SPRING 2013

CJD IN CANADA
FAMILY EDITION

IN THIS ISSUE

Mission Statement

The mission of the Prion Diseases Program of the Public Health Agency of Canada is to continually assess, mitigate, and ultimately eliminate risks to human health posed by infectious prion diseases in Canada, through surveillance, laboratory services, research and education.

INTRODUCTION

The **Canadian Creutzfeldt-Jakob Disease Surveillance System** (CJDSS), which is part of the Public Health Agency of Canada's Prion Diseases Program, was established in 1998 as a national surveillance system for Creutzfeldt-Jakob disease (CJD). The main role of the CJDSS is to help protect Canadians from health risks posed by CJD.

The CJDSS also works more directly to support patients, families and healthcare providers dealing with this difficult disease, through education and sharing of information. The CJD in Canada newsletter is one way in which this is done.

This issue of the newsletter includes an announcement about new cerebrospinal fluid (CSF) protein tests, a feature article on genetics, a brief report on the recent discovery of a second case of variant CJD (vCJD) in Canada, and a "You Asked Us" section where we strive to provide answers to your important questions about CJD. Your questions can also help others dealing with CJD. It is our hope that this newsletter provides you with helpful information about CJD in Canada.

(Note that definitions for words highlighted in *italics* can be found in the "Helpful Definitions" box following the article.)

Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

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NEW CEREBROSPINAL FLUID (CSF) PROTEIN TESTS OFFERED

The CJDSS laboratory offers testing for 14-3-3 *protein* in *cerebrospinal fluid* (CSF), which is often helpful in the diagnosis of patients with suspected CJD. As of October 2011, two newer tests – for tau protein and S100B protein – were added by the laboratory to better support physicians in their diagnostic work. These newer tests cannot confirm or rule out a diagnosis of CJD, which still requires a pathologist to examine brain tissue. However, they provide improved information that can often contribute to greater confidence in the diagnosis of a living patient. For more information on CSF testing, please contact the CJDSS toll-free at 1-888-489-2999.

HELPFUL DEFINITIONS

Cerebrospinal fluid (CSF) – CSF is a clear, colorless body fluid that surrounds the brain and spinal cord, and can be analyzed to help in the diagnosis of CJD. It is collected by a physician, who uses a fine needle to puncture the lower spine and take a small sample.

Proteins – Proteins are complex chemical substances that are made by all cells of the human body, including those of the brain. 14-3-3, tau and S100B proteins are often found in higher amounts in the CSF of patients with CJD.

GENETICS AND CREUTZFELDT-JAKOB DISEASE

Genetic differences play a number of important roles in CJD. For this reason, the CJDSS offers laboratory-based genetic testing services for people with suspected CJD, as well as for family members of CJD patients with a mutation. Some key information on genetic testing is provided here.

Since 1998, 39 cases of CJD in Canada have been linked to a disease-causing mutation.

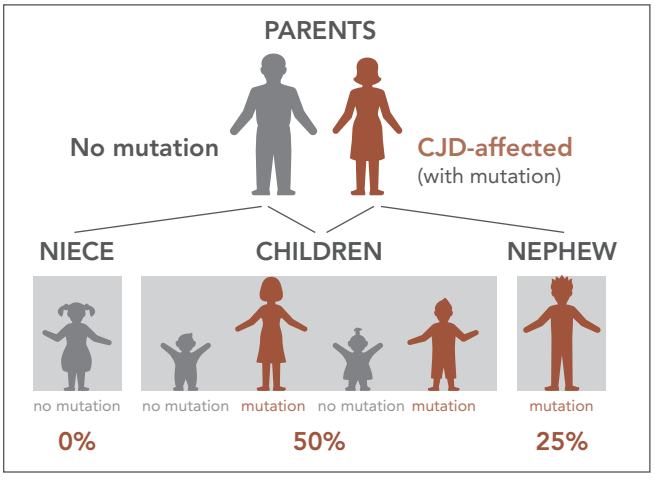
In genetic CJD (also known as *hereditary or familial* CJD) an altered form of a specific human gene (*PRNP*) is responsible for the affected person's disease. This contrasts with most cases of CJD in Canada which are sporadic (meaning that a specific genetic or infectious cause of the disease cannot be identified). The *PRNP* gene, which carries instructions for making the normal *prion protein* (PrP), is carried by everyone in two copies (one is received from each parent). In hereditary CJD, disease results even if only one of these two copies is altered by a *gene mutation* in such a way that the PrP protein is abnormal.

It is important to remember that in most cases, CJD is **sporadic**, meaning that it is not associated with any specific genetic or infectious cause.

As CJD tends to appear only later in life, some people with the altered gene may pass it to one or more of their children without knowing it. The altered gene may also be present in some of the person's other family members (for example brothers or sisters) who are presently healthy.

The closer one's degree of genetic relationship is to a person affected by genetic CJD, the greater one's own genetic risk will also be. This means, for example, that a child, brother or sister of a patient with genetic CJD has a 50% chance (1 in 2) of also carrying the mutation. For a niece or nephew

Figure 1: Risk of genetic CJD decreases with more distant genetic relationship to an affected person.



of the patient this chance is 1 in 4, and for a family member related only by marriage, nearly zero. Almost always, only one of two parents will be a carrier, so that one side of a family will be affected and the other not.

How do I know if genetic CJD is present in our family?

A blood test for genetic CJD is available through the Canadian CJD Surveillance System. An identical test can be done using brain tissue obtained during the autopsy. This test is able to show whether or not a person is carrying a CJD-causing mutation, and can also show whether a known case of CJD is genetic or sporadic. Because a complete analysis of the *PRNP* gene is carried out as part of this test, it can detect any known CJD-causing mutation in the gene. It can also find exceptionally rare mutations that have not been reported previously in any other CJD patient, and may be unique to a particular family.

Many patients with genetic CJD do not have a clear history of similar disease in their family.

If you or an affected family member are suspected to have CJD and are asked to enroll in the CJD Surveillance System, you will also be asked for consent to have the genetic test performed. Genetic counseling is extremely important, both before choosing whether to be tested and after the test results are received. Most genetic tests on CJD patients are negative for the presence of genetic mutations. Therefore, it is also strongly recommended that testing be done on the patient first, *before* undertaking any testing of family members who are presently healthy.

There are three possible results from a test for genetic CJD:

1. **No gene mutation is found.** Most of the time, a person with CJD will not have any abnormalities in the *PRNP* gene. If no mutation is found, then the disease is not considered to be genetically caused. Thus, for the patient's family members there is no more risk of acquiring CJD than there would be for a non-relative of the patient, and further genetic testing is not required or recommended.
2. **A gene mutation is found, of a type known to cause genetic CJD.** If such a mutation is found in a person who has been confirmed by a pathologist to have CJD, then the disease is determined to be genetic CJD. If a pathology examination has not been done, the finding of such a mutation is considered to be the likely cause of the patient`s disease. Other family members could therefore be at risk of developing the same condition. At this point, testing would be made available to family members who wish to know whether they carry the same mutation.
3. **A gene mutation of uncertain significance is found.** As testing for genetic CJD has been carried out on behalf of more families, some individuals with CJD have been found to carry a mutation in the *PRNP* gene that has not been seen previously in other families, or in only very few. In such cases, it may not be certain whether the genetic change is in fact the cause of the affected person's disease. However, often careful assessment of scientific information will help to answer this question.

What else should I know about genetic testing?

The main purpose of the genetic test is to distinguish between genetic and non-genetic forms of CJD, as the presence of a mutation may not be obvious from an affected individual's medical and family history alone. In genetic cases, other family members may have a mutation. These individuals may wish to pursue testing to know if they carry a *PRNP* mutation. Participation in genetic testing is always voluntary.

Genetic counseling is extremely important, so that patients and families can receive guidance from a medical professional. A genetic counselor will ask questions about your family history. They will also discuss in greater depth the issues involved in genetic testing.

The result of the test for genetic CJD does not normally change the approach to caring for the affected patient. Genetic testing is not presently able to help predict how long the illness will last, or when symptoms will appear in a mutation carrier.

Where can I get more information?

Medical genetics specialists (both physicians and counselors) are available in most major health-care centres in Canada. They will ensure that you understand the test results, as well as their interpretation and future implications. This information is useful both for affected individuals and for relatives who may be at risk for genetic CJD. In some cases genetic counseling may also be provided by your family doctor

For any question about the CJDSS consent process for genetic testing please call the CJDSS toll-free at 1-888-489-2999. A healthcare professional will assist you in completing the appropriate consent form, and will provide information on where and when a blood sample can be taken. The CJDSS can also assist you by providing more information on how to contact a genetics specialist in your area.

HELPFUL DEFINITIONS

DNA: The chemical substance that carries genetic instructions in the human body.

Gene: A segment of a *DNA* molecule, which carries coded biological information for the structure of a *protein*.

Genetic counselor: A medical professional who specializes in assisting patients and families who are affected by, or at risk of, a hereditary medical condition. They help patients and families in understanding their situation and the implications of genetic test results.

Mutation: An alteration in the structure of a *gene*, which can cause disease in an individual who carries it.

PRNP: The *gene* that carries the information for the human prion *protein*.

Protein: Any of a large number of different chemical molecules that are made by all living things, and carry out the biological work of cells and tissues. Humans have tens of thousands of different kinds of proteins, each of which is specified by a *gene*.

PrP: The prion protein which causes neurological disease when it becomes abnormal.

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THE SECOND CASE OF VARIANT CJD IN CANADA

In March of 2011, the CJDSS, working closely with Canadian physicians, identified a probable case of variant Creutzfeldt-Jakob disease (vCJD) in a Canadian resident[1]. Variant CJD results mostly from dietary exposure to a similar disease of cattle, bovine spongiform encephalopathy (BSE) that emerged internationally in the 1980s and 1990s. The CJDSS had previously identified only one other case of vCJD[2] (in 2002). Both individuals are believed to have contracted the disease while outside Canada. Evidence also indicates that the most recent case presents no risks for the safety of the Canadian food supply or to the health of Canadians. For more information on the second Canadian case of variant CJD, please refer to the original case report.[1]

Key Article Links

1. Public Health Agency of Canada. Variant Creutzfeldt-Jakob disease in a Canadian resident. Canadian Communicable Disease Report Weekly 2011;4(10). www.phac-aspc.gc.ca/ccdrw-rmtch/2011/ccdrw-rmtcs1011r-eng.php
2. Jansen GH et al. First Canadian Case of Variant Creutzfeldt-Jakob Disease (Variant CJD). Canadian Communicable Disease Report 2003;29(13):117-120. www.phac-aspc.gc.ca/cjd-mcj/vcjd-ca-eng.php

HELPFUL DEFINITIONS

Prion disease – A neurological disease caused by an altered form of the prion protein, *PrP*.

Variant Creutzfeldt-Jakob disease (vCJD) – The human form of Bovine Spongiform Encephalopathy (BSE), a *prion disease* of cattle. Scientists believe that vCJD is contracted after consuming BSE-contaminated food, or through transfusion of blood from a donor with unrecognized vCJD.

YOU ASKED US

This section gives us a chance to answer questions you may have when dealing with CJD. The CJDSS also invites you to contact us directly if you have any questions, comments or concerns – by telephone (toll free) at 1-888-489-2999, or *via* email at CJDSS@phac-aspc.gc.ca.

Q. Do we have to participate in the CJDSS?

A. Participation in the CJDSS is not mandatory. However, for public health purposes the CJDSS is interested in every suspected case of CJD in Canada, and invites participation in the CJDSS by patients and their representatives through a process of voluntary informed consent. Each type of participation (genetic testing, autopsy, interview and medical record review) requires a separate consent form. If you have further questions about the CJDSS, please call 1-888-489-2999.

Q. I have been recently caring for someone with CJD. Am I at risk of catching the disease?

A. No, doctors and scientists who study CJD do not believe you can catch it by caring for someone with the disease. You cannot catch CJD by social or sexual contact either. However, special care is taken during contact with the person during specific kinds of surgery, when handling samples in laboratories, and during an autopsy. Funeral service workers must also take special care when handling a person's remains.

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Q. How long does it take to receive the results of the autopsy?

A. The final autopsy report will be sent to your doctor, usually between 4 and 6 months after the autopsy takes place. The reason for this delay is that the brain tissue needs to be prepared and sometimes transported to another province before it is examined. Your doctor will give you the results as we cannot disclose results over the telephone. If you have additional questions about brain autopsy, you may contact the CJDSS at 1-888-489-2999.

Q. What are my options for receiving the results of a genetic test?

A. If you consent to genetic testing, the CJDSS consent form will present you with two main options for handling the results: you may choose to receive the results from your genetic counselor or doctor as soon as they are available; or you may choose not to receive the results. Please discuss your preference with your genetic counselor or doctor and the CJDSS will handle the result accordingly.

CONSENT FORM FOR DONATION OF BIOLOGICAL MATERIALS

Unused portions of the specimens of blood, brain tissue and cerebrospinal fluid that are received by the CJDSS for laboratory testing are very valuable for research. This research may lead to improved diagnostic tests, better understanding of the causes of CJD, and better ways to deal with public health risks. All participants or their representatives are asked whether or not these specimens may be used in future research, and to sign the Donation of Biological Materials for Research consent form. Please call 1-888-489-2999 if you have not completed this form, or would like more information. The CJDSS is very grateful for your participation.

SUBSCRIPTION INFORMATION

If you wish to continue receiving our newsletter, you may do one of the following:

› Visit our subscription page at www.phac-aspc.gc.ca/hcai-iamss/cjd-mcj/sub-abo-eng.php

If you do not have access to Internet, you may call 1-888-489-2999. If you give us your postal address, a member of our team will make sure you continue to receive our newsletter by regular mail.

CONTACT US

What would you like to see in the next newsletter? Was this newsletter helpful? Please let us know your thoughts or submit questions by contacting us at:

Toll free: 1-888-489-2999
Via email: CJDSS@phac-aspc.gc.ca

Mailing Address:
Canadian Creutzfeldt-Jakob Disease
Surveillance System
Prion Diseases Program
Public Health Agency of Canada
10th Floor, AL: 1910B
200 Églantine Driveway
Ottawa, ON K1A 0K9

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