Transmissible Spongioform Encephalopathy (TSE) or Prion Disease (includes CJD; vCJD) Investigation Guideline

CONTENT:	**VERSION DATE:**
Investigation Protocol:	
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Investigation Forms / Documentation Worksheets:	
• **TSE Patient Questionnaire**	**03/2011**
• **Appendix A (Medical Terms/Definitions)**	**03/2011**
Supporting Materials found in attachments:	
• **Fact Sheets**	**03/2011**

Revision History:

Date	Replaced	Comments
03/2011	09/2010	Minor formatting and editing of investigation guideline, fact sheet and questionnaire.

Transmissible Spongioform Encephalopathy (TSE)
Disease Management and Investigation Guidelines

Diagnostic Criteria for Creutzfeldt-Jakob Disease (CJD), CDC 2010

Sporadic CJD:

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

Probable: 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. atypical electroencephalography EEG (periodic sharp wave complexes) during an illness of any duration; and/or
b. a positive 14-3-3 cerebrospinal fluid (CSF) assay in patients with a disease duration of less than 2 years; and/or
c. Magnetic resonance imaging (MRI) high signal abnormalities in caudate nucleus and/or putamen on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR)

AND no alternative diagnosis

Possible: Progressive dementia; and at least two 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 a-c above)

AND duration of illness less than two years

AND no alternative diagnosis

Iatrogenic CJD:

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.

Familial CJD:

Definite or probable CJD plus definite or probable CJD in a first degree relative (e.g. mother, father, brother, sister); and/or neuropsychiatric disorder plus disease-specific PrP gene mutation.

Diagnostic Criteria for Variant Creutzfeldt-Jakob Disease (vCJD) in the United States, CDC 2003

Variant Creutzfeldt-Jakob Disease (vCJD):

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

- Numerous widespread kuru-type amyloid plaques surrounded by vacuoles in both the cerebellum and cerebrum - florid plaques.
- Spongiform change and extensive prion protein deposition shown by immunohistochemistry throughout the cerebellum and cerebrum..

Suspected:

a. Current age or age at death <55 years (a brain autopsy is recommended 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 month 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 greater than 6 months.
f. No alternative, non-CJD diagnosis.
g. No history of receipt of 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.

LABORATORY ANALYSIS

Testing for prion diseases is not provided by the Kansas Health and Environment Laboratories, but the National Prion Disease Pathology Surveillance Center (NPDPSC) does provide testing. The NPDPSC:

- Acquires tissue samples and clinical information from cases of human prion disease occurring in the United States (US) to monitor for vCJD.
- Diagnoses prion disease by analyzing cerebrospinal fluid (CSF), blood, and brain tissue obtained either at biopsy or autopsy.
- Identifies the precise type of prion disease (sporadic, familial, or acquired) by examining the prion protein and the prion protein gene.
- Report findings to caregivers in a timely fashion.
- Submits data to CDC and state health departments who monitor prevalence and investigate possible cases of transmissible disease.
- Stores tissues for future studies.

Diagnostic tests performed by NPDPSC:

- CSF: Search for the presence of the 14-3-3 protein, a marker for some prion diseases, such as Creutzfeldt-Jakob disease (CJD).
- Blood, brain, or other tissues: DNA extracted and examined for mutations in the prion protein gene and polymorphism at codon 129 and at other codons.
- Unfixed brain tissue: obtained either at biopsy or autopsy; examined for presence and type of the abnormal, protease-resistant form of the prion protein, also known as scrapie prion protein (PrPSc).
- Fixed brain tissue: Exclude or confirm and characterize the prion disease by microscopic examination following ordinary histological procedures and immunohistochemical demonstration of the prion protein.

Note: **Only an examination of frozen brain tissue** can confirm or exclude the diagnosis of prion disease and provide information to identify the type of prion disease. CSF and blood examinations provide information that may be helpful to physicians in making a clinical diagnosis.

Specimen collection, shipping, and testing:

- For details regarding the collection and shipment of clinical specimens, visit the NPDPSC website at www.cjdsurveillance.com.
    a. Protocols are available for specimen collection and test reporting (including turnaround times).
    b. Forms are available for autopsy consent, test request, and test reporting.
    c. Instructions for contacting and mailing to the NPDPSC are provided.

EPIDEMIOLOGY

Prion diseases or transmissible spongiform encephalopathies (TSEs) are a group of rare disease of the brain characterized by a degenterative neuropathology and tissue deposition of an abnormal form of a normal prion protein.

Human prion diseases are comprised of: Creutzfeld-Jakob In humans (CJD) and its four known variants: sporadic (sCJD); genetic (gCJD); variant (vCJD) and iatrogenic (iCJD) and the less common prion disease include Gerstmann-Straussler-scheinker syndrome (GSS); Kuru; and fatal familial insominia (FFI). The most common prion disease, sCJD, has a 1-2 per million mortality rate with the highest age-specific mortality rate in the 65-79 age group (more than 5 cases/million. Genetic CJD have been reported in familial clusters in Chile, Israel, and Slovakia.

In the 1990s, vCJD was recognized in the United Kingdom (UK) associated with the consumption of BSE-infected beef. BSE, or bovine spongiform encephalopathy, is an animal prion disease of cattle similar to scrapie in sheep, chronic wasting disease in deer and elk, and transmissible mink encephalopathy. As of March 2008, 206 cases of vCJD have been reported worldwide, mostly in the UK and Europe. In the United States there have not been any reported cases of endemically acquired vCJD though health care providers should be alert for cases in persons who have lived in the UK or Europe.

DISEASE OVERVIEW

A. Agent:

A prion is suspected; induces abnormal folding of normal cellular prions in the brain, leading to brain damage and the characteristic signs and symptoms.

B. Clinical Description:

Sporadic CJD begins with cognitive and behavioral changes and progresses to include physical neurologic abnormalities (e.g., myoclonus, ataxia, rigidity). Death is often caused by aspiration or sepsis. Typically, 90% of sCJD patients die within 12 months of illness onset; with a mean survival time of 5 months.

Varient CJD is characterized primarily by behavioral changes (e.g., psychosis, depression), painful sensory symptoms, a younger age of onset, and a longer duration of illness. Table 1 shows clinical and pathologic differences for vCJD and sCJD.

C. Reservoirs

It is unknown whether a reservoir exists for the most common human prion disease, sCJD.

Table 1: Clinical and pathologic characteristics distinguishing vCJD from sCJD

	vCJD	sCJD
Median age at death	28 years	68 years
Median duration of illness	13–14 months	4–5 months
Clinical signs and symptoms	Prominent psychiatric/ behavioral symptoms; painful dysesthesia; delayed neurologic signs	Dementia; early neurologic signs
Periodic sharp waves on EEG	Absent	Often present
"Pulvinar sign" on MRI*	Present in >75%	Not reported
Presence of "florid plaques" on neuropathology	Present in large numbers	Rare or absent
Immunohistochemical analysis of brain tissue	Marked accumulation of PrPres**	Variable accumulation
Agent present in lymphoid tissue	Readily detected	Not readily detected

*An abnormal signal in the posterior thalamus 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

D. Modes of Transmission

The mode of transmission of sCJD, is not known. Approximately 10–15% 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 vCJD was associated with consumption of beef products contaminated with the BSE prion but food protection measures have been implemented to prevent suspected or confirmed BSE infected cattle from being sold for consumption. Three UK cases of vCJD provided evidence for transmission of vCJD through blood transfusion; 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. No recent cases of iatrogenic CJD have been identified in the United States.

E. Incubation Period

The incubation period for the few prion diseases with known sources (i.e., vCJD, iatrogenically-acquired prion disease) is variable and extremely long, in the order of several years to decades.

F. Period of Communicability

There is no general communicable period as there is no evidence of transmission through casual or intimate person-to-person contact. In rare circumstances, transmission occurred through contaminated neurosurgical instruments, transplanted dura mater and corneas, human-derived pituitary hormones, and possibly for vCJD only, in transfused blood.

G. Treatment

No curative treatment; invariably fatal. Supportive care is needed and medications may be used to control aggressive or agitated behaviors.

NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

The Kansas Department of Health and Environment's (KDHE) Bureau of Epidemiology and Public Health Informatics will identify potential cases from three sources:

1. Reports from health care providers, upon the suspicion of disease
2. Death certificates, listing a TSE as the cause of death
3. National Prion Disease Pathology Surveillance Center (NPDPSC) reports

Cases TSE or prion disease, whether definite (confirmed) or suspected, shall be reported within 7 days:

1. Health care providers and hospitals: report to local health jurisdiction
2. Laboratories: report to KDHE
3. Local health jurisdiction: report to KDHE

KDHE Bureau of Epidemiology and Public Health Informatics receives ALL test reports for specimens submitted to the NPDPSC and then faxes the laboratory reports to the local health jurisdiction.

NPDPSC laboratory reports do NOT have to be reported to the local health jurisdiction or KDHE by other entities, but physicians and hospitals should still report any suspicion of TSE or prion disease to the local health jurisdiction.

INVESTIGATOR RESPONSIBILITIES

1) Complete the TSE Patient Questionnaire.
2) If the report is from a physician suspecting prion disease, inform the physician of the autopsy and laboratory services provided by the NPDPSC and provide the physician with the phone number (216-368-0587) and website information (www.cjdsurveillance.com).
3) For deaths, encourage the physician to discuss the role of autopsy in confirming the diagnosis of prion disease with the family.
4) Provide physicians with the contact information for the Creutzfeldt-Jakob Disease Foundation, which provides support to individuals and families dealing with CJD and other prion disease. (www.cjdfoundation.org/ or 1-800-659-1991)
5) Emphasize the importance of appropriate infection control procedures if invasive neurologic diagnostic testing is being considered.

STANDARD CASE INVESTIGATION AND CONTROL METHODS

If any assistance is needed, the local investigator can contact the KDHE Bureau of Epidemiology and Public Health Informatics at 1-877-427-7317

Case Investigation

1) **Evaluate the diagnosis.**
   - Follow the sequence described in the patient record form. In addition to discussions with the neurologist, medical record review may be required. (*Note: A definitive brain biopsy or autopsy results may preclude the need to obtain all clinical data listed on the worksheet/case report form*.)
   - Determine the status (alive or deceased) of the patient.
   - There is no need to interview the next of kin unless after consultation with KDHE: vCJD, iatrogenically transmitted CJD, a novel prion disease, or a disease cluster is suspected.
   - If the patient is alive but not expected to survive, strongly encourage the provider to discuss the essential role of autopsy for diagnosis with the patient's family.
     - If the family consents to having an autopsy performed, a completed NPDPSC autopsy consent form should be sent to NPDPSC (available at www.cjdsurveillance.com/pdf/consent-autopsy.pdf).
     - NPDPSC covers 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.
   - If the patient is deceased, determine the date of death and whether brain tissue has been collected postmortem for laboratory testing at a facility other than NPDSC. Ascertain which laboratory has the tissues and forward any pathology report with the case report form.
   - Refer to Appendix A for definitions of neurologic terms found on the case report form.

2) **Identify Potential Sources of Infection**
   - Ask the provider if the patient ever received human-derived pituitary hormones (especially human-derived growth hormone), dura mater or corneal grafts, had a neurosurgical procedure, or is biologically related to a person with heritable prion disease.
   - If a patient is suspected to have iatrogenically-acquired prion disease, vCJD or another novel acquired prion disease, a more extensive evaluation will be conducted.
     - Further instructions on conducting a more extensive evaluation will be provided by KDHE when they are needed.

Contact Investigation

There is no evidence of transmission through casual or intimate person-to-person contact, but iatrogenic transmission of the CJD agent has been linked to the use of contaminated human growth hormone, dura mater and corneal grafts, or neurosurgical equipment.

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 of these equipment-related cases occurred before the routine implementation of sterilization procedures currently used in health care facilities. No such cases have been reported since 1976, and no iatrogenic CJD cases associated with exposure to the CJD agent from surfaces such as floors, walls, or countertops have been identified.

1) To identify potentially exposed persons: determine if the patient had a neurosurgical procedure during this illness.
2) Notify the hospital where neurosurgical procedures were performed of the patient's diagnostic status.

Infection Control Recommendations

Information about infection control measures related to CJD is available from the CDC (www.cdc.gov/ncidod/dvrd/cjd/qa_cjd_infection_control.htm) and the World Health Organization (http://whqlibdoc.who.int/publications/2003/9241545887.pdf).

- Standard precautions are recommended for hospitalized patients; additional special precautions are necessary during invasive neurosurgical or ophthalmic procedures.
- Neurosurgical procedures: The brain and spinal cord of patients with prion disease are highly infectious and prions are resistant to routine physical and chemical sterilization methods used in medical facilities. As a result, neurosurgical equipment, surfaces and other objects in contact with nervous tissue of a person with a prion disease require special decontamination procedures. If a patient with confirmed or suspected prion disease requires or recently had a neurosurgical procedure or invasive EEG monitoring (implanted electrodes) that facility's infection control division should be informed of the patient's diagnostic status with reference to CJD. Additional updates to the facility may be necessary if a procedure has been performed and higher diagnostic specificity is obtained at a later date. If you suspect a patient had a neurosurgical procedure or invasive EEG monitoring when the hospital was unaware of the suspected prion disease status, contact KDHE.
- 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. (http://whqlibdoc.who.int/publications/2003/9241545887.pdf)

- 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 http://www.cdc.gov/ncidod/dvrd/cjd/funeral_directors.htm).
- 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 at risk cornea transplants, 2) have undergone at risk 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

Case Management

If routine case investigation activities have been completed, no case follow-up is typically needed after an autopsy is arranged. Once pathology results are available, the case can be classified.

Contact Management

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 neurosurgical procedures were performed, the hospital notified should internally review infection control practices; see Infection Control section. Consultation with KDHE is provided, as needed.

Environmental Measures

If neurosurgery has been performed, see Infection Control section.

Education

The CFD Foundation provides support to individuals and families dealing with CJD and other prion disease. Contact information: http://www.cjdfoundation.org/ or 1-800-659-1991.

DATA MANAGEMENT AND REPORTING TO THE KDHE

A. Organize, collect and report data with the TSE Patient Questionnaire.

B. Report data by fax to: 1-877-427-7318.

ADDITIONAL INFORMATION / REFERENCES

A. World Health Organization (WHO) Infection Control Guidelines for Transmissible Spongiform Encephalopathies. http://whqlibdoc.who.int/publications/2003/9241545887.pdf

B. CDC information on prion disease: www.cdc.gov/ncidod/dvrd/prions/index.htm

C. **Treatment / Differential Diagnosis:** American Academy of Pediatrics. 2009 Red Book: Report of the Committee on Infectious Disease, 28th Edition. Illinois, Academy of Pediatrics, 2009.

D. **Epidemiology, Investigation and Control:** Heymann. D., ed., Control of Communicable Diseases Manual, 19th Edition. Washington, DC, American Public Health Association, 2009.

E. **Case Definitions:** CDC Division of Public Health Surveillance and Informatics, Available at: www.cdc.gov/ncphi/disss/nndss/casedef/case_definitions.htm

F. **Kansas Regulations/Statutes Related to Infectious Disease:** http://www.kdheks.gov/epi/regulations.htm

Investigation Form(s)

Kansas Department of Health and Environment
TSE Patient Questionnaire

PATIENT DEMOGRAPHICS:

Last Name _____ **First Name**_____ **Middle** _____

Street _____ **City** _____ **State** _____ **Zip** _____

DOB_____ **Sex** ____

Ethnicity ❑ Hispanic or Latino ❑ Not Hispanic or Latino ❑ Unknown

Race ❑ American Indian/Alaska Native ❑ Asian ❑ Black/African American

❑ Native Hawaiian/Other Pacific Islander ❑ White ❑ Unknown

Day Phone (_____)_____-_____ **Evening Phone** (_____)_____-_____

MEDICAL HISTORY

Date of Illness Onset ____/____/_____

Is there an alternative non-CJD diagnosis for the patient's illness? ❑ Yes ❑ No ❑ Unknown

If *YES*, specify: _____

_____

_____

Is the patient still living? ❑ Yes ❑ No ❑ Unknown

If *NO*, Date of Death: _____

Is the patient hospitalized? ❑ Yes ❑ No ❑ Unknown

If YES, What hospital? _____

Diagnosing physician: _____ **Telephone: (____)____-_____**

Specialization: _____ **Address:** _____

CLINICAL INFORMATION

Is duration of illness > 6 months? ❑ Yes ❑ No ❑ Unknown

Did the patient have any of the following symptoms?

Progressive Dementia	❑ Yes ❑ No ❑ Unknown	
		Was the onset ≥ 4 months after onset of illness?
Myoclonus?	❑ Yes ❑ No ❑ Unknown	❑ Yes ❑ No ❑ Unknown
Chorea?	❑ Yes ❑ No ❑ Unknown	❑ Yes ❑ No ❑ Unknown
Dystonia?	❑ Yes ❑ No ❑ Unknown	❑ Yes ❑ No ❑ Unknown
Hyperreflexia?	❑ Yes ❑ No ❑ Unknown	❑ Yes ❑ No ❑ Unknown
Other Pyramidal/extrapyramidal signs?	❑ Yes ❑ No ❑ Unknown	❑ Yes ❑ No ❑ Unknown

Visual or cerebellar signs? (ataxia, poor coordination, visual signs, etc)	❑ Yes ❑ No ❑ Unknown	❑ Yes ❑ No ❑ Unknown
Akinetic Mutism?	❑ Yes ❑ No ❑ Unknown	
Psychiatric symptoms? (anxiety, apathy, delusions, depression, withdrawal)	❑ Yes ❑ No ❑ Unknown	If yes, was it present at onset of illness? ❑ Yes ❑ No ❑ Unknown
Persistent painful symptoms? (frank pain and/or dysethesia)	❑ Yes ❑ No ❑ Unknown	

POTENTIAL EXPOSURES

Has the patient had any of the following medical procedures? (Check all that apply.)

Procedure	Date	Location
❑ Human pituitary growth hormone receipt		
❑ Dura mater graft		
❑ Corneal graft		
❑ Other CNS invasive procedure (including implanted EEG electrodes), specify_____		
❑ Other invasive surgery, specify_____		

Has the patient ever:

Lived outside of the U.S. for >3 months?	❑ Yes ❑ No ❑ Unknown	If *YES*, Where?_____ When?_____
Traveled outside the U.S?	❑ Yes ❑ No ❑ Unknown	If *YES*, Where?_____ When?_____
Hunted deer or elk?	❑ Yes ❑ No ❑ Unknown	If *YES,* where and when was it harvested? _____
Consumed deer or elk?	❑ Yes ❑ No ❑ Unknown	If *YES, when* was it consumed? _____ _____

Is there history of CJD diagnosis in a first degree relative (e.g. mother, father, brother, sister)?
❑ Yes ❑ No ❑ Unknown

Did the patient have any other potential history of exposure to BSE? ❑ Yes ❑ No ❑ Unknown

If *YES*, explain_____

MEDICAL TESTS

Test	Date	Results
❑ EEG		Does it show a periodic or pseudoperiodic paroxysms of triphasic or sharp waves (0.5 – 2.0 Hz) against a slow background? ❑ Yes ❑ No Other, specify _____ _____ _____
❑ MRI		Bilateral pulvinar high sign ❑ Yes ❑ No Other, specify _____ _____ _____
❑ Tonsilar biopsy		
❑ Other, specify _____ _____		

Comments:

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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 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."

Ataxia: failure of muscular coordination due to cerebellar dysfunction. 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.

Cerebellar syndrome: in addition to ataxia, other cerebellar signs of CJD may include:

- 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, including disorientation and or impaired memory, judgment, and intellect.

Dysesthesia and painful sensory symptoms: New onset of pain or other uncomfortable sensations that is unrelated to injury or stimulus.

Dystonia: Abnormal tonicity in muscles resulting in impairment of voluntary movement.

Electroencephalograpy (EEG): A characteristic EEG pattern of periodic synchronous bi- or triphasic sharp wave complexes (PSWC) is observed in 67 to 95 percent of patients with sCJD at some time during the course of the illness. PSWCs have a very high specificity for the diagnosis of sCJD. Absence of PSWCs does not rule out the diagnosis of CJD. PSWCs are not found in patients with new variant CJD.

Hyperreflexia: Exaggerated reflexes

Myoclonus: Sudden, involuntary contractions or jerking of a muscle or group of muscles. Terms such as "myoclonic jerks", "myoclonic jerking", and "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-months) 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:

- 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 that we associate 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

Supporting Materials

- **Fact sheet**

Supporting Materials are available under attachments:

CLICK HERE TO VIEW ATTACHMENTS

Then double click on the document to open.

Other Options to view attachments:

Go to <View>; <Navigation Pane>; <Attachments>

– OR –

Click on the "Paper Clip" icon on the right.