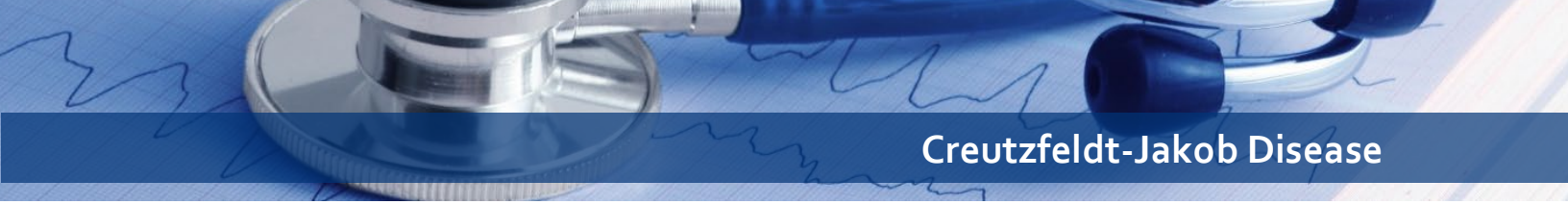

Creutzfeldt-Jakob Disease

Creutzfeldt-Jakob Disease (CJD) is a neurodegenerative disease that has been recognized since the early 1920's[1,2]. CJD is part of a group of universally fatal neurodegenerative diseases of humans and animals called transmissible spongiform encephalopathies (TSEs)[1–4]. Classic CJD is not related to variant CJD (vCJD) which also affects human[2–5]. Variant CJD is related to bovine spongiform encephalitis (BSE), "mad cow disease", and was first described in the United Kingdom in 1996[2,3,5,6].

Clinical and Pathologic Characteristics Distinguishing Classic CJD from Variant CJD[7]		
CHARACTERISTIC	**CLASSIC 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 dysesthesias; 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.

A. Agent:

CJD is caused by spontaneous structural change of a normal, ubiquitous prion protein[2,3,4]. Both the normal and infectious forms of the protein have the same sequence of amino acids but are folded differently. The abnormal folding of the protein causes them to clump together and destroy neurons. Abnormally folded prion proteins can attach to normal prion proteins causing them to change into the abnormal form[2].

B. Clinical Description:

CJD manifests as a rapidly progressive, dementia-causing illness with defects in memory, personality, and other high cortical function[2,3]. At presentation approximately one third of patients have cerebellar dysfunction, including ataxia (uncoordinated movement) and dysarthria (difficulty saying words). Myoclonus (involuntary muscle jerks) develops in at least 80% of affected patients at some point in the course of disease[3].

- Differential Diagnosis:
  Alzheimer's disease, dementia with Lewy Bodies, frontotemporal dementia, meningoencephalitis, corticobasal degeneration, progressive supranuclear palsy, CADASIL, and paraneoplastic encephalomyelitis[8].

There are four categories of CJD:

Classical (Sporadic or Spontaneous) CJD (sCJD) - CJD of an unexplained origin and presumably autochthonous. The prevalence of classical CJD is about one case per one million populations per year. This type of CJD typically strikes older individuals with the vast majority of cases occurring in those over 65 years of age (median = 68 years). Median duration of illness is 4 – 5 months. Approximately 85% of CJD cases are spontaneous[3,4,8].

Iatrogenic CJD (iCJD) - Occurs as a result of exposure to infectious prions during a medical procedure. Corneal transplants, dura mater grafts, brain surgery, and growth or gonadotropic hormones made from human pituitary glands have all been implicated in iatrogenic CJD cases[1,3,4]. Less than 1% of cases are iatrogenic[3].

Familial (Genetic) CJD - Same general characteristics as classical CJD, but a case may be given this classification when the patient has a known family history of rapid-onset dementia. Approximately 15% of CJD cases are familial[3,4].

Variant CJD (vCJD) - vCJD is associated with consumption of BSE infected beef. Only four cases of this form of CJD have been found in the United States and all cases almost certainly acquired the disease in countries with BSE-contaminated cattle products (United Kingdom and Saudi Arabia). The typical age of onset of vCJD is much younger (median = 28) than classical CJD. Median duration of illness is 13–14 months[3].

C. Reservoirs:
Humans are the only known reservoir for CJD[1–3,4,6]. Cattle infected with BSE are believed to be the reservoir for vCJD[2–6].

D. Mode of Transmission:
The mode of transmission for classical CJD is unknown as there is no recognizable pattern of transmission[1]. Iatrogenic transmission of the CJD agent has been reported via medical equipment, but occurred before the routine implementation of sterilization[4]. No cases of iatrogenic cases via equipment have been reported since 1976[4]. In familial CJD, a mutated PRNP (prion protein) gene is inherited. This mutated gene causes production of abnormal prion proteins[4]. Person-to-person transmission of classic CJD by blood, milk, saliva, urine, or feces has not been reported[1,2]. It is believed that all cases of vCJD have resulted from exposure to tissue from cattle infected with BSE. It is also believed to be possible to transmit the disease through blood transfusions or direct contact of infectious neurological tissues[2].

E. Incubation Period[3]:
Usually long, from 14 months to more than 30 years.

F. Period of Communicability:
There is no evidence that CJD is spread person-to-person by casual contact[1–3,6]. Central Nervous System (CNS) tissues are infectious throughout the period that CJD patients are symptomatic[1–3].

G. Susceptibility and Resistance[3]:
Immunization against prion diseases is not available, and no protective immune response to infection has been demonstrated.

H. Treatment:
No treatment has been shown in humans to slow or stop the progressive neurodegeneration in prion diseases[1–5]. Supportive therapy is needed to manage dementia, spasticity, rigidity, and seizures[2,3].

I. Clinical Case Definition[10]:

CJD is a fatal disease characterized by progressive dementia and a variety of other neurological symptoms including:

- Myoclonus (involuntary muscle jerk)
- Visual or cerebellar signs
- Pyramidal/extrapyramidal signs (movement disorders)
- Akinetic mutism (inability to move or speak)

CJD is typified by development of spongy spaces in brain tissue where cells have died.

J. Laboratory Criteria for Diagnosis[10]:

Confirmatory Testing

- Detection of characteristic lesions by examination of frozen brain tissue. The diagnosis can be made in the United States only by the National Prion Disease Pathology Surveillance Center (NPDPSC) in Cleveland, Ohio[9].
- Detection of abnormal prion protein by Western blot testing performed on frozen brain tissue, or by immunochemistry/histology performed on fixed tissue.

Presumptive Testing

- Detection of 14-3-3 protein in CSF
- Genetic analysis suggestive of the presence of the mutation associated with CJD
- Detection of characteristic patterns by EEG or MRI

When possible, each case of CJD should be classified into one of the types according to the mode of transmission.

Case Classification[10]			
Confirmed	A case that meets at least one of the confirmatory laboratory criteria and only when performed by the NPDPSC.		
	Iatrogenic CJD meets the above criteria **PLUS** • Progressive cerebellar syndrome in a recipient of human cadaveric-derived hormone or • A CJD recognized exposure risk (i.e. antecedent neurosurgery with dura mater implantation, corneal transplants, brain surgery).	Familial CJD meets the above criteria **PLUS** • Confirmed or Probable CJD in first degree relative	Sporadic CJD meets the above criteria **PLUS** • No evidence of iatrogenic and familial CJD
Probable	A case that meets one of the presumptive laboratory criteria and in which 3 of the 5 clinical findings described above are present. Findings must include progressive dementia with clinical duration lasting <2 years. Routine investigations should not suggest an alternative diagnosis.		
	Iatrogenic CJD meets the above criteria **PLUS** • Progressive cerebellar syndrome in a recipient of human cadaveric-derived hormone or • A recognized CJD exposure risk (i.e. antecedent neurosurgery with dura mater implantation, corneal transplants, brain surgery).	Familial CJD meets the above criteria **PLUS** • Confirmed or Probable CJD in a first degree relative	Sporadic CJD meets the above criteria **PLUS** • No evidence of iatrogenic and familial CJD
Suspect	A case that meets one of the presumptive laboratory criteria and in which on clinical information is known and routine investigations should not suggest an alternative diagnosis.		

K. Classification of Import Status:
N/A

L. Laboratory testing[10]:
All specimens should be sent to NPDPSC to be tested. NPDPSC can analyze brain tissue from a biopsy or autopsy, CSF, and blood. If sending brain tissue, both frozen and fixed brain tissue should be sent[9].

TEST[10]	SPECIMEN
Protein assay	Detects 14-3-3 protein in cerebrospinal fluid.
Western blot analysis	Identifies PrP on frozen biopsy tissue.
Histological analysis	Fixed biopsy tissue.
PRNP gene sequencing	Blood, brain, or other tissue.
Electroencephalography (EEG)	
Magnetic resonance imaging (MRI)	

M. Assessing Laboratory Results[9]:

Fixed brain tissue - A report is issued stating whether the tissue is positive or negative for prion disease based on immunostaining of the prion protein, and a tentative diagnosis regarding the type of prion disease when possible. Turn-around time is approximately 14 days from the receipt of the samples for autopsies and approximately 3 days for biopsies.

Frozen brain tissue - A report is issued whether the tissue is positive or negative for prion disease based on Western blot analysis of the tissue, and a tentative diagnosis regarding the type of prion disease will be added when possible. Turn-around time is approximately 14 business days from receipt of the samples for autopsies and approximately 3 days for biopsies.

PRNP gene sequencing in blood and other tissues - A report is issued stating whether a mutation was discovered in the gene which encodes the prion protein. The presence of a mutation indicates a diagnosis of CJD, Fatal Familial Insomnia, or Gerstmann-Straussler-Scheinker disease as noted in the report. In cases where only blood is available, the possibility of sCJD or iCJD cannot be ruled out as a possible diagnosis. Turn-around time is approximately one month from receipt of the samples.

N. Outbreak Definition:
An increase in cases in time or place that is greater than expected.

O. Time Frame[11]:

Providers	Submit a report to the Local Health Department within 5 working days after a case or suspect case is diagnosed, treated, or detected.
Local Health Agencies	• Notify ADHS within 5 working days after receiving a report. • Submit an epidemiologic investigation report to ADHS within 30 calendar days after receiving a report.

P. Forms:

- ADHS CJD and TSE Investigation Form

Q. Investigation Steps:

For a local health agency[11]:

A.A.C. R9-6-325. Creutzfeldt-Jakob Disease

A. Case control measures:

1. A local health agency shall:
   a. Conduct an epidemiologic investigation of each reported Creutzfeldt-Jakob disease case or suspect case; and
   b. For each Creutzfeldt-Jakob disease case, submit to the Department, as specified in Table 2.4, the information required under R9-6-206(D).

Confirm Diagnosis

Use current case definition to verify diagnosis

Conduct Case Investigation

- Collect case's demographic data and contact information:
- Obtain information from the provider or medical chart.
  - Obtain medical records, including admission notes, progress notes, lab report(s), and discharge summary.
  - Make a note of any tests being performed and the expected turn-around time.
- Examine the symptoms and clinical history, especially:
  - Date of illness onset, type of disease syndrome, hospitalization records (reason, location and duration of stay), and outcome status (survived or date of death).
- Examine the laboratory testing that was done:
  - Collection date, type of specimen that was collected, which tests were ordered.
  - Review reports from NPDPSC.
- Collect any information on travel outside of the United States.

Conduct Contact Investigation

Not applicable.

Initiate Control and Prevention Measures

- Standard precautions are recommended[3,6]. Available evidence indicates that even prolonged intimate contact with CJD-infected people has not resulted in transmission of disease[2–4].
- Tissues associated with high levels of infectivity (e.g. brain, eyes, and spinal cord of affected people) and instruments in contact with those tissues are considered biohazards;

incineration, prolonged autoclaving at high temperature and pressure after thorough cleaning, and especially exposure to a solution of 1 N or greater sodium hydroxide or a solution of 5.25% or greater sodium hypochlorite (undiluted household chlorine bleach) for 1 hour has been reported to decrease infectivity of contaminated surgical instruments[3].

Isolation, Work and Child Care Restrictions

Not applicable.

Case Management, including Susceptible Contacts

Not applicable.

R. Outbreak Guidelines:

Refer to outbreak section.

S. Special Situations:

N/A

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