Patients at increased risk of Creutzfeldt-Jakob Disease
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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.

A number of TSEs are recognised in both humans and animals. 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, which accounts for 85% of cases
- Variant CJD
- Inherited/genetic CJD and other prion diseases
- Iatrogenic CJD (through medical procedures).

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, 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 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, 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 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 variant CJD tend to live longer than people with most other forms of CJD, with an average of 14 months between symptoms starting and death.

Over 160 people have died from variant CJD in the UK and a small number have died in other countries. The number of cases in the UK is now declining and only one death was reported in the UK in 2008. The latest estimates are 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. There are between six and 10 new cases each year in the UK. The clinical features of genetic CJD vary from person to person, even within one 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. Over 190 people have been infected after having received dura mater grafts contaminated with sporadic CJD before 1992[1] 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.

Worldwide, there have been only four cases of people developing CJD after being operated on with instruments used before for neurosurgery on patients with sporadic CJD[10]. These people developed CJD between 12 and 28 months after being infected. Two cases have been linked to using infected electrodes on the brain and another two cases linked to corneal transplants. As far as we know, variant CJD has never been spread through surgery.

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[1] Brown P et al. Iatrogenic CJD. The waning of an era. Neurology, August 2006, 67:389-93.

6 Iatrogenic transmission of vCJD through blood

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

The first person to develop variant CJD disease following a blood transfusion was identified in December 2003[4]. This person developed variant CJD six and a half years after receiving a transfusion of red cells. The donor of the red cells developed symptoms of variant CJD three and a half years after giving blood.

Another case of variant CJD 'infection' in a blood recipient was identified a few months later[13]. This individual had been given red cells from a donor who developed symptoms of variant CJD 18 months after giving blood. This second case died from causes unrelated to variant CJD 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 variant CJD 6 years after receiving a transfusion of red blood cells, and died 8 years and 8 months after receiving the blood[5]. The blood donor developed variant CJD about 20 months after giving blood.

The fourth case developed symptoms of variant CJD 8 and a half years after receiving a transfusion of red blood cells[12]. The donor developed variant CJD about 17 months after giving blood. This donor had also donated blood to the 3rd case.

Other routes of exposure, including most notably dietary exposure to BSE, cannot be excluded as the source of these patients' variant CJD 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 variant CJD-implicated blood transfusions) has made this more probable.

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 has been found to have evidence of the prion that causes variant Creutzfeldt-Jakob Disease (vCJD) in his spleen at post mortem. 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 Surveillance Unit.

This haemophilia patient had been treated with several batches of UK-sourced clotting factors, including one batch of factor VIII that was manufactured using

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[2] 4th case of transfusion-associated vCJD infection. Health Protection Report 2007; 1;3,
[3] Peden AH et al. Preclinical vCJD after blood transfusion in a PRNP codon 129 heterozygous patients. The Lancet, 2004; 364:527-9.
[4] Llewellyn CA et al. Possible transmission of vCJD by blood transfusion. The Lancet, 2004; 363:417-21
[5] 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

plasma from a donor who went on to develop vCJD. The plasma donor developed symptoms of vCJD 6 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.

A final view as to how vCJD abnormal prion protein was transmitted to this haemophilia patient has yet to be reached because investigations are continuing to be sure of the source.

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.

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 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 arise:

- spontaneously (a possible explanation for sporadic CJD)
- acquired through eating meat or meat products from cattle infected with BSE (for variant CJD 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 everyone with variant CJD, have a particular form of the prion protein gene (methionine homozygous) found in 40% of people in the UK. 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, variant CJD infection was detected in the spleen and one cervical lymph node of someone who had a different form of the prion protein gene (MV heterozygous). This patient had received a blood transfusion from a donor who later developed variant CJD. The patient had received a blood transfusion from a donor who later developed variant CJD. The patient had had no

symptoms of variant CJD, and had died from an unrelated cause some years after receiving the transfusion.

10 How CJD spreads

Eating beef or beef products from BSE infected cattle is the most likely cause of variant CJD, 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, e.g., they are not spread 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 spread through breastfeeding.

Abnormal prion proteins resist most of the usual methods to 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 variant CJD spreading through blood. The Department of Health in England arranged for Det Norske Veritas Consulting to assess this risk[6]. 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[7].

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[6] Risk of Infection from variant CJD in Blood. DNV Consulting.

[7] http://www.seac.gov.uk/statements/statement0806.htm

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

- Withdrawal and recall of any blood components, plasma products or tissues donated by anyone who later develops variant CJD (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 variant CJD) from all blood used for transfusions (leucodepletion) (since November 1999).
- Importing fresh frozen plasma from the United States for patients born on or after 1st 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.
- Exclusion of blood donors whose blood has been transfused to recipients who later developed vCJD, where blood transfusion cannot be excluded as a source of the vCJD infection and where no infected donor has been identified (July 2005).

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 informed that they should not donate blood, tissues or organs.

We last revised this leaflet in February 2009. To check for any updates to this information, please see the current version of this leaflet at www.hpa.org.uk/cjd
We welcome your comments on this leaflet. Please send them to cjd@hpa.org.uk