CREUTZFELDT-JAKOB DISEASE (CJD), CLASSIC

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.

IATROGENIC CREUTZFELDT-JAKOB DISEASE (ICJD)

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***).

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 amorphic 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***).

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

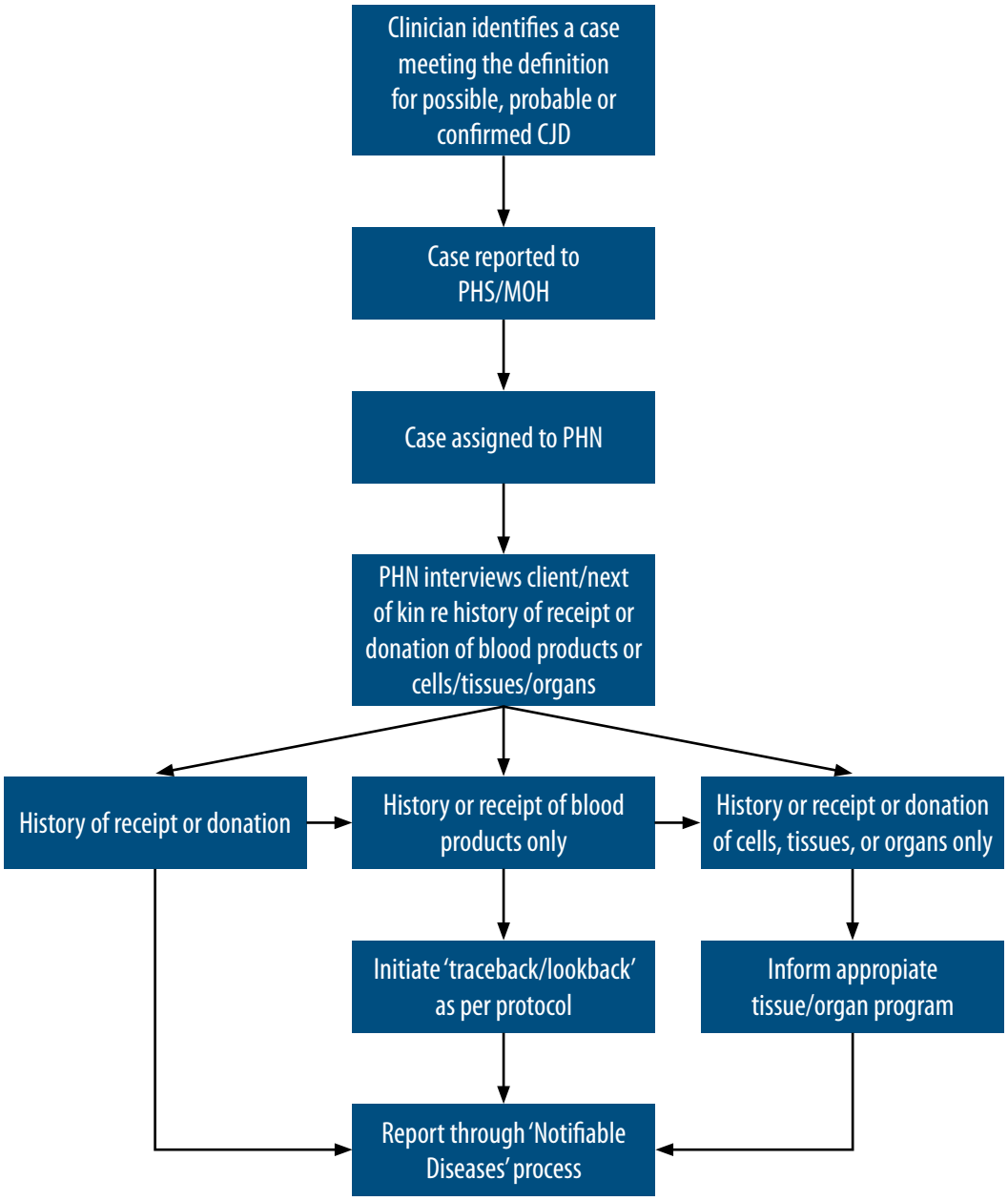
I. *PRNP* mutations associated with a neuropathologic phenotype of CJD (see ***Box 1***): P105T, G114V, R148H, D178N, V180I, V180I+M232R, T183A, T188A, T193I, E196K, E200K, V203I, R208H, V210I, E211Q, M232R; octapeptide repeat insertions (various lengths) and deletion (48 bp).

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).

Flow chart for Public Health follow-up of CJD



Causative agent

Thought to be a unique, self-replicating protein called a prion that replicates by a poorly understood mechanism.

Source

Humans

Incubation

Fifteen months to possibly more than 30 years

Transmission

The mode of transmission in most cases in unknown. CJD may either occur sporadically (approximately 90% of cases), through iatrogenic transmission of infective agents (<1% of cases) or as an autosomal dominant inheritance (approximately 10% of cases). Potential sources of iatrogenic transmission include any medical or surgical procedures involving tissues with “high infectivity” such as the brain, spinal cord, and eyes.

Communicability

Central nervous system (CNS) tissues are infectious throughout symptomatic illness. Other tissues and cerebral spinal fluids (CSF) are sometimes infectious.

Symptoms

- Classic CJD has an insidious onset, symptoms include: confusion, poor concentration, lethargy, progressive dementia, intermittent unsteadiness when standing or walking, and variable ataxia. As the disease progresses, mental impairment becomes more severe and cases may develop involuntary muscle jerks (myoclonus), lose the ability to move or speak, and eventually enter a comatose state. Death invariably occurs within three to twelve months.
- Approximately 80% of patients with sporadic CJD are between 50 and 70 years of age, although familial cases usually have an onset of around 40 years of age.

Diagnostic testing

Please contact your local lab

Treatment

There is no known effective treatment available to cure or control CJD and the disease appears to be uniformly fatal. Current treatment is therefore aimed at controlling symptoms and making the person as comfortable as possible

PUBLIC HEALTH MANAGEMENT & CONTROL

Case management

- Obtain the client's medical history including symptoms, date of onset, treatment surgical procedures of concern, and/or hospitalization and any potential sources of exposure, particularly a history of any receipt or donation of blood, blood products, cells, tissues or organs.
- If necessary, contact the client's physician to obtain further information and clarification of the client's history, especially with respect to past surgical procedures and blood/tissue/organ receipt and/or donation
- If the client has a history of receipt or donation of blood, cells, tissues or organs, inform the Medical Officer of Health immediately and fax the "CJD Case Report Form" to the Department of Health and Wellness so that appropriate lookback and traceback procedures may be initiated immediately.
- If client has a history of surgical procedures of concern when symptomatic, inform infection control program in hospital where procedure occurred.
- Discuss the role of public health and provide information to the client or family (i.e., general information sheets). Complete the "CJD/vCJD Case Report Form" and update as new information becomes available.
- If client is deceased, ensure that attending physician has notified the funeral director of CJD diagnosis so appropriate infection control precautions can be taken.

Follow-up of organ/tissue donors

If case has received or donated cells, tissue or organs, work with the Regional Tissue Bank and the Multi-Organ Transplant Program on a case-by-case basis to ensure appropriate follow-up.

Education

Any person who spent six or more cumulative months between January 1, 1980, and December 31, 1996, in the United Kingdom should not donate blood, organs or other body tissues or fluids.

Surveillance forms

novascotia.ca/dhw/populationhealth/surveillanceguidelines/NS_Notifiable_Disease_Surveillance_Case_Report_Form.pdf

novascotia.ca/dhw/populationhealth/surveillanceguidelines/CJD_Case_Report_Form.pdf

General Information Sheet