

Creutzfeldt-Jakob disease (CJD)

A topic in the Alzheimer's Association® series on understanding dementia.

Dementia is a condition in which a person has significant difficulty with daily functioning because of problems with thinking and memory. Dementia is not a single disease. It's an overall term — like heart disease — that covers a wide range of specific medical conditions, including Alzheimer's disease. Disorders grouped under the general term “dementia” are caused by abnormal brain changes. These changes trigger a decline in thinking skills severe enough to impair daily life and independent function. They also affect behavior, feelings and relationships.

Brain changes that cause dementia may be temporary, but they are most often permanent and worsen over time, leading to increasing disability and a shortened life span. Survival can vary widely, depending on such factors as the cause of the dementia, age at diagnosis and coexisting health conditions.

Creutzfeldt-Jakob disease (CJD)

Creutzfeldt-Jakob disease (CROYZ-felt YAH-cob) is the most common human form of a group of rare, fatal brain disorders affecting humans and certain other mammals. These disorders are known as prion (PREE-awn) diseases. They occur when prion protein, which is found throughout the brain and body but whose normal function isn't yet known, begins folding into an abnormal three-dimensional shape. This shape change gradually triggers prion protein in the brain to fold into the same abnormal shape.

Through a process scientists don't yet understand, misfolded prion protein destroys brain cells. The damage leads to rapid decline in thinking and reasoning, as well as involuntary muscle movements, confusion, difficulty walking and mood changes. CJD causes a type of dementia that worsens unusually fast. More common causes of dementia, such as Alzheimer's disease, dementia with Lewy bodies and frontotemporal dementia, typically progress more slowly.

An especially rare form of CJD can sometimes be transmitted like an infection from one person to another, from one animal to another or from certain animals to people. As a result of this infectious capability, prion diseases are also known as “transmissible spongiform encephalopathies.”

Many scientists suspect that some molecular processes driving abnormal protein folding in rare prion diseases may also play a role in more common disorders involving brain protein abnormalities, including Alzheimer's disease.

Prevalence

CJD is rare, occurring in about one in 1 million people annually worldwide. In the United States, this translates to about 350 new cases each year.

Experts generally recognize the following main types of CJD:

- **Sporadic CJD** develops spontaneously for no known reason. It accounts for 85% of cases. On average, sporadic CJD first appears between ages 60 and 65.
- **Familial CJD** is caused by certain changes in the chromosome 20 gene coding the biological blueprint for prion protein. People who develop familial CJD do so because they inherited the genetic changes from a parent. Familial CJD accounts for about 10% to 15% of cases. It develops, on average, at a younger age than sporadic CJD, with some genetic types appearing as early as ages 20 to 40.
- **Acquired CJD** results from exposure to an external source of abnormal prion protein. These sources are estimated to account for about 1% of CJD cases. The two most common outside sources are:

1. **Medical procedures** involving instruments used in neurosurgery, growth hormone from human sources or certain transplanted human tissues, including corneas (the clear outer covering of the eye) and dura mater (the fibrous membrane covering the brain and spinal cord). This type of acquired CJD is also known as iatrogenic CJD (iCJD). The risk of iCJD from medical procedures has been greatly reduced by improved neurosurgical instruments sterilization techniques, new single-use instruments and synthetic sources of growth hormone and dura mater.
2. **Meat or other products from cattle infected with bovine spongiform encephalopathy (BVE) or “mad cow disease”**, recognized in the mid-1990s as the cause of variant CJD (vCJD). Scientists traced this new type of CJD to consumption of beef from cattle whose feed included processed brain tissue from other animals. Since then, experts have diagnosed about 200 cases of vCJD, primarily in the United Kingdom and other European countries. Variant CJD tends to occur at a younger age than sporadic or familial forms, sometimes even in teenagers. New cases of vCJD have slowed

significantly, most likely due to changes in animal feeding practices.

Symptoms

The pattern of symptoms can vary depending on the type of CJD, and specific CJD symptoms experienced by an individual and the order in which they appear can differ significantly. Common neurological and psychological symptoms include:

- Depression.
- Agitation, apathy and mood swings.
- Rapidly worsening confusion.
- Disorientation.
- Problems with memory, thinking, planning and judgment.
- Difficulty walking.
- Muscle stiffness, twitches and involuntary jerky movements.
- Vision problems, such as double vision and hallucinations

Diagnosis

There is no single test — or any combination of tests — that can conclusively diagnose sporadic CJD in a living person. Rapid symptom progression is one of the most important clues that a person may have CJD. The following tests may help determine whether an individual has CJD, especially if more than one test result is consistent with CJD:

- **Electroencephalogram (EEG)**, which measures the brain's patterns of electrical activity similar to the way an electrocardiogram (ECG) measures the heart's electrical activity.
- **Brain magnetic resonance imaging (MRI)**, which can detect certain brain changes consistent with CJD.
- **Lumbar puncture (spinal tap)** to test cerebrospinal fluid (CSF) for the presence of certain proteins. CSF diagnostics include:
 - Real-time quaking induced conversion (RT-QuIC): RT-QuIC can detect the actual prions in the spinal fluid and is 98.5% diagnostic for prion disease.
 - 14-3-3: A marker of neurodegeneration or brain damage.
 - Tau: A marker of neurodegeneration or brain damage.
- **Protein misfolding cyclic amplification (PMCA)**: PMCA is an amplification technique for the detection of misfolded protein aggregates.

Causes and risk factors

Sporadic CJD has no known cause. Most scientists believe the disease begins when prion protein somewhere in the brain spontaneously misfolds, triggering a “domino effect” that misfolds prion protein throughout the brain. Genetic variation in the prion

protein gene at a location called “codon 129” may increase risk of this spontaneous misfolding.

Variation at codon 129 in the prion protein gene may also play a role in making people susceptible to acquired CJD from external sources. Scientists don't yet know why acquired CJD seems to be transmitted through such a limited number of external sources. Researchers have found no evidence that the abnormal protein is commonly transmitted through sexual activity or blood transfusions, although a few cases of vCJD seem to have been spread through blood transfusions. Professionals who regularly encounter blood from a human or animal, such as surgeons, pathologists or butchers, have not been shown to have a higher-than-normal risk through occupational exposure.

Familial CJD is caused by variations in the prion protein gene that increase the likelihood an individual will develop CJD. Researchers have identified more than 50 prion protein mutations in those with inherited CJD. Genetic testing can determine whether family members at risk have inherited a CJD-causing mutation. Experts strongly recommend professional genetic counseling both before and after genetic testing for hereditary CJD.

Age has an influence on sporadic CJD, which tends to develop later in life, usually around age 60. Onset of familial CJD occurs slightly earlier and vCJD has affected people at a much younger age, usually in their late 20s.

Chronic wasting disease is a prion disease similar to mad cow disease that's been found in wild deer, elk and moose in certain U.S. states, Canadian provinces, Korea and Norway. According to the U.S. Centers for Disease Control and Prevention (CDC), there's no evidence to date that chronic wasting disease has been transmitted to humans, including hunters who eat meat from affected animals. There's also no evidence that rates of CJD have increased in states or provinces where chronic wasting disease has been identified. Additional studies are under way to understand what risk, if any, chronic wasting disease poses to humans. The CDC recommends that hunters who plan to eat meat from deer, elk or moose in areas where chronic wasting disease occurs consider having the meat tested by their local state wildlife agency. The CDC also recommends wearing gloves while field dressing these animals to avoid handling the brain or spinal column.

Outcomes

CJD progresses rapidly and is fatal. Those affected lose their ability to move or speak and require full-time care to meet their daily needs. An estimated 70% of those diagnosed with CJD die within one year. Those affected by familial CJD tend to develop the disorder at an earlier age and survive somewhat longer than those with the sporadic form, as do those diagnosed with vCJD. Scientists have not yet learned the reason for these differences in survival.

Treatment

There is no treatment to slow or stop the underlying brain cell destruction caused by CJD and other prion diseases. Various drugs have been tested but have not shown any benefit. Clinical studies of potential CJD treatments are complicated by the rarity of the disease and its rapid progression.

Current therapies focus on treating symptoms and supporting individuals and families coping with CJD. Doctors may prescribe painkillers such as opiates to treat pain if it occurs. Muscle stiffness and twitching may be treated with muscle-relaxing medications or antiseizure drugs. In the later stages of the disease, individuals with CJD become completely dependent on others for their daily needs and comfort.

Additional resources

Creutzfeldt-Jakob Disease Foundation, Inc.

cjd.foundation.org

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