Clinical Directorate of Laboratory Medicine, Beaumont Hospital					
Doc No:	LI-NCJD-Diagnostic Criteria	**Revision**	2	**Active Date**	8-Jan-21
Title: Diagnostic Criteria for the Clinical Diagnosis of Creutzfeldt-Jacob Disease					

Purpose: To provide information for the clinical classification of CJD
Materials: N/A
Safety Precautions: As per RA on SOP
Procedure: Notification of CJD cases
Associated SOP No.: LP-NCJD-Notification Protocol

1. SPORADIC CJD (sCJD)

1.1. DEFINITE
Progressive neurological syndrome AND
Neuropathologically or immunocytochemically or biochemically confirmed

1.2. PROBABLE
1.2.1. I + 2 of II + III
OR
1.2.2. I + 2 of II + IV
OR
1.2.3. I + 2 of II + positive 14-3-3
OR
1.2.4. Progressive neurological syndrome and positive RT-QuIC in CSF or other tissues.

1.3. POSSIBLE
I + 2 of II + duration < 2 years

I Rapidly progressive dementia

II A Myoclonus
B Visual or cerebellar problems
C Pyramidal or Extrapyramidalfeatures
D Akinetic mutism

III Typical EEG (generalized periodic complexes)

IV High signal in caudate/putamen on MRI brain scan or at least two cortical regions (temporal, parietal, occipital) either on DWI or FLAIR

2. GENETIC/FAMILIAL CJD (fCJD)

2.1. DEFINITE
2.1.1. Definite TSE + Definite/ probable TSE in 1st degree relative.
OR
2.1.2. Definite TSE with a Pathogenic *PRNP* mutation (See box).

2.2. PROBABLE
2.2.1. Progressive neuropsychiatric disorder + definite/probable TSE in 1st degree relative.
OR
2.2.2. Progressive neuropsychiatric disorder + pathogenic *PRNP* mutation (See Box).

- *PRNP* mutations associated with **GSS** neuropathological phenotype
  P102L, P105L, A117V, G131V, F198S, D202N, Q212P, Q217R, M232T, 192bpi.
- *PRNP* mutations associated with **CJD** neuropathological phenotype
  D178N-129V, V180I, V180I+M232R, T183A, T188A, E196K, E200K, V203I, R208H, V210I, E211Q, M232R, 96bpi, 120bpi, 144bpi, 168bpi, 48bp*del*.
- *PRNP* mutations associated with **FFI** neuropathological phenotype
  D178N-129M
- *PRNP* mutations associated with vascular PrP amyloid
  Y145s
- *PRNP* mutations associated with proven but unclassified prion disease
  H187R, 216bpi
- *PRNP* mutations associated with neuropsychiatric disorder but not proven prion disease
  I138M, G142S, Q160S, T188K, M232R, 24bpi, 48bpi, 48bpi+nucleotide substitution in other octapeptides.
- *PRNP* mutations without clinical and neuropathological data
  T188R, P238S
- *PRNP* polymorphisms with established influence on phenotype
  M129V
- *PRNP* polymorphisms with suggested influence on phenotype
  N171S, E219K, 24 bp deletion
- *PRNP* polymorphisms without established influence on phenotype
  P68P, A117A, G124G, V161V, N173N, H177H, T188T, D202D, Q212Q, R228R, S230S

3. ACCIDENTALLY TRANSMITTED TSE - IATROGENIC CJD (iCJD)

3.1. DEFINITE
Definite CJD with a recognised iatrogenic risk factor (See Box).

3.2. PROBABLE
3.2.1. Progressive predominant cerebellar syndrome in human pituitary hormone recipients.
OR
3.2.2. Probable CJD with a recognised iatrogenic risk factor (See Box).

3.3. POSSIBLE
Possible CJD with a recognised risk factor (agreed at EURO meeting Bled, 2006)

Relevant Exposure Risks for the Classification as iCJD

The relevance of any exposure to disease causation must take into account the timing of the exposure in relation to disease onset.

- Treatment with human pituitary growth hormone, human pituitary gonadotrophin or human dura mater graft.
- Corneal graft in which the corneal donor has been classified as definite or probable human prion disease.
- Exposure to neurosurgical instruments previously used in a case of definite or probable human prion disease.

This list is provisional as previously unrecognised mechanisms of human prion disease may occur.

4. VARIANT CJD (vCJD)

4.1. DEFINITE
IA and neuropathological confirmation of vCJD[e].

4.2. PROBABLE
4.2.1. I and 4/5 of II and IIIA and IIIB.
OR
4.2.2. I and IVA[d].

4.3. POSSIBLE
I and 4/5 of II and IIIA

I A Progressive neuropsychiatric disorder
B Duration of illness >6months
C Routine investigations do not suggest an alternative diagnosis
D No history of potential iatrogenic exposure
E No evidence of fCJD.

II A Early psychiatric symptoms[a]
B Persistent painful sensory symptoms[b]
C Ataxia
D Myoclonus or chorea or dystonia.
E Dementia

III A EEG does not show the typical appearance of sporadic CJD[c] in the early stages of illness.
B Bilateral pulvinar high signal on MRI scan.

IV A Positive tonsil biopsy[d].

a depression, anxiety, apathy, withdrawal, delusions.
b this includes both frank pain and/or dysaesthesia
c the typical appearance of EEG in sCJD consists of generalised triphasic periodic complexes at approx. 1/sec. These may occasionally be seen in the late stages of vCJD.
d tonsil biopsy is NOT recommended routinely, nor in cases with EEG appearances typical of sCJD, 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.
e spongiform change and extensive PrP deposition with florid plaques throughout the cerebrum and cerebellum.