Prion Diseases

Information for Wisconsin Medical Providers

Introduction

Suspected or confirmed human cases of transmissible spongiform encephalopathy (TSE) are legally reportable to the patient's local health department under Wis. Admin. Code ch. DHS 145 Appendix A as a category II disease.

TSEs include any prion-related disease, including sporadic Creutzfeldt-Jakob disease (sCJD), familial CJD (fCJD), variant Creutzfeldt-Jakob disease (vCJD), fatal insomnia (FI), Gerstmann-Straüssler-Scheinker syndrome (GSS), and variably protease-sensitive prionopathy (VPSPr). Of these, only sCJD is known to occur with any frequency in the U.S. (with an incidence of approximately 1–1.5 cases per million). sCJD makes up 90% of all CJD cases, with the other 10% being comprised of mostly fCJD.

Criteria for reporting a suspect case of TSE in Wisconsin

A prion-related disorder, such as Creutzfeldt–Jakob disease (CJD), should be suspected and reported to the patient's local public health department electronically, through the Wisconsin Electronic Disease Surveillance System (WEDSS), by mail or fax using an Acute and Communicable Diseases case report, F-44151 (Word) or by other means within 72 hours upon recognition of a case. Reports can also be faxed to the prion diseases program of the Wisconsin DPH (Fax: 608-251-3035) in any patient diagnosed with dementia before the age of 55 years old or rapidly progressive dementia occurring at any age with one or more of the following:

- Movement disorders (such as myoclonus or ataxia)
- Painful sensory symptoms
- Visual disturbances

DPH prion disease program contact information:

- Phone number: 608-267-9003
- Email: DHSDPHPrions@dhs.wisconsin.gov

When suspecting a case

☐ **Explore differential diagnoses (blood panel, medical history evaluation)**

Treatable conditions with similar presentation:

- B12 Deficiency
- Hypothyroidism
- Syphilis
- HIV/AIDS
- Chronic Meningitis
- Toxic Exposure
- Whipple's Disease
- Cerebrovascular Disease
- Direct or Indirect effects of Cancer (B-cell Lymphoma)
- Wilson's Disease Seizure Disorder
- Tardive Dyskinesia
- Normal Pressure Hydrocephalus
- Organ Failure
- Psychiatric Disorders
- Unusual Presentation of Parkinson's Disease or Parkinson–plus Syndromes

Incurable conditions with similar presentation:

- Corticobasilar Degeneration
- Leukodystrophies
- Spinocerebellar Degenerations
- Pick's Disease
- MELAS Syndrome
- Unusual presentations of Alzheimer's Disease and Alzheimer's Disease Related Dementias
- Mitochondrial diseases

☐ **Order cerebrospinal fluid (CSF) testing including RT- QuIC analysis**

Cerebrospinal fluid (CSF): Constituents are usually normal aside from elevated levels of tau protein and 14-3-3 protein. The sensitivity and specificity of these CSF markers near 90%; however, the usefulness of these non-specific tests is questionable in early disease.

- We **strongly** recommend specimens be sent to the National Prion Disease Pathology Surveillance Center (NPDPSC) at Case Western Reserve University, Cleveland, Ohio for the completion of RT-QuIC analysis (98.5% specificity and 89–92% sensitivity in detecting the abnormal prion protein), autopsy, and subsequent genotyping following a diagnosis.
    - Phone: 216-368-0587
    - Emergency autopsy phone (nights and weekends only): 216-647-8148
    - Email: **cjdsurveillance@uhhospitals.org**
    - Test protocols/submission forms can be found on their website.

☐ **Order a neurology consult and EEG and MRI testing to search for abnormalities**

Expected results for CJD are:

- Electroencephalogram (EEG): Periodic sharp wave complexes
- Magnetic resonance imaging (MRI): High signal in caudate and/or putamen on MRI brain scan or at least two cortical regions (temporal, parietal, occipital) either on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR)

Following a tentative diagnosis

☐ **Clarify that treatment for the disease is supportive or palliative in nature**

☐ **Do not isolate patient, transmission is not possible from casual contact**

☐ **Inform family of the autopsy services offered by the NPDPSC**

Brain biopsy and autopsy: While conventional pathological investigation will show spongiform encephalopathy, we **strongly** recommend specimens be sent to the NPDPSC for further testing. Coordination of these autopsies can be done by contacting the center (See contact information above).

The NPDPSC is unique in that they can also perform genotyping on frozen specimens to determine the type of CJD-diagnose related conditions such as GSS and FFI and definitively distinguish between sporadic and familial CJD. Families interested in pursuing these services can do so by contacting the NPDPSC to be directed to one of their autopsy coordinators.

☐ **Report the case in WEDSS; be sure to include:**

- History and physical assessment for ample context.
- Neurology consult (if performed).
- MRI and EEG results (if performed).
- Discharge summary (if available).
- CSF testing results.

Variant CJD (vCJD), was a prion disease that resulted from the consumption of animal products harvested from cattle infected with Bovine Spongiform Encephalopathy (BSE) in the United Kingdom in the 1980's. Although new exposures are nearly impossible due to improved surveillance of cattle, cases in humans may still manifest as a result of a past exposure. vCJD can be confirmed only through examination of brain tissue—the nature and location of brain lesions combined with western blot testing of prion protein (performed at the NPDPSC) allow the definitive differentiation of vCJD from sCJD. Clinically, in contrast to sCJD, vCJD predominantly affects younger people, has a longer survival time after onset (greater than six months), and has an atypical presentation, with prominent psychiatric or sensory symptoms at the time of presentation. Patients with vCJD usually have delayed onset of neurologic abnormalities, including ataxia within weeks or months, with dementia and myoclonus occurring late in the illness. Only four cases of vCJD have occurred in the U.S., all of which had been acquired abroad.