Fact sheet: Variant CJD

About the CJD Support Network

The CJD Support Network is the leading care and support charity for all forms of CJD. The CJD Support Network:

- Provides practical and emotional support to individuals, families and professionals concerned with all forms of CJD
- Provides emotional support to people who have been told that they are at a 'higher risk' of CJD through blood or surgical instruments
- Links families with similar experiences of all forms of CJD
- Offers financial support for families in need
- Provides accurate, unbiased and up-to-date information and advice about all forms of CJD
- Provides a national helpline on all forms of CJD
- Promotes research and the dissemination of research findings
- Promotes good quality care for people with all forms of CJD
- Encourages the development of a public policy response for all forms of CJD
- Provides support, education and training to professionals concerned with CJD

For more information about the activities of the CJD Support Network, contact:

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Registered charity no. **1097173**

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Introduction to variant CJD (vCJD)

Variant CJD (vCJD) was initially named New variant CJD when it was first identified in 1995/96. It is a form of Creutzfeldt-Jakob disease, one of a group of rare, and currently always fatal, brain disorders called the prion diseases. vCJD first arose due to human dietary by exposure to Bovine Spongiform Encephalopathy (BSE), a prion disease found in cattle.

At the molecular level, all forms of CJD are characterised by the accumulation in the brain of an abnormal form of a normal protein called "prion protein". The normal form of prion protein (PrP^{C}) is made in various parts of the body, including the brain; its exact functions are not fully understood. Proteins are long molecules that fold into particular shapes that are important for their normal functions. In prion diseases, the molecule can fold into an abnormal shape which changes its physical and chemical properties. It becomes more resistant to being broken down and tends to aggregate into clumps that are deposited in tissues. This molecular abnormality results in neurons (brain cells) malfunctioning and dying, giving rise to neurological illness in the affected person, with disability and, ultimately, their death. Abnormal prion protein can cause normal prion protein to change shape and become abnormal, leading to a chain reaction and spread of the disease process.

In the case of vCJD, ingestion of abnormal prion protein from cattle affected by BSE, leads to conversion of the person's normal prion protein into an abnormal form and results in brain disease.

In this dietary-related form of CJD, although the abnormal prion protein gets into the brain via the rest of the body (initially via the gastro-intestinal system), and while there can be evidence of the abnormal protein outside the brain, the only symptoms of disease arise from the brain; other bodily tissues function normally.

A few cases of vCJD have resulted from person-to-person transmission via blood/blood products used in medical practice. This is discussed below. Most cases to date are thought to be BSE dietary related.

It should be stressed that there is no evidence of vCJD transmission via ordinary, including intimate, personal contact with someone affected by the disease.

There are other types of CJD and these are sometimes confused with each other; the details below relate specifically to vCJD (for more information on other forms of CJD see the related fact sheets at www.cjdsupport.co.uk).

A brief history

CJD was studied in England and Wales over the 1970-1985 period by researchers based in Oxford University. During this period, CJD was known to be mostly 'sporadic' with some cases being genetic or iatrogenic (for more information on other forms of CJD see the related fact sheets at www.cjdsupport.co.uk).

In the 1980s, a new prion disease of cattle, BSE, was identified in the UK. There was uncertainty as to whether this posed a risk to human health; certainly, there was no evidence that the known prion disease of scrapie in sheep transmitted to man via diet. However, it was decided that surveillance of CJD should be set up in the UK to see if there was any change that might indicate BSE transmission to humans. The surveillance centre being in the University of Edinburgh. During surveillance, a new variant of vCJD was recognised, initially distinguished from other CJD by its affecting an unusually young age group and by a somewhat different clinical illness course. Examination of the brain from such cases also revealed differences in the pathological picture. The first cases were identified in 1995 and, in 1996, when the number had risen to 10, this new disease was described in a medical publication.

BSE was suspected to be the likely cause; such CJD cases were not then identified in other countries with CJD surveillance systems and the UK was the country principally affected by BSE. Subsequent research involving a study of cases and the abnormal protein with laboratory animal transmission experiments provided proof (discussed in more detail below).

Various controls were introduced to reduce BSE in cattle and to protect human diet. Two important steps in relation to human dietary protection were: (1) The 1989 ban on specified offal (brain and spinal cord) from cattle in human food, and (2) The 1995 rules on mechanically recovered meat.

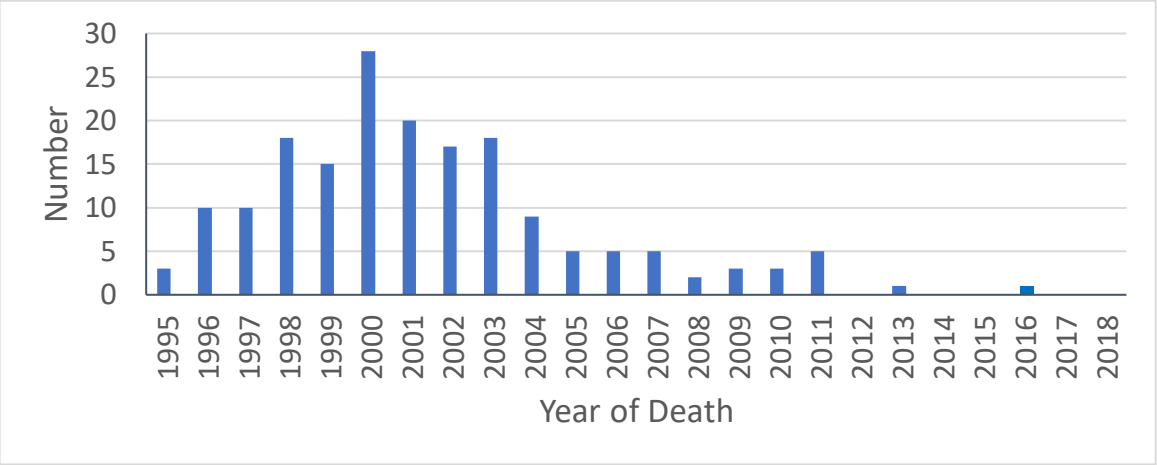
The number of deaths per year due to vCJD in the UK increased from 1995 up to 2000, but then declined, with no UK vCJD deaths since 2016 (this last individual's symptoms began in 2014). No deaths due to vCJD have occurred in the UK in people born after 1989; an indication that the dietary protection measures were effective.

From the outset, there was concern that the primary cause (BSE in diet) might be controlled, but that there was a risk of secondary, human-to-human transmission. With the exception of a very few cases related to blood/blood products (detailed below), this has not occurred.

Current vCJD figures

Current figures: UK

As of March 2024, there have been a total of 178 (definite and probable) deaths from of vCJD in the UK. Of these, 175 are considered BSE dietary-related cases, with 3 being related to blood transfusions. The number of deaths per year in the UK is shown in the graph below.



UK vCJD Deaths 1995-2018 [No deaths in 2019-2020] as at Jan 2022

Current figures: Worldwide

The below table details definite and probably cases of vCJD worldwide, as at March 2024.

Definite & Probable Cases	
UK	178 [last case onset 2014]
France	28 [last case onset 2019]
Spain	5
Rep of Ireland	4
USA	4
Italy	3
Netherlands	3
Portugal	2
Canada	2
Saudi Arabia	1
Japan	1
Taiwan	1

It is important to note that a case is attributed to a country according to residence at the time of illness; this does not necessarily mean that the person contracted the illness in that country. For example, none of the USA cases are considered to have been infected in the USA.

vCJD and BSE

As indicated above, variant CJD is thought to have arisen because of exposure to BSE infectivity in diet following the development of the BSE epidemic in UK cattle in the 1980s.
This view is supported by several lines of evidence:

1. The UK had the greatest number of cattle BSE cases and has had most of the vCJD cases.
2. The time interval between the appearance of BSE in cattle and the appearance of vCJD in humans is in keeping with what is known of prion infectivity incubation periods (the time from being exposed to infection and that of becoming ill).
3. Detailed epidemiological study of the vCJD cases did not provide evidence for other possible causes but did find support for a link with diet.
4. The abnormal prion protein (PrP^{Sc}) found in BSE cattle brains and that found in human vCJD brains has the same sort of laboratory characteristics. In particular, when the proteins are studied by a process called Western Blotting, they produce the same sort of pattern (which differs from that seen with sporadic CJD; sCJD).
5. Animal transmission experiments showed that cattle BSE and human vCJD infections behave in the same way and in a different way from other prion diseases.

In addition, the control of BSE and protection of human diet has been followed by a decline in vCJD and, indeed, in no recent cases. Variant CJD has not been identified in the UK in anyone born after 1989, the date of the main dietary protection measure.

Given all of this, there is no coherent doubt that BSE dietary infection was the origin of vCJD. However, it must be stressed that there is no known direct link between any specific dietary event and subsequent illness. In any individual case, it is impossible to identify a particular item of diet at some specific point in time that led to infection.

Beef itself may have contained infectivity but it is thought that mechanically recovered meat (MRM) may have been a significant source of infection. MRM was obtained by removing carcass material and it was then added to other products such as sausages, meat pies, and burgers etc. MRM prepared from vertebral columns might well contain spinal cord or other infective materials. This process was stopped in 1996.

vCJD and BSE (continued)

Why were young people particularly affected?

There is no definite answer to this question. However, it is thought that two factors may be important:

1. Young people may have consumed more of potentially infected material (such as burgers and sausages).
2. Young people may be more susceptible to dietary infection because they have more lymphoid tissue in the gastro-intestinal tract (such as tonsils, the appendix and lymphoid patches ('Peyer's Patches') in their intestines. Dietary-acquired BSE/vCJD infection seems to begin in such lymphoid tissue. In addition, younger people are more prone to infections in tonsils and the appendix that might make transmission more likely.

What does 'Codon 129' mean and how does it affect vCJD?

The prion protein gene (*PRNP*) is a string of code that instructs cells to make prion protein. There are common variations in the code that do not cause major changes in the protein, in that they do not directly cause disease; these are called polymorphisms and are present in many genes. The individual items of code (codons) in the gene are numbered and the 129th item in *PRNP* is the site of a common variation between 3 forms. In brief, all individuals are either *PRNP*-129 MM, MV or VV. About 39% of the normal UK population is MM, 50% MV and 11% VV. While this does not, in itself, cause any disease, the variation can have some effects on prion disease. It can influence how likely one is to get a prion disease, the clinical picture if one were to develop disease and, if it is acquired, the length of the incubation period (time from infection to first symptoms). In the case of vCJD, virtually all definite or probable cases to date have been in MM individuals. There has been 1 definite and 1 possible MV case. While there is uncertainty as to exactly how the 129 polymorphism affects BSE/vCJD, MM individuals are probably more likely to be at risk of developing vCJD after dietary exposure and MV or VV individuals are less likely to do so and, if they do, after a longer incubation period.

Are further cases of vCJD expected, and, if so, how many?

We do expect that further cases of vCJD will occur but it is impossible to be certain and it is very difficult to predict the number. We know that the incubation period of acquired prion diseases is long and varies from individual to individual. In acquired prion diseases other than vCJD, incubation periods of 3 or 4 decades have been reported. The incubation period for BSE/vCJD dietary infection is uncertain; it is thought that the minimum period is around 5 years, with an average around 10-15, and a maximum that could be as long as that reported in other forms of CJD. One publication in 2010 estimated that there might be up to 10 cases per year on average over the period 2010 to 2179, but this was on the basis of many uncertain assumptions and there have been only 10 deaths in the 13-year period between 2010 and the end of 2023.

Secondary transmission

'Secondary transmission' refers to the possibility of vCJD being transmitted from one person to another. It should be stressed that such transmission does not occur through ordinary, even intimate, human contact.

The three possible modes of transmission that have been considered are surgery (via possible contamination of instruments), blood transfusion and the use of blood-derived products as medical treatments.

Clearly, if a person is ill with vCJD, precautions can be taken. For example, such a person could not donate blood and any potentially contaminated surgical instruments could be withheld from further use.
The main problem concerns what is called 'asymptomatic infection'. If someone is silently infected with vCJD, they would not be identified as such, yet be potentially infectious to others if they donated blood or if they underwent surgery for some reason.

What is asymptomatic infection?

After dietary infection with BSE, abnormal prion protein can be found in lymphoid tissue (appendix, tonsil, lymph nodes etc) before the brain is involved and neurological vCJD illness starts. This gap between infection and developing vCJD is called the incubation period or the preclinical infection period. As the person has no symptoms, but is infected, the term 'asymptomatic infection' may be used. As mentioned above, this period is likely to be measured in years. During this time, the affected individual might be able to infect others via the routes already discussed. This is not simply a theoretical risk: the blood/blood product cases outlined above resulted from blood donated by individuals in this preclinical period. It is also possible that someone could be asymptomatically infected and never go on to develop clinical vCJD; this certainly happens with other infections (as discussed below).

How many people are asymptomatically infected in the UK?

It is not known. Anonymised studies of appendices (looking for abnormal prion protein) removed during routine surgery suggest that around 1:2000 of the UK population might be symptomatically infected with BSE. However, there is a lot of uncertainty around this estimation. It is taken as a figure for the purposes of public health policy considerations, but it cannot be regarded as a definite number.

Is it possible to be tested for asymptomatic infection?

Currently, there is no simple, reliable, validated way of testing a healthy person to see if they might be silently infected.

Does asymptomatic infection always result in CJD?

It is not known whether clinical vCJD always follows asymptomatic infection. For one thing, with very long incubation periods, it is possible that infected individuals might die from other causes before they have the chance to become ill with vCJD. In addition, there are experimental data that suggest that infection may be permanently asymptomatic in some people.

Has vCJD been transmitted via surgery?

There have been no identified instances of acquiring vCJD via surgery-whether neurosurgery, general surgery, eye surgery or dental practice.

Has vCJD been transmitted via Blood Transfusion?

Three cases of vCJD have resulted from blood (red blood cell) transfusions donated by people who later went on to develop vCJD. One further person, who had received blood from a donor who later developed vCJD, died without having vCJD but was found, at autopsy, to have evidence of infection with vCJD (not affecting the brain).

Has vCJD been transmitted via Blood Products?

One person has died without having vCJD but had evidence of vCJD infection (not affecting the brain). A blood product ("Factor VIII") is considered to be the probable cause of the infection. More details concerning vCJD, blood and blood products are given in a separate factsheet: Variant CJD and Blood (see www.cjdsupport.co.uk).

The clinical picture of vCJD

vCJD has a clinical picture that typically differs in important respects from that of the most common form of CJD (sCJD), particularly in relation to the first symptoms and the rate of illness progression.
It is important to note that, although the clinical pictures of variant and sporadic CJD are rather different, there is some overlap and, sometimes, there can be uncertainty as to the type of CJD in specific cases. Any uncertainty is usually-though not always-resolved by investigations (see below).

First symptoms

vCJD often presented with psychological/psychiatric problems such as anxiety, depression, social withdrawal, behavioural changes and, sometimes, hallucinations or delusions. As a result, patients were sometimes referred initially to a psychiatrist rather than to a neurologist. In addition, some patients complained of pain or unpleasant sensations in the face, trunk or limbs. The neurological physical examination was sometimes normal in early stages, despite these symptoms.

Subsequent symptoms

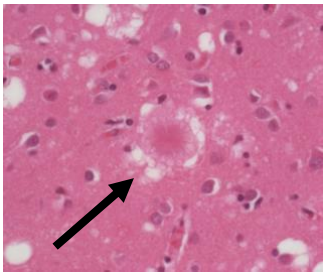
More definite neurological problems developed, often beginning with unsteadiness, incoordination and clumsiness. Progressive mental function/cognitive loss took place, along with increasing impairment of speech and motor function. Involuntary movements occured, such as tremor, fidgety movements and myoclonus (muscular jerks of parts of the body). The affected person became increasingly dependent on care, immobile and bedbound.

Rate of Progression

The rate of change was generally rapid but typically slower than that seen in sCJD; the average duration of vCJD being around 14 months compared with 4 months for sCJD.

Diagnosis

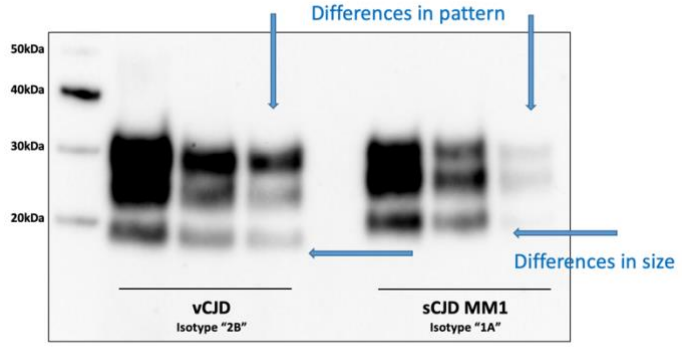
CJD in general is rare; vCJD is very rare (with, in 2024, no cases identified in the UK for around 8 years). While general practitioners should be aware of the condition, most of them have never seen a case and most will never do so in the whole of their professional life.



Microphotograph of florid plaques in brain tissue taken from a person with vCJD. **Courtesy of NCJDRSU**

It is also the case that anxiety and depression are very common symptoms in general practice and virtually always are not the result of serious neurological disease. However, the development of progressive neurological symptoms should lead to appropriate referral to a clinical neurologist and then detailed neurological assessment and investigation can take place. However, as with prion diseases in general, the presenting neurological picture is not unique to vCJD and neurologists will need to consider other diagnoses.

Currently there is no simple, absolute test for vCJD in life. An absolutely definite diagnosis requires the examination of tissue from the brain. This is usually undertaken after death, however, in certain very specific situations, a brain biopsy may be considered in life. The general hallmarks of CJD (spongiform change, loss of neurons and abnormal prion protein deposition) are present, but, in vCJD, the abnormal prion protein deposition takes the form of so-called florid plaques which are not seen typically in sCJD. In addition, the abnormal protein has a different molecular signature to that of the abnormal protein found in other forms of CJD. The protein can be extracted from the brain and studied by a laboratory technique called 'Western Blotting'.



Western Blots showing protein differences in vCJD & sCJD. **Courtesy of Angie Chong & Marcelo Barria Mateus, NCJDRSU**

Fortunately, a confident -even very confident- diagnosis can be made in life in most instances, without the need for a brain biopsy. Such a diagnosis is based on:

(1) The clinical picture being in keeping with vCJD.

(2) The exclusion of other possible diagnoses.

(3) Positive results from specific investigations.

Diagnosis (continued)

Blood tests will be needed for a variety of reasons; brain scans performed to exclude tumours or other disorders and a lumbar puncture may be needed to exclude things like viral infections. 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, under local anaesthetic, into the lower part of the back.

Some tests which can be very helpful in diagnosing other forms CJD are not so useful in vCJD: the electroencephalogram (EEG), the CSF 14-3-3 test, the CSF RT-QuIC test. In particular, the CSF RT-QuIC test, which is nearly always positive in sCJD, is negative in vCJD (which can, therefore, be helpful in distinguishing these two forms of CJD).

The most helpful diagnostic tests for vCJD are:

1. **Brain Magnetic Resonance Imaging (Brain MRI)**

While this is important in excluding other problems, it has an important positive role as in 80 per cent or more of vCJD cases, a characteristic abnormality, known as the Pulvinar sign, is seen.

2. **Specific Blood Tests**

Aside from blood tests that may be done to exclude other illnesses, specific blood tests have been developed that can detect the abnormal form of prion protein in vCJD. These are important advances in diagnosis, but they are not performed as routine tests in ordinary clinical practice. Blood would need to be sent to the particular laboratories that developed the tests. Results need to be interpreted with caution as these tests have not been evaluated in extensive numbers of patients.

3. **Tonsil Biopsy**

In vCJD, unlike other forms of CJD, the abnormal prion protein can be readily detected in tissues outside the brain, including the tonsil. In cases where the diagnosis of vCJD remains significantly uncertain, despite other investigations, tonsil biopsy may be considered.

The diagnosis of vCJD often takes time. Several neurological conditions can look very similar in the early stages; it is important to see how the illness develops over time and to exclude other conditions (some potentially treatable). In addition, clinicians do not wish to perform unnecessary unpleasant investigations on individuals. This time to make diagnosis can be a very distressing period for the family, particularly as their relative or friend may be deteriorating very rapidly. It is important that clinicians support families and friends through this difficult period and additional support is available from organisations such as the CJD Support Network.

Is there a cure for vCJD?

At present (March 2024), there is no proven treatment for any form of CJD. However, research into possible treatments is being undertaken with some potential promise; details of the current treatment situation are discussed elsewhere.

There are a number of drugs which can relieve some of the symptoms of the illness and make the patient more comfortable – for example, treatments for psychiatric symptoms, pain and the jerking movements.

Support and care

General support and care for the patient, family and friends is equally important. Social services should be involved in an early stage to advice on financial matters, respite and long term care. Various therapists – including speech and language therapists, physiotherapists and occupational therapists – will provide help with specific problems. Community nursing may provide more general nursing care outside of hospital.

There are specialist prion disease nurses based in the NPC (National Prion Clinic) in London and in Edinburgh. There is a national care package (administered by the NCJDRSU) that, in certain circumstances, provides finance for care that cannot be met by local services.

Notification

Clinicians are asked to let two organisations know of individuals suspected of having CJD: the National CJD Diagnostic Advisory Service (NCJDDAS, based in Edinburgh), and the National Prion Clinic (NPC, based in London). These organisations are able to provide information, advice and help to clinicians, patients and families. Involvement with them is entirely voluntary for the patients and their families.

Research

There is much prion disease research underway including that relevant specifically to vCJD.
Surveillance continues in order to identify any further cases, with continuing consideration of the possible risks of asymptomatic infection.

Further information and contacts

Further information about CJD may be found on the CJD Support Network website at www.cjdsupport.co.uk, our fact sheets are also available by post on request to the Network.

Support and information may be obtained from the organisations below:

CJD Support Network

Address – PO Box 3936, Chester, CH1 9NG
Website – www.cjdsupport.co.uk
Phone – 0800 774 7317
Email – admin@cjdsupport.co.uk or support@cjdsupport.co.uk

National CJD Diagnostic Advisory Service

Based at the Royal Infirmary of Edinburgh
Website page with contact information - www.cjd.ed.ac.uk
Email - loth.securecjd@nhs.scot

UK National CJD Nursing Service & National Care Fund

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