From: "Dewhurst Lynne (RW3) CM&MC Manchester" <GRO-C>
To: "UK Haemophilia Centre Directors" <GRO-C>
Date: 14/11/2006 13:14:53
Subject: Variant Creutzfeldt-Jakob Disease (vCJD) and Plasma Products: look back and patient notification

Dear Centre Director,

Re: Variant Creutzfeldt-Jakob Disease (vCJD) and Plasma Products: look back and patient notification

Please find enclosed letters and papers in relation to two further batches of factor VIII / IX concentrate which include donations from patients who subsequently developed vCJD. These relate to products released in 1988 through the transfusion service in Tooting, Wales, Colindale and Birmingham, not previously notified because it was not possible at that time to trace their distribution. If you received these products you may have to notify your patients.

Further details are enclosed in the attached papers

Yours sincerely

Charles Hay

Chairman UKHCDO

CC: <GRO-C>

UKHCDO
UNITED KINGDOM HAEMOPHILIA CENTRE DOCTORS' ORGANISATION

November 2006

To UK Haemophilia Centre Doctors

Variant Creutzfeldt-Jakob Disease (vCJD) and Plasma Products

Dear Colleague,

I am writing to inform you about a batch of Factor VIII and a batch of Factor IX that were manufactured using plasma including that from donors who later developed vCJD. Neither are within shelf life, and neither have been included in previous notifications.

These batches were not included in the previous vCJD plasma product patient notification exercise in 2004, because, at the time, records for fate of the products could not be identified. Since then, due to further intensive work between BPL and the NBS, it has been possible to trace the likely fate of these products.

There are no other outstanding batches connected to plasma donors who have been diagnosed with vCJD. From now on, we will only notify you if newly diagnosed cases of vCJD are found to have been plasma donors.

Table 1: vCJD implicated batches of plasma product

Plasma product	Batch Number	Date of release	Expiry Date	Vial Size	Please report patients who received at least:
Factor VIII (8Y)	FHC0059	06/09/1988	13/07/89	240 iu	1 vial
Factor IX (9A)	FJA0020	06/10/1988	17/08/89	485 iu	1 vial

The implicated batch of Factor VIII was distributed by regional blood transfusion centres in Wales and Tooting. It is thought that the Birmingham and Colindale transfusion centres also distributed bottles of this batch.

The implicated batch of Factor IX is likely to have been distributed by the transfusion centres in Birmingham and Colindale.

Only haemophilia centres that received clotting factors from these centres in 1988 and 1989 need to take any action.

In 2004 all patients with bleeding disorders[1] who have been treated with UK-sourced pooled factor concentrates or antithrombin[2] between 1980 and 2001[3] were classified as at-risk of vCJD for public health purposes. This meant that infection control precautions and other safety measures applied to all these patients. This letter does not change this advice. There is no need for any additional public health actions.

If your centre did receive clotting factors from the above regional centres, then please take the following actions:

1 Please review your records

Please review your records to see if your centre received the implicated batches of Factor VIII and IX. If you did not receive any of the implicated batches, then you need do nothing further. If you did, then please check to see if you can identify which patients received the implicated batches. The manager of your trust's blood transfusion laboratory, and your medical director have received separate notifications.

2 Please record patients' exposures to implicated batches

If you can identify which 'at risk' patients have received the newly notified implicated batches of Factor VIII and IX, then please record this information on a vCJD Exposure Assessment Form for each patient. The UKHDCO is collecting this information on the National Haemophilia Database. Please send patient exposure information to the UKHCDO National Haemophilia Database Co-ordinator by post or electronically {DETAILS}.

3 Please tell your patients

If you used any of the implicated batches, please write to all your patients with bleeding disorders who are 'at risk' of vCJD for public health purposes to tell them about the newly implicated batches of Factor VIII and Factor IX. We have enclosed an 'Information for Patients' sheet to accompany this letter.

Please give your patients the opportunity of finding out whether they were treated with these clotting factors. Please try to ensure that patients have an opportunity to discuss this with you.

---

[1] defined here as congenital and acquired haemophilia (Haemophilia A and Haemophilia B), Von Willebrand Disease, other congenital bleeding disorders and congenital antithrombin III deficiency.

[2] ie. clotting factors and antithrombin made from pooled plasma. These include factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complex concentrates as well as antithrombin.

[3] The start date of 1980 is when BSE is thought to have entered the human food chain. The end date of 2001 is the last possible expiry date of any product manufactured by the UK fractionators that was sourced from UK donors until 1998.

If any of these patients have transferred to another haemophilia centre, please contact their new haemophilia centre director. S/he should then record their patients' exposures and inform them of this new notification.

This new notification does not change the vCJD 'at risk' status of these patients.

Background to the 2004 notification

In 2004 the HPA, the UKHCDO and colleagues notified patients who had received plasma products manufactured using plasma from donors who had developed vCJD. That notification dealt with plasma donations which had been used to manufacture factor VIII, factor IX, antithrombin, intravenous immunoglobulin G, albumin, intramuscular human normal immunoglobulin and anti-D.

Patients treated with these plasma products were managed according to an assessment of potential vCJD infectivity carried out by the Health Protection Agency with the CJD Incidents Panel (Panel)[4].

The UK Haemophilia Doctors and patient representatives, the Panel and UK Health Departments agreed that it was likely that many patients with bleeding disorders would have had a sufficient exposure to these implicated plasma products to put them 'at risk' of vCJD for public health purposes. We also thought that it was likely that further batches of UK-sourced plasma products would be implicated in the future as more cases of vCJD arose.

Therefore all patients with bleeding disorders who were treated with UK-sourced pooled factor concentrates or antithrombin between 1980 and 2001 are 'at-risk' of vCJD for public health purposes and special precautions should be taken.

Information given to patients in 2004

All patients with bleeding disorders were told if they had received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001. Patients who had were:

a) informed that they had an additional risk of vCJD because they could have been treated with plasma made from donations from individuals who later developed vCJD.

b) given the opportunity to find out whether they had been treated with an implicated batch. They were told that if any more implicated batches were reported, then their exposure assessment might change.

c) informed that they were 'at-risk' of vCJD for public health purposes, and that their 'at-risk' status would be recorded in their hospital medical records and primary care notes. Their exposure to implicated batches, and whether they had asked to know if they have received implicated batches, was recorded in their hospital medical records on a

[4] The CJDIP is an expert committee set up on behalf of the UK Chief Medical Officers to advise on the management of 'incidents' of potential transmission of CJD between patients.

Patient vCJD Exposure Assessment Form. Patients who had **NOT** received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001 had this fact clearly recorded on this form.

d) informed that special precautions needed to be taken to reduce the chance of any further spread of vCJD, and were given the following advice:
   - They should not donate blood, organs or tissues (many patients who have received plasma products may already be excluded from donation because of their underlying condition)
   - They should inform their doctors and other healthcare professionals of their 'at-risk' status, so that special infection control precautions could be taken before surgery and other invasive procedures should they require future medical care. They were advised to inform their families, in case they needed emergency surgery in the future.

e) reassured that their clinical care should not be compromised in any way.

Further information

Information about vCJD and plasma products with useful links is available from the HPA website http://www.hpa.org.uk/infections/topics_az/cjd/menu.htm.

The Information for Clinicians document gives further information on the assessment of risk, special public health precautions, and infection control issues for affected patients. http://www.hpa.org.uk/infections/topics_az/cjd/information_documents.htm

A version for patients is enclosed.

If you would like to ask any questions about this notification, please contact

- Professor Frank Hill (Chairman of UKHCDO Working Party on Transfusion Transmitted Infections) on GRO-C
- The CJD Section at the Health Protection Agency's Centre for Infections (Colindale) by e-mail to cjd@hpa.org.uk or by phone on 020 8327 7771.
- (Wales only) Dr Roland Salmon (Consultant Epidemiologist, National Public Health Service for Wales) on GRO-C

Yours sincerely

GRO-C

GRO-C

Dr Charles Hay
Chairman
UK Haemophilia Centre Doctors' Organisation

Dr Nicky Connor
Consultant Epidemiologist
Health Protection Agency (Colindale)

Enclosed documents

a) vCJD and plasma products - Information for patients with bleeding disorders
b) vCJD and plasma products – Clinical Information

Health Protection Agency

CJD Section
Centre for Infections
Health Protection Angecy
61 Colindale Avenue
London NW9 5EQ

November 2006

To: Medical Directors of Trusts

Variant Creutzfeldt-Jakob Disease (vCJD) and Plasma Products: look back and patient notification

Dear Doctor,

The Health Protection Agency (HPA) is co-ordinating a patient notification exercise for vCJD implicated batches of plasma products. Your Trust should take specific actions to try to trace patients treated with these products.

This notification relates to four batches of plasma products that were manufactured using plasma from donors who later developed vCJD (Table 1). These include two batches of albumin 4.5%, one batch of Factor VIII and one batch of Factor IX. None of the implicated batches is within shelf life.

These four batches were not included in the previous vCJD plasma product patient notification exercise in 2004, because, at the time, records for fate of the products could not be identified. Since then, due to further intensive work between BPL and the NBS, it has been possible to trace the likely fate of these products.

The CJD Incidents Panel (Panel) has assessed the risk of vCJD from these batches of plasma products. The Panel advises that some of the patients who were treated with these batches of plasma products may have been exposed to a vCJD infection risk. You should now try to trace these patients and ask them to take specific public health precautions to reduce the risk of spreading vCJD to other people.

Table 1: vCJD implicated batches of plasma product

Plasma product	Batch Number	Date of release	Expiry Date	Vial Size	Please report patients who received at least:
Albumin 4.5%	AD1667	09/12/1987	01/06/90	400 ml	8,700 ml
Albumin 4.5%	AD1668	12/11/1987	01/06/90	400 ml	
Factor VIII (8Y)	FHC0059	06/09/1988	13/07/89	240 iu	Patients to be managed by haemophilia centres
Factor IX (9A)	FJA0020	06/10/1988	17/08/89	485 iu	1 vial. Patients with bleeding disorders to be managed by haemophilia centres

Please try to trace and identify patients treated with sufficient quantities of the implicated batches of albumin 4.5% and Factor IX for them to be considered 'at-risk' of vCJD for public health purposes. There are two groups of these patients:

1. Patients who have received at least 8,700ml of implicated batches of albumin 4.5%. These are likely to include plasma exchange recipients and patients with severe burns.
2. Patients without a bleeding disorder, who have been treated any of the implicated batch of Factor IX e.g. patients undergoing rapid warfarin reversal.

Patients with bleeding disorders are being traced and managed by haemophilia centres. In 2004 all patients with bleeding disorders who could have been exposed to vCJD through treatment with UK sourced plasma products were classified as 'at risk of vCJD for public health purposes'. This current notification does not change the 'at risk' status of patients with bleeding disorders. Haemophilia centres will inform their patients about the newly notified batches of clotting factors, and will record any new vCJD risk information on a UK Haemophilia Centres Doctors Organisation (UKHCDO) database.

Please now take the following actions:

1. Please find out whether your trust can trace these batches of plasma products to individual patients.

Please ask the head of your pharmacy and the manager of your blood transfusion laboratory or hospital blood bank to try to trace these batches. The manager of the trust blood transfusion laboratory has received a separate notification from the National Blood Service.

Please complete and return the enclosed traceability questionnaire to the CJD Section, HPA-CFI (address on form). Please do this even if you can't identify which patients were treated with these batches, or how much plasma product they received.

2. Please report how much of the implicated batches of plasma products each patient received.

If records are readily accessible, and you can easily identify which patients received implicated batches, then please find out how much of the implicated batches your patients received. If you are not able to readily access this information, the trace back effort is unlikely to be proportionate to any possible public health benefit.

If you can identify patients who received implicated batches, and who are not already "at risk of vCJD for public health purposes" (i.e. those with bleeding disorders), then the hospital clinician responsible for their care should record the doses received on the enclosed Patient vCJD Exposure Assessment Form.

You only need to complete exposure assessment forms for patients treated with 8,700ml or more of albumin 4.5%. You do not need to report patients who received smaller amounts of albumin 4.5%. Please complete exposure assessment forms for all patients (except those with bleeding disorders) treated with any of the implicated batch of Factor IX.

Please return the Patient vCJD Exposure Assessment Forms to the CJD Section, HPA-CFI (address on form).

You should base patients' individual risk assessments on the batches of implicated product that a patient is known to have received. Do not report treatments if there is uncertainty e.g. where there are gaps in a patient's treatment record.

You should also assess patients who have died within the last year. This is because if any are identified as 'at-risk', you will need to review their clinical history to identify any recent surgery which could pose a vCJD infection risk to other patients.

Next Steps

A. The HPA will identify patients 'at risk of vCJD for public health purposes'

The CJD Section at the HPA will assess each patient's risk, based on the amount of implicated plasma product received, and infectivity data for each batch of plasma product. The CJD Section will report back promptly and directly to each clinician, with information on whether patients are 'at-risk' of vCJD for public health purposes, and the further action that may need to be taken. All patient data is managed in accordance with Caldicott guidance, the requirements of the Data Protection (1998), and the Health and Social Care (section 60, 2001) Acts.

B You will then inform, advise and support patients 'at risk of vCJD for public health purposes'

You will need to ensure that suitable arrangements are made to inform any patients identified as 'at risk of vCJD for public health purposes'.

The hospital clinician responsible for the care of that patient will need to liaise with the patient's GP to agree the best way to inform each patient, advise them of the special public health precautions required, and arrange for on-going support. The HPA will distribute relevant clinician and patient literature when they report the result of each individual risk assessment. The clinician will also need to liaise with your Director of Infection Protection and Control and local Health Protection Unit to ensure that certain special public health precautions are followed.

Patients with bleeding disorders

The UK Haemophilia Centre Doctors' Organisation is contacting its members directly with details of how to manage their patients. The Trusts with haemophilia centres may need to review whether the support available is likely to be adequate for the work that will be required.

Further information

This notification completes the actions from all cases of vCJD which have been identified to date. There are no other outstanding batches from previously notified cases and any further notifications will relate to newly diagnosed cases of vCJD.

The Clinical Information document (attached) gives background information on the assessment of risk, special public health precautions, and infection control issues for staff caring for affected patients.

Information about vCJD and plasma products with useful links is available from the HPA website http://www.hpa.org.uk/infections/topics_az/cjd/menu.htm.

If you would like to ask any questions about this notification, please contact the CJD Section at the Health Protection Agency's Centre for Infections (Colindale) by e-mail to cjd@hpa.org.uk or by phone on 020 8327 7771.

Yours sincerely

GRO-C

Dr Nicky Connor

Consultant Epidemiologist,

Health Protection Agency (Colindale)

Enclosed documents

a) Patient vCJD Exposure Assessment Form

b) Traceability questionnaire

c) vCJD and Plasma Products - Clinical Information

cc Consultant Haematologist in charge of the blood transfusion laboratory

Variant Creutzfeldt-Jakob disease (vCJD) and plasma products

Information for medical staff

This information is for clinicians and other staff caring for patients 'at risk' of variant CJD (vCJD) following treatment with plasma products.

In this document, 'CJD' means all types of human prion disease, unless we say sporadic CJD or variant CJD.

Patients with bleeding disorders

In 2004 all patients with bleeding disorders[1] who have been treated with UK-sourced pooled factor concentrates or antithrombin[2] between 1980 and 2001[3] were classified as at-risk of vCJD for public health purposes. This meant that infection control precautions and other safety measures applied to all these patients. **This current notification does not change the vCJD 'at risk' status of these patients.**

Public health advice for people who are 'at risk of vCJD for public-health purposes'

Advice for patients

If you are 'at risk of vCJD for public-health purposes', you have been treated with plasma products which may have been produced using plasma donated by someone who has developed vCJD.

Although we believe the chances of you developing vCJD are very low, you should do the following things to reduce the chances of passing vCJD to other people.

- **Don't donate blood.**
- **Don't donate organs or tissues.**
- **Tell whoever is treating you before you have any surgical, endoscopy or dental procedures, so they can make special arrangements for the instruments used in your care.**
- **It would be best if you tell your family about this in case you need health care in the future for any reason and your family can help by telling the health-care staff.**

Blood, tissue and organ donations

If you are at risk of vCJD for public-health purposes, you should not donate organs, tissues or blood.

---

[1] defined here as congenital and acquired haemophilia (Haemophilia A and Haemophilia B), Von Willebrand Disease, other congenital bleeding disorders and congenital antithrombin III deficiency.

[2] ie. clotting factors and antithrombin made from pooled plasma. These include factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complex concentrates as well as antithrombin.

[3] The start date of 1980 is when BSE is thought to have entered the human food chain. The end date of 2001 is the last possible expiry date of any product manufactured by the UK fractionators that was sourced from UK donors until 1998.

There is no evidence that vCJD can be passed from a women to her unborn baby or by breast feeding. To be cautious, if you are a man you should not donate sperm, and if you are a women you should not donate eggs or breast milk.

Family and friends

You should not pass vCJD to your family, friends, health-care workers or other people. vCJD is not passed on by sneezing or coughing, by touching or by having sex. There is no evidence that vCJD could pass from a mother to her child.

Advice for health-protection teams

Patients at risk of vCJD may have had surgery since the time when they were exposed to vCJD. If this is the case, instruments used on tissues with medium-low, medium or high infectivity levels, could infected other patients (see table 1 below). This is because infectious prion proteins on the surgical instruments are not completely removed by the usual decontamination processes.

Table 1: Tissue infectivity levels for patients with, or at risk of vCJD

Infectivity level	Tissues of patients with, or at risk of vCJD
High	Brain Spinal cord Posterior eye
Medium	Olfactory epithelium Lymphoid tissue
Medium–low	Anterior eye
Low or not detectable	Other

The risk of transmitting vCJD from one patient to another on surgical instruments will fall each time the instruments are used and decontaminated. After being used and decontaminated around 10 times (20 times for high-risk tissue), the instruments are not likely to infect other patients.

Health-protection teams should report to the CJD Incidents Panel any surgery carried out on medium-low and medium-risk tissues involving instruments that may have been used and decontaminated less than 10 times (20 times for high-risk tissues) since being used on a patient at risk of vCJD. Please use the reporting form available on our website at www.hpa.org.uk/infections/topics_az/CJD/incidents_panel.htm.

Surgical departments reuse instruments at different rates. Reviewing the medical history over the last 12 months for each patient who is at risk of vCJD for public-health purposes should reveal any instruments that could still infect other patients.

You should also review the medical records of patients at risk of vCJD who have died in the last year.

The CJD Incidents Panel may decide that the instruments used on a patient at risk of vCJD should be quarantined immediately or destroyed. The panel currently advises that there is no need to contact the patients these instruments were used on. However, the panel will review this advice in line with any relevant new scientific evidence.

There is no need to investigate or report other operations that have been done on patients at risk of vCJD, as long as standard processes for decontaminating the surgical instruments have been used.

Please also report to the panel any donations of blood, tissues or organs made by these patients since they became at risk of vCJD. The panel advises that there is no need to contact patients who have received blood, tissues or organs donated by someone at risk of vCJD following treatment with plasma products. The panel will review this advice in line with any relevant new scientific evidence.

Infection control advice

If you are carrying out an invasive procedure, operation, or are part of an infection control team, please follow the guide to controlling infections published by the Advisory Committee on Dangerous Pathogens Transmissible Spongiform Encephalopathy (ACDP TSE) Working Group in 2003. You can find the guide at www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm. This tells you what action you should take to control vCJD infection in hospital, during surgery, and in community health-care such as dentistry.

If you are a patient who is 'at risk' of vCJD and you need to have an invasive medical procedure, you should tell the health-care staff in charge of your care about this so they can take action to stop vCJD being passed on to other people.

Infection control abroad

If you are at risk of vCJD and you need an operation or endoscopy while you are abroad, you should do the following things to reduce the chances of vCJD being passed on to other people.

- Tell the medical staff caring for you that, in the UK, doctors must take special infection control measures when you have surgery, to reduce the risk of infecting other patients with vCJD.

- Tell the medical staff that they should contact their own national organisation for advice on controlling infections, who can then contact the Health Protection Agency (HPA) duty doctor on 0044 208 200 6868 to get advice about the safety measures recommended for the medical procedure they are planning to do, or have already done.

The duty doctors are available 24 hours a day every day, and have information about:

- where to find the relevant guidelines for controlling infection; and
- contact numbers for experts who can help interpret the guidelines if necessary.

If it is not possible to tell medical staff before they operate or give you treatment, you should tell them as soon as possible afterwards. This may happen in the UK as well as abroad, for example, if you are unconscious and need treatment straight away. Procedures for controlling infection can still be effective, even if you tell the health staff after your operation (or other medical procedure).

Advice for GPs and other medical staff

If you are are responsible for telling a patient they are at risk of vCJD for public-health purposes, you should make sure that the patient's GP is informed.

The GP should do the following things.

- Know that their patient is being told they are at risk of vCJD for public-health purposes.
- In the patient's primary-care records, record that the patient is at risk of vCJD for public-health purposes and that special infection control measures are needed.
- Include this information in any referral letters if the patient needs surgery, an invasive procedure or dental surgery. Remember to inform consultants who are providing ongoing care to patients at risk of vCJD.
- Check if the patient has had surgery in the past year. If this is the case, the GP should tell the local Health Protection Team, who will take action if necessary.

The doctor caring for patients who are at risk of vCJD should make sure that their 'at risk' status is recorded in their hospital medical records and primary-care notes. This should only be done once the patient knows that they are at risk of developing vCJD.

Doctors should ensure that patients at risk of vCJD receive the same medical and dental care that they would if they were not at risk.

Advice for dentists

If you have a patient who is at risk of vCJD, they should tell you about this. This will allow you to follow satisfactory standards for infection control. You should include the information if you refer your patient to specialists such as maxillofacial surgeons.

There is no reason why you should refuse dental care to any patients with, or at risk of, vCJD, or their relatives. You can treat them in the same way as any other patient.

In February 2005, the English Chief Dental Officer sent a letter to all dentists in England to give information and advice about treating patients with (or at risk of) vCJD. You can find this letter on our website at www.hpa.org.uk/infections/topics_az/CJD/incidents_panel.htm.

The TSE guidance for controlling infection 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."

You can deal with dental instruments you have used on patients with (or at risk of) vCJD in the same way as in any other low-risk surgery (that is, you can decontaminate them in line with best practice and use them again). Remember, you should never use any instruments that are labelled 'single use' more than once.

You can find advice on decontaminating dental instruments in the British Dental Association's (BDA's) guide 'Infection control in dentistry'. You can get this document (known as the 'A12') from the BDA's website, www.bda-dentistry.org.uk.

Discussing vCJD risks with patients

Patients may find the news that they are at risk of vCJD distressing. They may want an absolute guarantee that they will not develop vCJD. This is clearly not possible.

Variant CJD (vCJD)

Many people in the UK will have eaten food that could have been infected with BSE, which causes vCJD. We do not know how large the extra risk of developing vCJD is from treatment with plasma products, but it is likely to be very low.

Three patients have been infected with vCJD following blood transfusions in the UK. One of these patients did not develop clinical disease. No cases have been reported among patients who received plasma products sourced from people who went on to develop vCJD.

As far as we know, vCJD has never been spread through surgery.

Sporadic CJD and other types of CJD

Everyone has a very small risk of developing sporadic CJD. We do not know how large the extra risk of developing CJD is from being operated on with instruments used before on someone with sporadic CJD, but it is likely to be very low.

In the whole world, there have been four cases of people developing CJD after being operated on with instruments used before for neurosurgery (surgery to the brain and spinal cord) on patients with sporadic CJD. These people developed CJD within about 18 months of being infected. Two cases have been linked to using infected depth electrodes on the brain and another two to corneal transplants.

Before informing at risk patients, you should consider their risks carefully and make such preparations as giving patients the opportunity to discuss these issues with appropriate health-care staff afterwards.

You will need to decide who should be involved in telling patients about their risk of developing vCJD, and how this should best be done. Many patients are likely to need more than one session to discuss what this means for them if they are to come to terms with what they have been told. You may consult a trained counsellor for advice on managing this process.

Annex 1 – How and why patients are identified as at risk of CJD for public-health purposes

The CJD Incidents Panel

CJD incidents happen when there is a possibility that patients could have come into contact with CJD through:

- treatment with plasma products such as clotting factors and albumin
- receiving a blood transfusion
- surgical instruments contaminated with CJD
- organ or tissue transplants.

In 2000 the UK Chief Medical Officers set up an independent committee of experts, the CJD Incidents Panel (the panel). The panel gives advice to all organisations responsible for providing health care on how to manage situations when CJD could have been passed on from one patient to another. In particular, the panel gives advice to local infection-control teams and health protection teams.

Medical teams should ask for Panel advice when they are dealing with patients who might have come into contact with CJD. The panel assesses the risk to these patients, and advises whether the team should contact the patients and tell them that they are at risk of CJD. Teams will then need to tell these patients about the safety measures which are necessary to prevent CJD spreading to others.

You can get more information on the panel from our website at www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm. This includes the panel framework document, which sets out the principles of managing incidents where a patient may have come into contact with CJD. Our CJD section provides the secretariat for the CJD Incidents Panel, and provides help to health-care teams which are following the Panel's advice.

The panel's recommendations

The CJD Incidents Panel advises on the need to contact patients who have a risk of at least 1% of being infected with CJD through medical procedures such as treatment with plasma products. The patients should be told they are at risk of CJD for public-health purposes, and that they should take certain safety measures to prevent CJD being spread to other patients.

Much of the scientific data that underpins the vCJD risk assessment models is uncertain. Where there has been doubt, the Panel has made cautious assumptions. The risk assessment and 1% threshold provide a guide for deciding to when safety measures are needed to limit CJD spreading from person to person. They should not be used as precise guides for telling people their exact risk of developing CJD.

Previous vCJD plasma products notification in 2004

Patients who had received plasma products manufactured from plasma donated by individuals who later developed vCJD were notified in 2004. Plasma from these donors had been used to manufacture factor VIII, factor IX, antithrombin, intravenous immunoglobulin G, albumin, intramuscular human normal immunoglobulin and anti-D.

Patients treated with these plasma products were managed according to an assessment of potential vCJD infectivity carried out by the Health Protection Agency with the Panel. Plasma product infectivity data were combined with batch manufacturing data to calculate the likely infectivity of each batch of the implicated plasma products.

Three groups of patients were involved: patients with bleeding disorders, patients with primary immunodeficiency disease and patients with other disorders who had been treated with sufficient quantities of plasma products to put them at 1% risk of vCJD.

The UK Haemophilia Doctors and patient representatives, the Panel and UK Health Departments agreed that it was likely that many patients with bleeding disorders would have had a sufficient exposure to these implicated plasma products to put them 'at risk' of vCJD for public health purposes. We also thought that it was likely that further batches of UK-sourced plasma products would be implicated in the future as more cases of vCJD arose.

Therefore all patients with bleeding disorders who were treated with UK-sourced pooled factor concentrates or antithrombin between 1980 and 2001 were informed that they were 'at-risk' of vCJD for public health purposes and that special precautions should be taken.

This current notification does not change the vCJD 'at risk status' of any patient with bleeding disorders.

Information given to patients in 2004

All patients with bleeding disorders were told if they had received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001. Patients who had were:

a) informed that they had an additional risk of vCJD because they could have been treated with plasma made from donations from individuals who later developed vCJD.

b) given the opportunity to find out whether they had been treated with an implicated batch. They were told that if any more implicated batches were reported, then their exposure assessment might change.

c) informed that they were 'at-risk' of vCJD for public health purposes, and that their 'at-risk' status would be recorded in their hospital medical records and primary care notes. Their exposure to implicated batches, and whether they had asked to know if they have received implicated batches, was recorded in their hospital medical records on a Patient vCJD Exposure Assessment Form. Patients who had **NOT**

received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001 had this fact clearly recorded on this form.

d) informed that special precautions needed to be taken to reduce the chance of any further spread of vCJD, and were given the following advice:

   - They should not donate blood, organs or tissues (many patients who have received plasma products may already be excluded from donation because of their underlying condition)
   - They should inform their doctors and other healthcare professionals of their 'at-risk' status, so that special infection control precautions could be taken before surgery and other invasive procedures should they require future medical care. They were advised to inform their families, in case they needed emergency surgery in the future.

e) reassured that their clinical care should not be compromised in any way.

The HPA and the CJD Incidents Panel also worked with hospitals throughout the UK to identify other groups of patients treated with implicated batches of plasma products. Clinicians who identified these patients sent their details to the HPA which calculated patients' vCJD exposure risks. Patients identified as at risk of vCJD were then contacted by their doctors and informed about their exposure and the public health measures that they would need to take.

CJD risk from surgical instruments

Surgical (or other) instruments may be contaminated with prion protein (the protein that carries CJD) when they touch infectious tissues of a patient with CJD. Prion proteins are not completely destroyed in normal decontamination processes, and the instruments may spread CJD to other patients when they are used again.

The amount of material on an instrument after surgery depends on the type of instrument, the tissues it was used on, and the decontamination processes the instrument has been through. Usually, there are two stages for decontaminating surgical instruments. First, they are cleaned, for example in a mechanical washer and drier. Then, infectious material is inactivated, for example, by high-pressure steam autoclaving.

Studies show that the first cycle of decontamination may reduce the amount of protein on instruments with flat surfaces by a thousand-fold. However, instruments with serrated edges and hinges, or with narrow lumens (for example, flexible endoscopes) are much more difficult to clean. Cleaning the instruments again is not likely to be as effective, as any material that has survived the first cleaning stage may have been baked on during autoclaving or, in the case of flexible endoscopes, fixed to the equipment by the chemicals used in processing. It is possible that even after using and

decontaminating the instruments a great many times, some infectious prion proteins could remain on the instruments.

The Department of Health has modelled the infection risk to patients coming into contact with surgical instruments that were used on a patient with CJD. These assessments show that the risk to patients is highest if the surgical instruments used on them have only been used and decontaminated a small number of times since being used on a patient with CJD. You can find this risk assessment on our website.

The panel's advice on whether to contact patients in an incident is based on these models. The panel assesses the risk of patients coming into contact with CJD by reviewing the information collected by the local incident team. In each case the panel considers a range of factors including:

- the clinical condition of the patient with CJD;
- the infectivity levels of the tissues that the instruments have been used on;
- the type of instruments used;
- the processes in place for decontaminating the surgical instruments; and
- whether the instruments can be traced.

Annex 2 – More information about 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 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 or mad cow disease). In humans, there are four main types of CJD.

- Sporadic CJD, which accounts for 85% of cases.
- Variant CJD (vCJD)
- Inherited CJD
- Iatrogenic CJD (through medical procedures)

At the moment, we can diagnose CJD by histological examination of the brain, following a brain biopsy or after a post-mortem. If someone has symptoms suggestive of variant CJD, tonsil biopsies may also be used. There is no proven treatment or cure for CJD, and the disease always leads to death.

Research is being done on the causes, tests and possible treatments for the disease. One trial of a treatment has taken place at the NHS National Prion Clinic (NPC) and the Medical Research Council's (MRC's) Prion and Clinical Trials Unit.

Sporadic 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.

Variant CJD (vCJD)

Variant CJD was first recognised in 1996 and is thought to be caused by eating beef from cattle infected with BSE, although no-one knows the exact cause of infection. 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 inside, 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.

About 150 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 only five deaths were reported in the UK in 2005. 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. More information, including monthly numbers of cases and the latest short-term incidence projections are available from the National CJD Surveillance Unit's website, www.cjd.ed.ac.uk.

Inherited CJD

Inherited 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 inherited 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.

Iatrogenic CJD and CJD transmission through blood

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

- Surgery and other invasive medical procedures;
- receiving infectious material (such as blood components); or
- having treatment with human hormones derived from the pituitary gland such as human growth hormone.

The clinical features of iatrogenic CJD partly depend on the route of infection. About 150 people have been infected after having received contaminated dura mater grafts. Over 100 people have been infected through treatment with contaminated human growth hormone.

Infection with variant CJD (vCJD) has probably been transmitted to three patients through blood transfusions in the UK. One of these patients did not develop clinical disease. No cases have been reported among patients who received plasma products sourced from people who went on to develop vCJD.

There is no epidemiological evidence that blood transfusions from donors who later develop sporadic CJD, can infect people. However, experiments in which blood from humans with sporadic CJD is injected into the brains of animals, suggest that blood might be infectious at a relatively low level. It is possible that some cases could have occurred, without this source being recognised.

How CJD spreads

Prion diseases like CJD can spread from one person to another in certain circumstances, but they are not infectious in the usual way. 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.

Eating beef or other 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 sources of vCJD infection include inoculation from contaminated medical equipment or receiving infected transplant material.

Preventing CJD from spreading between patients

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

- Improving the standards for decontaminating instruments
- Taking special infection control measures when operating on patients with, or at risk of, CJD
- Measures to protect the blood supply (see below)

Measures to protect the blood supply

Sporadic and inherited CJD

There have been no reports of CJD being spread by blood transfusions from a patient with sporadic or inherited CJD. Sporadic CJD has been monitored for many years in many countries, and this shows that transmission through blood is unlikely.

Variant CJD (vCJD)

We do not know the exact risk of vCJD spreading through blood. The Department of Health in England arranged for Det Norske Verita Consulting to assess this risk. The Spongiform Encephalopathy Advisory Committee (SEAC) accepted the risk assessment in early 1999.

As a result, the blood services take 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 1998).
- Removing white blood cells (which may carry the highest risk of spreading vCJD) from all blood used for transfusions (leucodepletion) (since October 1999).
- Importing fresh frozen plasma from the United States for patients born on or after 1st January 1996 (since August 2002).

- 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.
- Promoting the appropriate use of blood, tissues and alternatives throughout the NHS.

What is an infectious prion protein?

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. We think it builds up by inducing the normal prion protein to mis-fold, but we do not know how this change happens. The abnormal prion protein then builds up 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 abnormal prion protein that starts these changes may arise:

- spontaneously (a possible explanation for sporadic CJD);
- associated with an inherited abnormality of the prion protein gene (inherited CJD);
- acquired in a medical setting from contamination with tissue from someone with CJD (iatrogenic CJD); or
- acquired most likely through eating meat from cattle infected with BSE (for variant CJD only).

The immune system does not seem to respond to CJD infection. Also, the infected prion protein resists 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. We cannot rely on autoclaving to denature abnormal prion proteins contaminating surgical instruments following use on a patient with CJD.

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 that is found in 40% of people in the UK. This genotype probably makes the 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. The patient had died from a cause unrelated to vCJD. This happened some years after receiving a blood transfusion from a donor who later developed vCJD. The patient had not become ill with vCJD and we do not know if they would ever have done so.

Annex 3 – Useful websites

You can get more information about CJD from the following websites and phone numbers.

Health Protection Agency
Website: www.hpa.org.uk/infections/topics_az/cjd/menu.htm

CJD Incidents Panel

Website: www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm

Infection control guidance
Website: www.advisorybodies.doh.gov.uk/acdp/tseguidance/

Department of Health information for dentists
Website:
www.dh.gov.uk/PublicationsAndStatistics/LettersAndCirculars/DearColleagueLetters/DearColleagueLettersArticle/fs/en?CONTENT_ID=4102752&chk=7HspA

National CJD Surveillance Unit
Website: www.cjd.ed.ac.uk/index.htm

National Prion Clinic
Website: www.uclh.org/services/national_prion_clinic/index.shtml
Phone: 020 7837 3611

Patient support groups

CJD Support Network
Website: www.cjdsupport.net/
Phone: 01630 673973

Human BSE Foundation
Website: www.hbsef.org/

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

Department of Health
Website: www.doh.gov.uk/cjd/index.htm

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

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

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

We last revised this leaflet in November 2006.
To check for any updates to this information, please see the current version of this leaflet, 'Variant Creutzfeldt-Jacob Disease (vCJD) and plasma products – clinical information'. You can find this document at
www.hpa.org.uk/infections/topics_az/cjd/information_documents.htm

Health Protection Agency

National Public Health Service for Wales
Gwasanaeth Iechyd Cyhoeddus Cenedlaethol Cymru

Variant Creutzfeldt-Jacob Disease and clotting factors

This leaflet is for patients who are 'at-risk of variant CJD (vCJD) for public health purposes'. We hope it will give you some answers to your questions.

Information for patients

This leaflet is for individuals with bleeding disorders or congenital antithrombin III deficiency[1] and who have received clotting factors or antithrombin derived from UK-sourced plasma[2] manufactured between 1980 and 2001.

This means that you are part of a group of patients who might have been treated with clotting factors made from the plasma of a donor who has developed vCJD, or from the plasma of donors living in the UK who might go on to develop vCJD. This is why you are 'at-risk' of vCJD for public health purposes.

Three people have become infected with vCJD after receiving blood donated by people who later developed vCJD themselves. No one has ever developed vCJD following treatment with clotting factors for bleeding disorders. We believe that the chances of you developing vCJD are low, but we need to take some simple safety measures to make sure you do not pass the infection on to someone else. This could happen, even if you become infected with vCJD, but never become ill with this disease. That is why you are described as 'at risk of vCJD for public health purposes'.

Why am I at risk of vCJD for public health purposes?

In order to prevent further spread of vCJD a decision was taken in 2004 to consider all patients with bleeding disorders who have been treated with UK sourced factor VIII, factor IX and antithrombin III plasma products as 'at risk' of vCJD.

You are in this 'at risk' group because you have been treated with clotting factors which were made from UK plasma between 1980 and 2001. It is possible that some of the people donating plasma in the UK at that time were infected with vCJD, even if they currently remain well.

---

[1] congenital and acquired haemophilia (Haemophilia A and Haemophilia B), Von Willebrand Disease, other congenital bleeding disorders and congenital antithrombin III deficiency.
[2] factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complexes, as well as antithrombin.

What should I do now?

You should do the following things to reduce the chance of passing on variant CJD to other people:

Don't donate blood.

Don't donate organs or tissues.

Tell whoever is treating you before you have any medical, surgical or dental procedures, so they can make special arrangements for the instruments used in your care.

It would be best if you tell your family about this in case you need health care in the future for any reason, and your family can help by telling the healthcare staff.

Will this affect my family and friends?

If you are carrying vCJD, your family and friends should not catch vCJD from you, and you do not need to do anything in your day-to-day life to avoid passing it on. There is no evidence that it can be passed from one person to another by sneezing or coughing, sharing cups, knives, forks and so on, by touching, kissing or having sex.

There is no evidence that vCJD can be passed from a woman to her unborn baby, or by breast feeding. To be cautious, if you are a man you should not donate sperm, and if you are a woman you should not donate eggs or breast milk.

There is no evidence that vCJD has spread between people through work. There is no need to inform your employer unless they ask. If you are a doctor or nurse or other health-care worker, there is no evidence that you could infect your patients or that patients could infect you.

What is vCJD?

Creutzfeldt-Jakob Disease, or CJD, is one of a group of diseases called TSEs (transmissible spongiform encephalopathies). These are rare diseases in humans and animals that affect the structure of the brain and always lead to death. In animals the best-known TSE is BSE (bovine spongiform encephalopathy), sometimes referred to as 'mad-cow disease'.

There are four main types of CJD:

- Sporadic CJD (we don't know why this disease happens). This is the most common type of CJD and accounts for 85 out of 100 cases

- Inherited (with genetic causes)
- Iatrogenic (passed on through medical treatment)
- Variant CJD (vCJD). Variant CJD is believed to be the human form of BSE. Many people in the UK have been exposed to BSE through eating BSE-infected beef and beef products in the 1980s and early 1990s.

Am I going to get vCJD?

You are at-risk of vCJD for public health purposes. This does not mean you will actually develop vCJD. This risk is not known, but the chances of it happening are thought to be low.

It is impossible to say exactly what the chances are of getting vCJD from treatment with plasma products such as Factor VIII and Factor IX. No one has ever developed vCJD following treatment with plasma products. Nevertheless, it is believed that this could happen, and that we should try to prevent any spread of the disease in this way.

It is unlikely that any unusual symptoms that you have will be the start of vCJD. However, your doctor will be able to arrange for you to see an expert if appropriate. vCJD can cause a range of symptoms, including psychiatric, neurological and physical symptoms.

How might surgery spread variant CJD?

Surgical instruments used on patients who are infected with vCJD might spread the infection to other patients having surgery. This is because the infected 'prion' proteins, which are thought to cause vCJD, are very hard to destroy. (Prion proteins are proteins in our cells that can cause and spread vCJD.) Surgical instruments could still have infected prion proteins on them, even after they have been thoroughly washed and disinfected. If this happens, when the instruments are used again the prion proteins could infect other patients with vCJD.

Can I have a test to see if I am infected?

No. Scientists are working very hard to develop tests, but there is no blood test available yet which could show if you are infected with vCJD.

However, if you have an illness which might be vCJD, a doctor could test tissue samples removed from your body (a biopsy). Biopsies can help to confirm whether or not an illness is vCJD. However, if you are well, a biopsy is not a helpful way of testing to see if you are infected with vCJD.

What about my medical and dental care?

You should still receive the same medical and dental care as you would if you were not at risk of vCJD for public-health purposes – it will be just the surgical instruments that may be treated differently. Your doctors will include this information in your hospital medical records and your general practitioner's records.

Your routine dental care should not be affected. If routine dental care leads on to more complicated surgery of your head or neck, your doctors may need to take special safety measures (only for the surgical instruments they use) to reduce the chance of spreading vCJD to other patients. Please tell your dentist that you are at risk of vCJD so they can include this information in their letter if they refer you for surgery.

You will not need extra medical checks because you are at risk of variant CJD. However, your doctor will always be willing to see you if you have any worries about your health.

What about life insurance?

Companies registered with the Association of British Insurers do not refuse life assurance just because someone is 'at risk for public-health purposes'. Nor will being 'at risk' affect your current life insurance policy (if you have one). If you take out a new policy, you must answer all questions truthfully, or your policy may not be valid.

Who decided that I am 'at risk' of vCJD for public health purposes?

In 2000, the Department of Health set up a committee of experts called the CJD Incidents Panel (the panel) to give advice on the risk that CJD could pass from patient to patient. The panel assesses the risk to patients, and advises doctors whether to contact people about the chance that they may have come into contact with CJD.

The panel advises contacting patients who have a higher risk of developing CJD than is normal in the UK from having eaten beef in the past. Because you have a higher risk, you are 'at-risk of variant CJD for public-health purposes'.

Can you treat CJD?

At the moment, there is no treatment or cure for CJD and the disease always leads to death. Scientists are researching the causes and possible tests and treatments for the disease.

How many cases of vCJD are there?

By the end of 2005, there had been just over 150 deaths from vCJD in the UK and a handful in other (mainly European) countries. The number of deaths was highest in 2000, and has fallen ever since. In 2005 there were only five deaths. However, nobody knows how many people will develop this disease in the future.

Can blood spread vCJD?

It is possible that vCJD can be spread by blood transfusions. Three people have been shown to be infected with vCJD after receiving blood donated by people who developed vCJD themselves later. Blood services in the UK have taken safety measures to reduce the risk of vCJD being spread by blood.

How can I find out more?

Medical staff who provide your care will talk to you about your risk of developing vCJD and the things you should do to avoid passing it on to other people. The Health Protection Agency (HPA) can help these staff.
You can find more information about CJD from the following:

Our website: www.hpa.org.uk/infections/topics_az/cjd/menu.htm

National CJD Surveillance Unit website: www.cjd.ed.ac.uk

National Prion Clinic website: www.nationalprionclinic.org/

CJD Support Network website: www.cjdsupport.net Helpline: 01630 673973

Human BSE Foundation website: www.hbsef.org

Department of Health website:
www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/CJD/fs/en

Information for dentists at:

www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm

We last updated this information sheet in November 2006.
To check for any new information, please see the latest version of this information sheet, 'Variant CJD and Clotting Factors – Information for patients' that can be found at www.hpa.org.uk/infections/topics_az/cjd/information_documents.htm