



Protecting and improving the nation's health

# Patients at increased risk of Creutzfeldt-Jakob disease (CJD): background Information for healthcare staff

## 1 General information on CJD

Creutzfeldt-Jakob disease (CJD) is one of a rare group of diseases, known as transmissible spongiform encephalopathies (TSEs), which affect the structure of the brain. TSEs cause dementia and a range of neurological symptoms, including ataxia, myoclonus, chorea or dystonia.

TSEs are recognised in both animals and humans. In animals, the best-known TSE is bovine spongiform encephalopathy (BSE or “mad cow disease”). In humans, there are four main types of CJD:

- Sporadic CJD
- Variant CJD
- Genetic CJD and other inherited prion diseases
- Iatrogenic CJD

At the moment, a CJD diagnosis can be confirmed only by histological examination of the brain following a brain biopsy, or after a post-mortem. If someone has symptoms suggestive of variant CJD (vCJD), a full neurological examination would be conducted by a specialist. There is no proven treatment or cure for CJD, and the disease leads to death. Research is being carried out on the causes, tests and possible treatments for the disease.

The National CJD Research and Surveillance Unit carries out surveillance of CJD throughout the UK and provides further information on CJD for clinicians and members of the public on its website. This includes information on diagnostic criteria, the number of cases, epidemiology, research and the latest short-term incidence projections.

## 2 Sporadic CJD

The most frequent form of CJD (accounting for 85% of cases), sporadic CJD is most common in people over 50 and affects about one in a million people in the world. It is thought to arise spontaneously. Early symptoms are usually of behavioural disturbance or mental deterioration. A rapidly progressive dementia with obvious multifocal neurological involvement soon develops. Within weeks the patient may become unsteady on their feet, lack co-ordination and become very clumsy. In some people these are the first symptoms. Later symptoms may include blurred vision or even blindness, rigidity in the limbs, sudden jerky movements, and incontinence. Death usually occurs within months of the symptoms starting.

### **3 Variant CJD**

Variant CJD was first recognised in 1996 and is thought to be caused by eating beef and beef products from cattle infected with BSE. It usually affects younger people, with a median age of onset in the late 20s. The clinical picture is different from sporadic CJD in that it often starts with psychiatric symptoms, such as anxiety and depression. There may be persistent pain, with odd sensations in the face and limbs. These symptoms are followed by more obvious neurological symptoms and progressive dementia. Variant CJD (vCJD) is also different from other human TSEs because infectious prion proteins are found outside the nervous system as well as within it, especially in the lymphoid tissues throughout the body. People with vCJD tend to live longer than people with most other forms of CJD, with an average of 14 months between symptoms starting and death.

More than 170 people have died from vCJD in the UK and a small number have died in other countries. The number of cases in the UK is now declining and the last death reported in the UK was in 2016. The latest estimates are much lower than some of the pessimistic forecasts that were made in the mid-1990s. However, nobody knows how many people will get this disease in the future.

### **4 Inherited/genetic CJD and other prion diseases**

Genetic CJD has an autosomal dominant inheritance. The patients are often younger and live longer than people who develop sporadic CJD. Between 5 and 10 cases are reported each year in the UK. The clinical features of genetic CJD vary from person to person, even within the same family. Some patients have signs and symptoms similar to those seen in sporadic CJD, while others develop ataxia and other movement disorders before dementia starts. Close blood relatives of people with genetic CJD have a one in two chance of carrying the gene and developing the disease.

More details, including information on current research, are available from the National Prion Clinic.

### **5 Iatrogenic transmission of CJD through medical treatment**

People may develop iatrogenic CJD after infectious tissue enters their body through:

- receiving infectious material such as blood components or dura mater grafts
- treatment with human-derived hormones derived from the pituitary gland such as human growth hormone or gonadotrophin
- surgery and other invasive medical procedures using contaminated instruments

The clinical features of iatrogenic CJD partly depend on the route of infection. More than 220 people have been infected after having received dura mater grafts contaminated with sporadic CJD before 1992.<sup>1</sup> A similar number have been infected through treatment with contaminated human growth hormone before 1985. More information on human growth hormone and CJD is available from the Institute of Child Health.

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<sup>1</sup> 1 Brown P et al. Iatrogenic Creutzfeldt Jakob Disease, final assessment. *Emerging Infectious Diseases*, June 2012,18:901-06.

Worldwide, there have been only four instances of people developing CJD after being operated on with instruments used during neurosurgical procedures on the brain and spinal cord and two instances of people infected with CJD from electrodes used on the brain.<sup>1</sup> These people developed CJD between 12 and 28 months after being infected. A further two cases have been linked to corneal transplants. As far as we know, variant CJD has never been spread through surgery.

## **6 Iatrogenic transmission of vCJD through blood**

Infection with vCJD has probably been transmitted to four patients through blood transfusions in the UK<sup>2</sup> from three donors who were diagnosed with vCJD after donating the blood. One of these patients had not developed clinical disease before dying from another cause.<sup>3</sup> All four cases had received transfusions of non leucodepleted red blood cells between 1996 and 1999.

The first person to develop vCJD disease following a blood transfusion was identified in December 2003.<sup>4</sup> This person developed vCJD six and a half years after receiving a transfusion of red cells. The donor of the red cells developed symptoms of vCJD three and a half years after giving blood.

Another case of vCJD 'infection' in a blood recipient was identified a few months later.<sup>3</sup> This individual had been given red cells from a donor who developed symptoms of vCJD 18 months after giving blood. This second case died from causes unrelated to vCJD five years after receiving the transfusion. At post-mortem abnormal prion protein was found in the spleen and a cervical lymph node, but not in the brain.

A third case developed symptoms of vCJD six years after receiving a transfusion of red blood cells, and died eight years and eight months after receiving the blood.<sup>5</sup> The blood donor developed vCJD about 20 months after giving blood.

The fourth case developed symptoms of vCJD eight and a half years after receiving a transfusion of red blood cells.<sup>2</sup> The donor developed vCJD about 17 months after giving blood. This donor had also donated blood to the third case.

Other routes of exposure, including most notably dietary exposure to BSE, cannot be excluded as the source of these patients' vCJD infections. However, it is highly probable that they were infected by their blood transfusion: each new case (amongst the relatively small group of individuals exposed to vCJD-implicated blood transfusions) has made this more probable.

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<sup>2</sup> 4th case of transfusion-associated vCJD infection. Health Protection Report 2007; 1;3

<sup>3</sup> Peden AH et al. Preclinical vCJD after blood transfusion in a PRNP codon 129 heterozygous patients. The Lancet, 2004; 364:527-9.

<sup>4</sup> Llewellyn CA et al. Possible transmission of vCJD by blood transfusion. The Lancet, 2004; 363:417-21

<sup>5</sup> Wroe SJ et al. Clinical presentation and pre-mortem diagnosis of variant Creutzfeldt-Jakob disease associated with blood transfusion: a case report. The Lancet, 2006; 368: 2061-67

Sporadic CJD has been monitored for many years in many countries. To date, no other forms of human prion disease, including sporadic CJD, have been transmitted by blood transfusions.

## **7 Iatrogenic transmission of vCJD through plasma products**

In 2008, a person with haemophilia was found to have evidence of the prion that causes variant Creutzfeldt-Jakob Disease (vCJD) in his spleen at post-mortem.<sup>6</sup> Tissue taken at post-mortem was examined as part of a study jointly co-ordinated by the UK Haemophilia Centre Doctors Organisation and the National CJD Research and Surveillance Unit.

This haemophilia patient had been treated in the 1990s with over 390,000 units of UK-sourced Factor VIII, including over 9,000 units from two implicated batches of Factor VIII 8Y (linked to a donor who later developed clinical vCJD). The plasma donor developed symptoms of vCJD six months after donating the plasma in 1996. The haemophilia patient was in his 70s when he died of a condition unrelated to vCJD, 11 years and one month after receiving the batch of implicated Factor VIII. He had no signs or symptoms of vCJD or other neurological disease when alive.

The investigations into the possible routes of infection for this patient are now complete and a risk assessment has been carried out by the Department of Health.<sup>7</sup>

Assuming that the abnormal prion protein did indicate vCJD infection, the risk assessment considers four possible infection routes: dietary exposure to BSE; surgical procedures; transfusions with several units of red cells; and treatment with large amounts of UK-sourced Factor VIII. This included two batches of Factor VIII 8Y that were sourced from plasma pools which included plasma from a single donor who later developed clinical vCJD. The calculations in the risk assessment depend on the likely prevalence of subclinical vCJD infections among the UK population, the infectivity of plasma products and blood components - both of which are subject to great uncertainties - and the number of donors contributing to the plasma pools. The risk assessment concludes that in scenarios based on current evidence, the most likely source of this patient's infection was treatment with UK-sourced clotting factors.

This is the first time that vCJD abnormal prion protein has been found in a patient with haemophilia or any patient treated with plasma products. To date, no haemophilia or bleeding disorder patients have been diagnosed with or died from clinical vCJD.

## **8 How might prions cause CJD?**

The cause of CJD is thought to be an abnormal form of the naturally occurring prion protein. The normal form of this protein is found in the brain and other parts of the body, in humans and many animal species, but we know little about its function. The abnormal infectious prion

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<sup>6</sup> Health Protection report, 20 February 2009, 3:7.

<sup>7</sup> vCJD risk assessment calculations for a patient with multiple routes of exposure. Department of health, 9 June 2009:

[http://webarchive.nationalarchives.gov.uk/20130124050233/http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/documents/digitalasset/dh\\_100337.pdf](http://webarchive.nationalarchives.gov.uk/20130124050233/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_100337.pdf)

protein is chemically identical to the normal form, but its physical shape is different, and it resists normal cell degradation. It is thought to build up by inducing the normal prion protein to mis-fold, but it is not known how this change happens. The abnormal prion protein then accumulates in various tissues, particularly in the central nervous system, where tissue damage is most severe. As the disease progresses, neuronal tissue is lost, and the brain becomes 'spongiform'. The immune system does not seem to respond to CJD infection.

The abnormal prion protein that starts these changes may be:

- a spontaneous change (a possible explanation for sporadic CJD)
- acquired through eating meat or meat products from cattle infected with BSE (for vCJD only)
- associated with an inherited abnormality of the prion protein gene (genetic CJD)
- acquired in a medical setting through inoculation with contaminated tissue from someone with CJD (iatrogenic CJD)

## 9 The effect of genotype on CJD infection

Of those who have been tested, most people with sporadic CJD, and, until 2009, everyone with clinical vCJD, has had a particular form of the prion protein gene (methionine homozygous at codon 129, MM) found in about a third of the UK population. This genotype probably makes the host prion protein more vulnerable to conversion into the abnormal form.

In a post-mortem carried out in July 2004, vCJD infection was detected in the spleen and one cervical lymph node of someone who had a different form of the prion protein gene (methionine valine heterozygous, MV). This patient had received a blood transfusion from a donor who later developed vCJD. The patient had had no symptoms of clinical vCJD, and had died from an unrelated cause some years after receiving the transfusion.

One possible and one confirmed clinical diagnosis of vCJD have been made in heterozygous (MV) individuals. The first patient developed symptoms in 2007 and died in 2009.<sup>8</sup> A post-mortem was not undertaken. The second patient died in 2016 and vCJD was confirmed through a post mortem.<sup>9</sup>

## 10 How CJD spreads

Eating beef or beef products from BSE infected cattle is the most likely cause of vCJD, and most of the people in the UK would have been exposed in this way. Other potential sources of CJD infection include contaminated medical equipment or infected transplant material.

Prion diseases like CJD can spread from one person to another only in certain circumstances through healthcare. They are not infectious in usual ways, eg by coughing or sneezing, touching or by having sex, nor is there evidence that the disease can spread from a mother to her unborn baby or through breastfeeding.

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<sup>8</sup> Kaski D et al. Variant CJD in an individual heterozygous for PRNP codon 129. *The Lancet*, 19/26 December 2009, 374:2128

<sup>9</sup> Mok T et al. Variant Creutzfeldt–Jakob disease in a patient with heterozygosity at PRNP codon 129. *New England Journal of Medicine*. 2017 Jan 19;376(3):292-4.

Abnormal prion proteins resist most of the usual methods which inactivate bacteria and viruses. Prions are not totally inactivated by heat, ultraviolet light or other standard sterilisation procedures such as immersion with sodium hypochlorite at normal concentrations. This is why autoclaving cannot be relied on to denature abnormal prion proteins contaminating surgical instruments following use on a patient with CJD

### **11 Measures to prevent CJD from spreading through healthcare between patients**

The following public health measures aim to reduce as far as possible the chances of spreading CJD between people:

- improving the standards and processes for decontaminating instruments
- taking special infection control measures in relation to instruments when operating on patients with, or at increased risk of, CJD
- measures to protect the blood supply (see below)
- excluding transfused donors from the living bone donation programme

### **12 Measures to protect the blood supply**

We do not know the exact risk of vCJD spreading through blood. The Department of Health in England arranged for Det Norske Veritas Consulting to assess this risk.<sup>10</sup> The Spongiform Encephalopathy Advisory Committee (SEAC) accepted the risk assessment in early 1999 and issued a position statement on TSE infectivity in blood in July 2006.<sup>11</sup>

As a result, the blood and transplant services have taken the following safety measures to reduce any possible risk of spreading vCJD through blood:

- withdrawal and recall of any blood components, plasma products or tissues donated by anyone who later develops vCJD (since December 1997) importing plasma from the USA for fractionation to make plasma products (since July 1998)
- removing white blood cells (which may carry the highest risk of spreading vCJD) from all blood used for transfusions (leucodepletion) (since November 1999)
- importing fresh frozen plasma from the USA for patients born on or after 1 January 1996 (since August 2002) later extended to patients under the age of 16 years (July 2005)
- not accepting (since April 2004) donations from people who have received a blood transfusion in the UK since 1980. In August 2004 this was extended to include people who are not sure if they have had a blood transfusion, and apheresis donors. The exclusion criteria were later extended to the recipients of blood transfusion anywhere in the world
- promoting the appropriate use of blood, tissues and alternatives throughout the NHS. This has led to a reduction in the amount of blood transfused during and following surgery

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<sup>10</sup> Risk of Infection from variant CJD in Blood. DNV Consulting

<sup>11</sup><http://webarchive.nationalarchives.gov.uk/20110316163217/http://www.seac.gov.uk/statements/statement0806.htm>

In addition, individuals who have been informed that they are at increased risk of CJD/vCJD for public health purposes because they have been exposed to a possible risk through blood transfusion, surgery, or tissue transplantation are all asked not to donate blood, tissues or organs.

We last revised this leaflet in June 2018. To check for any updates to this information, please see the current version of this leaflet at:

<https://www.gov.uk/government/publications/cjd-information-leaflets-for-patients-andhealthcare-professionals>

<http://www.hps.scot.nhs.uk/haic/creutzfeldtjakobdisease.aspx>

We welcome your comments on this leaflet. Please send them to:

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