Michigan Department Of Community Health

MDCH

Creutzfeldt-Jakob Disease (CJD) Fact Sheet for Physicians and Healthcare Workers

A) Etiologic Agent: CJD is caused by an abnormal form of the brain prion protein, which is thought to replicate by inducing normal proteins to fold into the abnormal disease-causing conformation.

B) Disease Description: CJD is a rare, rapidly progressive, and fatal neurodegenerative disease. Clinical disease is thought to result from the accumulation of the abnormal prion protein resulting in damage to brain tissue and characteristic "spongy" appearance. The onset of CJD symptoms is typically around age 60.

C) Disease Types: There are four distinct types of CJD.

1) Sporadic CJD- the most common type of CJD, accounts for approximately 85-90% cases. Sporadic CJD is believed to be caused by the spontaneous conversion of the normal prion protein into the disease causing abnormal form.

2) Familial CJD- an inherited form of CJD caused by a genetic mutation that makes it more likely the prion protein will convert to the abnormal disease causing form. Familial CJD accounts for 5-15% of cases.

3) Iatrogenic CJD- transmitted by direct exposure to abnormal prion proteins from an external source during a medical procedure. In rare situations, CJD has been spread by the re-use of contaminated surgical instruments or the transplantation of infectious tissue (cornea, dura mater grafts, human growth hormone).

4) Variant CJD (vCJD)- the human form of bovine spongiform encephalopathy (BSE) or "Mad Cow Disease," caused by a different prion protein than the sporadic or familial forms of CJD. Variant CJD is linked to the consumption of products from cattle infected with BSE or by blood transfusion from a donor with variant CJD.

Additional types of human prion diseases that are not classified as CJD

Gerstmann-Straussler-Scheinker disease (GSS)- is an extremely rare prion disease. It is almost always inherited and is found in only a few families around the world. Onset of the disease generally occurs between the ages of 35 and 55.

Fatal Familial Insomnia (FFI)- is an extremely rare prion disease that affects the thalamus and interferes with the ability to sleep. The disease can occur spontaneously or as a result of an inherited genetic mutation. Onset of the disease generally occurs between the ages of 40 and 60.

D) Incidence: The worldwide overall incidence of CJD is approximately 1 case per million people per year. However, the risk of CJD increases with age; the rate of disease is 3.4 cases per million people in individuals over the age of 50. Based on the population of Michigan, approximately 10 cases of sporadic CJD per year would be expected.

E) Clinical Description: Initial symptoms of CJD generally include progressive dementia, confusion, behavioral changes, and muscle incoordination including ataxia and myoclonus. Other symptoms may include depression, insomnia, and problems with vision and speech. After clinical symptoms begin, the progression of the disease is rapid; nearly all individuals diagnosed with CJD die within one year.

F) Incubation: The incubation period of CJD is very long. Cases with incubation from 15 months to 30 years have been documented.

G) Diagnosis: The use of computed tomography (CT) scans, magnetic resonance imaging (MRI), electroencephalogram (EEG), clinical signs, and the use of specific tests for elevated 14-3-3 and tau proteins in cerebrospinal fluid can provide supporting evidence for the diagnosis of CJD. The 14-3-3 and tau tests alone are not considered diagnostic; false negatives and false positives have been reported. A confirmed diagnosis of CJD can only be made by examination of brain tissue from a biopsy or autopsy. Due to the varied distribution of the abnormal prions in the brain, a positive brain biopsy can confirm the diagnosis of CJD, but a negative biopsy cannot rule out CJD or prion disease. The use of brain biopsies is generally suggested to be reserved for cases where a treatable condition is suspected. Currently no cure for CJD exists and treatment relies on supportive care for the patient.

H) Laboratory Testing: Prion disease testing including 14-3-3 and tau protein testing, brain biopsy and autopsy examination are available through the National Prion Disease Pathology Surveillance Center (NPDPSC) at Case Western Reserve University. For help with the coordination of an autopsy or other testing protocols please contact the NPDPSC at (216) 368-0587. Information can also be found on the center's website http://www.cjdsurveillance.com.

I) CJD Case Classification

1) Sporadic CJD

Definite case

- Neuropathological confirmation; and/or
- Confirmation of protease-resistant prion protein by immunocytochemistry (IHC) or Western Blot

Probable case (in the absence of an alternative diagnosis from routine investigation)

- Progressive dementia;
- at least two of the following four clinical features: myoclonus, visual or cerebellar disturbance, pyramidal/extrapyramidal dysfunction, akinetic mutism, with
- atypical EEG (generalized triphasic periodic complexes at approximately one per second), whatever the clinical duration of the disease, and/or
- a positive 14-3-3 or tau protein assay in CSF and a clinical duration leading to death in <2 years.

Suspect case

- Progressive dementia; and
- EEG atypical or not carried out; and
- duration <2 years; and
- at least two out of the following clinical features**:** myoclonus, visual or cerebellar disturbance, pyramidal, extrapyramidal dysfunction, akinetic mutism.

2) Familial CJD

Definite Case
- Definite CJD with a recognized disease-specific prion protein gene mutation; and
- Definite or probable prion disease in a first-degree relative

Probable Case
- Probable CJD plus confirmed or probable CJD in a first degree relative; and/or neuropsychiatric disorder disease-specific prion protein gene mutation

Note. For surveillance purposes, this definition includes Gerstmann-Sträussler-Scheinker (GSS) syndrome and fatal familial insomnia (FFI).

3) Iatrogenic CJD

Definite Case
- Definite CJD with a recognized iatrogenic risk.

Probable Case
- Progressive cerebellar syndrome in a recipient of human cadaver-derived pituitary hormone; or
- Probable CJD with a recognized iatrogenic risk.

4) Variant CJD

Variant CJD cannot be diagnosed with certainty on clinical criteria alone; this requires neuropathological confirmation. The following combinations of signs, symptoms and clinical investigations serve to define suspect, probable and definite vCJD:

(I)
- Progressive psychiatric disorder
- Clinical duration >6 months
- Routine investigations do not suggest an alternative diagnosis
- No history of potential iatrogenic exposure
- No evidence of a familial form of TSE (transmissible spongiform encephalopathies).

(II)
- Early psychiatric symptoms (depression, anxiety, apathy, withdrawal, delusions)
- Persistent painful sensory symptoms (pain and/or dysaesthesia)
- Ataxia
- Chorea / dystonia or myoclonus
- Dementia

(III)

- EEG unknown or does not show the typical appearance of sporadic CJD (generalized triphasic periodic complexes at approximately one per second)
- Bilateral symmetrical pulvinar high signal on MRI brain scan (relative to other deep gray-matter nuclei).

(IV)

- Positive tonsil biopsy.
  Note- Tonsil biopsy not recommended routinely nor in cases with EEG appearances typical of sporadic CJD, but useful in suspect cases where clinical features are compatible with vCJD and MRI does not show bilateral pulvinar high signal. Cerebral biopsy in living patients is to be discouraged unless its purpose is to arrive at an alternative diagnosis of a treatable disorder.

vCJD case classification

Definite Case

- A patient with the items under (I) above
- Neuropathological confirmation of vCJD.

Probable Case

- A patient with the items under (I) and at least four items under (II)
- Bilateral pulvinar high signal on MRI brain scan
- EEG does not show the typical appearance of sporadic CJD although generalized periodic complexes may occasionally be seen at the later stages of the disease.

OR

- A patient with items under (I) and a positive tonsil biopsy.

Suspect Case

- A patient with the items under (I) above and at least 4 items under (II)
- EEG does not show the typical appearance of sporadic CJD

J) Clinical and Pathologic differences between sporadic and vCJD

Characteristic	Sporadic CJD	Variant CJD
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 dyesthesiasis; delayed neurologic signs
Periodic sharp waves on electroencephalogram	Often present	Often absent
"Pulvinar sign" on MRI*	Not reported	Present in >75% of cases
Presence of "florid plaques" on neuropathology	Rare or absent	Present in large numbers
Immunohistochemical analysis of brain tissue	Variable accumulation	Marked accumulation of protease-resistance prion protein
Presence of agent in lymphoid tissue	Not readily detected	Readily detected
Increased glycoform ratio on immunoblot analysis of protease-resistance prion protein	Not reported	Marked accumulation of protease-resistance prion protein
*An abnormal signal in the posterior thalami on T2- and diffusion-weighted images and fluid-attenuated inversion recovery sequences on brain magnetic resonance imaging (MRI); in the appropriate clinical context, this signal is highly specific for vCJD.		
Source: Adapted from Belay E., Schonberger L. Variant Creutzfeldt-Jakob Disease and Bovine Spongiform Encephalopathy. Clin Lab Med 2002;22:849-62. Chart source: http://www.cdc.gov/ncidod/dvrd/vcjd/index.htm		

K) Case Reporting:

All spongiform encephalopathies, including CJD, are required reportable diseases in Michigan. If you have a suspected or confirmed case of CJD or other prion disease, please contact the appropriate local health depart to report the case.

References:

Belay E., Schonberger L. Variant Creutzfeldt-Jakob Disease and Bovine Spongiform Encephalopathy. Clin Lab Med 2002;22:849-62

Centers for Disease Control and Prevention (CDC), “CJD (Creutzfeldt-Jakob Disease, Classic)” Webpage: http://www.cdc.gov/ncidod/dvrd/cjd/

Centers for Disease Control and Prevention (CDC), “vCJD (Variant Creutzfeldt-Jakob Disease)”. Webpage: http://www.cdc.gov/ncidod/dvrd/vcjd/index.htm

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National Institute of Neurological Disorders and Stroke, “NINDS Creutzfeldt-Jakob Disease Information Page”. Webpage: http://www.ninds.nih.gov/disorders/cjd/cjd.htm

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National Prion Disease Pathology Surveillance Center. Webpage: http://www.cjdsurveillance.com/

World Health Organization, “*WHO recommended standards and strategies for surveillance, prevention and control of communicable diseases". Webpage:* http://www.who.int/zoonoses/diseases/Creutzfeldt.pdf