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EU case definition

1. **Variant form of Creutzfeldt Jakob Disease (vCJD)**
2. **Other forms of Creutzfeldt Jakob Disease (sCJD, iCJD, fCJD)**

The legal basis, rationale and purposes of the EU case definitions can be found here, the case definitions for CJD can be found here.

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Case Classification 6

A. DEFINITE 6

B. PROBABLE 6

1. Variant form of Creutzfeldt Jakob Disease (vCJD)

Preconditions

- Any person with a progressive neuropsychiatric disorder with a duration of illness of at least six months.
- Routine investigations do not suggest an alternative diagnosis.
- No history of exposure to human pituitary hormones or human dura mater graft.
- No evidence of a genetic form of transmissible spongiform encephalopathy.

Clinical Criteria

Any person with at least four of the following five:

- Early psychiatric symptoms [3]
- Persistent painful sensory symptoms [4]
- Ataxia
- Myoclonus or chorea or dystonia
- Dementia

Diagnostic Criteria

Diagnostic criteria for case confirmation:

- Neuropathological confirmation: spongiform change and extensive prion protein deposition with florid plaques throughout the cerebrum and cerebellum.

Diagnostic criteria for a probable or a possible case:

- EEG does not show the typical appearance [5] of sporadic CJD [6] in the early stages of the illness.
- Bilateral pulvinar high signal on MRI brain scan.
- A positive tonsil biopsy [7].

Epidemiological Criteria

An epidemiological link by human to human transmission (e.g. blood transfusion)

Case Classification

A. Possible case

Any person fulfilling the preconditions AND

meeting the clinical criteria AND

a negative EEG for sporadic CJD [8]

https://www.ecdc.europa.eu/en/infectious-disease-topics/variant-creutzfeldt-jakob-disease/disease-information/eu-case-definition

B. Probable case

Any person fulfilling the preconditions AND

meeting the clinical criteria AND

a negative EEG for sporadic CJD [9] AND

a positive MRI brain scan

OR

any person fulfilling the preconditions AND

a positive tonsil biopsy

C. Confirmed case

Any person fulfilling the preconditions AND

meeting the diagnostic criteria for case confirmation

Footnotes

(3) Depression, anxiety, apathy, withdrawal, delusions.

(4) This includes both frank pain and/or dysaesthesia.

(5) The typical appearance of the EEG in sporadic CJD consists of generalised periodic complexes at approximately one per second. These may occasionally be seen in the late stages of vCJD.

(6) See footnote 5.

(7) Tonsil biopsy is not recommended routinely nor in cases with EEG appearances 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 pulvinar high signal.

(8) See footnote 5.

(9) See footnote 5.

Reference

Commission Implementing Decision 2012/506/EU of 8 August 2012, amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council.

Factsheet about variant Creutzfeldt-Jakob disease

https://www.ecdc.europa.eu/en/infectious-disease-topics/variant-creutzfeldt-jakob-disease/disease-information/eu-case-definition

2. Other forms of Creutzfeldt Jakob Disease (sCJD, iCJD, fCJD)

2.1 SPORADIC CJD (from 1 January 2017)

Clinical presentation:

I Rapidly progressive cognitive impairment

II
- A Myoclonus
- B Visual or cerebellar problems
- C Pyramidal or extrapyramidal features
- D Akinetic mutism

*Generalised periodic complexes on EEG

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

Case Classification

A. DEFINITE

Progressive neurological syndrome AND
Neuropathologically OR
immunocytochemically OR
biochemically confirmed

B. PROBABLE

2.2.1 I + two of II and typical EEG*
OR 2.2.2 I + two of II and typical MRI brain scan**
OR 2.2.3 I + two of II and positive CSF 14-3-3
OR 2.2.4 Progressive neurological syndrome and positive RT-QuIC in CSF or other tissues

*Generalised periodic complexes

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

C. POSSIBLE

I + two of II + duration <2 years

https://www.ecdc.europa.eu/en/infectious-disease-topics/variant-creutzfeldt-jakob-disease/disease-information/eu-case-definition

2.2 IATROGENIC CJD

Case Classification

A. DEFINITE

Definite CJD with a recognised iatrogenic risk factor (see below)

B. PROBABLE

Progressive predominant cerebellar syndrome in human pituitary hormone recipients

OR

Probable CJD with recognised iatrogenic risk factor:

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

https://www.ecdc.europa.eu/en/infectious-disease-topics/variant-creutzfeldt-jakob-disease/disease-information/eu-case-definition

2.3 FAMILIAL CJD/TSE (GENETIC)

Case Classification

A. DEFINITE

Definite TSE + definite or probable TSE in 1st degree relative OR

Definite TSE with a pathogenic PRNP mutation (see right)

B. PROBABLE

Progressive neuropsychiatric disorder + definite or probable TSE in 1st degree relative

OR

Progressive neuropsychiatric disorder + pathogenic PRNP mutation:

- **PRNP MUTATIONS ASSOCIATED WITH GSS NEUROPATHOLOGICAL PHENOTYPE:**
  P102L, P105L, A117V, G131V, F198S, D202N, Q212P, Q217R, M232T, 192 bpi
- **PRNP MUTATIONS ASSOCIATED WITH CJD NEUROPATHOLOGICAL PHENOTYPE**:
  D178N129V, V180I, V180I+M232R, T183A, T188A,
  E196K, E200K, V203I, R208H, V210I, E211Q, M232R, 96 bpi, 120 bpi, 144 bpi, 168 bpi, 48 bp *del*
- **PRNP MUTATIONS ASSOCIATED WITH FFI NEUROPATHOLOGICAL PHENOTYPE**:
  D178N129M
- **PRNP MUTATION ASSOCIATED WITH VASCULAR PRP AMYLOID**: Y145s
- **PRNP MUTATIONS ASSOCIATED WITH PROVEN BUT UNCLASSIFIED PRION DISEASE**: H187R, 216 bpi,
- **MUTATIONS ASSOCIATED WITH NEUROPSYCHIATRIC DISORDER BUT NOT PROVEN PRION DISEASE**: I138M, G142S, Q160S, T188K, M232R, 24 bpi, 48 bpi, 48 bpi + nucleotide substitution in other octapeptides

Additional list of mutations:

- **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

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