GP only.

VARIANT CREUTZFELDT-JAKOB DISEASE (vCJD) and BLOOD TRANSFUSION

CLINICAL INFORMATION

This document contains information relating to people who are to be considered to be *'at-risk of vCJD for public health purposes'* due to having received a blood transfusion from a donor who also donated blood to a patient who later developed vCJD. We hope it will provide answers to some queries these people, or their healthcare staff, may have.

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Health Protection Agency

Health Protection Scotland

1. Introduction

In 2000 an independent expert advisory committee, the CJD Incidents Panel (the Panel), was established on behalf of the UK Chief Medical Officers to advise all those bodies responsible for the provision and delivery of health care on how to manage incidents involving the potential transmission of CJD between patients. 'Incidents' include blood transfusion, organ transplantation and exposure to contaminated instruments used in healthcare interventions.

The CJD Section of the Health Protection Agency (HPA), based at Colindale, North-West London, provides the secretariat to the CJD Incidents Panel, and provides assistance to healthcare workers implementing Panel advice. Health Protection Scotland (HPS) provides assistance in Scotland.

This document is aimed at clinicians and other staff at local level who may be involved in notifying individuals who have been identified as ***recipients of blood from donors to vCJD cases*** where it is suspected that the vCJD case may have been infected by their transfusion and that therefore other recipients from this donor are to be considered to be ***'at-risk of vCJD for public health purposes'***. This document contains more detailed information than the 'Information for Patients' document, and will hopefully provide answers to some further questions patients may ask. This document is therefore primarily intended for use by the staff who are involved in direct communication with a transfusion recipient, to supplement the 'Information for Patients' document. However, if considered appropriate and likely to be useful, this document may also be given to a recipient.

2. Background

Transfusion as a route of transmission

In 2003, a recipient of blood from a donor known to have later developed variant CJD (vCJD) died and post-mortem investigations resulted in a diagnosis of vCJD[1]. This patient had suffered onset of depression 6½ years after transfusion, and died 13 months later. The donor to this patient had died of vCJD 3½ years after the implicated donation.

In 2004, the recipient of an implicated component (in 1999) from another donor died of causes unrelated to vCJD. Post-mortem investigations found abnormal prion protein, the vCJD agent (PrP^{Sc}), in spleen and lymph node tissue: there were no signs of vCJD disease in the brain of this patient[2].

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[1] Llewelyn CA, Hewitt PE, Knight RSG, Amar K, Cousens S, Mackenzie J, Will RG. Possible transmission of variant CJD disease by blood transfusion. 2004 Lancet 363;417-421.
[2] Peden AH, Head MW, Ritchie DL, Bell JE, Ironside JW. Preclinical vCJD after blood transfusion in a PRNP codon 129 heterozygous patient. 2004 Lancet 364;527-529.

Although other exposures, including most notably dietary exposure to BSE, cannot be excluded as the source of these patients' infections, it is considered highly probable that these patients were infected by blood transfusion. These two reports add to previous evidence of infectivity in blood obtained from experiments in animals.

Actions already taken for recipients

Between 2000 and 2003, the Panel developed and consulted on proposals for the appropriate management and notification of patients identified as at an increased risk of CJD due to iatrogenic exposures, including receipt of blood transfusion from a donor who subsequently developed vCJD (i.e. an implicated blood component).

In 2003, after the first case above had been reported, the HPA was asked to implement the recommendations of the Panel and to coordinate the notification of patients who may have been exposed to vCJD through implicated blood components in England, Wales and Northern Ireland, starting with those already identified, and continuing as further cases are identified. HPS takes responsibility for this notification in Scotland.

Actions already taken for donors to vCJD cases

During 2004, the question arose about whether the donors of blood given to recipients who later developed vCJD were at increased risk of having a sub-clinical (asymptomatic) vCJD infection. The key question here is the likelihood of such donors being the source of the recipients' infection and therefore themselves infected. A risk assessment was conducted by the Department of Health's Standards and Quality Analytical Team (www.dh.gov.uk/cjd). This risk assessment, and its implications, were considered by the CJD Incidents Panel during the first half of 2005. The Panel recommended that these donors should be informed of their *implied* increased risk of vCJD infection and considered to be 'at-risk of vCJD for public health purposes'. This recommendation has been implemented by the HPA and HPS since July 2005.

Actions now being taken for other recipients of blood from donors to vCJD cases

In September 2005, the CJD Incidents Panel considered the estimated risks for other patients who had received blood from donors to vCJD cases, and made further recommendations to the Chief Medical Officer.

3. Recommendations of the CJD Incidents Panel

The potential risk of vCJD infection that is implied by being the recipient of blood from a donor who also donated blood to a patient who later developed vCJD is very uncertain, and several assumptions are involved in estimating

this risk of infection. However, some individuals identified in this way could pose a potential (and avoidable) risk to others in certain circumstances.

The Panel has recommended the classification of some individuals as 'at-risk of vCJD for public health purposes' in order to enable the implementation of certain public health precautions to limit any possible human-to-human transmission of CJD.

The Panel recommends that:

- Recipients of blood from donors to vCJD cases (with transfusion as a suspected route of infection) should be considered to be 'at-risk of vCJD for public health purposes' if the probability of being infected with vCJD is estimated to be well above 1%.
- These recipients and their clinicians should be informed and asked to implement certain public health precautions (see below), as already advised for other asymptomatic patients identified as 'at-risk' for public health purposes i.e. not to donate blood or other tissues/organs, and to tell their healthcare staff (including dentists) who should then apply the ACDP TSE Working Group Infection Control Guidelines (see Sources for additional information at the end of this document).

Neither the threshold, nor the exact risk estimate value for any individual recipient should be considered useful as an indicator of an individual's risk of developing vCJD. This risk is unknown.

4. Advice and care for 'at-risk' individuals

Care for individuals being notified

The information that has to be given to individuals who are considered to be 'at-risk' of vCJD may be distressing.

It is quite likely that these individuals will ask for definite information about their risk of developing vCJD. Unfortunately, this is not possible.

Many people in the UK will have had possible dietary exposure to the BSE agent responsible for vCJD between 1980 and 1996. Whether these recipients (and their donors who have donated blood to a vCJD case) do actually have a higher risk of being infected than the rest of the population, is not known. However, at this point in time, with the information available, there is more reason to suspect these individuals may be infected with vCJD.

Providing this information requires careful consideration and preparation, including making arrangements for follow-up discussions with appropriate healthcare staff.

Some individuals may require consultations to discuss the implications of the information from the UK Blood Services to help them understand and come to terms with what they have been told. Advice should be sought from local counsellors if required.

Advice for individuals being notified

The following advice may answer some queries from individuals who are notified as 'at-risk of vCJD for public health purposes'.

Infectivity:

Routine contact with people who have vCJD, including those considered 'at-risk' of vCJD, does not pose a risk for relatives, healthcare workers (nor patients of healthcare workers) or the community at large. vCJD is not infectious in the usual way - by airborne droplets (like colds and flu) or by skin contact or through sexual intercourse. There is no evidence that vCJD could be vertically transmitted from mother to child.

5. Public health precautions against vCJD

From animals to humans: Several public health measures have been implemented to minimise the risk of transmission of vCJD to humans from meat and meat products infected with Bovine Spongiform Encephalopathy (BSE or 'mad-cow disease'). These include banning the feeding of mammalian protein to other mammals, and removing certain high-risk tissues (e.g. brain and CNS) from the human food chain.

From humans to humans: Several public health measures are aimed at minimising any possible risk of transmitting vCJD between people. These include: improving decontamination standards for instruments used in healthcare interventions; taking special infection control precautions for instruments used on patients with, or considered 'at-risk' of, vCJD; and measures to prevent infectious blood being transfused to patients or being used to manufacture plasma products.

Special precautions for certain medical procedures are needed because standard decontamination processes cannot be relied on to remove all the infectivity from instruments used for healthcare interventions on patients with vCJD.

Special precautions for individuals considered 'at-risk of vCJD for public health purposes': When someone is considered to be 'at-risk of vCJD for public health purposes', they are asked to take certain special precautions to reduce the risk of spreading the infection to others. These are:

- **Not to donate blood;**
- **Not to donate organs or tissues;**
- **To tell whoever is treating them before they undergo medical, surgical or dental treatment, so they can then arrange any special procedures for the instruments used in their healthcare. (This subject is considered in more detail in Section 9);**
- **That it would be best if they told their family about this in case, for any reason, they need health care in the future, and their family can help by telling the doctors (e.g. for emergency care).**

Special measures to protect the blood supply:

Several public health precautions have been taken to reduce any possible risk of transmitting vCJD through blood. These precautionary measures include:

- Withdrawal and recall of any blood components, plasma products or tissues obtained from any individual who later develops vCJD (December 1997).
- Importing plasma from the USA for fractionation to manufacture plasma products (1998).
- Removal of white blood cells (which may carry the greatest risk of transmitting vCJD) from all blood used for transfusion (leucodepletion) (October 1999).
- Importing fresh frozen plasma from the United States for patients born on or after 1st January 1996 (March 2004), extended to all children under 16 years of age (Summer 2005).
- Not accepting donations from people who have themselves received a blood transfusion in the UK since 1980 (April 2004). This has been extended to include two new groups: apheresis donors and donors who are unsure if they have previously had a blood transfusion (August 2004).
- Promotion of appropriate use of blood and tissues and alternatives throughout the NHS.

Asking individuals who are identified as 'at-risk of vCJD for public health purposes', not to give blood is one further measure to reduce the risk of vCJD transmission by blood transfusion.

6. CJD-related healthcare incidents

CJD 'incidents' occur when there is a possibility that patients could have been exposed to CJD, either through exposure to contaminated instruments used

in healthcare interventions, through transplantation, blood transfusion or treatment with plasma products.

The Panel advises on the handling of these incidents, including advice on the management of patients who could have been exposed to vCJD, and individuals identified as at an increased risk of vCJD. The Panel assesses the risk to patients, and advises whether individuals should be contacted and informed about their possible exposure/risk. These individuals are then advised whether special public health precautions need to be taken to prevent possible transmission to others.

More information on the Panel is available on the HPA website at: http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm. This includes the Panel's framework document, which sets out the principles of managing CJD incidents and also describes some of the risk assessments that underpin the risk management, particularly relating to incidents involving blood or instruments used in healthcare interventions.

7. Calculation of potential vCJD risk for donors to vCJD cases

Evidence of transmission of vCJD by blood transfusion

In vCJD, the disease process involves many tissues (more than in the sporadic form of CJD), including the lymphoid tissue. This raised concerns about the possibility of infectivity in blood.

The Department of Health (England) commissioned an assessment of the risk of transmitting vCJD through blood by Det Norske Veritas Consulting (DNV), which was assessed by the Spongiform Encephalopathy Advisory Committee (SEAC). An update was published in 2003. This can be found at http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm.

As mentioned above, early in 2004, a case of vCJD was reported in a patient who some years earlier had received a blood transfusion from a donor who later died of vCJD[1(page 2)]. This was the first case of transfusion-associated vCJD infection and increased the existing concern (based on experiments in animals) that blood might be infective for vCJD. A second probable case of transmission of vCJD infection by transfusion was reported in July 2004[2(page 2)]. In this second case, the recipient did not develop clinical vCJD and died of unrelated causes.

Based on this and other evidence available from animal experiments, blood transfusion is considered able to transmit vCJD infection between humans.

Animal data suggest that infection in blood may get higher (or more likely) as the donor gets closer to developing disease. However, it is not possible to know whether a donor's blood would have been infectious at the time it was

donated. It is also not known whether a recipient is likely to become infected, or to develop disease.

Rationale for assessing donors to vCJD cases and their other recipients as 'at-risk'

If a patient with vCJD has received blood, and this blood is suspected as a possible source of that patient's vCJD infection, this suggests that the donors of these blood transfusions may have an increased risk of infection, i.e. the patient with vCJD may have got the infection from their blood transfusion. This 'reverse' risk was analysed by the Department of Health's Standards and Quality Analytical Team during 2004 (http://www.dh.gov.uk/assetRoot/04/11/53/12/04115312.pdf). The results of this analysis and the implications of those results were reviewed by the CJD Incidents Panel in 2005.

If these donors, with an *implied* increased risk of vCJD due to their donation to a vCJD case, have given other blood donations, the recipients of these other donations may also have an increased risk of vCJD infection.

Assessment of each recipient

Recipients of blood who develop vCJD might have been infected via their transfusion, or via their own dietary exposure to BSE. The risk assessment considers the chance of any given donor (contributing to a recipient's transfusion(s)) being the source of infection.

The calculations used to assess the risk of vCJD associated with transfusion are based on a number of 'worst case' assumptions, including that any blood component[3] from an infected donor would pass vCJD infection on to the recipient. This is a precautionary approach. The assessment also assumes (unless other information is available) that blood recipients and blood donors are equally likely to have been infected by dietary exposure to BSE.

Given these assumptions, estimates can be made of a) the probability of a donor to a vCJD case being infected with vCJD, and b) the probability of other recipients of blood from this donor being infected with vCJD.

The probability of a) above, depends heavily on the number of blood components the vCJD case has received. The more blood components a patient has received, the more likely it looks that they were infected by blood transfusion. However, because the risk is now split between more possible sources, each individual donor has a lower chance of being the source of infectivity.

[3] Blood components are derived from a single blood or plasma donation or, in the case of platelets, a small pool usually of about four donations. These are labile products with a short shelf life. Blood components include whole blood; red cell preparations; platelets; granulocytes; fresh frozen plasma; and cryoprecipitate (made by freezing and thawing plasma).

The Panel has recommended that:

- all donors with a chance of being infected that is not clearly below 1% should be considered 'potentially at-risk of vCJD for public health purposes';
- all recipients of other donations from these donors with a chance of being infected that is well above 1% should be considered 'at-risk of vCJD for public health purposes'.

The threshold of 1% is a guide for implementing special public health precautions to limit any possible human-to-human transmission of vCJD. The uncertainties underlying the assessment of 'risk' are great, and several precautionary assumptions are involved. Also, this estimate only concerns the probability of being *infected*, not of becoming *diseased*. Therefore, **neither the threshold, nor the exact risk estimate value for any individual recipient should be considered useful as an indicator of an individual's risk of developing vCJD.** This risk is unknown.

8. Identifying individuals who have received blood from a donor who also donated blood to a patient who later developed vCJD.

In 1997, a system was established between the National CJD Surveillance Unit (NCJDSU) and the United Kingdom Blood Services (UKBS) to investigate whether any type of CJD (sporadic, familial or variant) was transmitted by blood transfusion. This study (the Transfusion Medicine Epidemiology Review (TMER), http://www.cjd.ed.ac.uk/TMER/TMER.htm) reviews data for any evidence of CJD infection in the recipients of blood from CJD cases, and for any evidence of CJD infection in the donors of blood to CJD cases.

When a patient is diagnosed with vCJD, the UKBS are informed and checks are made (of UKBS and hospital records) to find out whether the patient ever ***donated*** blood, and whether the patient ever ***received*** blood donated by others.

Patients with vCJD who have received blood

All vCJD patients are investigated to see if they ever received a blood transfusion. When past transfusions are identified, hospitals are asked to identify the donations given to these patients, and these details are passed to the relevant UKBS Medical Director to identify the donors. To date, review of the medical history of all reported vCJD cases in the UK has identified 6 cases with confirmed past transfusion. In one case, blood transfusion occurred after the onset of vCJD, and can therefore be excluded as a possible source of infection. Blood transfusion has been discounted as the likely source of infection in another case, based on timing of transfusion and onset of disease in the recipient. For one case, a donor with vCJD had already been identified and is thought to have probably been the source of the recipient's infection. This leaves three cases (to October 2005) for which transfusions are suspected as a possible source of vCJD infection.

Donors to these cases
The donors of these donations have been traced and informed, and asked to take precautions to avoid the risk of passing infection on to others (as in Section 5).

Other recipients of blood from these donors
The UKBS and hospitals are tracing the recipients of other donations from these donors, and these individuals are now being informed and asked to take precautions (as in Section 5).

9. Public health precautions for 'at-risk' patients

9.1 Advice to individuals and their general practitioners

Individuals considered 'at-risk' for public health purposes due to having received a blood transfusion from a donor who also donated blood to a patient who later developed vCJD are asked to take certain public health precautions in order to reduce the chance of passing on vCJD to other people:

- **Do not donate blood.**
- **Do not donate organs or tissues.**
- **Tell whoever is treating you before you undergo medical, surgical or dental treatment, so they can arrange any special procedures for the instruments used in your healthcare.**
- **It would be best if you tell your family about this in case, for any reason, you need medical care in the future and your family can help by telling healthcare staff.**

All individuals considered to be 'at-risk' for public health purposes should be advised to inform healthcare staff of this fact so that extra infection control precautions can be taken when required. They should be asked to inform all healthcare professionals, for example, in private clinics, not just those working in the NHS. Individuals should also be asked to inform their families, in case they need emergency surgery in the future, and their families can alert the healthcare staff.

The general medical practitioners of these individuals should:

- know that their patient is being informed about their 'at-risk' status;
- record their patient's vCJD 'at-risk' status and the special precautions required in their primary care records (the Panel advises that this should only be done once the patient is aware of their exposure to vCJD);
- include this information in any referral letters should their patient require invasive healthcare interventions, for example a surgical

operation; (Guidance on infection control for patients considered 'at-risk' of vCJD is produced by the ACDP TSE Working Group [http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm])

- check if their patient has given any donations of tissues or organs (during life, or at death if the patient is now deceased), and check if their patient has undergone any invasive healthcare interventions (e.g. surgery, endoscopy, in hospital or primary care) in the past 12 months and, if they have, liaise with their local Health Protection Team in order to ascertain whether any further action needs to be taken.

The clinical care of patients identified as 'at-risk' should not be compromised in any way.

9.2 Future donation of blood, tissue and organs

Patients who are considered 'at-risk' for public health purposes are asked not to donate organs, tissues or blood.

There is no evidence that vCJD can be sexually transmitted or transmitted from parent to child. However, as a precautionary measure, men who are 'at-risk' of vCJD should be advised not to be sperm donors, and women who are 'at-risk' of vCJD should be advised not to donate breast milk.

9.3 Future invasive healthcare interventions (in UK and abroad)

Guidance on infection control ***in the UK*** for any patient who is considered 'at-risk' of CJD is provided by the ACDP TSE Working Group: http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm. This guidance describes the infection control measures that should be taken in hospital care, in surgery, and community healthcare including dentistry. This TSE Infection Control Guidance should be followed.

When individuals who are 'at-risk' for public health purposes need to undergo an invasive healthcare intervention, they should inform the healthcare professional in charge of their care about this so that special infection control precautions can be taken, if required. This information should also be included in the referral letter from their GP.

Should an 'at-risk' individual require invasive treatment while ***abroad***, it is recommended that they:

- inform the foreign medical staff that, in the UK, certain special infection control precautions are advised when they have surgery/invasive treatments, and that this is in order to reduce the risk of vCJD transmission

- advise the foreign medical staff to contact their own national source of Infection Control Advice, who can contact the HPA Centre for Infection Duty Doctor on +44 208 200 6868 to obtain advice about infection

control precautions recommended for the procedure they are planning to perform, or have performed.

HPA Duty Doctors are on call 24 hours a day, and have information about what to do in the event of such a call, where to find the Guidance on Infection Control relevant for these patients, and contact numbers for experts who can assist in the interpretation of the Guidelines if/as necessary.

In situations where it is not possible to inform healthcare staff prior to treatment, they should be informed after treatment. This situation may occur in the UK as well as abroad, for example in the event of an emergency where the patient is unconscious. The infection control precautions can still be effective even if known about after the operation (or other procedure) has been performed.

9.4 Dentistry

Individuals considered 'at-risk' for public health purposes should inform their dentist about this. This will enable the dentist to ensure satisfactory standards of infection control are used. Dentists should also include the information in referrals to specialists such as maxillofacial surgeons.

The ACDP TSE Infection Control Guidance states that:
"The risks of transmission of infection from dental instruments are thought to be very low provided optimal standards of infection control and decontamination are maintained. General advice on the decontamination of dental instruments can be found in guidance prepared by the British Dental Association (BDA) on 'Infection control in dentistry'. This document (known as the 'A12') is available from the BDA and can be accessed on their website at www.bda-dentistry.org.uk. Dental instruments used on patients defined in Table 4a [this includes patients 'at-risk' in relation to CJD] can be handled in the same way as those used in any other low risk surgery i.e. these instruments can be reprocessed according to best practice and returned to use. Optimal reprocessing standards must be observed. Additionally, dentists are reminded that any instruments labelled by manufacturers as 'single use' should not be re-used under any circumstances.

"There is no reason why any of the categories of patients defined in Table 4a [including those 'at-risk'] or their relatives should be refused routine dental treatment. They can be treated in the same way as any member of the general public."

A letter from the English Chief Dental Officer was sent to all dentists in England in February 2005 to give information and advice about the treatment of patients with or 'at-risk' of vCJD. This letter can be found via http://www.hpa.org.uk/infections/topics_az/cjd/guidance.htm .

9.5 Previous invasive healthcare interventions and donations

Past invasive healthcare interventions

Patients considered 'at-risk' of vCJD may have undergone invasive healthcare interventions in the past. If this is the case, instruments that have come into contact with medium- or high-infectivity tissues (i.e. brain, spinal cord, posterior or anterior eye, olfactory epithelium or lymphoid tissue) could pose an infection risk to other patients. This is because the infective agent for vCJD, the abnormal 'prion' protein (PrP^{Sc}), may not be completely removed by routine decontamination processes.

The CJD Incidents Panel (see Introduction) advises on the actions to be taken in the event of such past procedures.

Any risk of transmitting vCJD on such instruments will decrease each time they are used and decontaminated. For past procedures the Panel generally considers that instruments are unlikely to pose a significant risk of infection to other patients if they have been through more than ten cycles of use and satisfactory decontamination.

Recent procedures on medium or high risk tissues in which instruments may not have undergone more than ten cycles of use and satisfactory decontamination since being used on an 'at-risk' patient should be reported promptly to the Panel as described at: http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm. These procedures should be reported (in liaison with local health protection unit/team) using the reporting form available on this website.

Medical services vary in how often different instruments are re-used and decontaminated. For some procedures, all instruments may be re-used and decontaminated many more than 10 times each month; for other procedures instruments are re-used far less frequently. A review of each 'at-risk' patient's medical history over the previous 12 months is expected to reveal any instruments that may still pose a potential risk to other patients. For some instruments that are particularly difficult to clean satisfactorily, the Panel may advise action even after more than 10 cycles of use and decontamination.

The medical records of patients who are considered 'at-risk' of vCJD who have died within the last year should be reviewed in the same way (i.e. to detect any instrument that may not have been re-used and satisfactorily decontaminated more than 10 times since use on the patient).

The Panel may advise that instruments used in medium- or high-risk procedures should be quarantined immediately or destroyed. (It is advisable to consider quarantining such instruments if identified while awaiting Panel advice.) Usually, the removal of instruments from use will only be advised for

instruments that may not have undergone more than ten cycles of use and satisfactory decontamination since their use on the 'at-risk' individual.

The Panel currently advises that patients exposed to these instruments in subsequent operations do *not* need to be contacted. This advice would be reviewed should an 'at-risk' patient develop vCJD.

Provided that standard decontamination processes have been used, other operations (either not involving any high- or medium- infectivity tissue, or where instruments have all been through more than ten cycles of use and satisfactory decontamination) that have been undertaken on these 'at-risk' patients do not need to be reported to the Panel or investigated further.

Past donations of tissues or organs

Any donations of tissues or organs made by these 'at-risk' individuals since their transfusion should be reported to the Panel. The Panel will advise what should be done for patients who have received tissues or organs donated by any of these 'at-risk' individuals.

Past donations of blood

These individuals may have themselves made donations of blood after the transfusion that has put them 'at-risk' – some transfusion recipients go on to be motivated blood donors. Any donations of blood made by these 'at-risk' individuals since their transfusion should be reported to the Panel. The Panel will advise what should be done about such donations.

10. About CJD

10.1 General

Creutzfeldt-Jakob Disease (CJD) is one of a rare group of diseases, known collectively as 'transmissible spongiform encephalopathies' (TSEs), which affect the structure of the brain causing dementia and a range of neurological symptoms, including ataxia and jerky movements.

A number of TSEs are recognised in both humans and animals. In animals, the best-known TSE is bovine spongiform encephalopathy (BSE - sometimes referred to in the news as 'mad-cow disease'). In humans, there are four main types of CJD: of these, sporadic CJD accounts for 85% of cases. The other types are familial, iatrogenic and vCJD.

At present, TSEs, including vCJD, can only be reliably diagnosed by the histological examination of tissues taken by biopsy or after a post mortem. There is no blood test for CJD as yet, no proven treatment and in all patients who have developed disease, the disease has been fatal.

10.2 Types of CJD

Sporadic CJD

Sporadic CJD is most common in people over 50 years of age, and affects about one person per million per year worldwide. It appears to arise spontaneously. Early symptoms are usually of mental deterioration or behavioural disturbance. A rapidly progressive dementia with obvious multifocal neurological involvement soon develops and within weeks the patient may become unsteady on their feet, lacking in co-ordination and markedly 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. The course of the disease is typically measured in months.

Familial CJD

Familial CJD has an autosomal dominant inheritance. The patients are often younger and the duration of the illness has a longer time course than sporadic CJD. Between six and ten cases are seen each year in the UK. The clinical features of genetic CJD are variable, even within affected families. Some patients exhibit clinical features that resemble sporadic CJD, while others present with ataxia and other movement disorders before the onset of dementia.

Iatrogenic CJD

Iatrogenic CJD has occurred through inoculation with infected tissue either via surgical procedures or transfer of infective material, or through treatment with human pituitary derived hormones such as human growth hormone. The clinical features of this diverse group of patients are partially dependent on the route of transmission. Worldwide there have been four cases of CJD (of the sporadic/classical form) associated with neurosurgery with a mean incubation period of about 18 months. Two cases have been linked to the use of depth electrodes used on the brain and a further two to corneal transplants. About 150 people have been infected following grafting with contaminated dura mater, and over 100 people through treatment with contaminated human growth hormone. There have been two cases of probable transmission of vCJD infection (one without clinical disease) associated with blood transfusion in the UK (announced late 2003 and 2004) to date [1,2 (page 2)].

Variant CJD (vCJD)

Variant CJD was first recognised in 1996 and is thought to be caused, in the first instance, by dietary exposure to the BSE agent of cattle, although no-one knows the exact route of infection. It typically affects younger people with a

median onset age in the late 20s, and symptoms differ from those of sporadic CJD in that they are often psychiatric at onset, such as anxiety and depression, and there may be persistent pain, with odd sensations in the face and limbs. These are followed by more obvious neurological symptoms and progressive dementia. Variant CJD also differs from other human TSEs in that the transmissible agent is detected outside the nervous system, as well as inside, especially in the lymphoid tissues throughout the body. Variant CJD has a relatively longer time course than most other forms of CJD, with an average period of 14 months between the onset of symptoms and death.

Just over 150 cases of vCJD have occurred in the UK and a small number in other countries. The UK epidemic reached a peak in 2000, and since 2000 the number of cases each year has been declining. Estimates of the total number of patients have been revised downwards from some of the pessimistic forecasts that were made in the mid-1990s. However no-one knows how many people will be diagnosed with this disease in the future, and no-one knows how many people may be infected but not develop disease. Further information, including monthly numbers of cases and the latest short-term incidence projection is available from the National CJD Surveillance Unit's website: http://www.cjd.ed.ac.uk.

10.3 Abnormal prion protein (PrP^{Sc})

The cause of CJD is thought to be an abnormal form of the naturally occurring prion protein (PrP) that can be infectious. In its normal form, designated as PrP^{C}, this protein occurs in the brain and other parts of the body in humans and a wide range of animals; its function is unknown. The abnormal prion protein, designated as PrP^{Sc}, is chemically identical to the normal form but its physical shape is different, making it resistant to normal cell degradation. It is thought to build up by inducing normal protein to misfold, although how this change occurs is unknown. These changes lead to accumulation in various tissues, with the highest levels occurring in the central nervous system where tissue damage is most severe. As the disease progresses there is loss of neuronal tissue which gives rise to the characteristic 'spongiform' appearance of the brain.

One important effect is that there is no discernible response from the immune system. In addition, the abnormal prion protein is resistant to most of the common methods used for inactivating bacteria and viruses. As a consequence, prions are not totally inactivated by heat, ultraviolet light or other standard sterilisation procedures such as immersion in sodium hypochlorite at normal concentrations. Autoclaving cannot be relied upon to denature any abnormal prion protein remaining on surgical instruments following surgery.

The initial abnormal prion protein needed to seed the above process may occur spontaneously as a rare event (a possible explanation for sporadic CJD); be associated with an inherited genetic abnormality of the PrP gene

(familial CJD); or be acquired, either from contamination with tissue from an infected person in a medical setting (iatrogenic CJD) or, as in vCJD, most likely following oral exposure to the BSE agent.

The majority of people with sporadic CJD and all the people diagnosed with vCJD who have been tested, have a particular form of the PrP gene that is found in 40% of the UK population. This genotype probably makes PrP^C more vulnerable to conversion into the abnormal form associated with disease. In July 2004, a patient with a different form of the PrP gene had vCJD infection detected in their spleen and one cervical lymph node during a post mortem[2(page 2)]. The patient had died from a cause unrelated to vCJD. This was some years after a transfusion of red blood cells from a donor who later developed vCJD. The patient had not become ill with vCJD and it is unclear whether they would ever have done so.

10.4 Transmission of CJD

Prion diseases are transmissible in certain circumstances, but they are not infectious in the usual way. They are not spread by respiratory droplets, direct skin contact or sexual contact, nor is there evidence of mother-to-child transmission.

There is no epidemiological evidence that transfusion of blood from people with sporadic CJD has resulted in transmission of infection. However, experiments in which blood from humans with sporadic CJD is injected intra-cerebrally into animals suggest that blood may contain infectivity, albeit at a relatively low level. It is possible that some cases of transmission by transfusion could have occurred without this being recognised. Experiments in several animal models have shown that blood from an animal infected with a TSE can be infective when inoculated intra-cerebrally into the same species. An on-going experiment in sheep has shown transmission of experimentally induced BSE via blood transfusion. Other evidence suggests that infectivity of blood from animals that are infected but asymptomatic is less than when symptoms develop.

There have been two cases of probable transmission of vCJD infection via blood transfusion from donors who themselves died of vCJD[1,2 (page 2)]. These reports strongly suggests that there is infectivity in human blood, at least at some stages of disease, and that this can be transmitted by blood transfusion.

The consumption of BSE-contaminated beef or other bovine-derived products between 1980 and 1996 in the UK remains the most likely source of acquiring vCJD, and the source to which most of the UK population would have been exposed. Other sources of vCJD infection may include inoculation from contaminated medical equipment or infected transplant material. So far, there are no recorded instances of vCJD being spread through surgery, nor have there been any cases amongst recipients of plasma products made from

pools of plasma including donations from individuals who later developed vCJD.

10.5 Treatment and tests for vCJD

There are no proven treatments or cures for vCJD at present, although research is underway into potential treatments for the disease. One trial of a treatment is in progress at the NHS National Prion Clinic and the Medical Research Council Prion Unit. Entry into this trial is now discussed with all patients who are diagnosed with vCJD (and those with other forms of CJD).

There is no blood test currently available for vCJD. Tests for vCJD can sometimes be done on certain tissues by 'biopsy'. Biopsies can be useful in helping confirm a diagnosis of vCJD in someone who is actually suffering symptoms suggestive of the disease. However, their use in people who are well is nowhere near as helpful and is not generally recommended.

Blood tests are under development and may become available in the future. It is not yet known how accurate these blood tests will be, and whether they will be reliable enough to tell an individual whether they really are infected or not.

Clinical tests (e.g. MRI scans, and physical tests) are also not generally thought to be informative, or helpful, for asymptomatic individuals.

Patients who are interested in finding out more about available possibilities of testing, e.g. tonsil biopsy, or who would like a clinical assessment, should be referred to a specialist at a local neurology department in the first instance. A decision can then be made as to whether to refer to a specialist in prion diseases at either the National CJD Surveillance Unit or National Prion Clinic (addresses are given at the end of this document) where the pros and cons of available options could be discussed in more detail.

11. Sources for additional information

The process of informing transfusion recipients about their 'at-risk' status, and the special precautions needed, is being undertaken by the UK Blood Services, with additional information and support being provided by their GP with help from their local public health doctor. The Health Protection Agency (HPA) in England, Wales and Northern Ireland, and Health Protection Scotland (HPS) in Scotland, are providing assistance to these staff and will provide further information as appropriate.

More information about CJD with useful links is available from the HPA and HPS websites:

HPA: http://www.hpa.org.uk/infections/topics_az/cjd/menu.htm

Including other Information leaflets concerning 'vCJD and Blood Components' and 'vCJD and Plasma-products' at:
http://www.hpa.org.uk/infections/topics_az/cjd/information_documents.htm

Health Protection Scotland (formerly the Scottish Centre for Infection and Environmental Health - SCIEH): http://www.hps.scot.nhs.uk

Patient Support Groups

CJD Support Network http://www.cjdsupport.net/ Helpline: tel 01630 673973

Human BSE Foundation http://www.hbsef.org/

Further information is available as follows:

CJD Incidents Panel
http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm

Transmissible Spongiform Encephalopathy Agents: Safe Working and the Prevention of Infection. Guidance from the Advisory Committee on Dangerous Pathogens and the Spongiform Encephalopathy Advisory Committee. 1998 and 2003.http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/

Assessing the Implications for Blood Donors if Recipients are infected with vCJD, Department of Health

http://www.dh.gov.uk/assetRoot/04/11/53/12/04115312.pdf

CJD Therapy Advisory Group guidance
http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/CJD/CJDGeneralInformation/CJDGeneralArticle/fs/en?CONTENT_ID=4032403&chk=LVJY6b

Det Norske Veritas vCJD blood risk assessment
http://www.dnv.com/consulting/news/riskofinfectionfromvariantcjdinblood.asp

Department of Health
www.dh.gov.uk/cjd
including information for dentists at:
http://www.dh.gov.uk/PublicationsAndStatistics/LettersAndCirculars/DearColleagueLetters/DearColleagueLettersArticle/fs/en?CONTENT_ID=4102752&chk=7HspvA
also accessible via link from
http://www.hpa.org.uk/infections/topics_az/cjd/guidance.htm

National CJD Surveillance Unit http://www.cjd.ed.ac.uk/index.htm
The National Creutzfeldt-Jakob Disease Surveillance Unit
Western General Hospital
Crewe Road

Edinburgh EH4 2XU
Clinical Office Telephone: 0131 537 2128
including the TMER study: http://www.cjd.ed.ac.uk/TMER/TMER.htm

National Prion Clinic
http://www.uclh.org/services/national_prion_clinic/index.shtml
The National Hospital for Neurology & Neurosurgery
Queen Square
London
WC1N 3BG
Switchboard: 020 7837 3611

UK Blood Services:
England and North Wales http://www.blood.co.uk/,
Scotland http://www.scotblood.co.uk/,
South and West Wales http://www.welsh-blood.org.uk,
Northern Ireland http://www.nibts.org/

UK Blood Services position statement:
http://www.transfusionguidelines.org.uk/docs/pdfs/position_statement_01_2005_02.pdf

National Public Health Service for Wales
http://www.wales.nhs.uk/sites/home.cfm?OrgID=368

Department of Health, Social Services and Public Safety, Northern Ireland
http://www.dhsspsni.gov.uk/phealth/index.asp

Spongiform Encephalopathy Advisory Committee http://www.seac.gov.uk/

Department for Environment, Food and Rural Affairs BSE home page
http://www.defra.gov.uk/animalh/bse/index.html

This information sheet was prepared in November 2005.
To check for any update to the information in this leaflet, please see the current version of this leaflet, 'vCJD and Transfusion – Clinical Information' that can be found at
http://www.hpa.org.uk/infections/topics_az/cjd/information_documents.htm