



# Creutzfeldt-Jakob Disease

U.S. DEPARTMENT OF HEALTH  
AND HUMAN SERVICES  
National Institutes of Health



# Creutzfeldt-Jakob Disease

## What is Creutzfeldt-Jakob disease?

**C**reutzfeldt-Jakob disease (CJD) is a rare, degenerative, fatal brain disorder. It affects about one person in every one million per year worldwide; in the United States there are about 350 cases per year. CJD usually appears in later life and runs a rapid course. Typical onset of symptoms occurs at about age 60, and about 70 percent of individuals die within one year. In the early stages of the disease, people may have failing memory, behavioral changes, lack of coordination, and visual disturbances. As the illness progresses, mental deterioration becomes pronounced and involuntary movements, blindness, weakness of extremities, and coma may occur.

There are three major categories of CJD.

- In *sporadic CJD*, the disease appears even though the person has no known risk factors for the disease. This is by far the most common type of CJD and accounts for at least 85 percent of cases.
- In *hereditary CJD*, the person may have a family history of the disease and test positive for a genetic mutation associated with CJD. About 10 to 15 percent of cases of CJD in the United States are hereditary.

- In *acquired CJD*, the disease is transmitted by exposure to brain or nervous system tissue, usually through certain medical procedures. There is no evidence that CJD is contagious through casual contact with someone who has CJD. Since CJD was first described in 1920, fewer than one percent of cases have been acquired CJD. A type of CJD called *variant CJD* (or vCJD) can be acquired by eating meat from cattle affected by a disease similar to CJD called bovine spongiform encephalopathy (BSE) or, commonly, “mad cow” disease.

CJD belongs to a family of human and animal diseases known as the transmissible spongiform encephalopathies (TSEs) or *prion* diseases. A prion—derived from “protein” and “infectious”—causes CJD in people and TSEs in animals. Spongiform refers to the characteristic appearance of infected brains, which become filled with holes until they resemble sponges when examined under a microscope. CJD is the most common of the known human TSEs. Other human TSEs include kuru, fatal familial insomnia (FFI), and Gerstmann-Straussler-Scheinker disease (GSS). Kuru was identified in people of an isolated tribe who practiced ritual cannibalisms in Papua, New Guinea and has now almost disappeared. Kuru is considered an acquired prion disease. FFI and GSS are extremely rare hereditary diseases, found in just a few families around the world. To date, about 260 cases of vCJD, mostly in the United Kingdom, have been reported related

to consuming beef but none in which the disease was acquired in the U.S. Other TSEs are found in specific kinds of animals. These include BSE, mink encephalopathy, feline encephalopathy, and scrapie, which affects sheep and goats. Chronic wasting disease (CWD) affects elk and deer and is increasingly prevalent in certain areas in the United States. To date no transmission of CWD to humans has been reported.

## **What are the symptoms of the disease?**

**A**lthough sporadic TSE includes five distinct subtypes of sporadic CJD and sporadic fatal insomnia (sFI), overall they are characterized by rapidly progressive dementia. Initially, individuals experience problems with muscle coordination, personality changes (including impaired memory, judgment, and thinking), and impaired vision. People with the disease, especially with FFI, also may experience insomnia, depression, or unusual sensations. As the illness progresses, mental impairment becomes severe. People often develop involuntary muscle jerks called myoclonus, and they may go blind. They eventually lose the ability to move and speak, and enter a coma. Pneumonia and other infections often occur in these individuals and can lead to death.

Variant CJD begins primarily with psychiatric symptoms, affects younger individuals than other types of CJD, and has a longer than usual duration from onset of symptoms to death.

Some symptoms of CJD can be similar to symptoms of other progressive neurological disorders, such as Alzheimer's and Huntington's disease. However, CJD causes unique changes in brain tissue which can be seen at autopsy. It also tends to cause more rapid deterioration of a person's abilities than Alzheimer's disease or most other types of dementia.

## What causes CJD?

**C**urrent scientific consensus maintains that abnormal forms of normal cellular proteins called prions cause CJD in people and TSE in animals. The normal, harmless prion is usually designated PrP<sup>C</sup> (C stands for cellular) and the abnormal, infectious form (which causes the disease) is PrP<sup>Sc</sup> (Sc stands for prototypical prion disease—scrapie).

Proteins are long chains of amino acids that have to fold together into a unique shape or conformation to gain function in the cells. Research findings indicate that the infectious prion originates from a normal protein whose conformation has changed to one that causes the disease. The normal prion protein is found throughout the body but is most abundant in the nervous system. Its overall role is not fully understood. It is believed that the harmless to infectious protein conformational change is common to the all major forms of human prion disease, including CJD. In the acquired form of the disease, the PrP<sup>Sc</sup> comes from the outside the body, for example, through contaminated meat as is seen in vCJD. It then clings to and changes the conformation of the normal prion

protein of the host and progressively spreads in domino-like fashion toward the brain where it causes lesions.

In the hereditary form, infectious prions can arise when a mutation occurs in the gene for the body's normal prion protein. As the mutated PrP<sup>C</sup> replicates itself, it spontaneously changes shape into the infectious form. (Prions themselves do not contain genetic information and do not require genes to reproduce themselves.) If the prion protein gene is altered in a person's sperm or egg cells, the mutation can be transmitted to the person's offspring. Several different mutations in the prion gene have been identified. The particular mutation found in each family affects how frequently the disease appears and what symptoms are most noticeable. However, not all people with mutations in the prion protein gene develop CJD.

In the sporadic form, the infectious prions are believed to be made by an error of the cell machinery that makes proteins and controls their quality. These errors are more likely to occur with aging, which explains the general advanced age at onset of CJD and other prion diseases. Once they are formed, abnormal prion proteins aggregate, or clump together. Investigators think these protein aggregates lead to the nerve cell loss and other brain damage seen in CJD. However, they do not know exactly how this damage occurs.

## How is CJD transmitted?

**C**JD cannot be transmitted through the air or through touching or most other forms of casual contact. Spouses and other household members of people with sporadic CJD have no higher risk of contracting the disease than the general population. However, exposure to brain tissue and spinal cord fluid from infected persons should be avoided to prevent transmission of the disease through these materials.

In some cases, CJD has spread to other people from grafts of dura mater (a tissue that covers the brain), transplanted corneas, implantation of inadequately sterilized electrodes in the brain, and injections of contaminated pituitary growth hormone derived from human pituitary glands taken from cadavers. Doctors call these cases that are linked to medical procedures *iatrogenic* cases. Since 1985, all human growth hormone used in the United States has been synthesized by recombinant DNA procedures, which eliminates the risk of transmitting CJD by this route.

Many people are concerned that it may be possible to transmit CJD through blood and related blood products such as plasma. Some animal studies suggest that contaminated blood and related products may transmit the disease, although this has never been shown in humans. Recent studies suggest that while there may be prions in the blood of individuals with vCJD, this is not the case in individuals with sporadic CJD. Scientists do not know how many abnormal prions a person must



receive before he or she develops CJD, so they do not know whether these fluids are potentially infectious or not. They do know that, even though millions of people receive blood transfusions each year, there are no reported cases of someone contracting sporadic CJD from a transfusion. Even among people with hemophilia (a rare bleeding disorder in which the blood does not clot normally), who sometimes receive blood plasma concentrated from thousands of donors, there are no reported cases of CJD.

While there is no evidence that blood from people with sporadic CJD is infectious, studies have found that infectious prions from BSE and vCJD accumulate in the lymph nodes (which produce white blood cells), the spleen, and the tonsils. At present, four cases of vCJD infection have been identified following transfusion of red blood cells from asymptomatic donors who subsequently died from vCJD. Recently, one case of likely transmission of vCJD infection by concentrates of blood-clotting protein has been reported in an elderly individual with hemophilia in the United Kingdom. The possibility that blood from people with vCJD may be infectious has led to a policy preventing individuals in the United States from donating blood if they have resided for more than three months in a country or countries where BSE is common.

Both brain biopsy and autopsy pose a small, but definite, risk that the surgeon or others who handle the brain tissue may become accidentally infected by self-inoculation.

Special surgical and disinfection procedures can markedly reduce this risk. A fact sheet with guidance on these procedures is available from the National Institute of Neurological Disorders and Stroke (NINDS) (<https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Creutzfeldt-Jakob-Disease-Fact-Sheet-Healthcare>) and the World Health Organization ([http://www.who.int/csr/resources/publications/bse/WHO\\_CDS\\_CSR\\_APH\\_2000\\_3/en/](http://www.who.int/csr/resources/publications/bse/WHO_CDS_CSR_APH_2000_3/en/)).

## How is CJD diagnosed?

**S**everal tests can help diagnose Creutzfeldt-Jakob disease.

- *Electroencephalography* (EEG), which records the brain's electrical pattern, can be particularly valuable because it shows a specific type of abnormality in major but not all types of CJD.
- *Cerebrospinal fluid-based tests*. In April 2015, the National Prion Disease Pathology Surveillance Center began reporting a new diagnostic test for human prion diseases, called second generation Real Time-Quaking-Induced Conversion (RT-QuIC). RT-QuIC is based on an ultrasensitive detection of the pathogenic prion protein in the cerebrospinal fluid of individuals affected by CJD and other forms of human prion diseases. This new advanced test demonstrates a very high sensitivity and specificity of the disease. RT-QuIC differs from traditional surrogate markers of prion disease—14-3-3 and tau proteins—in that it detects directly

a disease-defining pathogenic prion protein as opposed to a surrogate marker of rapid neurodegeneration. Detection of these traditional surrogate marker proteins is accurate in approximately three-fourths of cases.

- *Magnetic resonance imaging* (MRI) has recently been found to be accurate in about 90 percent of cases.

The only way to confirm a diagnosis of CJD is by *brain biopsy* or *autopsy*. In a brain biopsy, a neurosurgeon removes a small piece of tissue from the person's brain so that it can be examined by a neuropathologist. This procedure may be dangerous for the individual, and the operation does not always obtain tissue from the affected part of the brain. Because a correct diagnosis of CJD does not help the individual, a brain biopsy is discouraged unless it is needed to rule out a treatable disorder. In an autopsy, the whole brain is examined after death.

## How is the disease treated?

**C**urrently, there is no treatment that can cure or control CJD, although studies of a variety of drugs are now in progress. Current treatment for CJD is aimed at easing symptoms and making the person as comfortable as possible. Opiate drugs can help relieve pain if it occurs, and the drugs clonazepam and sodium valproate may help relieve myoclonus. During later stages of the disease, intravenous fluids and artificial feeding also may be used.

## How can people avoid spreading the disease?

**T**o reduce the already very low risk of CJD transmission from one person to another, people should never donate blood, tissues, or organs if they have suspected or confirmed CJD, or if they are at increased risk because of a family history of the disease, a dura mater graft, or other factor.

Normal sterilization procedures such as cooking, washing, and boiling do not destroy prions. Although there is no evidence that caregivers, healthcare workers, and those who prepare bodies for funerals and cremation have increased risk of prion diseases when compared to general population, they should take the following precautions when they are working with a person with CJD:

- Cover cuts and abrasions with waterproof dressings.
- Wear surgical gloves when handling the person's tissues and fluids or dressing any wounds.
- Avoid cutting or sticking themselves with instruments contaminated by the person's blood or other tissues.
- Use disposable bedclothes and other cloth for contact with the person. If disposable materials are not available, regular cloth should be soaked in undiluted chlorine bleach for an hour or more, and then washed in a normal fashion after each use.

- Use face protection if there is a risk of splashing contaminated material such as blood or cerebrospinal fluid.
- Soak instruments that have come in contact with the person in undiluted chlorine bleach for an hour or more, then use an autoclave (pressure cooker) to sterilize them in distilled water for at least one hour at 132 - 134 degrees Celsius.

## What research is taking place?

**T**he mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge of the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. The NINDS is a component of the National Institutes of Health (NIH), the leading supporter of biomedical research in the world.

Other NIH Institutes, including the National Institute of Allergy and Infectious Diseases and the National Institute on Aging, also conduct research on CJD.

Researchers are examining and characterizing the prions associated with CJD and other human and animal prion diseases and trying to discover factors that influence prion infectivity and transmission, and how the disorder damages the brain. For example, researchers are investigating the cellular mechanisms involved in abnormal prion formation and accumulation, as well as their replication by select cellular subsets in the brain. Other projects are

examining how abnormal prions cross the protective blood-brain barrier and spread throughout the central nervous system, and tests that measure the biological activity of prions. Findings may identify new therapeutic targets to treat prion diseases.

More information about CJD research supported by NINDS and other NIH Institutes and Centers can be found using NIH RePORTER (<http://projectreporter.nih.gov>), a searchable database of current and past research projects supported by NIH and other federal agencies. RePORTER also includes links to publications and resources from these projects.

## How can I help research?

**S**cientists are conducting biochemical analyses of brain tissue, blood, spinal fluid, urine, and serum in the hope of determining the nature of the transmissible agent or agents causing CJD. To help with this research, they are seeking biopsy and autopsy tissue, blood, and cerebrospinal fluid from individuals with CJD and related diseases. The following investigators have expressed an interest in receiving such material:

Dr. Brian Appleby, Director  
National Prion Disease Pathology  
Surveillance Center  
Case Western Reserve University  
2085 Adelbert Road, Room 419  
Cleveland, OH 44106  
216-368-0587  
<http://case.edu/med/pathology/centers/npdpssc/>

Dr. Laura Manuelidis  
Yale University School of Medicine  
Section of Neuropathology  
310 Cedar Street  
New Haven, CT 06510  
203-785-4442

## Where can I get more information?

**F**or more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

### **BRAIN**

P.O. Box 5801  
Bethesda, MD 20824  
800-352-9424  
[www.ninds.nih.gov](http://www.ninds.nih.gov)

The following organizations can provide information and support for people and families affected by Creutzfeldt-Jakob disease:

### **National Institute of Allergy and Infectious Diseases**

Office of Communications and  
Government Relations  
6610 Rockledge Drive, MSC 6612  
Bethesda, MD 20892-6612  
866-284-4107  
[www.niaid.nih.gov](http://www.niaid.nih.gov)

**National Institute on Aging  
Alzheimer's Disease Education and  
Referral Center**

P.O. Box 8250

Silver Spring, MD 20907-8250

800-438-4380

[www.nia.nih.gov/alzheimers](http://www.nia.nih.gov/alzheimers)

**Creutzfeldt-Jakob (CJD) Foundation**

3610 W. Market Street, Suite 110

Akron, OH 44333

800-659-1991

[www.cjdfoundation.org](http://www.cjdfoundation.org)

**National Prion Disease Pathology  
Surveillance Center**

Case Western Reserve University

Institute of Pathology Building, Room 419

2085 Adelbert Road

Cleveland, OH 44106-4907

216-368-0587

<http://case.edu/med/pathology/centers/npdpssc/>

**National Organization for Rare Disorders**

55 Kenosia Avenue

Danbury, CT 06813-1968

203-744-0100

800-999-6673 (voicemail only)

[www.rarediseases.org](http://www.rarediseases.org)

**Alzheimer's Association**

255 N. Michigan Avenue, Floor 17

Chicago, IL 60601-7633

312-335-8700

800-272-3900

[www.alz.org](http://www.alz.org)



## **Centers for Disease Control and Prevention**

Office of Public Inquiries

1600 Clifton Road, NE

Atlanta, GA 30333

404-639-3311

800-232-4636

[www.cdc.gov](http://www.cdc.gov)

## **Genetics Home Reference**

<https://ghr.nlm.nih.gov/condition/prion-disease>

To learn more about steps taken to ensure the safety of beef and other agricultural products in the United States, contact:

## **United States Department of Agriculture (USDA)**

National Agricultural Library

10301 Baltimore Avenue

Beltsville, MD 20705-2351

301-504-5755

[www.nal.usda.gov](http://www.nal.usda.gov)

For information on the safety of medical products and procedures, contact:

## **U.S. Food and Drug Administration**

10903 New Hampshire Avenue

Silver Spring, MD 20993

888-INFO-FDA (1-888-463-6332)

[www.fda.gov](http://www.fda.gov)







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