7. CREUTZFELDT-JAKOB DISEASE (CJD)

Cause/Epidemiology

Creutzfeldt-Jakob disease (CJD) is a rare, fatal degenerative disorder. It affects approximately one person in every one million people per year worldwide.

Typically the average age of onset is 50 years of age. In rare instances, CJD can be dormant for as long as 30 years. Approximately 90 percent of patients die within 1 year of symptom onset.

Some researchers believe an unusual slow-growing virus causes CJD. However, a virus or other organism has never been isolated from people with the disease. Furthermore, the agent that causes CJD has several unusual characteristics, is difficult to eliminate, and usually has a long incubation period before symptoms appear.

CJD belongs to a family of human and animal diseases known as the transmissible spongiform encephalopathies (TSEs). TSEs, also known as prion diseases, are a group of rare degenerative brain disorders characterized by tiny holes, giving the brain a "spongy" appearance. These holes are caused by pathological changes in the brain involving a specific protein called Prion Protein, or PrP.

CJD is the most common of the known human TSEs. Other human TSEs include kuru, fatal familial insomnia (FFI), and Gerstmann-Straussler-Scheinker disease (GSS). There is no evidence CJD is contagious through casual contact with a CJD patient.

There are 3 major categories of Classic CJD:

- **Sporadic**: the disease appears even though the person has no known risk factors for the disease. This is by far the most common type of CJD and accounts for at least 85 percent of cases.
- **Hereditary** (familial): the person has a family history of the disease and/or tests positive for a genetic mutation associated with CJD.
- **Acquired** (iatrogenic): person-to-person transmission has occurred via transfer of tissue from an affected donor (corneal transplant and dura mater grafts), through peripheral injection of pooled cadaveric pituitary gland extract (growth hormone injection and human gonadotropin injection), and by use of contaminated neurosurgical instruments. Since CJD was first described in 1920, fewer than 1 percent of cases have been acquired CJD.

A new category of CJD, called variant CJD (nv-CJD, v-CJD), was first described in 1996 and has been found in Great Britain and several other European countries. **Variant CJD should not be confused with the classic form of CJD endemic throughout the world.** The initial symptoms of vCJD are different from those of other classic forms of CJD and the disorder typically occurs in younger patients. Research suggests vCJD may have...
resulted from human consumption of beef from cattle with a TSE disease called bovine spongiform encephalopathy (BSE), also known as "mad cow disease."

**Clinical Presentation**

CJD usually appears in later life and runs a rapid course. Some CJD symptoms can be similar to symptoms of other progressive neurological disorders, such as Alzheimer’s or Huntington’s disease, though a more rapid deterioration is noted. CJD causes unique changes in brain tissue that can be seen at autopsy.

Clinical presentation includes rapidly progressive dementia, myoclonus, impaired vision, progressive motor dysfunction, and behavioural changes, including impaired memory, judgment, and thinking. People with the disease also may experience insomnia, depression, or unusual sensations. They eventually lose the ability to move and speak and enter a coma. Pneumonia and other infections often occur in these patients and can lead to death. Death usually occurs within one year of symptom onset.

New variant CJD affects younger patients than other types of CJD (i.e., 30-70 years of age versus 50-70 years of age in classic CJD). It begins primarily with psychiatric symptoms and has a longer than usual duration from onset of symptoms to death.

**Incubation Period**

Classic CJD usually has a long incubation period before symptoms appear. In some cases, the incubation period may be as long as 40 years. The incubation period for vCJD is unknown but is likely measured in terms of many years or decades.

**Transmission**

The highest risk of transmission of CJD is related to tissues of the brain, dura mater, spinal cord, and cornea. Exposure to these tissues from suspected/infected patients should be avoided to prevent disease transmission.

The appearance of the new variant of CJD (nv-CJD or v-CJD) in several younger than average people in Great Britain and France has led to concern BSE may be transmitted to humans through consumption of contaminated beef. Although laboratory tests have shown a strong similarity between the prions causing BSE and v-CJD, there is no direct proof to support this theory.

Studies have found infectious prions from BSE and vCJD may accumulate in the lymph nodes, the spleen, and the tonsils. These findings suggest blood transfusions from people with vCJD might transmit the disease. There has been concern it may be possible to transmit CJD through blood and related products such as plasma; however this has never been shown in humans.
CJD cannot be transmitted through the air or through touching or most other forms of casual contact. Spouses and other household members of CJD patients have no higher risk of contracting the disease than the general population.

**Diagnosis**

There is currently no single diagnostic test for CJD.

The only way to confirm a diagnosis of CJD is by brain biopsy or autopsy. Brain biopsy may be dangerous for the patient, and the procedure does not always obtain tissue from the affected part of the brain. Brain biopsy is discouraged unless needed to rule out a treatable disorder.

Imaging techniques are useful in excluding other causes of sub-acute dementia. A lumbar puncture is often done to exclude other disease processes. A diagnostic test for detection of 14-3-3 protein in CSF has a high sensitivity and specificity for diagnosis of sporadic CJD during clinical illness.

Standard diagnostic tests include:

- A spinal tap to rule out more common causes of dementia
- An electroencephalogram (EEG) to record the brain’s electrical pattern (which can show a specific abnormality in CJD)
- Computerized tomography (CT) of the brain to help rule out alternative diagnoses such as stroke or a brain tumor
- Magnetic resonance imaging (MRI) brain scans to reveal characteristic patterns of brain degeneration that can help diagnose CJD

All specimens containing high or low infectivity tissue from high-risk patients, or high infectivity tissue and CSF from at risk patients, should be labeled “suspect CJD” on the requisition.

Refer to Appendix A (pp 7.8.15 – 7.8.16) for national surveillance case definitions for classic CJD.

**Risk Assessment for CJD**

Determining potential for CJD transmission requires consideration of multiple factors. Assessments of patient, tissue, and instrument risks are necessary. The following sections present information helpful in the determination of risk associated with each factor.

A. **Patient Risk for CJD**
1. **High-risk patients**

Patients considered to be at high risk of transmitting CJD are those diagnosed, prospectively or retrospectively, with:

<table>
<thead>
<tr>
<th>CJD</th>
<th>Either confirmed, probable, or possible CJD, familial CJD, GSS, or FF) depending on pathological, laboratory, and clinical evidence and following Surveillance Definitions for Classic CJD (Appendix A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected CJD</td>
<td>Undiagnosed, rapidly progressive dementia and CJD not ruled out</td>
</tr>
<tr>
<td>Asymptomatic Carrier of Genetic TSE</td>
<td>Person without signs or symptoms of TSE, but meets one or more of the following:</td>
</tr>
<tr>
<td></td>
<td>- Confirmed by genetic testing to carry a genetic mutation causative of TSE</td>
</tr>
<tr>
<td></td>
<td>- At least one first-degree relative confirmed by genetic testing to carry such a mutation, with or without pathologic TSE confirmation</td>
</tr>
<tr>
<td></td>
<td>- Two or more first-degree relatives diagnosed with either confirmed or probable TSE, with or without confirmation by genetic testing</td>
</tr>
</tbody>
</table>

To minimize the risk of transmitting CJD, elective procedures in high-risk patients (involving high-risk or low-risk tissues) should be well justified and carefully planned in advance. Refer to tissue risk tables, pp 7.8.5 - 7.8.7.

2. **At-risk patients**

The following patients are at risk of iatrogenic CJD:

- Recipients of a dura mater graft (until 1992 for Lyodura grafts, until 1997 for Tutoplast Dura grafts)
- Recipients of human tissue derived pituitary hormone treatment (either growth hormone or gonadotrophin)
- Recipients of a corneal graft originating in a jurisdiction that does not require graft donors to be screened for neurological disease
- Patients who have been exposed, via contact with instruments, to high-infectivity tissue of a confirmed CJD patient

The risk of transmission via instruments used on at-risk, asymptomatic patients is negligibly low, and therefore such instruments may be routinely decontaminated and then reused.
Screening procedures should be performed to identify high-risk patients, and not to identify at-risk patients.

A patient who self-identifies as being at-risk should be evaluated clinically for evidence of CJD.

B. **Tissue Risk for CJD**

The procedures recommended for managing instruments used on **high-risk** patients depend on the potential infectivity of the tissue contacted. Human tissue is classified into three categories, according to its risk of transmitting CJD. This information is subject to change as further information becomes available.

<table>
<thead>
<tr>
<th>1. <strong>High Infectivity</strong></th>
<th>2. <strong>Low Infectivity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>Dura Mater</td>
</tr>
<tr>
<td>Pituitary Gland</td>
<td>Trigeminal ganglia</td>
</tr>
<tr>
<td>Posterior eye (optic nerve and retina)</td>
<td>Spinal cord and spinal ganglia</td>
</tr>
<tr>
<td>Cerebrospinal fluid (CSF)²</td>
<td>Lung</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. <strong>No Detected Infectivity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Adipose tissue</td>
</tr>
<tr>
<td>Adrenal gland</td>
</tr>
<tr>
<td>Appendix</td>
</tr>
<tr>
<td>Blood (including cord blood)</td>
</tr>
<tr>
<td>Blood vessels</td>
</tr>
<tr>
<td>Bone marrow</td>
</tr>
<tr>
<td>Breast milk (including colostrum)</td>
</tr>
<tr>
<td>Dental pulp</td>
</tr>
<tr>
<td>Epididymis</td>
</tr>
<tr>
<td>Esophagus</td>
</tr>
</tbody>
</table>
### 3. No Detected Infectivity

<table>
<thead>
<tr>
<th>Feces</th>
<th>Prostate</th>
<th>Trachea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gingival tissue</td>
<td>Saliva</td>
<td>Urine</td>
</tr>
<tr>
<td>Heart</td>
<td>Semen</td>
<td>Uterus (non-gravid)</td>
</tr>
</tbody>
</table>

Note: While CSF is a low-infectivity tissue, contact with CSF necessarily implies contact with high-infectivity tissue and should be managed as a high infectivity tissue/fluid for infection prevention and control purposes.

#### Instrument Risk for CJD

To minimize the risk posed by instruments, the following strategies are needed:

- Limit the number of instruments used for any procedure
- Use disposable rather than reusable instruments whenever possible and especially when contacting high-infectivity tissue
- When using reusable instruments, choose, whenever possible, those that can tolerate the rigors of CJD decontamination
- Track the use of reusable instruments

Instrument identification

Without detailed information as to which reusable instruments were in contact with potentially infectious tissue, the only way to eliminate all risk of iatrogenic transmission is to discard all potentially contaminated instruments, creating considerable waste. Without such information, the opportunity to reduce the risk of transmission by instruments already in circulation – risk a risk to which some patients have already been exposed – is lost.

**NOTE:** To reduce or eliminate such risk without waste, it is strongly recommended all reusable instruments be tracked.

Once an evaluation of the patient, tissue, and instrument risks has occurred, utilize the risk assessment tool, “Recommendations for Managing Instruments Used on CJD Patients” (algorithm, pp 7.8.10 – 7.8.11 text version pages) to identify recommended actions for instrument management.
Risk Assessment Tool - Recommendations for Managing Instruments used on CJD Patients

For explanations of each of the four steps in the above graphic, including definitions, see the corresponding numbered sections in the text below.

1. No detected infectivity tissue: No CJD precautions, reprocess as usual.
2. >9 times: no evidence that it removes all risk.
3. Recipients of human tissue derived pituitary hormone treatment, dura mater graft, corneal graft and patients exposed via contact with instruments to high-infectivity tissue in a confirmed CJD patient.

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REVISION DATE: April 15, 2010
Risk Assessment Tool

Recommendations for Managing Instruments used on CJD Patients (Text Version)

High-risk CJD Patients Managed Prospectively

<table>
<thead>
<tr>
<th>Instruments in contact with: ***</th>
<th>Action to be taken:</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-infectivity tissue**</td>
<td>Discard</td>
</tr>
<tr>
<td>Low-infectivity tissue**</td>
<td>Can the instruments tolerate CJD decontamination?</td>
</tr>
<tr>
<td></td>
<td>– Yes → CJD decontaminate and reuse</td>
</tr>
<tr>
<td></td>
<td>– No → Discard</td>
</tr>
<tr>
<td>No detected infectivity tissue**</td>
<td>Routine reprocessing &amp; reuse</td>
</tr>
</tbody>
</table>

Suspected CJD

<table>
<thead>
<tr>
<th>Instruments in contact with: ***</th>
<th>Action to be taken:</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-infectivity tissue**</td>
<td>Routine reprocessing separately and quarantine</td>
</tr>
<tr>
<td></td>
<td>Is diagnosis of CJD excluded?</td>
</tr>
<tr>
<td></td>
<td>– Yes → Reuse</td>
</tr>
<tr>
<td></td>
<td>– No → Discard</td>
</tr>
<tr>
<td>Low-infectivity tissue**</td>
<td>Can the instruments tolerate CJD decontamination?</td>
</tr>
<tr>
<td></td>
<td>– Yes → CJD decontaminate &amp; reuse</td>
</tr>
<tr>
<td></td>
<td>– No → Routine reprocessing separately and quarantine</td>
</tr>
<tr>
<td></td>
<td>Is diagnosis of CJD excluded?</td>
</tr>
<tr>
<td></td>
<td>– Yes → Reuse</td>
</tr>
<tr>
<td></td>
<td>– No → Discard</td>
</tr>
<tr>
<td>No detected infectivity tissue**</td>
<td>Routine reprocessing &amp; reuse</td>
</tr>
</tbody>
</table>

Asymptomatic Carrier of Genetic TSE*

<table>
<thead>
<tr>
<th>Instruments in contact with: ***</th>
<th>Action to be taken:</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-infectivity tissue**</td>
<td>Discard</td>
</tr>
<tr>
<td>Low/No detected infectivity tissue**</td>
<td>Routine reprocessing and reuse</td>
</tr>
</tbody>
</table>

* Refer to: Is the patient a potential CJD transmitter?
** Refer to: Was infectious tissue contacted?

7.8.8

DATE ISSUED: February 1, 2006

REVISION DATE: April 15, 2010
*** Refer to: Which instruments were used?

High-risk CJD Patients Managed Retrospectively

<table>
<thead>
<tr>
<th>Instruments in contact with: ***</th>
<th>Action to be taken:</th>
</tr>
</thead>
<tbody>
<tr>
<td>High/Low infectivity tissue**</td>
<td>Can specific instruments or sets be identified?</td>
</tr>
<tr>
<td></td>
<td>- Yes → Proceed as for prospectively managed CJD</td>
</tr>
<tr>
<td></td>
<td>- No → Were instruments reprocessed more than 9 times?</td>
</tr>
<tr>
<td></td>
<td>o Yes → Proceed as for prospectively managed CJD (option A) or reuse (option B)</td>
</tr>
<tr>
<td></td>
<td>o No → Proceed as for prospectively managed CJD (option A)</td>
</tr>
<tr>
<td>No detected infectivity tissue**</td>
<td>Continue to reuse</td>
</tr>
</tbody>
</table>

* Refer to: Is the patient a potential CJD transmitter?
** Refer to: Was infectious tissue contacted?
*** Refer to: Which instruments were used?

At-risk CJD Patients for CJD

Recipients of human tissue derived pituitary hormone treatment, dura mater graft, corneal graft, and patients exposed via contact with instruments to high infectivity tissue in a confirmed CJD patient*

<table>
<thead>
<tr>
<th>Instruments in contact with: ***</th>
<th>Action to be taken:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any tissue**</td>
<td>Routine reprocessing &amp; reuse.</td>
</tr>
</tbody>
</table>

* Refer to: Is the patient a potential CJD transmitter?
** Refer to: Was infectious tissue contacted?
*** Refer to: Which instruments were used?

Infection Prevention and Control

Health care workers must employ Routine Practices when caring for patients with CJD.

Consult Infection Prevention and Control regarding autopsy and handling deceased patients. When performing medical/surgical procedures and post-mortem examinations, the most important safety rule is to avoid self-induced injury from instruments used in the course of removing and processing tissues for pathological examination. In particular, avoid contact between contaminated material and skin with cuts or abrasions.
Spills

Spills of fluids containing high or low infectivity tissue from high risk patients or high infectivity tissue and CSF from at risk patients should be flooded with full strength sodium hypochlorite for 10 minutes before the absorbent material is applied. After the absorbent material has been used to remove the fluid it should then be sealed in a leak proof, puncture-resistant container, labeled 'biohazardous', and incinerated. The surface should then be disinfected using the hard surface decontamination process.

Solid Waste

All solid waste exposed to high or low infectivity tissues from a high risk patient or high infectivity tissues and CSF from an at risk patient should be sealed in a leak proof, puncture-resistant container, labelled 'biohazardous', and incinerated. Employees should use personal protective equipment and engineering controls (e.g., splash guards) to prevent exposure from splashing and aerosols during the emptying of waste containers. Liquids used for cleaning can be flushed down the drain.

Consult Infection Prevention and Control and Waste Management for management and pick-up of instruments.

Medical Devices

Normal sterilization procedures do not prevent transmission of CJD. Re-used instruments and materials should be kept moist until they can be appropriately decontaminated and cleaned. Neurosurgical and ophthalmic instruments used on a suspect patient with CJD should be quarantined until diagnosis of CJD is confirmed.

1. Quarantine

After routinely reprocessing separately from other instruments, store instruments in dry conditions. Do not reuse unless a diagnosis is made eliminating the possibility the patient on whom the instruments were used had CJD. A confirmed diagnosis other than CJD, either clinical or pathological, or a postmortem examination excluding CJD, is required to take instruments out of quarantine. A brain biopsy that is negative for CJD, in the absence of a confirmed alternate diagnosis, does not suffice to take instruments out of quarantine.

A combination of the following measures is necessary to manage or reduce the risk of transmitting CJD infection through reused instruments. It is important to separate instruments used on known cases from those used on suspect cases.
2. **Discard**
   - To discard means to ensure an instrument cannot possibly transmit infection to another patient. Incineration is the most unambiguous means of doing so.
   - Whenever possible, contaminated instruments and other materials should be discarded as medical pathological waste or destroyed by incineration.
   - When this is not possible, special decontamination methods may be employed as described below, followed by disposal in landfill.

3. **CJD decontamination**
   - Where appropriate, a combined method of CJD decontamination in four steps:
     1. Clean thoroughly: removal of adherent particles through mechanical or manual cleaning must be completed prior to any chemical/sterilizer decontamination of instruments. Instruments and other materials to be decontaminated should be kept moist between the time of exposure to infectious materials and subsequent decontamination.
        - Clean and decontaminate reusable instruments that have been exposed to high or low infectivity tissues separately from those reusable instruments that have been exposed to no detected infectivity tissues
        - Reusable instruments should be manually cleaned using an enzymatic cleaner prior to CJD decontamination. Reusable instruments to be cleaned in an automatic mechanical processor must be manually cleaned before they are put in the processor. After the instruments have been through the processor, the mechanical washer/disinfector should be run through a complete empty cycle before any further use
     2. Soak in 1N sodium hydroxide (NaOH) for 1 hour (acceptable to substitute 2% NaOCl [20,000 ppm available chlorine] for NaOH)
     3. Thoroughly rinse
     4. Sterilize in a pre-vacuum-method autoclave at 134°C for 60 minutes
   - Instruments made of high-quality stainless steel can tolerate CJD decontamination using NaOH
   - Instruments containing plastic or electronic devices, such as bronchoscopes, cannot tolerate CJD decontamination and must be discarded
   - Instruments containing both steel and other metals, and particularly aluminum, should never be exposed to NaOH and must be discarded

**Environmental Surfaces**

Surfaces (e.g., floors, counter-tops) exposed to high or low infectivity tissues from a high risk patient or high infectivity tissues and CSF from an at risk patient should be cleaned and decontaminated thoroughly following guidelines for hard surface
decontamination. When possible, efforts should be made to prevent contamination to surfaces (i.e., through the use of temporary covers, shields, or guards made of disposable, liquid-resistant materials that can then be removed, sealed in a leak proof, puncture-resistant container, labeled ‘biohazardous’, and incinerated).

**Hard Surface Decontamination**
1. Remove visible soil
2. Flood with 2N NaOH or undiluted sodium hypochlorite; let stand for 1 hour; then mop up and rinse with water; or
3. If surfaces cannot tolerate NaOH or undiluted sodium hypochlorite, thorough cleaning will remove most infectivity by dilution


**Occupational and Environmental Safety and Health**

**Background**
TSE agents exhibit an unusual resistance to conventional chemical and physical decontamination methods. They are not adequately inactivated by most common disinfectants, or by most tissue fixatives, and some infectivity may persist under standard hospital or healthcare facility autoclaving conditions (e.g. 121°C for 15 minutes). They are also extremely resistant to high doses of ionizing and ultra-violet irradiation and some residual activity has been shown to survive for long periods in the environment.

**Route of Exposure Risks**
When determining risk, infectivity of a tissue must be considered together with the route of exposure. Cutaneous exposure of intact skin or mucous membranes (except those of the eye) poses negligible risk; however, it is prudent and highly recommended to avoid such exposure when working with any high infectivity tissue. Transcutaneous exposures, including contact exposures to non-intact skin or mucous membranes, splashes to the eye and inoculations via needle or scalpel and other surgical instruments pose a greater potential risk. Thus, it is prudent to avoid these types of exposures when working with either low infectivity or high infectivity tissues. A CNS exposure (i.e., inoculation of the eye or CNS) with any infectious material poses a very serious risk, and appropriate precautions must always be taken to avoid these kinds of exposures.

**Occupational Injury**
Although there have been no confirmed cases of occupational transmission of TSE to humans, cases of CJD in healthcare workers have been reported in which a link to occupational exposure is suggested. Therefore, it is prudent to take a precautionary approach. In the context of occupational exposure, the highest potential risk is from exposure to high infectivity tissues through needle-stick injuries with inoculation; however exposure to either high or low infectivity tissues through direct inoculation (e.g., needle-sticks, puncture wounds, sharps injuries, or contamination of broken skin) must be avoided. Exposure by splashing of the mucous membranes (notably the conjunctiva) or unintentional ingestion may be considered a hypothetical risk and must also be avoided. Healthcare personnel who work with patients with confirmed or suspected TSEs, or with their high or low infectivity tissues, should be appropriately informed about the nature of the hazard, relevant safety procedures, and the high level of safety which will be provided by the proposed procedures described throughout this document.

**Definition of Occupational Exposure:**

A healthcare worker who has had a percutaneous exposure or direct contact with high or low infectivity tissues of a person with suspect CJD

- Refer to the above table for tissue risk for CJD
- Non-invasive contact does not transmit CJD

**Healthcare Worker Exposed to CJD:**

*Post-exposure management*

Appropriate counseling should include the fact no case of human TSE is known to have occurred through occupational accident or injury. Health and safety guidelines mandate reporting of injuries, and records should be kept for no less than 25 years. A number of strategies to minimize the theoretical risk of infection following accidents have been proposed, but their usefulness is untested and unknown. For the present the following common-sense actions are recommended:

**Unbroken Skin Exposure**

- Wash skin with detergent and copious amounts of warm water (avoid scrubbing). Rinse and dry or, for maximum safety, one minute soak with 0.1 Sodium Hydroxide (NaOH) or a 1:10 dilution of bleach
  - Refer to Materials Safety Data Sheets (MSDS)
- Exposed healthcare workers shall contact Occupational and Environmental Safety and Health for clinical management
Percutaneous Exposure
- Gently encourage bleeding. Immediately wash the wound with copious amounts of warm soapy water (avoid scrubbing). Rinse, dry, and cover with a waterproof dressing
- Exposed healthcare workers shall contact Occupational and Environmental Safety and Health for clinical management

Mucous Membrane Exposure
- Immediately irrigate with either saline (eye) or tap water (mouth)
- Exposed healthcare workers shall contact Occupational and Environmental Safety and Health for clinical management

Healthcare Worker Symptomatic or Infected with CJD
- Physician confirmed diagnosis
- Healthcare workers shall be referred to Occupational and Environmental Safety and Health for clinical management

References


### Appendix A: National Surveillance Case Definition for Classic CJD

#### Sporadic Case

- **Confirmed CJD**
  - Spongiform encephalopathy in cerebral and/or cerebellar cortex and/or sub-cortical grey matter
  - **AND/OR** Encephalopathy with prion protein (PrP) immunoreactivity (plaque and/or diffuse synaptic and/or patchy/perivacuolar types)
  - **AND/OR** Scrapie associated fibrils (SAF)

- **Probable CJD**
  - Rapidly progressive dementia
  - **AND** Typical EEG
  - **AND** At least two of the following four clinical features: myoclonus, visual or cerebellar disturbances (ataxia), pyramidal/extrapyramidal dysfunction, akinetic mutism
  - **OR**
    - Rapidly progressive dementia
  - **AND** Two of the four clinical features listed above
  - **AND** Duration of illness < 2 years
  - **AND** 14-3-3 positivity (in CSF)

- **Possible CJD**
  - Rapidly progressive dementia
  - **AND** Two of the four clinical features listed above
  - **AND** Duration of illness < 2 years

- **Iatrogenic CJD**
  - Progressive cerebellar syndrome in a pituitary hormone recipient
  - Sporadic CJD with a recognized exposure risk (e.g., dura mater transplant)
### Familial CJD

<table>
<thead>
<tr>
<th>Confirmed or probable sporadic CJD plus confirmed or probable CJD in a first degree relative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AND/OR</strong> Neuropsychiatric disorder plus disease-specific PrP mutation</td>
</tr>
</tbody>
</table>

### Gerstmann-Sträussler-Scheinker (GSS)

<table>
<thead>
<tr>
<th>GSS in a family with dominantly inherited progressive ataxia</th>
</tr>
</thead>
</table>
| **AND/OR** Dementia and one of a variety of PrP gene mutations
  - Encephalo(myelo)pathy with multicentric PrP plaques |

### Familial Fatal Insomnia (FFI)

| FFI in a member of a family with PrP178 mutation
  - Thalamic degeneration, variable spongiform change in cerebrum |

### Kuru

| Kuru in the Fore population of Papua New Guinea:
  - Although most neurologic features correspond to those of CJD with plaques, kuru should be diagnosed only in members of the Fore population in Papua New Guinea |