low to no detectable infectivity so the majority of samples taken or procedures performed will carry low to no risk for transmission (Table 1). If a patient with suspected or confirmed prion disease requires an invasive procedure, healthcare providers should contact the facility's infection control division to assure that recommended infection control measures are implemented.

Table 1. Infectivity in Organs, Tissue, and Body Fluids of Humans with Prion diseases (CJD)

Infectivity category	Tissues, secretions, and excretions			
High infectivity	Brain	Cranial nerves	Cranial ganglia	Pituitary gland
	Posterior eye	Spinal cord		
Low infectivity	CSF	Kidney	Liver	Lung
	Lymph nodes	Olfactory epithelium	Placenta	Spleen
No detectable infectivity	Adipose tissue	Adrenal gland	Blood / serum	Bone marrow
	Feces	Gingival tissue	Heart muscle	Intestine
	Milk	Nasal mucosa	Peripheral nerves	Prostate
	Saliva	Semen	Serous exudate	Skeletal muscle
	Sputum	Sweat	Tears	Testis
	Thyroid gland	Urine	Vaginal secretions	

Prion Diseases in Washington State

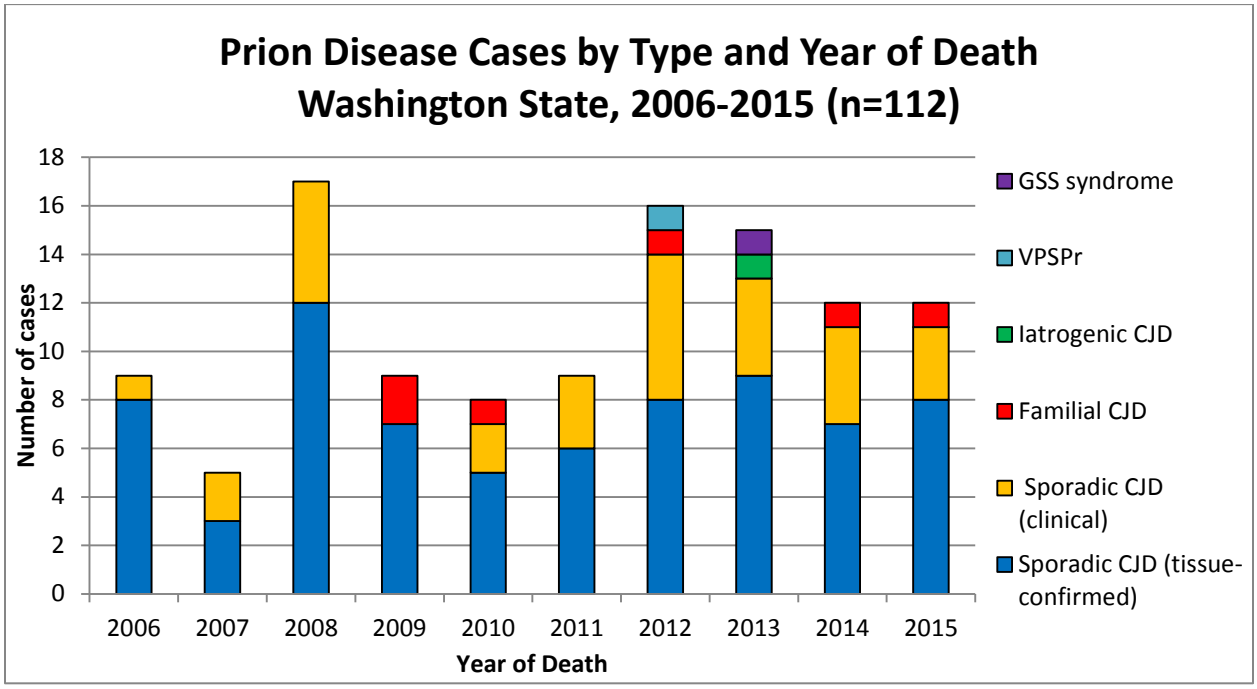
Beginning in 2004, the Washington State Department of Health (DOH) has collaborated with the Centers for Disease Control and Prevention (CDC) and the NPDPSC to track prion disease in the State. Healthcare providers in Washington should report suspected human prion disease to the local health jurisdiction of the patient (WAC 246-101-101). From 2006-2015, an annual average of 11 prion disease cases have been reported in Washington State (Table 2).

Table 2. Characteristics of Prion Disease Cases, Washington State, 2006–2015 (n=112)

Characteristic	No. Cases (%)
Male	58 (52%)
Median age [range]	67 years [36–84 years old]
Median duration of illness [range]	4.5 months [1-70 months]
Average incidence	1.6 cases/million population
Autopsy and/or biopsy performed	80 (71%)

The distribution of the different types of human prion disease in Washington is consistent with national and global reports (Figure).

Figure. Prion Disease Cases in Washington State, 2006-2015



A complete assessment of any risks for acquired disease (e.g. pituitary hormone or dura mater recipient) or risk to others (i.e. neurosurgery performed while symptomatic) should be completed for each possible, probable, or definite prion disease case. Also obtain information on family history of prion disease, residence in the United Kingdom for over three months since 1980, and organ and tissue donation/receipt to support the etiology (i.e. sporadic, familial, acquired). Only brain tissue examination can confirm the type of prion disease, although some families may be uncomfortable with the autopsy. However the results contribute to public health knowledge and can provide information that lets the family assess whether others are at risk.

Resources for Patients and Families

The CJD Foundation operates a national toll-free line at (800) 659-1991 and a web site: http://www.cjdfoundation.org/ offering support, information, and practical advice for patients and families.

Resources

CDC Creutzfeldt-Jakob Disease web page: http://www.cdc.gov/prions/cjd/index.html

National Prion Disease Pathology Surveillance Center (NPDPSC), Case Western Reserve University: (216) 368-0587 or http://case.edu/med/pathology/centers/npdpsc/

Washington Department of Health Communicable Disease Epidemiology (206) 418-5500
http://www.doh.wa.gov/ForPublicHealthandHealthcareProviders/NotifiableConditions/PrionDisease

World Health Organization (WHO) Infection Control Guidelines for Transmissible Spongiform Encephalopathies for suspected or confirmed human prion disease:
http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf