

CREUTZFELDT-JAKOB DISEASE

Sporadic Creutzfeldt-Jakob Disease, Iatrogenic Creutzfeldt-Jakob Disease, Genetic Prion Diseases, Creutzfeldt-Jakob Disease Variant

SPORADIC CREUTZFELDT-JAKOB DISEASE (sCJD)

Case Definition

Confirmed Case:

Neuropathologically and/or immunocytochemically and/or biochemically confirmed, through observation of one or more neuropathologic features (see [Box 1](#)) and no evidence of iatrogenic CJD or genetic human prion disease (described below).

Probable Case:

Routine investigation should not suggest an alternative diagnosis:

- Rapidly progressive dementia + at least two features of list I + II (see [Box 2](#)).
- OR
- Suspect CJD + cerebrospinal fluid positive for 14-3-3 by immunoblot + duration < 2 years.

Suspect Case:

Rapidly progressive dementia + two of list I (see [Box 2](#)) + duration < 2 years + no electroencephalography (EEG) or atypical EEG.

Clinical Evidence

See [Boxes 1 and 2](#) (as noted in definitions).

Reporting Requirements

- Report confirmed or probable cases to DHW Surveillance Team via Panorama.
- Select appropriate initial staging option in the “staging” field in Panorama
 - Update the staging field if/when new information becomes available

Additional Forms

None.

Data Entry

Complete data entry in Panorama.

IATROGENIC CREUTZFELDT-JAKOB DISEASE (iCJD)

Case Definition

Confirmed Case:

Confirmed CJD (see [Box 1](#)) with a recognized risk factor for iatrogenic transmission (see [Box 3](#)).

Probable Case:

Progressive predominant cerebellar syndrome in a recipient of cadaverically derived human pituitary growth hormone.

OR

Probable CJD with a recognized risk factor for iatrogenic transmission (see [Box 3](#)).

Clinical Evidence

See case definitions above

Reporting Requirements

- Report confirmed or probable cases to DHW Surveillance Team via Panorama.
- Select appropriate initial staging option in the “staging” field in Panorama
 - Update the staging field if/when new information becomes available

Additional Forms

- None.

Data Entry

Complete data entry in Panorama.

GENETIC PRION DISEASES

Case Definition

Confirmed Case:

- Definite (pathologically confirmed) prion disease + definite or probable prion disease in a first-degree relative.
OR
- Definite prion disease + pathogenic mutation in prion protein gene (PRNP) (see [Box 4](#)).
OR
- Typical neuropathologic phenotype of Gerstmann-Sträussler-Scheinker disease (GSS)*.

*Presence of multicentric PrP-immunoreactive plaques in cerebral and/or cerebellar cortex, with neuron loss and spongiosis. Other large amorphous plaques or neurofibrillary tangles immunoreactive for PrP have been described in subsets of GSS, but these are associated with less frequent PRNP mutations (A117V and F198S). Florid or Kuru plaques are not considered diagnostic for GSS.

Probable Case:

- Progressive neuropsychiatric disorder + definite or probable prion disease in a first degree relative.
OR
- Progressive neuropsychiatric disorder + pathogenic mutation in PRNP (see [Box 4](#)).

Clinical Evidence

See case definitions

Reporting Requirements

- Report confirmed or probable cases to DHW Surveillance Team via Panorama.
- Select appropriate initial staging option in the “staging” field in Panorama
 - Update the staging field if/when new information becomes available

Additional Forms

- None.

Data Entry

Complete data entry in Panorama.

CREUTZFELDT-JAKOB DISEASE, VARIANT

Case Definitions

Confirmed Case:

IA (see [Box 5](#)) and neuropathologic confirmation as per pathologic features (see [Footnote^a](#), Box 5).

Probable Case:

I + four or five criteria of II, IIIA and IIIB (see Box 5).

OR

I + IVA (see [Box 5](#)).

Suspect Case:

I + four or five criteria of II + IIIA (see [Box 5](#)).

Clinical Evidence

See case definitions.

Reporting Requirements

- Report confirmed, probable, and Suspect cases **immediately** to DHW Surveillance Team.
- Enter into Panorama.
- Select appropriate initial staging option in the “staging” field in Panorama
 - Update the staging field if/when new information becomes available

Additional Forms

None.

Data Entry

Complete data entry in Panorama.

Box 1

- I. Spongiform encephalopathy in cerebral and/or cerebellar cortex and/or subcortical grey matter.
- II. Encephalopathy with prion protein (PrP) immunoreactivity in plaque-like and/or diffuse synaptic and/or patchy/perivacuolar patterns, by examination of tissue either directly or with assistance of capillary transfer from paraffin-embedded tissue (PET) to secondary support (PET blot).
- III. Presence of scrapie-associated fibrils (SAF) by electron microscopy.
- IV. Presence of protease-resistant PrP by Western blot.

Box 2

- I. A – Myoclonus
B – Visual disturbances or cerebellar dysfunction (ataxia)
C – Pyramidal or extrapyramidal features
D – Akinetic mutism
- II. Typical EEG pattern: periodic sharp-wave complexes ca. 1 HZ.

Box 3

Note: Assessment of the relevance of any proposed risk factor to disease causation should take into account the timing of the putative exposure in relation to disease onset, especially where the putative exposure is recent. As well, this list is provisional, as the risks of iatrogenic transmission of prion disease by other routes are currently incompletely understood.

- I. Treatment with human cadaveric pituitary growth hormone, human pituitary gonadotrophin or human dura mater graft.
- II. Corneal graft in which the corneal donor has been classified as having a definite or probable prion disease.
- III. Neurosurgical exposure to instruments previously used on a patient classified as having definite or probable prion disease.

Box 4

- I. *PRNP* mutations associated with a neuropathologic phenotype of CJD (see [Box 1](#)): P105T, G114V, R148H, D178N, V180I, V180I+M232R, T183A, T188A, T193I, E196K, E200K, V203I, R208H, V210I, E211Q, M232R; octapeptide repeat insertions (various lengths) and deletion (48 bp).
- II. *PRNP* mutations associated with a neuropathologic phenotype of GSS (see previous footnote above): P102L, P105L, A117V, G131V, A133V, Y145Stop, H187R, F198S, D202N, Q212P, Q217R, M232T; octapeptide repeat insertions (various lengths).
- III. *PRNP* mutations associated with a neuropathologic phenotype of Familial Fatal Insomnia (FFI): D178N.

- IV. *PRNP* mutations associated with other neuropathologic phenotypes: I138M, G142S, Q160Stop, T188K, T188R, P238S, M232R; octapeptide repeat insertions (various lengths).

Box 5

- I. A – Progressive neuropsychiatric disorder
B – Duration > 6 months
C – Routine investigations do not suggest alternative diagnosis
D – No history of potential iatrogenic exposure
E – No evidence of genetic prion disease
- II. A – Early psychiatric symptoms ^b
B – Persistent painful sensory symptoms ^c
C – Ataxia
D – Myoclonus or chorea or dystonia
E – Dementia
- III. A – EEG does not show typical appearance of sporadic CJD ^d (or no EEG performed) in the early stages of the illness.
B – Bilateral pulvinar high signal on magnetic resonance imaging (MRI) scan ^e.
- IV. A – Tonsil biopsy positive for prion protein immunoreactivity ^f

Footnotes

- a) Spongiform change, extensive PrP deposition, florid plaques throughout the cerebrum & cerebellum.
- b) Depression, anxiety, apathy, withdrawal, delusions.
- c) Frank pain and/or dysaesthesia.
- d) Generalized triphasic period complexes at ca. 1 Hz. Rarely, these may occur in the late stages of vCJD.
- e) Relative to the signal intensity of other deep grey matter nuclei & cortical grey matter.
- f) Tonsil biopsy is not recommended routinely or in cases with EEG appearance typical of sporadic CJD, but may be useful in suspect cases in which the clinical features are compatible with vCJD and MRI does not show bilateral pulvinar high signal.