A brain autopsy is recommended for all physician-diagnosed CJD cases.

Creutzfeldt-Jakob Disease (CJD)

2019 Case Definition (North Carolina)[i]

1. Sporadic CJD

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

- Neuropsychiatric disorder plus positive RT-QuIC in cerebrospinal fluid (CSF) or other tissues

OR

- 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 typical EEG (periodic sharp wave complexes) during an illness of any duration; and/or
- a positive 14-3-3 CSF assay in patients with a disease duration of less than 2 years
- High signal in caudate/putamen on magnetic resonance imaging (MRI) brain scan or at least two cortical regions (temporal, parietal, occipital) either on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR)

AND without routine investigations indicating an alternative diagnosis.

Suspect

- Progressive dementia; and at least two out 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 (listed above) that would classify a case as “probable”
AND duration of illness less than two years

AND without routine investigations indicating an alternative diagnosis.

2. 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.

3. Familial CJD
Definite or probable CJD plus definite or probable CJD in a first degree relative; and/or neuropsychiatric disorder plus disease-specific PrP gene mutation.

4. Variant CJD

Confirmed

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

a. Numerous widespread kuru-type amyloid plaques surrounded by vacuoles in both the cerebellum and cerebrum - florid plaques.

b. Spongiform change and extensive prion protein deposition shown by immunohistochemistry throughout the cerebellum and cerebrum.

Probable

a. Current age or age at death <55 years (a brain autopsy is recommended, however, 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 months 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 over 6 months.

f. Routine investigations of the patient do not suggest an 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.

---

[i] Adapted from the CDC Diagnostic Criteria for Creutzfeldt-Jakob Disease (CJD), 2018 and Variant Creutzfeldt-Jakob Disease (vCJD)accessible at: https://www.cdc.gov/prions/cjd/diagnostic-criteria.html and https://www.cdc.gov/prions/vcjd/diagnostic-criteria.html