

# **Creutzfeldt-Jakob Disease** **and other Prion Diseases**



**Creutzfeldt-Jakob Disease**  
*Foundation, Inc.*

The CJD Foundation HelpLine  
1.800.659.1991  
[help@cjd.foundation.org](mailto:help@cjd.foundation.org)  
[www.cjd.foundation.org](http://www.cjd.foundation.org)

**The CJD Foundation  
Toll-Free HelpLine  
1-800-659-1991  
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www.cjd.foundation.org**

The Creutzfeldt-Jakob Disease Foundation, Inc. (CJDF), a non-profit 501(c)(3), has established a HelpLine at **1.800.659.1991** or **help@cjd.foundation.org**. The HelpLine's toll-free number is answered Monday – Friday, 9:00 am – 5:00 pm ET. Messages left on the CJDF's voicemail after hours concerning patients will be returned evenings and weekends.

Patients, family members, medical professionals, funeral directors, embalmers and others are encouraged to call or email with questions about:

- Suspected or confirmed CJD diagnosis
- Patient care
- Hospice care
- Family support
- Physician referrals
- Autopsy
- Research
- Surveillance
- Funeral arrangements
- Participation in the CJDF's questionnaire
- The CJDF's educational DVDs for medical and funeral professionals
- Political and public advocacy
- Donations
- General CJD information

The CJD Foundation has produced the following DVDs:

- *Confronting CJD and other Prion Diseases*
- *CJD Infection Control and Patient Care for Health Care Professionals*
- *CJD Information for Funeral Directors and Embalmers*

The CJD Foundation's DVDs are available for medical and funeral professionals at no cost. To request a copy, please contact the CJD Foundation at **1.800.659.1991** or **help@cjd.foundation.org**.

Please visit our website for additional information on Creutzfeldt - Jakob Disease and the CJD Foundation: **www.cjd.foundation.org**

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## Who We Are

### History and Mission

The Creutzfeldt-Jakob Disease Foundation, Inc. (CJDF), a registered 501(c)(3) non-profit organization, was established in Miami, Florida in 1993 by two women who had lost loved ones to CJD. Mayra Lichter and Cecile Sardo established the CJDF's firm commitment to reach out to families affected by this terrible disease. In 2001, Ana Betro, Monica Curtis, Ruthie George and Florence Kranitz created a CJD task force in Akron, Ohio to work closely with the CJDF. In 2002, the task force was asked to assume the reigns of the Foundation. The CJDF moved to Akron, Ohio where it remains today.

#### **The CJDF's mission is to:**

- Provide education and support to families affected by CJD
- Educate affected families and the community at large about CJD and the care of CJD patients
- Advocate for continued and increased research funds aimed at finding a treatment and eventually a cure for CJD

#### **Services We Provide:**

- HelpLine support and education to families, caregivers, healthcare professionals, funeral directors and embalmers and the general public
- Physician referrals
- Autopsy information
- Medical education
- Comprehensive educational materials about CJD
- Information about providing quality care for those suffering from CJD
- Annual CJD Foundation Family Conference in Washington, DC
- Educational DVDs for healthcare and funeral professionals
- Political and public advocacy
- Website: **[www.cjdfoundation.org](http://www.cjdfoundation.org)**

### **The CJD International Support Alliance (CJDISA)**

The CJDISA, co-founded by the CJDF, was formed in 2006 and includes a group of grassroots non-profit organizations that share one vital factor: a commitment to prion disease victims, their families and those at risk for prion disease. The CJDISA was formed to fill the gap that exists on an international level and to assure excellence in service to individuals affected by or at risk of a prion disease, their families and caregivers. The participating organizations collaborate on educational initiatives, information dissemination, resource allocation, program design and implementation and advocacy. The CJDISA speaks with one voice in support of all issues of concern regarding prion diseases around the world. As of May 2009, the CJDISA membership includes the following organizations: The CJD Foundation (U.S.), CJD Insight (U.S.), CJD Support Group Network (Australia), CJD Alliance (U.K.), CJD Support Network (U.K.), Associazione Italiana Encefalopatie da Prioni (Italy), and CJD Support Network (Japan).

### **The CJD Foundation's HelpLine Statistics, 2008**

|                     |               |                  |            |
|---------------------|---------------|------------------|------------|
| New Cases Reported: | <b>289</b>    | Deaths Reported: | <b>209</b> |
| Help Line Calls:    | <b>1,379</b>  | Emails:          | <b>727</b> |
| Website Visitors:   | <b>81,643</b> |                  |            |

*Note: Not all new cases and deaths reported are confirmed by autopsy*

For current HelpLine statistics, please visit our website: **[www.cjdfoundation.org](http://www.cjdfoundation.org)**

## Introduction

Prion diseases are a group of rare, invariably fatal brain diseases that occur both in humans and animals. They first came to wide public attention in the mid-1980s when the epidemic of bovine spongiform encephalopathy (BSE), a prion disease of cattle, arose in the United Kingdom (U.K.). It is now believed that BSE may have appeared spontaneously in British cattle sometime in the early 1970s. Tissue from infected animals may have contaminated cattle feed, leading to the silent spread of the BSE epidemic. There is also a theory that BSE came from feed contaminated with scrapie, the long established sheep prion disease. Inevitably, concern over whether BSE could pass to humans mounted.

In humans, the best known prion disease is Creutzfeldt-Jakob Disease (CJD), first documented in 1920 by two German doctors, Hans Gerhard Creutzfeldt (1885-1964) and Alfons Maria Jakob (1884-1931). CJD reportedly affects approximately one person per million per population each year worldwide. In the United States (U.S.), this translates to approximately 300 new cases annually. It is well known that CJD is very difficult to diagnose, leading to speculation that the one case per million statistics may be incorrect. Most of the cases are sporadic CJD (sCJD), occurring for no, as of yet, proven reason. The sporadic form accounts for approximately 85% of the cases. The familial form of CJD (fCJD) is associated with a genetic mutation that is passed on from parent to child. fCJD accounts for approximately 10-15% of the cases. The third type of CJD is acquired by infection from an outside source; there are at least three types of acquired CJD:

1. Kuru – Acquired through cannibalism
2. Iatrogenic CJD (iCJD) – Acquired through contaminated surgical instruments or tissue transplants
3. Variant CJD (vCJD) – Exposure to BSE contaminated meat

The main indications leading to a possible diagnosis of CJD are rapid dementia and one or many of a range of neurological symptoms including unsteady gait, hallucinations and sudden jerking movements. The brains of people and animals infected with a prion disease show characteristic damage known as spongiform changes. When seen under a microscope, the brain tissue shows many tiny holes almost like a sponge. For this reason, prion disease is known as spongiform encephalopathy, although the term prion disease is preferred.

Most prion diseases are transmissible in the laboratory, although the infectious agent is not a conventional bacterium or virus. Instead, the infectivity is associated with an abnormal protein or prion. Because prions are so unusual and prion diseases are unique in that they can both be inherited and transmitted, the area has attracted enormous scientific and medical interest. This provides a ray of hope that all of this attention may one day lead to a cure.<sup>1</sup>

## Human Prion Diseases

| FORM  | CAUSE   | DISTINGUISHING FEATURES   |
|---|---|---|
| <b>Sporadic CJD (sCJD)</b>  | Unknown   | Affects mainly people over the age of 60. Common symptoms include ataxia and dementia. Short course. Upon tissue examination there is spongiform change, but plaques are rarely present.  |
| <b>Sporadic Fatal Insomnia (sFI)</b>  | Unknown   | Has clinical and histopathologic features indistinguishable from those of FFI, but does not have the mutation on the prion gene that characterizes FFI. <sup>2</sup>  |
| <b>Inherited Prion Diseases</b><br>- Familial CJD (fCJD)<br>- Gerstmann-Straussler-Scheinker Disease (GSS)<br>- Fatal Familial Insomnia (FFI) | Inherited mutation in PrP gene  | Often younger onset than sCJD. Symptom pattern depends on type of mutation, but can be similar to sporadic. Course of illness is usually longer.  |
| <b>Acquired CJD</b><br>-latrogenic CJD (iCJD)   | Contamination through brain surgery, corneal transplant, dura mater graft or growth hormone | Age at onset depends on the age at exposure and on the incubation time. Clinical and pathological features are often indistinguishable from sCJD. Growth hormone cases show plaques.  |
| -Variant CJD (vCJD)   | Exposure to BSE through consumption of infected beef or blood or plasma transfusion         | With exposure to BSE, younger onset and longer duration than sporadic CJD. Psychiatric symptoms often seen at disease presentation. Distinctive “daisy” plaques upon tissue examination. For blood or plasma transfusion, age at onset depends on the time of exposure. |

A new type of prion disease, called protease-sensitive prionopathy or PSPr, has been recently reported. The age at onset is similar to that of sporadic CJD but the duration is longer. Clinically, PSPr is different from CJD and often is misdiagnosed as atypical dementia. Pathologically, PSPr is similar to CJD but the characteristics of the abnormal prion protein associated with PSPr are distinctly different and allow for the definitive diagnosis of PSPr on Western blot. To date (May 2009), PSPr has not been experimentally transmitted.<sup>2</sup>

## More About Prions...

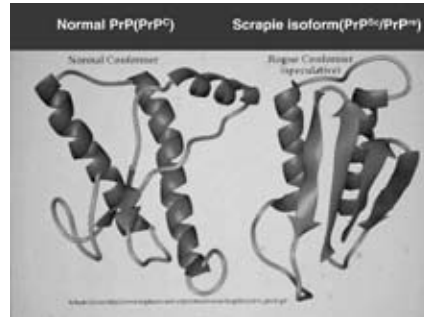
### Prions are Different from Bacteria and Viruses

The discovery that prion diseases were transmissible led researchers to the natural conclusion that the infective agent had to be a bacterium or a virus. When, however, infectious tissue remained transmissible after treatment with both heat (which destroys most bacteria) and ultraviolet light (which should inactivate a virus), it was concluded some other kind of infectious agent was responsible. In 1982, neurologist Stanley Prusiner of the University of California at San Francisco, provided the first direct evidence that the infectious agent was a protein. The word 'prion' comes from proteinaceous infectious particle. The idea, originally put forward by the British investigators Griffith and Patterson, was highly unusual and even heretical at first, although it has slowly gained acceptance over the years.

### Abnormal Prions are Infectious Proteins

Proteins are essential to life. They are molecules made up of thousands of smaller chemical units called amino acids, joined together like beads on a necklace. Once formed in a living cell, a protein molecule folds into a curl. Protein molecules are fairly flexible and can adopt a number of subtly different shapes.

The prion protein, PrP, can exist in two forms: normal and abnormal. For convenience, these are written PrP<sup>C</sup> (normal) and PrP<sup>Sc</sup> (abnormal). The normal form exists in the human brain and in other parts of the body. It is also found in many other mammals and even in birds, however, its function is unknown. Genetic modification can produce seemingly healthy laboratory mice which do not have PrP<sup>C</sup>, suggesting that it is not essential to life.

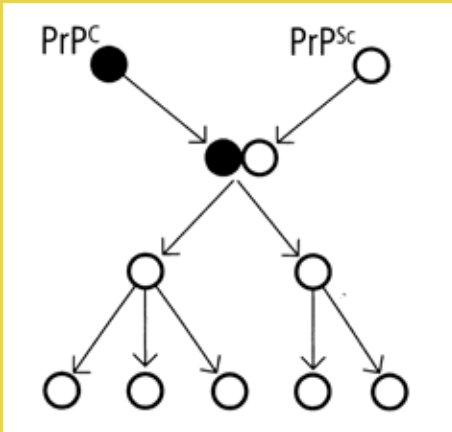


*A computer model of the structure of a prion molecule. Such models give useful insights into the pathology of CJD and may point to potential treatments.<sup>3</sup>*

### The Strange Behavior of Abnormal Prions

The abnormal form of a protein has unusual properties. First, unlike a normal protein, it is not broken down by enzymes. It also forms tiny fibers called scrapie associated fibrils (SAFs) in the test tube. Tissue that forms many SAFs have been noted to frequently be the most infectious. The SAFs often clump together to form a chemical structure called amyloid. In some cases of CJD and other prion diseases, amyloid deposits, known as plaques, are found in the brain during autopsy examination under the microscope. Plaques are also found in other non-prion diseases such as Alzheimer's Disease and in aging brains, although the plaques in these cases are not made of prions.

3 - Photo courtesy of Fred E. Cohen, MD, Dept. of Cellular & Molecular Pharmacology, University of California at San Francisco



*Conversion of a PrP<sup>C</sup> molecule to PrP<sup>Sc</sup>, leading to a cascade of PrP<sup>Sc</sup>, and eventually brain damage.*

### **Ways in Which Abnormal Proteins are Transmitted**

Dr. Stanley Prusiner's idea is that a single molecule of PrP<sup>Sc</sup> can convert molecules of PrP<sup>C</sup> into the abnormal form. These newly converted molecules can in turn "corrupt" more normal molecules leading to a cascade effect which would eventually cause brain damage.

It may be that once in a while a molecule of PrP<sup>C</sup> spontaneously converts into the abnormal form setting the scene for sporadic CJD, which would explain the relatively low worldwide annual incidence of sporadic CJD: one person per million per population.

In familial CJD, it is known that there are mutations in the PrP gene which are inherited from one parent. These mutations may produce forms of the PrP molecule which are unstable and likely to spontaneously convert into the abnormal form. In CJD acquired by transmission (iatrogenic and variant), PrP<sup>Sc</sup> molecules enter the body from an infected source and set about corrupting the normal PrP of their "host."



# Sporadic CJD

Sporadic means “occurring here and there” and that no major risk factors have been discovered.

Sporadic CJD is subdivided into five subtypes, some of which have different ages at onset, duration and clinical presentation. The typical subtype, which accounts for over 50% of all prion diseases, generally presents over the age of 60 years old. The incidence of sporadic CJD worldwide is around one case per million per population. The incidence of sporadic CJD does not seem to be significantly higher in countries where BSE and scrapie are common than it is in countries free of these diseases. Therefore, based on the present evidence, a link between animal prion diseases and sporadic CJD seems unlikely.

Figure 1

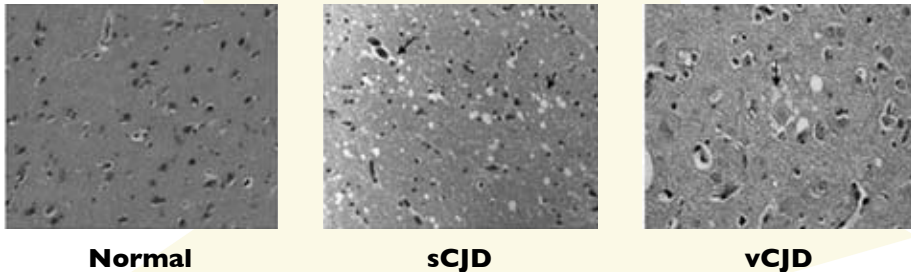


Figure 1. Microphotographs comparing normal brain tissue, brain from a subject with sporadic CJD-MM1 (sCJD), and from variant CJD (vCJD). Note the fine spongiform degeneration that is evenly distributed in sCJD (some of the vacuoles are identified by arrows) and mostly clustered around a plaque in vCJD (arrowheads). The plaques surrounded by vacuoles are commonly referred to as “florid” or “daisy” plaques and are the hallmark of vCJD.

Figure 2



Figure 2. Immunohistochemical staining of the prion protein (PrP) in the same brain tissues. With the procedures used, there is no PrP staining in the normal brain. In contrast, sCJD-MM1 shows a fine “synaptic” staining (brown color) indicating a fairly even distribution of scrapie PrP. In vCJD, the staining is unevenly distributed and forms areas of intense staining, especially in the plaques (arrowheads).

## **What are the Symptoms of Sporadic CJD?**

Sporadic CJD usually comes “out of the blue,” although the pattern of symptoms may vary from person to person.

- In the “typical” subtype of sporadic CJD (sCJD M/M 1), early symptoms are often like those of depression, mood swings, memory lapses, social withdrawal and lack of interest. However, rapid progression to dementia and obvious neurological symptoms distinguish CJD from depression.
- Within weeks, the patient may become unsteady on their feet, lacking in coordination and markedly clumsy. This pattern of symptoms is clinically known as cerebellar ataxia because it is caused by damage to the cerebellum, the part of the brain which controls movement. In some people, these are the first symptoms.
- Later symptoms may include blurred vision, hallucinations, blindness, rigidity in the limbs, sudden jerking movements and incontinence.
- Speech may become more difficult or slurred. Swallowing may become difficult.
- Eventually, the patient loses the ability to move or speak and will require full time nursing care. In this state, clinically known as akinetic mutism, the patient may appear to be following what is going on around them, but in fact they may not be aware of their surroundings.

*Most patients die within a few months of onset of symptoms, some within a few weeks. Other subtypes can linger for several years.*

*In some subtypes, the first clinical signs may affect movements, often resulting in unsteady gait rather than dementia.*

## Familial CJD

Approximately 10-15% of all cases of CJD account for familial CJD. In the familial form of CJD, there is a mutation in the PrP gene that makes the conversion into the abnormal form likely. Over 50 different mutations in the gene that encodes the prion protein are known. The translated portion of the gene has 253 codons and mutations may occur in many different regions. The most common mutations are at codons 102, 178, 200, and 210. Other mutations have been observed only in one or two families.

All of the mutations are inherited in an autosomal dominant pattern. Therefore, if one parent carries the mutation there is a 50-50 chance for each child to inherit the mutation. The presence of a mutation in only one allele is sufficient to cause the disease. If a family consisted of 100 children, half of them would carry the mutation and half of them would not. In the more realistic situation of families with smaller numbers of children, the proportion that inherits the mutation may not reflect these statistical odds: one, two or three of four children may be found to be mutation-positive.

Since CJD does not usually strike until later in life, people carrying the gene may not realize that they possibly passed it on to their children, although they may well be aware of a problem with neurological disease within the family. However, since CJD was recognized only relatively recently as a disease in its own right, some family members in years past may have been wrongly diagnosed. Their condition may have been thought to be a psychiatric illness, Parkinson's Disease, or some other neurological disease such as Alzheimer's Disease or Huntington's Chorea.

People with a relative who has or had CJD can be genetically tested for the CJD mutation. Genetic testing can be easily accomplished from a small sample of blood, but the choice of learning the result is a very individual matter and should never be made without the involvement of a knowledgeable genetic counselor and serious thought about the consequences. For example, it might be assumed that getting a negative test result would be cause for great relief and happiness, but it may also be cause for intense guilt: how is it that I escaped and my sister did not?<sup>4</sup>

*Familial CJD means "occurring in families." Some families have a mutated gene which makes the development of abnormal prion protein more likely.*

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

*Deana Simpson, RN is the Founder and Director of CJD Insight, a website that provides information and support to those affected by familial CJD.*

*If you would like to contact Ms. Simpson, please see her contact information in the back of the pamphlet.*

## Prevention and Therapy

Familial CJD could, in principle, be eradicated in a single generation by the use of prenatal genetic testing of the fetus and therapeutic abortion. This extremely sensitive issue is a matter of individual choice based on ethical and religious considerations and will certainly never be accepted by all families with inherited disease. Another therapeutic approach that would probably be met with much less resistance is genetic engineering to neutralize the gene that encodes the prion protein, which we know to be essential to the development of the disease. However, the technical difficulties of genetic engineering have so far impeded this strategy in all inherited human diseases, including CJD. When these difficulties are solved, familial CJD may be the first kind of CJD to be successfully treated.<sup>5</sup>

### What are the Symptoms of Familial CJD?

The symptoms of familial CJD vary depending on the type of mutation involved. There may even be great variation in the symptoms within affected members of the same family. Often familial CJD strikes at an earlier age than the sporadic form.

*Symptoms may include but are not limited to:*

- Initially depression, bizarre or uncharacteristic behavior and memory lapses
- Fatigue and visual disturbances
- Within weeks, unsteadiness (gait ataxia) and lack of coordination (cerebellar ataxia)
- Difficulties with speech and/or swallowing
- Sudden jerking movements (myoclonus), rigid limbs, possible blindness and incontinence

# Iatrogenic CJD

The first indication that human prion diseases might be transmissible through infected tissue came with the discovery of a strange disease called kuru among the Fore Tribe in Papua, New Guinea in the 1950s. Kuru mainly affected women and children and was similar to CJD except that ataxia was the predominant symptom and dementia was rare. The brains of these patients showed severe damage to the cerebellum, the part of the brain which controls movement, along with the spongiform change, which is a characteristic of prion disease. A further feature was the appearance of deposits called plaques within the brain tissue; this distinguished kuru from CJD, where plaques only occur in a minority of cases.

Kuru was eventually linked to the cannibalistic funeral practices of the Fore people in which it was common for the women and children to eat raw brain and other internal organs while men ate mostly skeletal muscle, which we now know is much less infectious. Since the victims of kuru continued to be given these funeral rites, the disease perpetuated itself.

The incubation time for kuru is between three and 40 years. When the Fore people stopped these funeral rites and the country was taken over by Australia, the number of new cases went down dramatically, but there is still the occasional case occurring in an older person in whom the disease has had a very long incubation period. Kuru has been of great importance in helping understand human prion diseases, in particular the risks of transmission from person to person. Brain tissue from a person with CJD contains prions. If the abnormal PrP from a CJD-affected person comes in contact with the normal PrP of the body of an uninfected person, the latter can change into the abnormal form and thereby transmit the disease.

Some medical procedures carry a risk of transmitting CJD. For instance, some people have contracted CJD from brain surgeries performed with instruments which were previously used on a CJD patient. In these cases, the infection was delivered intracerebrally, that is, directly into the brain. The prion agent survives the normal disinfection procedures which would normally destroy bacteria and viruses, but this was not known at the time. Now, instruments which have been used on the brain of someone with suspected CJD are destroyed.

Intracerebral transmission of CJD has also occurred with corneal transplants and grafts of dura mater, the rough membrane which covers the brain and is used in various types of surgery. The incubation time for intracerebral iatrogenic CJD is 19-46 months.

Iatrogenic means “caused by medical treatment,” but more generally this form of CJD is mostly due to transmission by direct contact with infected tissue from someone with the disease.

CJD has also been transmitted by treatment with human growth hormone. This is known as peripheral transmission because the route to the brain of the infective agent is through the body, not directly into the brain. Human growth hormone, which is used to treat children with short stature, used to be prepared from human pituitary glands, its natural source. Typically 2,000 glands would be pooled to make one batch of growth hormone which, in turn, would be split into hundreds of doses and distributed. Therefore, the inclusion of just one gland from someone with CJD had the potential to infect many people.

The incubation time for peripheral iatrogenic CJD is longer than that of the intracerebral form, and is more like kuru (itself a peripherally transmitted disease), possibly around 15 years. Therefore, there could be more growth hormone related cases to come. Since 1987, the U.S. has synthetically made growth hormone rather than extracting them from pituitary glands. Because of this, there is no current CJD risk from this source.

### **What are the Symptoms of Iatrogenic CJD?**

Where transmission is intracerebral, the symptoms are more like sporadic CJD (see page 8). However, peripherally acquired CJD is more like kuru, with symptoms of ataxia predominating and dementia being a rare feature.

## Variant CJD

In 1995, two cases of CJD were found among teenagers in the U.K. This was extremely unusual and alarming because only four cases of CJD (one in Britain) had ever been reported in this age group. By 1996, the number had increased to ten, and it was evident that a new type of prion disease, called variant CJD (vCJD), had arrived in Britain. The occurrence of a 1986 epidemic of bovine spongiform encephalopathy (BSE) among U.K. cattle was thought to be of no coincidence. vCJD was soon linked to exposure to BSE prior to the 1989 ban of specified offal (brain and spinal cord) from cattle in the human food supply.

The total number of deaths from vCJD detected in the U.K. since 1995 currently stands at 168 (March 2009). A total of 44 cases of vCJD have been found in other countries, mainly in Europe, including France (23), Spain (5), Ireland (4) and the Netherlands (3). Three cases have been found in the U.S. and one in Canada, but in two of these cases, evidence indicates that the disease was acquired in the U.K., and in the other cases, the infection likely took place in Saudi Arabia.<sup>6</sup>

vCJD differs from sporadic CJD in several respects. The average age at onset of symptoms for vCJD is 28 years old. The course of the illness is longer than that of sporadic CJD, typically around a year. The symptoms, at least at the onset, are usually more psychiatric than neurological. Finally, although the post-mortem examination of brains of people with vCJD show the characteristic spongiform change, there are also other changes that are described below.

Scrapie PrP (PrP<sup>Sc</sup>) is known to exist in different forms, called strains, that are classified as PrP<sup>Sc</sup> type 1 A or B and 2 A or B, according to the pattern they form on Western blot. In 1996, it was shown that all of the vCJD cases were affected by the same strain of PrP. The vCJD PrP strain was type 2B that at the time had never been seen before in non-familial human prion disease and, moreover, it bore a marked similarity to the strain of PrP seen in BSE. Later, laboratory mice were injected with vCJD prions and developed symptoms like BSE, but unlike those of sporadic CJD. The pattern of the disease resembles that of kuru. All of this is strong evidence that vCJD is caused by exposure to BSE.

But how might these young people have been exposed to BSE? Spinal cord from infected animals may have ended up in mechanically recovered meat, used in the manufacturing of sausages, hot dogs and hamburgers. Both the vCJD cases and controls without the disease had consumed these products prior to 1989, in addition to a substantial proportion of the rest of the population. There was no other obvious link between diet and exposure to BSE, nor to occupation or surgery.

Variant CJD is so-called because it differs in some ways from other forms of CJD, especially that it mostly occurs in young people. vCJD was first identified in 1995.

6 – Robert G. Will, MD, FRCP(E), Consultant Neurologist, Former Director and Founder, CJD Surveillance Unit, Edinburgh, Scotland, UK

It is not yet known for sure the likely route of transmission in vCJD. It may be that young people consume more of whatever foodstuffs carried the most infectivity, or it may be that young people are just more susceptible to transmission of CJD via BSE. BSE contaminated products were also fed to sheep, pigs and poultry, so exposure through their consumption cannot be ruled out.

It is not known how many other people will develop vCJD without knowing the route of exposure. However, if it is like kuru, which has an incubation time of up to 40 years (time from exposure to onset of symptoms), there could be many more cases of vCJD in the future.

On May 21, 2004 a report was released by the U.K. indicating that scientists who examined 12,674 stored appendix and tonsil samples identified three positive for prion proteins. Applying these findings to the U.K. population (60 million), experts estimate about 3,800 people could test positive for prion proteins. Scientists suspect these findings might indicate people can carry the disease without developing symptoms. They would still be able to spread the disease to others via contaminated surgical instruments, blood transfusions or organ donations.

Up until 2009, all tested cases of vCJD worldwide (192 out of 212) have had a particular genotype, MM at codon 129 of the human prion protein gene. In March 2009, a possible case of vCJD was reported in the U.K. with an MV genotype. On the reasonable assumption that this was truly a case of vCJD, it is possible that the 50% of the population with this genotype in the U.K. and other countries in Europe may be at risk of BSE infection. This raises the concern that further cases with an MV genotype are likely to occur in the future and the outbreak of vCJD may continue.

One important feature of vCJD is that, until recently, there had been only one case in any family. In 2008, a mother and her son who lived in Spain both developed vCJD. Investigation suggests that the reason for two cases in this family is that they regularly ate cattle brain coming from an area with BSE. In other countries, it is thought that the infection was due to eating processed meat products and this may be why there had previously been only one case per family. There is no evidence of transmission of vCJD directly from mother to child, and the facts of the Spanish patients exclude the possibility in these two cases.<sup>7</sup>

### **CJD and Blood Transfusion**

There is no evidence that sporadic, familial or iatrogenic CJD can be transmitted through blood transfusion. However, it is now clear that vCJD can be spread from person to person in this way. There have been three instances in the U.K. in which vCJD infection has been transmitted from a blood donor incubating vCJD to recipients who also developed vCJD, on average 8 years after the blood transfusion. In December 2003, the U.K. reported its first case of suspected transmission of vCJD by blood transfusion; the donor gave blood 3.5 years prior to becoming symptomatic. The recipient was 69 years old and died of vCJD 6.5 years after transfusion. As of January 2006, two more transfusion transmission cases have been reported, one in the U.K. and one in Ireland. In 2009, the U.K. authorities also reported possible transmission of variant CJD through a treatment for hemophilia produced from blood plasma.<sup>7</sup>

In January 2009, the American Red Cross (ARC) released the results of their five year CJD Look Back Study. The study examined 36 blood donors who later developed CJD and 436 blood recipients. The ARC found no proof of transfusion transmission of non-variant forms of CJD and considers the transmission risk, if any, significantly lower than the variant form of CJD (Dorsey et al Transfusion 2009).

7 – Robert G. Will, MD, FRCP(E), Consultant Neurologist, Former Director and Founder, CJD Surveillance Unit, Edinburgh, Scotland, UK



### What Are the Symptoms of vCJD?

The symptoms of vCJD are quite different from those of sporadic CJD. Often, the patient will first be referred to a psychiatrist rather than a neurologist, which may lead to a delay in diagnosis. After several weeks or months, more obvious neurological symptoms may set in including:

- Unsteadiness in walking and sudden jerking movements
- Anxiety, depression, withdrawal and behavioral changes
- Progressive dementia (loss of mental function marked by symptoms such as memory loss)
- Persistent pain and odd sensations in the face and limbs

Eventually, the patient may lose the ability to move or speak and will need 24 hour nursing care. Death occurs approximately a year after the onset of symptoms.

Please see page 7 for two sets of microphotographs that show comparisons of normal, sporadic and variant CJD.

### Variant Creutzfeldt-Jakob Disease Current Data (March 2009)

| COUNTRY         | TOTAL NUMBER OF PRIMARY CASES (NUMBER ALIVE) | TOTAL NUMBER OF SECONDARY CASES: BLOOD TRANSFUSION (NUMBER ALIVE) | RESIDENCE IN UK > 6 MONTHS DURING PERIOD 1980-1996 |
|-----------------|--|---|--|
| UK              | 165 (4)                                      | 3 (0)   | 168  |
| France          | 23 (0)                                       | -   | 1  |
| Rep. of Ireland | 4 (0)  | -   | 2  |
| Italy           | 1 (0)  | -   | 0  |
| United States   | 3 <sup>†</sup> (0)                           | -   | 2  |
| Canada          | 1 (0)  | -   | 1  |
| Saudi Arabia    | 1 (1)  | -   | 0  |
| Japan           | 1* (0)                                       | -   | 0  |
| Netherlands     | 3 (0)  | -   | 0  |
| Portugal        | 2 (0)  | -   | 0  |
| Spain           | 5 (0)  | -   | 0  |

<sup>†</sup> Two of these cases' evidence indicates that vCJD was acquired in the U.K. The third U.S. patient with vCJD was born and raised in Saudi Arabia and lived permanently in the United States since late 2005. According to the U.S. case report, the patient was most likely infected as a child when living in Saudi Arabia.

\*The case from Japan had resided in the U.K. for 24 days during 1980 - 1996.

Chart courtesy of Robert G. Will, MD, FRCP(E), Consultant Neurologist, Former Director and Founder, CJD Surveillance Unit, Edinburgh, Scotland, UK

## Diagnostic Aids

General Practitioners should be aware of CJD, although they may never see a case. A prompt referral to a neurologist should follow observation of any suspicious pattern of symptoms.

### **A number of investigations should be carried out including:**

- **Clinical Observation**

A complete patient history and physical examination are sufficient to make a suspected diagnosis fairly early in the course of the illness in nearly all patients with the typical features of CJD, and at least raise a suspicion in most patients with an atypical illness.

- **Magnetic Resonance Imaging (MRI)**

This type of scan produces an image of the brain. In CJD the scan looks normal, except in some cases a certain amount of brain shrinkage (atrophy) may be revealed. In about 80% of the cases, an increased signal can be seen to “light up” the basal ganglia on one or both sides of the brain. Because radiologists are usually searching for asymmetrical radiological changes, the significance of these often bilateral bright spots was overlooked for many years. They may also be seen in cases of Wilson’s Disease and in carbon monoxide poisoning, disorders that are readily clinically distinguishable from CJD. MRI is important for ruling out other conditions, such as a brain tumor. The MRI may also show relatively specific changes which aids diagnosis, particularly in vCJD. The **Diffusion Weighted MRI** has also been proven to be a valuable diagnostic tool.

- **Electroencephalography (EEG)**

An electroencephalogram, which measures the electrical activity of the brain, is currently one of the most useful aids in diagnosing CJD, as it may show changes which are characteristic of the disease. These changes have not been seen in any of the cases of vCJD. A periodic sharp wave pattern occurs in about 80% of the cases with the typical subtype, or sCJD MM (MV)1, but is not common in the other subtypes. In its most characteristic form, electrocardiogram-like regularity is seen in very few other diseases. A less definite but still suggestive periodic pattern is called “burst wave suppression” in which short periods of comparative electrical silence are broken by a quick succession of sharp waves.

- **Lumbar Puncture (Spinal Tap)**

In a lumbar puncture, a sample of the cerebrospinal fluid (CSF), which surrounds the brain and spinal cord, is taken by inserting a hollow needle into the lower part of the spinal column. The spinal fluid is analyzed for the presence of a protein designated as “14-3-3” that is released from damaged or dying nerve cells as well as other proteins, especially the tau protein. The 14-3-3 protein is detectable in over 90% of patients with typical CJD.

As with the EEG, it is not entirely specific and can be detected in some patients with other disorders including viral encephalitis, acute oxygen deficiency often associated with strokes, and Alzheimer's Disease. These disorders can usually be distinguished from CJD by looking at clinical history and routine spinal fluid examination. Examination of CSF is also done to exclude inflammation or infection of the brain as a cause of the symptoms.

Recently, it has become apparent that another protein named "tau" is almost equally informative as 14-3-3. Therefore, the National Prion Disease Pathology Surveillance Center (NPDPS) has decided to report both 14-3-3 and tau together to maximize accuracy and reliability. Overall, this combination is accurate in 85% of the cases in detecting CJD and about 75% in excluding it. The test is more accurate (over 95%) in detecting "typical" sporadic CJD, or sCJD MM (MV) I.

- **Computerized Tomography (CT)**

Scans of the brain are useful in excluding other conditions but do not show the specific changes useful for CJD diagnosis.

- **Blood Tests**

Blood and other biochemical tests are usually normal in CJD testing unless the disease is familial - in this case the genetic analysis identifies the mutation.

- **Brain Biopsy**

A sample of tissue is removed from the brain, usually from the frontal lobe, by a neurosurgical procedure (brain operation). The brain biopsy leads to the identification of prion disease with 99% accuracy provided both fixed tissue - for microscopic and immune staining examinations, and frozen tissue - for Western blot examination is available. Microscopic examination only is less accurate. The NPDPS conducts biopsy and post-mortem stains and biochemical analysis that allows for ruling out or establishing the diagnosis of CJD in virtually all of the cases. Brain biopsy is not routinely done because it poses possible risks to the patient and the medical team performing the surgery.

- **Tonsil Biopsy**

It has been shown that infectivity can be seen in tonsil tissue in cases of vCJD but not in sCJD. A tonsil biopsy may therefore be only useful in the diagnosis of vCJD. Other research has also found infectivity in the appendix (which had been previously removed) of a man who went on to develop vCJD.

Tests that are not based on tissue examination are not sensitive enough to identify every case of CJD, and no test is entirely specific for a CJD diagnosis. However, if two or more of the tests are positive, the diagnosis is almost certain to be CJD. Unfortunately, the chances are low that all tests may be positive in atypical subtypes. Because of the availability of this battery of laboratory tests, brain biopsy is no longer needed or advised in the diagnostic evaluation of suspected cases of CJD. However, brain biopsy may be in order when a treatable disease such as encephalitis must be ruled out.<sup>8</sup>

## Post-Mortem Tissue Examination (Autopsy)

Currently, the only way to diagnose the presence and type of CJD with certainty is by examination of brain tissue or tonsil tissue in vCJD. There are four tests that are carried out to establish or exclude the diagnosis of prion disease.

### 1) Histological Examination

The brain of someone with CJD nearly always shows signs of spongiform change; the brain tissue has the appearance of a sponge when seen under the microscope. Spongiform change results from a mixture of tiny bubbles within neurons and bigger holes distributed throughout the brain tissue. It affects mainly the grey rather than white matter of the brain. It may be found in the cerebral cortex, basal ganglia, thalamus and cerebellum. An increased number of astrocytes, the cells in the brain that support and supply nutrients to neurons, are often seen in CJD. Often neurons are decreased in number. Plaque deposits of prion protein are seen in only 10% of sporadic CJD cases or in the sCJD MV2 subtype. However, plaques are seen in some cases of familial CJD and in all cases of iatrogenic CJD caused by growth hormone treatment. In vCJD, where the brain pathology is very characteristic, a particular type of plaque known as a florid or “daisy” plaque is typical of the disease. The florid plaque is surrounded by an area of spongiform change.

### 2) PrP Immunohistochemical (IHC) Examinations

IHC is a technique that allows for the identification of abnormal PrP in the brain tissue using antibodies. The presence and distribution of the abnormal PrP is established and correlated to that of the tissue lesions examined histologically.

### 3) Western Blot (WB)

While the above techniques are carried out on fixed tissue, Western blot requires the unfixed (frozen) tissue. This means PrP<sup>Sc</sup> is separated from other brain proteins and visualized with specific antibodies to PrP. This technique can detect much smaller amounts of PrP<sup>Sc</sup> than IHC and can establish whether the affected tissue contains PrP<sup>Sc</sup> type 1 A or B, or type 2 A or B. However, it cannot establish the distribution of PrP<sup>Sc</sup>. Therefore, the two techniques are complementary. See page 19 for Western blot image.

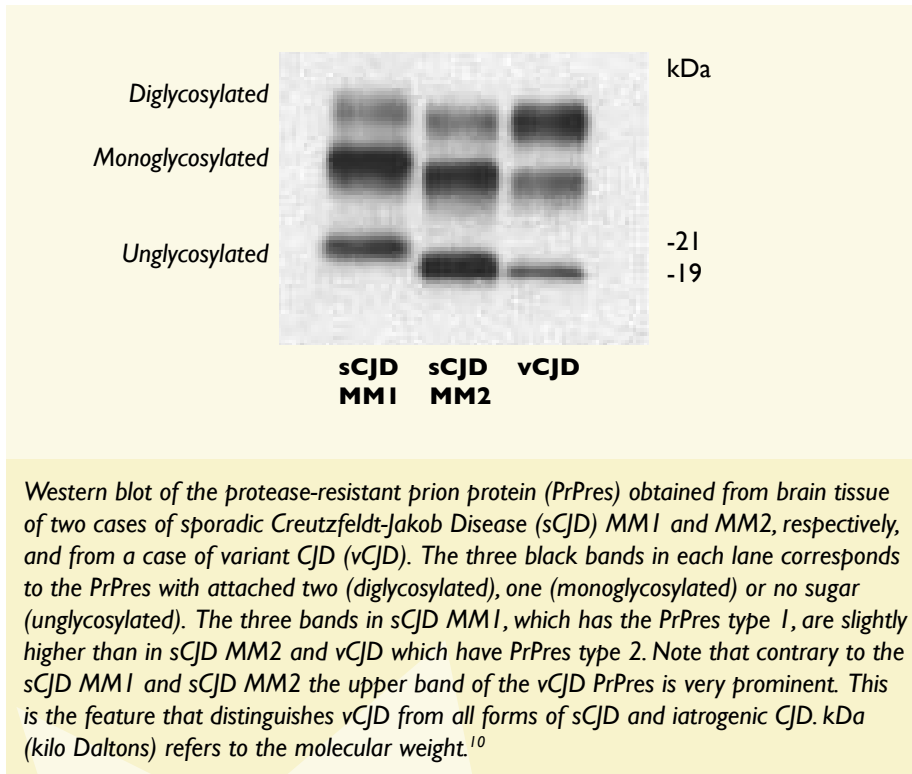
### 4) Gene Analysis

Since, as stated before, the gene of the PrP can modify the subtype of CJD, it is very important to determine the PrP genotype in every patient with a prion disease. Genetic analysis can be carried out on unfixed tissue, commonly brain tissue or blood.<sup>9</sup>

### [www.cjdsurveillance.com](http://www.cjdsurveillance.com)

The National Prion Disease Pathology Surveillance Center (NPDPS) offers a free autopsy to any suspected case of CJD. The autopsy provides answers to families and assists with prion disease research. If you would like to set up an autopsy, or if you need more information, please contact the NPDPS at 216.368.0587.

The difficulties involved in diagnosing CJD may have prevented the identification of the disease in some cases. Since the disease progresses rapidly, the patient may die before a diagnosis can be made. Furthermore, some physicians may not even consider the possibility of a CJD diagnosis because the disease is deemed to be rare and the clinical symptoms of CJD can often be attributed to other ailments. Consequently, CJD may be mistaken for a variety of psychological illnesses and other neurological disorders like Alzheimer's Disease, Pick's Disease, Huntington's Disease, cerebral hematomas or vascular irregularities. The extent to which such misdiagnosis may occur is presently unknown.



Western blot of the protease-resistant prion protein (PrPres) obtained from brain tissue of two cases of sporadic Creutzfeldt-Jakob Disease (sCJD) MM1 and MM2, respectively, and from a case of variant CJD (vCJD). The three black bands in each lane corresponds to the PrPres with attached two (diglycosylated), one (monoglycosylated) or no sugar (unglycosylated). The three bands in sCJD MM1, which has the PrPres type 1, are slightly higher than in sCJD MM2 and vCJD which have PrPres type 2. Note that contrary to the sCJD MM1 and sCJD MM2 the upper band of the vCJD PrPres is very prominent. This is the feature that distinguishes vCJD from all forms of sCJD and iatrogenic CJD. kDa (kilo Daltons) refers to the molecular weight.<sup>10</sup>

### **Information helpful in understanding an autopsy report**

The PrP gene, as with other genes, may have variations. Some of these variations can cause an inherited prion disease. Others do not cause disease and are called polymorphisms. This issue is further complicated by the fact that the PrP gene, as with other genes, consists of halves called alleles - one from each parent. To some extent, the two alleles function independently and each encodes for a PrP molecule. Because of the presence of mutations and polymorphisms, the two alleles may be different. For example, mutations causing familial prion disease are generally inherited only from one parent, therefore, they are located only in one of the two alleles. In this case, the patient is heterozygous for the mutation. An important polymorphism of the PrP gene is located at codon 129.\* Codon 129 of the PrP gene may encode either for the amino acid Methionine (M) or the amino acid Valine (V). Because each allele may have either M or V, people may have M in each of the two alleles, i.e. they are M/M (homozygous M), V/V (homozygous V), or M/V (heterozygous). The presence of M or V does not cause disease by itself, but if an individual develops CJD, the disease is likely to be different according to whether the CJD patient is M/M, V/V or M/V. Therefore, the polymorphism at codon 129 is a modifier of the disease in sporadic CJD. Another modifier is the type of PrP<sup>Sc</sup> present in the brain tissue of patients with sporadic CJD. Commonly two types, type 1 and 2, of PrP<sup>Sc</sup> are distinguished. The combination of the polymorphism at codon 129 and the PrP<sup>Sc</sup> identify fairly accurately the subtype of sporadic CJD. For example, sporadic CJD M/M1 (sporadic CJD in a homozygous M patient with PrP<sup>Sc</sup> type 1) corresponds to typical sporadic CJD. In addition, each PrP molecule may carry two sugars, one sugar and no sugar. When the PrP<sup>Sc</sup> present in a prion disease-affected individual contains mostly the monoglycosylated (one sugar), PrP<sup>Sc</sup> is identified as A; when it contains mostly the diglycosylated (two sugars), the form is identified as B. Therefore, there are basically two types of PrP<sup>Sc</sup>: 1 and 2, each of which has the A and B subtypes.<sup>11</sup>

*\* - The codon is the coding unit of the gene and directs the synthesis of an individual amino acid; it is generally identified with a number, such as 129, that refers to the position of the amino acid it encodes in the protein (i.e. the 129th amino acid of PrP).*

## Animal Prion Diseases

Prion diseases have been found in several animals. Scrapie, a prion disease in sheep and goats, has been recognized since the 18<sup>th</sup> century and is found at a low level in many parts of the world. The name scrapie comes from a Scottish word and refers to the peculiar tendency of affected animals to scrape their fleece against trees and bushes. Animals with scrapie become unsteady and startle easily. There is no evidence that scrapie has ever jumped the species barrier to cause prion disease in humans.

It has long been the practice to add protein from the carcasses of ruminants (sheep and cows) to animal feed. In the U.K., tissue from a cow with bovine spongiform encephalopathy (BSE) is believed to have contaminated the animal feed. Once the feed entered the bodies of other cows, they too contracted BSE and, in turn, this led to further cases when those carcasses were turned into feed. This “cascade effect” led to the BSE epidemic.

Prion diseases have also been found in ranched mink, called transmissible mink encephalopathy (TME), and in deer and elk, called chronic wasting disease (CWD). The last case of TME in the U.S. was discovered in 1985. In addition, there have been a few cases in zoo animals and in domestic cats. However, there is no evidence of transmission to humans in any of these cases.

### **Bovine Spongiform Encephalopathy and Chronic Wasting Disease**

In December 2003, the first case of BSE was discovered in the United States in Washington State. The infected cow was imported from Canada. Although technically this cow was “Canadian,” the concern over a case of BSE discovered in North America points out the need for more serious attention to be paid to cattle testing. A second case of BSE was announced in June 2005. The cow, born in the U.S., was slaughtered in November 2004, tested and found inconclusive. In June 2005, the tissue was retested and found to be positive. These two cases were considered to be a direct result of contaminated animal feed.

In 2006, a third case of BSE was discovered in a cow in Alabama. This case presented a more disturbing picture as reported on the Centers for Disease Control and Prevention website: In August 2008, several U.S. Agricultural Service investigators reported that a rare, genetic abnormality that may persist within the cattle population is considered to have caused BSE in the atypical BSE animal from Alabama in 2006.

On April 25, 2008, the FDA issued a new regulation scheduled to take effect in 2009 in order to allow livestock, meat, rendering and feed industries time to adapt their practices to comply with the new regulation. This regulation bars high-risk materials from all animal feed, including pet food. Banning these materials helps prevent the accidental feeding of cattle with ingredients that may be contaminated with the BSE agent. Such contamination of ruminant feed may occur during the manufacturing or transportation process.<sup>12</sup>

CWD was first recognized in 1967 among deer in several Colorado research institutions. Since that time, CWD has been discovered in wild deer and elk in several states. For a full list of states that have identified chronic wasting disease in their local deer and elk, please visit the following website<sup>13</sup>:

[www.nwhc.usgs.gov/disease\\_information/chronic\\_wasting\\_disease/index.jsp](http://www.nwhc.usgs.gov/disease_information/chronic_wasting_disease/index.jsp)

Surveillance programs are being conducted by individually affected states, as well as nationally by the Department of Agriculture. CWD is being closely studied for any potential risk to human health.

At the present time, there is no epidemiological and no experimental evidence that CWD can infect humans, however, one study reported that abnormal CWD proteins in vitro can convert normal human proteins into abnormal forms, although inefficiently. Since the transmissibility of CWD to humans cannot be completely ruled out, experts caution people against consuming any part of a deer or elk showing evidence of CWD. Experts also warn against eating the brain, spinal cord, eyes, spleen, tonsils and lymph nodes of any harvested animal, as these tissues are known to harbor the CWD agent in infected animals.<sup>14</sup>





## Frequently Asked Questions

### **Is there any treatment or cure for CJD?**

At the present time, there is no confirmed effective treatment to arrest or cure CJD. Currently, the disease is inevitably fatal. The only medications available for CJD patients focus on easing their symptoms and discomfort. Such measures may include drugs to control distress, myoclonus and hallucinations, catheters to collect urine, intravenous fluids, feedings through tubes and frequent repositioning of the patient to avoid bedsores.

Researchers have been experimenting with drugs like doxycycline, prograf, quinacrine, pentosan polysulphate, chlorpronazine and flupertine as potential therapies for CJD. Scientists are also examining the use of certain antibodies for the prevention and treatment of prion diseases. The development of a vaccine is also being studied.

### **Can you catch CJD from someone?**

Prion diseases are not infectious in the usual way. For example, they are not spread by airborne droplets like colds and flu, or by body fluids or sexual contact like HIV. The overall evidence suggests that there is no increased risk of developing CJD from contact with a person suffering from the condition. Special precautions are not required by anyone coming into contact with a CJD patient, however, it is sensible for anyone who might be exposed to the blood of a CJD patient to wear gloves and take standard precautions.

### **How can we be sure that the clinical diagnosis of CJD is correct?**

Each individual case of CJD can be assigned to one of three forms: sporadic, familial, or acquired (variant or iatrogenic). The diagnostic methods may vary depending on the type. In sporadic CJD, the spinal fluid test has improved the diagnostic accuracy while the patient is alive, and it is now included as one of the diagnostic criteria along with the electroencephalogram (EEG). However, the only way to currently be sure of the diagnosis is by brain biopsy or autopsy. In familial CJD, the diagnosis depends on development of particular neurological symptoms and the identification of a PrP gene mutation by genetic analysis. In acquired CJD, iatrogenic CJD is diagnosed on the basis of symptoms developing in someone with a relevant exposure. In vCJD, diagnosis is very difficult while the patient is alive, unless the diagnosis of vCJD is suspected and tonsil biopsy is carried out. An MRI scan may prove to be useful, however, a definitive diagnosis depends on examination of brain tissue or lymphoreticular tissue such as the tonsils.

### **Is the U.S. blood supply safe from CJD?**

When it became evident in the mid 1990s that a significant proportion of plasma pools used in the production of therapeutic protein derivatives were “contaminated” by donations from individuals who later died of sporadic CJD, regulatory agencies responded with guidance about quarantine and/or destruction of implicated product lots. These precautions were based upon laboratory evidence that low levels of infectivity were present in blood during both the incubation and clinical phases of disease in experimental rodent models.

However, it was also noted that there was a serious discrepancy between the experimental data and epidemiological observations that, although anecdotal, failed to identify any instance of a human case of sCJD that could be traced to blood or blood products. With the passage of time, systematically collected epidemiological data substantiated the absence of sCJD transmissions in blood recipients, and began to weigh more heavily on the perception of risk to humans. Although it was finally decided that any such risk was negligible and plasma pools were no longer discarded, upon knowledge of a contributing CJD donor, new evidence from the U.K. shows a transmission risk from vCJD cases (see page 14), although deferrals designed to eliminate “high risk” donor categories, such as human growth hormone and dura mater recipients remained in force.<sup>15</sup>

### **Is there a risk in contracting CJD from organ transplant surgery?**

The risk of contracting CJD from organ transplants is not known with certainty, with the possible exception of a case of CJD occurring after liver transplant (Creange et al Ann. Neurol. 1995), there are no reported instances in which such an event has occurred. As for tissue, there is only a single known instance in 1972 in which a transplant was proven to be the cause of disease from a corneal donor who had died of undiagnosed CJD. In the past 30-40 years, we know of one case in which a CJD patient had some years earlier received a bone transplant and it was investigated in detail. None of more than two dozen other individuals who had received transplants from the same donor ever developed the disease. In the second case, corneal and scleral tissue from a patient with unrecognized CJD were used for grafting procedures in three individuals, none of whom developed the disease. Although the tissue banking community is perhaps less well regulated than the blood banking community, everyone is much more aware today than in the past of the small but finite risks involved with tissue transfers, and donor criteria have been strengthened. In the vast majority of cases, the benefit of having the transplant far outweighs the risk of contracting CJD from a donor who has no symptoms but could be in the incubation period for CJD. Note also that there is a risk of infection in any transplant.<sup>15</sup>

### **I have had a spinal tap. Am I at risk?**

A lumbar puncture is performed with a single use kit which is destroyed after the test, so there is no risk of CJD transmission through spinal tap.

### **Am I at risk because of brain surgery?**

Instruments used on the brain or nervous tissue of someone known to have or suspected of having CJD must be destroyed. Ideally, single use disposable instruments should be used.

### **Is the CJD patient in pain?**

Clinical observation of people in the later stages of CJD indicates that they lose awareness of their condition as the disease progresses. Obviously this saves them, but not their families, from suffering. However, in the early stages, patients with CJD can develop marked fear which can be very distressing and is probably associated with visual hallucinations. They may feel discomfort, and some of the symptoms of the disease such as myoclonus are distressing to caregivers. Neurologists believe there is no pain associated with the disease itself. For example, there is no rise in pressure in the head which could cause headache or any other obvious cause of pain.

### **Is an autopsy necessary in CJD?**

Post-mortem examination is not mandatory in the U.S. When CJD is suspected, the doctor will need the permission of the next of kin. An autopsy helps the family to know the definite cause of death. At present, this can be done with examination of brain tissue or, in the case of vCJD, tonsils obtained at biopsy or autopsy. Furthermore, autopsy examination to confirm the diagnosis of CJD helps protect public health and makes tissue available for research. The NPDPS, in cooperation with the Centers for Disease Control and Prevention (CDC), examines tissue from as many cases as possible of suspected CJD in order to confirm or exclude the diagnosis of prion disease. The purpose of the NPDPS is to detect, in a timely manner, the presence of atypical cases in the U.S. such as human cases of prion disease acquired from animals, i.e. BSE infected beef, deer and elk, and monitor the number and distribution of cases of prion disease in the U.S. to identify other possible sources of infection such as the use of contaminated surgical instruments or tissue implants. Tissue examination from as many cases as possible is needed for the NPDPS to provide effective surveillance. The NPDPS provides a free autopsy to any suspected case of CJD. For more information, contact the NPDPS at 216.368.0587.<sup>16</sup>

### **Is the occurrence of sporadic CJD increasing?**

There is no consistent evidence that the number of cases of sporadic CJD is increasing, except for an isolated report from Switzerland where a two-fold increase had been recorded for the year 2001. CJD is not reportable in all states, but no evidence of increase in the number of cases has been observed in the U.S. However, the NPDPS examines about 64% of the approximately 300 cases expected to occur in the U.S. per year. Again, the number of cases examined by the NPDPS must be increased for the surveillance to be effective.

### **What is being done to protect us from CJD?**

At present, there is no way of protecting people from sporadic CJD. Iatrogenic CJD can be prevented by destroying surgical instruments that have been used on people suspected of having CJD, and by not using their organs for transplant.

### **Is CJD research currently being conducted?**

Yes, government agencies and public and private institutions around the world are engaged in researching all aspects of CJD for the ultimate purpose of finding the means for preventing, treating and curing this disease. The crisis in Great Britain involving BSE and vCJD has generated a great deal of research.

Among the many areas being studied are the unique nature of the infectious agent and how it destroys the brain. Scientists are also trying to ascertain which factors affect infectivity, susceptibility to disease and the onset of symptoms. Many researchers are trying to develop new, reliable diagnostic tests that can detect the disease before symptoms of the disease occur. Such pre-clinical tests in people can be useful, not only for the development of therapies before significant damage occurs, but also to ensure the safety from transmissible agents to blood, blood products, organs and surgical instruments.

## National Prion Disease Pathology Surveillance Center Statistics

### Cases Examined<sup>1</sup> (12/31/08)

| Year           | Total Referrals <sup>2</sup> | Prion Disease           | Sporadic    | Familial   | Iatrogenic | Variant        |
|----------------|------------------------------|-------------------------|-------------|------------|------------|----------------|
| 1996 & Earlier | 42                           | 32                      | 28          | 4          | 0          | 0              |
| 1997           | 115                          | 68                      | 59          | 9          | 0          | 0              |
| 1998           | 93                           | 53                      | 45          | 7          | 1          | 0              |
| 1999           | 115                          | 69                      | 61          | 8          | 0          | 0              |
| 2000           | 151                          | 103                     | 89          | 14         | 0          | 0              |
| 2001           | 210                          | 118                     | 108         | 9          | 0          | 0              |
| 2002           | 258                          | 147                     | 123         | 22         | 2          | 0              |
| 2003           | 273                          | 176                     | 735         | 41         | 0          | 0              |
| 2004           | 335                          | 184                     | 162         | 21         | 0          | 1 <sup>3</sup> |
| 2005           | 346                          | 193                     | 154         | 38         | 1          | 0              |
| 2006           | 380                          | 192                     | 159         | 32         | 0          | 1 <sup>4</sup> |
| 2007           | 370                          | 212                     | 185         | 26         | 0          | 0              |
| 2008           | 383                          | 228                     | 182         | 23         | 0          | 0              |
| <b>TOTAL</b>   | <b>3071<sup>5</sup></b>      | <b>1775<sup>6</sup></b> | <b>1490</b> | <b>254</b> | <b>4</b>   | <b>2</b>       |

*1 Listed based on the year of death or, if not available, on year of referral*

*2 Cases with suspected prion disease for which brain tissue and/or blood (in familial cases) were submitted*

*3 Disease acquired in the United Kingdom*

*4 Disease acquired in Saudi Arabia*

*5 Includes 20 cases in which the diagnosis is pending, and 17 inconclusive cases*

*6 Includes 25 cases with type determination pending in which the diagnosis of vCJD has been excluded.*

*For current statistics, visit the NPDPC's website: [www.cjdsurveillance.com](http://www.cjdsurveillance.com)*

## Glossary

**14-3-3:** The name of the protein being tested for in the spinal fluid which may indicate the presence of a prion disease.

**AKINETIC MUTISM:** A state in which patients cannot speak (mutism) or move (akinesia) due to damage of the brain.

**AUTOPSY:** In cases of suspected CJD, this is a post-mortem, brain only procedure. At present, it is the only conclusive method to confirm a diagnosis of CJD.

**AUTOSOMAL DOMINANT:** One of several ways a trait or disorder can be passed down through families. If a disease is autosomal dominant, it means a child requires an abnormal gene from only one parent in order to inherit the disease.

**BOVINE SPONGIFORM ENCEPHALOPATHY (BSE):** A prion disease in cattle. Also known as “Mad Cow” disease.

**BRAIN BIOPSY:** A surgical procedure to remove a small specimen of tissue from the brain to test for CJD.

**CEREBROSPINAL FLUID (CSF):** A bodily fluid composed mostly of water, glucose, salt and proteins that surrounds, cushions and provides nutrients to the brain and spinal cord. CSF is the fluid collected in a spinal tap test.

**CEREBELLAR ATAXIA:** Shaky movements, unsteady gait and clumsiness caused by damage to the cerebellum, a part of the brain which controls movement.

**CHRONIC WASTING DISEASE (CWD):** A prion disease in deer and elk.

**ELECTROENCEPHALOGRAPHY (EEG):** A non-invasive test of brain wave patterns in which changes can often be seen in CJD cases.

**ENCEPHALOPATHY:** A disorder or disease of the brain.

**FAMILIAL:** Occurring in or affecting blood relatives. Indicates a condition that can be inherited.

**IATROGENIC:** Unintentionally induced by a physician, surgeon, medical treatment, or diagnostic procedure.

**INTRACEREBRAL:** Occurring or situated within the brain.

**KURU:** A prion disease caused by the consumption of human tissue by members of the Fore Tribe in Papua, New Guinea.

**MAGNETIC RESONANCE IMAGING (MRI):** A non-invasive radiology scan used as a possible diagnostic tool. A **Diffusion Weighted MRI** is a specific type of MRI which has proven to be a helpful CJD diagnostic tool.

**MYOCLONUS:** Jerking movements of a muscle or groups of muscles that are caused by sudden spasms.

**PRION:** The name given to a protein that has become infectious. It stands for proteinaceous infectious agent

**PROTEIN:** A large molecule made up of amino acids. Proteins perform many different functions in the body.

**RUMINANT:** Any variety of hoofed, even footed, and usually horned mammals that characteristically have their stomachs divided into four sections, including cows, sheep, goats and deer.

**SCRAPIE:** A prion disease in sheep and goats characterized by chronic itching, loss of muscular control and progressive degeneration of the central nervous system.

**SPINAL TAP or LUMBAR PUNCTURE:** A diagnostics procedure that uses a hollow needle to enter the spinal canal in the lower (lumbar) spine to remove CSF for analysis.

**SPONGIFORM CHANGE:** Brain damage characterized by a spongy appearance of brain tissue as seen under a microscope.

**SPORADIC:** In an occasional, infrequent or random manner.

**TAU:** Microtubule-associated protein that accumulates in neurons in neurofibrillary degeneration in a wide variety of disorders including CJD. A spinal tap is performed to test for the tau protein.

**TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHY (TSE):** Any fatal, incurable degenerative disease of the human or animal brain caused by prions.



## What organizations can be contacted for further information on Creutzfeldt-Jakob Disease?

### **The CJD Foundation, U.S.**

P.O. Box 5312  
Akron, Ohio 44334  
Helpline/Office: 1.800.659.1991  
Fax: 330.668.2474  
[www.cjdfoundation.org](http://www.cjdfoundation.org)  
[help@cjdfoundation.org](mailto:help@cjdfoundation.org)

### **American Red Cross**

Jerome H. Holland Laboratory  
For the Biomedical Sciences  
15601 Crabbs Branch Way  
Rockville, MD 20855-2736  
Offices: 301.738.0592 or 301.738.0644  
Fax: 301.738-0495  
[dorseyke@usa.redcross.org](mailto:dorseyke@usa.redcross.org)  
[zous@usa.redcross.org](mailto:zous@usa.redcross.org)

### **Associazione Italiana Encefalopatie da Prioni (A.I.En.P.), Italy**

Phone: 39.348.88.11.514  
[www.aienp.it](http://www.aienp.it)  
[info@aienp.it](mailto:info@aienp.it)

### **Centers for Disease Control and Prevention (CDC)**

1600 Clifton Road  
Atlanta, Georgia 30333  
Phone: 404.639.3396 or 1.800.232.4636  
[www.cdc.gov](http://www.cdc.gov)  
[prion@cdc.gov](mailto:prion@cdc.gov)

### **Centro de Investigaciones Biomédicas de Occidente Laboratorio de Enfermedades Neurodegenerativas, Mexico**

Director: Victor Sanchez, MD, PhD  
Sierra Mojada 800  
Guadalajara, Jalisco 44340  
Phone: 33.36.73.09.57, ext. 31951

### **The CJD Alliance, U.K.**

[www.cjdalliance.net](http://www.cjdalliance.net)  
[info@cjdalliance.net](mailto:info@cjdalliance.net)

### **CJD Aware!, U.S.**

[www.cjdaware.com](http://www.cjdaware.com)

### **CJD Insight, U.S.**

*Information and support for  
those affected by familial CJD*  
Director: Deana Simpson, RN  
Phone: 586.786.6260  
[www.cjdinsight.org](http://www.cjdinsight.org)  
[dsimpson2@dmc.org](mailto:dsimpson2@dmc.org)

### **CJD Support Group Network, Australia**

Phone: 61.2.98998905  
[www.cjdsupport.org.au](http://www.cjdsupport.org.au)  
[contactus@cjdsupport.org.au](mailto:contactus@cjdsupport.org.au)

### **CJD Support Network, Japan**

Phone: 81.573.62.4970  
[www.cjd-net.jp/EnglishPage.htm](http://www.cjd-net.jp/EnglishPage.htm)  
[cs-net@takenet.or.jp](mailto:cs-net@takenet.or.jp)

### **CJD Support Network, U.K.**

Phone: 44.1630.673973  
[www.cjdsupport.net](http://www.cjdsupport.net)  
[support@cjdsupport.net](mailto:support@cjdsupport.net)

### **CJD Voice, U.S.**

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

### **Johns Hopkins Hospital, Creutzfeldt-Jakob Disease Program**

Director: Brian Appleby, MD  
Meyer 279, Johns Hopkins Hospital  
600 North Wolfe Street  
Baltimore, Maryland 21287  
Phone: 410.502.2981  
Fax: 410.614.1094  
[bappleb1@jhmi.edu](mailto:bappleb1@jhmi.edu)  
[www.hopkinsmedicine.org](http://www.hopkinsmedicine.org)



**National Surveillance Center for Prion Diseases, Germany**

Phone: 49.(0)5.51.39.70.20  
www.cjd-goettingen.de  
epicjd@med.uni-goettingen.de

**National Organization for Rare Diseases (NORD)**

P.O. Box 8923  
New Fairfield, CT 06812  
Phone: 1.800.6673  
Fax: 203.746.6481  
www.rarediseases.org

**National CJD Surveillance Unit, University of Edinburgh, Western General Hospital, U.K.**

Director: Hester Ward, MD  
Phone: 44.131.537.2128  
www.cjd.ed.ac.uk

**National Prion Disease Pathology Surveillance Center**

Director: Pierluigi Gambetti, MD  
Case Western Reserve University  
2085 Adelbert Road, Room 419  
Cleveland, Ohio 44106  
Phone: 216.368.0587  
Fax: 216.368.2546  
www.cjdsurveillance.com  
cjdsurv@case.edu

**NeuroPrion, France**

European Network of Excellence  
Jean-Philippe Deslys, CEA, MD, PhD  
www.neuroprion.org  
jpdeslys@cea.fr

**PrioNet Canada**

Scientific Director:  
Neil Cashman, MD, FRCP(C), FCAHS  
University of British Columbia  
Gerald McGavin Building  
Suite 200, 2386 East Mall  
Vancouver, BC V6T 1Z3 Canada  
Phone: 604.222.3600  
Fax: 604.222.3606  
www.prioNetcanada.ca  
admin@prioNetcanada.ca

**US Department of Agriculture (USDA)**

Food Safety and Inspection Services  
1400 Independence Ave., SW  
Washington, DC 20250  
Phone: 1.888.674.6854  
www.fsis.usda.gov  
MPHotline.fsis@usda.gov

**University of California at San Francisco**

Director: Bruce L. Miller, MD  
Memory and Aging Center  
350 Parnassus Ave Suite 905  
San Francisco CA 94143  
Phone: 415.476.6880  
Fax: 415.476.4800  
http://memory.ucsf.edu

**University of Chicago**

Director: James A. Mastrianni, MD, PhD  
Center for Comprehensive Care and  
Research on Memory Disorders  
Windermere Senior Health Center  
5549 Cornell Avenue  
Chicago, IL 60637  
Phone: 773.834.4340  
http://memorycenter.bsd.uchicago.edu  
memory@medicine.bsd.uchicago.edu



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**P.O. Box 5312**  
**Akron, Ohio 44334**  
**HelpLine/Office: 1.800.659.1991**  
**Fax: 330.668.2474**  
**[www.cjdfoundation.org](http://www.cjdfoundation.org)**  
**[help@cjdfoundation.org](mailto:help@cjdfoundation.org)**

**Acknowledgements:**

*The CJD Foundation acknowledges the valuable help of:*  
Pierluigi Gambetti, MD, Director, National Prion Disease Pathology Surveillance Center,  
Medical Director, the CJD Foundation.

*We also extend our gratitude to:*

Paul Brown, MD, Gillian Turner, CJD Support Network, United Kingdom for providing  
a template for this pamphlet, Fred Cohen, MD, James Ironside, MD, Mayra Lichter, Silvio  
Notari, PhD, Deana Simpson, RN, Robert Will, MD, FRCP(E), and the U.S. Geological Survey  
National Wildlife Health Center.

Edited by Marisa Boarman, Wanda Culp-Lias, Pierluigi Gambetti, MD, Ruthie George,  
Mimi Kent and Florence Kranitz

Creutzfeldt-Jakob Disease and other Prion Diseases  
June 2009, Fourth Edition.  
Creutzfeldt-Jakob Disease Foundation, Inc.



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**The printing of this pamphlet was made possible through  
a generous grant from the C.R. Bard Foundation, Inc.**