Creutzfeldt-Jakob disease and other spongiform encephalopathies

Epidemiology in New Zealand

Creutzfeldt-Jakob disease (CJD) is one of the transmissible spongiform encephalopathies that affect humans. There are generally three or four cases of CJD in New Zealand each year.

Other transmissible spongiform encephalopathies include kuru and hereditary forms such as Gerstmann-Straussler-Scheinker syndrome and fatal familial insomnia. CJD is subdivided into sporadic (previously known as classic), familial, iatrogenic and variant forms. The variant form of CJD (vCJD) is linked epidemiologically and through laboratory studies to bovine spongiform encephalopathy (BSE) in cattle.

All spongiform encephalopathies are caused by proteinaceous infectious particles (termed ‘prions’) that undergo conformational change, leading to cellular death and inducing a similar conformational change in other proteins around them.

More detailed epidemiological information is available on the Institute of Environmental Science and Research (ESR) surveillance website at www.surv.esr.cri.nz

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**

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Description</th>
<th>Predominant features</th>
<th>Mean age of onset</th>
<th>Mean duration of illness before death</th>
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<tbody>
<tr>
<td>Sporadic</td>
<td>Accounts for around 85 percent of all cases of CJD globally. Thought to arise spontaneously.</td>
<td>Dementia, myoclonus, ataxia</td>
<td>65 years</td>
<td>4.5 months</td>
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<tr>
<td>Familial</td>
<td>A hereditary form of CJD that accounts for 10–15 percent of all cases of CJD, occurring 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.</td>
<td>Dementia, myoclonus</td>
<td>45–49 years</td>
<td>15 months</td>
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<tr>
<td>Variant</td>
<td>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.</td>
<td>Mood and behavioural abnormalities, paraesthesias, dementia</td>
<td>26 years</td>
<td>14 months</td>
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<tr>
<td>Iatrogenic</td>
<td>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 United Kingdom.</td>
<td>Lack of coordination, dementia (late)</td>
<td>Depends on age of exposure</td>
<td>4.5 months (8 months if related to human growth hormone)</td>
</tr>
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</table>

Source: Health Protection Agency (United Kingdom), and personal communication Professor Martin Pollock, University of Otago
Laboratory tests for diagnosis

Histopathological examination of brain tissue confirms the diagnosis. The sensitivity and specificity of 14-3-3 protein detection in CSF are diagnostically helpful. Levels increase during the course of disease. Using a cut-off value of 8.3 ng/mL, the test has a sensitivity of 93 percent and specificity of 98 percent for sporadic CJD. The sensitivity is substantially lower for familial and variant subtypes. MRI [DWI] has a sensitivity and specificity in CJD of 91 and 96 percent respectively.

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:** Laboratory confirmation of CJD.
- **Not a case:** A case that has been investigated and subsequently found not to meet the case definition.

Spread of infection

Incubation period

Sporadic and familial cases

Arises spontaneously. See Table 1: Types of CJD, above, for mean age of onset.

Variant cases

Based on the small number of vCJD cases, the incubation period for foodborne transmission is approximately 13 years.

Iatrogenic cases

- Neurosurgical cases and EEG depth electrodes: 12–28 months
- Dural grafts: 1.5–18 years
- Growth hormone: 6–30 years
- Based on the small numbers of vCJD cases, the blood transfusion-related transmissions is around 5–9 years.
Mode of transmission

Sporadic and familial
Not applicable (arises spontaneously).

Variant
Variant CJD is most likely to have been caused by consumption of food products contaminated by BSE-infected cattle.

Iatrogenic
Infection passed on as a result of medical treatment or invasive medical intervention through exposure to infectious material from a case is considered iatrogenic. Most cases of iatrogenic CJD 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 cases of 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 variant CJD, 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.

Period of communicability
Cases are increasingly likely to be infective during the last 40 percent 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
Attending medical practitioners must immediately report suspected cases directly to the New Zealand CJD register, at the Department of Preventive and Social Medicine, University of Otago Dunedin School of Medicine, and inform the local medical officer of health and Director of Public Health at the Ministry of Health.
Management of case

Investigation
As for the CJD register protocol, completed by the clinician.

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 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

<table>
<thead>
<tr>
<th>Symptomatic cases</th>
<th>As per case classification.</th>
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<tbody>
<tr>
<td>Asymptomatic individuals at risk from familial forms of CJD linked to genetic mutations</td>
<td>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.</td>
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</tbody>
</table>
Asymptomatic individuals identified as potentially at risk due to iatrogenic exposures

<table>
<thead>
<tr>
<th>Recipients of hormone derived from human pituitary glands, for example, growth hormone, gonadotrophin. (In New Zealand, the human pituitary hormone programme ceased in 1985.)</th>
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<tr>
<td>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.)</td>
</tr>
<tr>
<td>Cases who have been contacted as potentially at risk, including individuals considered to be:</td>
</tr>
<tr>
<td>• 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</td>
</tr>
<tr>
<td>• at risk of vCJD due to receipt of blood components or plasma derivatives</td>
</tr>
<tr>
<td>• at risk of CJD/vCJD due to receipt of tissues/organs</td>
</tr>
<tr>
<td>• at risk of vCJD due to the probability they could have been the source of infection for a case transfused with their blood who was later found to have vCJD.</td>
</tr>
</tbody>
</table>

Source: Adapted from UK Advisory Committee on Dangerous Pathogens (ACDP) 2007.

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 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.

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 following website addresses:


Reporting

Attending medical practitioners must immediately report suspected cases directly to the New Zealand CJD register, at the Department of Preventive and Social Medicine, University of Otago Dunedin School of Medicine, and inform the local medical officer of health and Director of Public Health at the Ministry of Health.

If there are risk factors associated with health care, then the Ministry of Health will convene the CJD Response Group.

References and further information


