Creutzfeldt-Jakob Disease (CJD)

Manitoba Health
Public Health

Communicable Disease Control Unit

Case Definition

Confirmed case: Cerebral histopathology with characteristic lesions, usually found in post-mortem specimens.

Clinical case: Clinical constellation of characteristic EEG and clinical signs (see below), in particular a rapid onset of dementia.

Reporting Requirements

- Pathology positive results, including new variant CJD, are reportable by laboratory.
- All cases, including new variant CJD, are reportable by attending health care professional.

Clinical Presentation/Natural History

CJD is characterized by rapid onset of confusion, behavioural and cognitive abnormalities, progressive dementia, and variable ataxia in persons age 16 to 80 years and older. However, almost all persons with classical CJD (≥99%) are over 35 years old. Later, myoclonic jerks appear, together with a variable spectrum of other neurologic signs. Characteristically, routine laboratory studies of the cerebrospinal fluid (CSF) are normal and there is no fever. Typical periodic, high-voltage complexes are common on electroencephalogram (EEG). The disease progresses rapidly; death usually occurs within three to 12 months (median four months, mean seven months). About 5-10% of persons with CJD have a positive family history of pre-senile dementia, associated with one of several mutations in the gene on chromosome 20. Pathologic changes are limited to the central nervous system (CNS). New variant CJD has recently been described in the United Kingdom and to a lesser extent elsewhere in Europe, and may affect persons at younger ages. The clinical picture may be similar to classical CJD, but it has been linked to the consumption of prion-contaminated beef from cows with bovine spongiform encephalopathy (BSE) or "mad cow disease." About 30 to 40 cases have been described in Europe, but none in North America. Persons who have consumed beef in the United Kingdom during the BSE era (early 1980s to mid 1990s) are at risk for new variant CJD, but it appears to be an extremely rare occurrence.

CJD must be differentiated from other forms of dementia, especially Alzheimer disease, from other slow infections, from toxic and metabolic encephalopathies, and occasionally, from tumors and other space-occupying lesions.

Etiology

CJD is probably caused by a filterable, self-replicating, biologically stable protein called a prion.

Epidemiology

Reservoir: Humans are the only proven reservoir of classical CJD, but new variant CJD may be transmitted to humans from ingestion of contaminated beef (see above).

Transmission: Unknown in most cases; *de novo* spontaneous generation of the self-replicating protein has been hypothesized. Iatrogenic cases have been recognized from corneal transplants, cortical electrodes that had been used on known CJD patients, human dura mater grafts, and injections of growth or gonadotropic hormones prepared from human pituitary glands. Some cases have had a history of brain surgery within two years of onset. As indicated above, new variant CJD may be acquired by the ingestion of beef from cows with BSE.

Occurrence:

General: Worldwide. Average annual mortality rates are 0.5-1/1,000,000 population, with familial clusters reported from Slovakia, Israel and Chile. In North America, the highest age-specific average annual mortality rates (more than five cases/1,000,000) occur in the 65 to 79 year age group.

Manitoba: Since becoming reportable in January 1999, there have been three confirmed cases, all classical.

Incubation Period: Fifteen months to possibly more than 30 years in some iatrogenic cases. Those with known direct CNS tissue exposures have been associated with incubation periods of less than 10 years. The incubation period in sporadic cases is unknown.

Susceptibility and Resistance: Genetic differences in susceptibility, resembling those of autosomal dominant traits, have been shown to explain patterns of occurrence of the disease in families. Genetic differences in susceptibility to scrapie have been found in animals. Mutations in the "prion protein" gene have been found linked to all forms of familial disease.

Period of Communicability: CNS tissues are infectious throughout symptomatic illness. Other tissues and CSF may also be infectious, but data are limited. Infectivity during the incubation period is not known, but studies in animals suggest that lymphoid and other organs are probably infectious before signs of illness appear.

Diagnosis

Diagnosis is based on clinical signs and a characteristically periodic EEG. It is confirmed by histopathologic findings (generally at autopsy), at times aided by immunocytochemistry, and in research settings by transmission of disease to animals from biopsy specimens. Neurological consultation is advised.

Key Investigations

- History of relevant exposure.
- Familial history of CJD.

Control

Management of Cases:

- No specific treatment is available.
- Although transmission via blood or blood products has never been documented in humans (nor definitively in animal models), such transmission is theoretically possible. Persons with CJD or other forms of dementia should be excluded from donating blood, organs or other body tissues or fluids.
- To identify potential sources of infection, a complete medical history should be obtained, including history of invasive neurological or neuro-surgical procedures, corneal transplants, and possible exposure to human growth hormone or transplanted tissue, as well as a family history of dementia. Neurological referral is recommended.

Management of Contacts:

- As no specific diagnostic test for CJD or the presence of prions is available, contact notification must be considered on an individual basis. In general, because transmission through blood or blood products has not been demonstrated, it is not recommended that recipients of blood or blood products from donors who subsequently develop CJD be notified.
- Persons with potential exposures to CJD, such as invasive neurological or neuro-surgical procedures, dura mater grafts, corneal transplants, or administration of growth or gonadotropic hormones prepared from human pituitary glands, should be informed of their potential risk.

Preventive Measures:

- Persons with CJD, as well as their first-degree relatives (parents, children or siblings), should be excluded from donating blood, organs, or other body tissues hormone or gonadotropin, or corneal transplants, should also be excluded. Persons who have received dura mater implants, human growth hormone or gonadotropin or corneal transplants, should also be excluded.
- Persons with CJD who have donated blood, blood products, organs, or other body tissues or fluids are reported to Canadian Blood Services (CBS) by Manitoba Health. CBS may also by informed by CBS laboratories or other sources, that hospitals have been supplied blood or blood

products derived, in part, from persons who subsequently develop CJD. When such information is obtained, CBS performs a lookback to identify and notify the hospital(s) that received the blood, and recalls any available product. It is not recommended that recipients of such products be notified.

- Surgical instruments that have been in contact with high-risk tissue from CJD patients (brain, spinal cord, cornea, retina, pituitary gland, dura mater and cerebrospinal fluid) should be considered contaminated and must be inactivated. High vacuum steam autoclaving (for at least 18 minutes at 132-136°C) should be employed. Chemical agents such as 5% sodium hypochlorite and 1N to 2N sodium hydroxide may not be effective; after one hour, they are best followed by steam autoclaving. Aldehydes are ineffective.
- Single-use cardiac catheters, pacemakers and other single-use devices, should not be re-used after being used on a CJD patient.