CREUTZFELDT-JAKOB DISEASE

and Other Spongiform Encephalopathies

Based on the MoH Communicable Diseases Control Manual 2012[1]

Associated Documents

Case Report Form:
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Fact sheet**:**
https://www.tewhatuora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/creutzfeldt-jacob-disease-and-other-spongiform-encephalopathies/

The Illness[1-3]

Creutzfeldt-Jakob disease (CJD) is the most common of the known human Transmissible Spongiform Encephalopathies (TSEs). Others include kuru and hereditary forms such as Gerstmann-Straussler-Scheinker syndrome and fatal familial insomnia. All spongiform encephalopathies are caused by proteinaceous infectious particles (termed 'prions') that undergo abnormal folding, leading to cellular death and inducing a similar misfolding in other proteins around them. These human prion diseases share certain common neuropathologic features including neuronal loss, proliferation of glial cells, absence of an inflammatory response, and the presence of small vacuoles within the neuropil, which produces a spongiform appearance.

CJD exists in four forms:

- sporadic: occurs throughout the world at the rate of about one per million people, and accounts for about 85% of CJD cases.
- familial: associated with a gene mutation and makes up 5–15% of CJD cases
- iatrogenic: results from accidental transmission via contaminated surgical equipment or as a result of corneal or meningeal (dura mater) transplants or the administration of human-derived pituitary growth hormones; this accounts for less than 1% of CJD cases.
- variant (vCJD): a rare and fatal human neurodegenerative condition which is classified as a TSE because of its ability to be transmitted and the characteristic spongy degeneration of the brain that it causes. vCJD was first described in the United Kingdom in March 1996 and has been linked with exposure to a TSE of cattle called Bovine Spongiform Encephalopathy (BSE) which was first reported in the United Kingdom in 1986. In contrast to the traditional forms, vCJD has affected younger patients (median age at death of 28 years, as opposed to 68 years) and has a relatively longer duration of illness (median of 14 months as opposed to 4.5 months).

Early in the illness, patients usually experience psychiatric or sensory symptoms, which most commonly take the form of depression, apathy or anxiety, and occasionally (in a third of the cases) unusual persistent and painful sensory symptoms. Neurological signs, including unsteadiness, difficulty walking and involuntary movements, develop as the illness progresses and, by the time of death, patients become completely immobile and mute.

Epidemiology in New Zealand[1,4]

All suspected cases are referred to the New Zealand CJD registry (see Notification procedure below) for diagnosis. There are generally three or four cases of CJD in New Zealand each year. However in 2012, 9 cases were identified; two were classified as definite and seven as probable sporadic CJD cases. Their age distribution was 60 to >90 years; six were males. Since 1997, 65 cases of CJD have been identified, 17 definite and 48 probable. No cases of variant CJD have ever been identified in New Zealand.

Case definition

This is based on diagnostic criteria developed by the New Zealand CJD registry, which include case history and examination findings, cerebral magnetic resonance imaging (MRI), electroencephalogram (EEG), cerebrospinal fluid (CSF) 14-3-3 protein and definitively, brain histopathology.

Clinical description

CJD is a rapidly progressive, universally fatal neurodegenerative disease. Subtypes of CJD are differentiated by causative mechanism and clinical picture, as summarised in Table 1.

Table 1: Types of CJD

Subtype	Description	Predominant features	Mean age of onset	Mean duration of illness before death
Sporadic	Accounts for around 85% of all cases of CJD globally. Thought to arise spontaneously.	Dementia, myoclonus, ataxia	65 yrs	4.5 months
Familial	A hereditary form of CJD that accounts for 10–15% of all cases of CJD, occurs in geographic clusters. Autosomal dominant inheritance. Close blood relatives of people with genetic CJD have a 1 in 2 chance of carrying the gene and developing the disease.	Dementia, myoclonus	45–49 yrs	15 months
Iatrogenic	Accounts for less than 1% of all cases of CJD. Infection passed on from treatment or procedures from any case (sporadic, familial, variant) can be considered iatrogenic. Historically from pituitary hormones and dura mater grafts derived from human cadavers (treatments no longer in use), and more recently through corneal transplantation and contaminated neurosurgical instruments. Infection with variant CJD has been linked with blood transfusion in 4 patients in the UK.	Lack of coordination, dementia (late)	Depends on age of exposure	4.5 months (8 months if related to human growth hormone)
Variant	Suspected to occur from eating beef and beef products from cattle infected with BSE. Often starts with psychiatric symptoms, such as anxiety and depression. Infectious prion proteins are found outside the nervous system as well as within it, especially in the lymphoid tissues throughout the body. No cases of vCJD have been reported in New Zealand to date.	Mood and behavioural abnormalities, paraesthesias, dementia	26 yrs	14 months

Incubation

Sporadic CJD: Arises spontaneously. See Table 1 for mean age of onset.
Familial CJD: Arises spontaneously. See Table 1 for mean age of onset.
Variant CJD: Based on the small number of cases, the incubation period for foodborne transmission is approximately 13 years.
Iatrogenic CJD:
- neurosurgical cases and EEG depth electrodes: 12–28 months
- dural grafts: 1.5–18 years
- growth hormone: 6–30 years
- blood transfusion-related: 5–9 years.

Transmission

Sporadic CJD: Not applicable (arises spontaneously).
Familial CJD: Not applicable (arises spontaneously).
vCJD: most likely from consumption of food products contaminated by BSE-infected cattle.
Iatrogenic CJD: passed on by medical treatment or invasive medical intervention through exposure to infectious material from a case. Most cases have been transmitted through cadaveric dural grafts or treatment with human pituitary hormones; a few cases have been transmitted through corneal transplantation, contaminated neurosurgical instruments or from EEG depth electrodes. Each acquired form involves the inoculation, implantation or transplantation of infectious material.

Transmission from cases
For Sporadic, Familial and Iatrogenic CJD, only the tissues of the central nervous system, including the brain, dura mater, spinal cord ganglia, CSF (low risk), posterior eye and the olfactory tract, appear to be infective. Infective material is rarely found in blood.
For **vCJD**, abnormal prion protein has also been detected in various lymphoid tissues, including tonsils, spleen, gastrointestinal lymphoid tissues (for example, Peyers patches of the appendix and rectum), lymph nodes, thymus and adrenal gland. Some vCJD cases have been linked to blood transfusions, and it is thought that vCJD can be transmitted by blood components from people who are asymptomatic but later develop the disease.
There have been no isolations of infective material from human faeces, saliva, tears, vaginal secretions, semen or milk.

Communicability
Cases are increasingly likely to be infective during the last 40% of the incubation period (that is, approximately 8 years before the onset of symptoms for sporadic CJD). Central nervous system tissue is infective throughout symptomatic illness.

Notification Procedure

To be notified immediately on suspicion. On receiving a notification, the Medical Officer of Health should:
a) Forward details to:

Amanda West
NZ CJD Registry Coordinator
Department of Medicine
Dunedin School of Medicine
University of Otago
PO Box 56
DUNEDIN
Email: cjd.registry@otago.ac.nz
Phone: 021 081 34217

b) Inform the Director of Public Health, Ministry of Health.

CASE CLASSIFICATION
This is largely based on specific diagnostic criteria of definite, probable or possible CJD or vCJD, and assessed by the CJD Registry and reporting clinician.

- **Under investigation:** Cases with neurological disease of unknown aetiology who do not fit the criteria for possible CJD or vCJD but where the diagnosis of CJD is being actively considered.
- **Probable:** Clinical criteria met for probable or possible CJD.
- **Confirmed:** A case that has laboratory confirmation.
- **Not a case:** A case that has been investigated and subsequently found not to meet the case definition.

Laboratory testing

Histopathological examination of brain tissue confirms the diagnosis. For the technical aspects refer to the chapter on CJD in the MoH Communicable Diseases Control Manual 2012.

Management of Case

Investigation

- Notification details are forwarded to Dr M. Pollock and the Director of Public Health (MoH) informed (refer Notification Procedure above).
- Details of the CJD Register protocol are completed by the attending physician.
- No involvement of CPH is usually required.

Restriction
There is no reason to defer, deny or in any way discourage the admission of a person with CJD into any health care setting. Based on current knowledge, isolation of patients is not necessary; they can be nursed in the open ward system using standard precautions. Private room nursing care is not

required for infection control, but may be appropriate for compassionate reasons. In regard to invasive medical interventions, people with confirmed or suspected CJD are the highest-risk patients. They must be managed according to infection control policies using specific precautions (see documents referred to in 'Other Control Measures', below). Cases must not donate blood, tissues or organs.

Treatment
Supportive.

Counselling
Provided by the clinician or by a psychologist.

Management of Others At Risk

For infection control purposes, individuals with confirmed or suspected CJD are the highest-risk patients. Intermediate precautionary measures and counselling are also important for people who are identified as having been exposed to CJD or as being at risk of CJD (for example, have a family history).

Table 2: Categorisation of individuals at risk of CJD

Symptomatic individuals	As per case classification (under investigation, probable, confirmed, not a case).
Asymptomatic individuals at risk from familial forms of CJD linked to genetic mutations	Individuals who have been shown by specific genetic testing to be at significant risk of developing CJD or other prion disease. Individuals who have a blood relative known to have a genetic mutation indicative of familial CJD. Individuals who currently have, or have had two or more blood relatives affected by CJD or other prion disease.
Asymptomatic individuals identified as potentially at risk due to iatrogenic exposures	Recipients of hormone derived from human pituitary glands, for example, growth hormone or gonadotrophin. (*In New Zealand, the human pituitary hormone programme ceased in 1985.*) Individuals who have received a graft of dura mater. *(In October 1988 the New Zealand Department of Health, now Ministry of Health, recommended that commercially produced dura mater not be used.)* Cases who have been **contacted** as potentially at risk, including individuals considered to be: • at risk of CJD/vCJD due to exposure to certain instruments used on a case who went on to develop CJD/vCJD or was at risk of vCJD • at risk of vCJD due to receipt of blood components or plasma derivatives • at risk of CJD/vCJD due to receipt of blood, tissues or organs • at risk of vCJD due to the probability they could have been the source of infection for a case

Note:
• Categorisation of individuals by risk is in descending order.
• This table does not include people who may theoretically be at increased risk because of food-related exposures (eg, eating beef from areas with previous BSE). This risk is thought to be extremely low.

Restrictions

- Individuals at risk of disease must not donate blood, tissue or organs. They must notify their health care providers of their risk of developing prion disease as this has implications for lumbar puncture, endoscopy and surgical procedures and for transport and laboratory processing of samples.
- Individuals who have spent 6 months or more in the United Kingdom, France or the Republic of Ireland between January 1980 and December 1996 must not donate blood; however, organ donation is allowed with informed consent.
- Individuals who have a history of blood or blood product transfusion in the United Kingdom, France or the Republic of Ireland since 1980 must not donate blood. In addition, the New Zealand Blood Service does not accept tissues from individuals with the above blood transfusion history.

Counselling
Provide information on the disease. A fact sheet is available in the following location:
https://www.tewhatuora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/creutzfeldt-jacob-disease-and-other-spongiform-encephalopathies/

Other Control Measures

Identification of source
Follow the CJD register protocol.

Disinfection and decontamination
Comprehensive advice on case care, occupational exposure, laboratory safety, decontamination of instruments and surfaces, waste disposal and post-mortem care can be found in control guidance documents published by both the Australian Department of Health and Ageing and the United Kingdom's Department of Health. These documents are the basis of New Zealand's national policy approach recommended by the Ministry of Health. They can be located at the website addresses of References 5-7.

Reporting

- Refer Notification Procedure above.
- File.

References and further information

1) Te Whatu Ora Communicable Diseases Control Manual, Creutzfeldt-Jacob disease https://www.tewhatuora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/creutzfeldt-jacob-disease-and-other-spongiform-encephalopathies/

2) WHO media centre, Variant Creutzfeldt-Jakob Disease fact sheet. No. 180, Revised Feb.2012 http://www.who.int/mediacentre/factsheets/fs180/en/

3) UpToDate, Creutzfeldt Jakob disease https://www.uptodate.com/contents/creutzfeldt-jakob-disease

4) Notifiable And Other diseases in New Zealand: Annual Surveillance Reports 2014 https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2014/2014AnnualReportFinal.pdf

5) Department of Health and Ageing, Australia, *Creutzfeldt-Jacob Disease Infection Control Guidelines December 2007* www.health.gov.au/internet/main/publishing.nsf/Content/icg-guidelinesindex.htm

6) National Health and Medical Research Council (NHMRC), Australia, *Australian Guidelines for the Prevention and Control of Infection in Healthcare (2010)* www.nhmrc.gov.au/guidelines-publications/cd33

7) Department of Health, UK. Minimise transmission risk of CJD and vCJD in healthcare settings (Creutzfeldt-Jakob disease (CJD): guidance, data and analysis). 27 Nov. 2012 Last updated: 22 October 2015. https://www.gov.uk/government/publications/guidance-from-the-acdp-tse-risk-management-subgroup-formerly-tse-working-group