HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT

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20th September 2004

GRO-B

Dear Doctor,

Re: GRO-B

Variant Creutzfeldt-Jakob Disease (vCJD) and Plasma Products

You will be aware that an exercise is underway to trace and inform patients who have received batches of plasma products prepared from plasma donated by people who later developed vCJD (vCJD 'implicated batches'). Haemophilia doctors and immunologists caring for patients with primary immunodeficiency have been asked to trace patients who have received sufficient of the implicated batches to be considered 'at-risk' for public health purposes.

The Health Protection Agency's Communicable Disease Surveillance Centre (Colindale) is handling the patient notification in England, Wales and Northern Ireland. The Scottish Centre for Infection and Environmental Health is handling this notification in Scotland.

I am writing to inform you that your patient [as attached] falls into this group of patients who are being asked to take special precautions to reduce any possible risk of further transmission of vCJD.

Your patient has been asked:

- not to donate blood, tissues or organs
- to inform people providing their medical, surgical or dental treatment so any special procedures recommended for the instruments used in their care can be arranged, and to consider informing their family in case emergency surgery is needed in the future.

As part of these public health measures I should be grateful if you would:

- record the patient's vCJD 'at-risk' status and the special precautions required in their primary care record,

- include this information in any referral letters should the patient require certain surgery or other invasive medical procedures (guidance on infection control for any patient who is considered 'at-risk' of vCJD was published by the ACDP TSE Working Group in 2003: http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm)

- check if the patient has undergone any surgery within the past 12 months at other hospitals. If they have, please liaise with your local Health Protection Team in order to ascertain whether any further action needs to be taken.

Being identified as 'at-risk' for public health purposes should not compromise the clinical care your patient receives in any way. However you may wish to consider your patient's 'at-risk' status should they develop symptoms indicative of vCJD.

I enclose copies of the 'Clinical Information' and 'Information for Patients', developed by the Health Protection Agency alongside the Scottish Centre for Infection and Environmental Health, that contain detailed information about the special precautions to be taken and the background to this notification, as well as useful links. Your patient has already been given a copy of the patient information sheet.

Please do not hesitate to contact me should you require any further information.

Yours sincerely

GRO-C	GRO-C	GRO-C	GRO-C
Professor CA Lee Director	Dr Simon Brown Consultant Haematologist	Dr Thynn Thynn Yee Associate Specialist	Christine Harrington Nurse Consultant

Enclosures
Clinical Information
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GRO-B
GRO-B
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GRO-B

20th September 2004

IMPORTANT INFORMATION

Dear GRO-B ,

Variant Creutzfeldt-Jakob Disease (vCJD) and Plasma Products

This letter is being sent out to all patients and the parents of children with haemophilia, other bleeding disorders and congenital antithrombin III deficiency. It gives new information about certain plasma products available between 1980 and 2001, the possible risk of vCJD and the need for precautionary health care measures following certain medical procedures and surgical operations.

This information does NOT affect ALL patients.

- **PATIENTS AFFECTED** by this information are those with haemophilia, other bleeding disorders or congenital antithrombin III deficiency who received treatment between 1980 and 2001 with clotting factors or antithrombin manufactured by the UK Bio Products Laboratory (BPL) or the Protein Fractionation Centre (PFC) of the Scottish National Blood Transfusion Service (SNBTS) using plasma pools sourced from the UK. These include concentrates of factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complexes as well as antithrombin.

- **PATIENTS NOT AFFECTED** by this information are those who have only ever received recombinant products, DDAVP (desmopressin), clotting factors or antithrombin made with non-UK sourced plasma, or who have never been treated.

If you have ever received a blood transfusion or immunoglobulin this is treated differently and is not covered in this letter.

We realise this information creates uncertainty and may cause you concern.

It is important for everyone to read the rest of this letter and the enclosed 'Information for Patients' that has been prepared to help you understand this changing situation.

What has happened?

You may be aware of product recalls in 1997, 1999 and 2000 when donors who provided plasma used to make clotting factors or antithrombin were subsequently found to have vCJD. These previous notifications involved products made by the Bio Products Laboratory in England and the Scottish National Blood Transfusion Service. You may have been informed at the time.

We are writing to you now to give you further information about these and about further batches of clotting factors or antithrombin that have been made using plasma from donors who later developed vCJD; what action is being taken; and to offer you the opportunity to discuss this with us. None of these batches are now in use.

Who is looking into this?

The CJD Incidents Panel (the Panel) is an expert committee set up by the UK Chief Medical Officers to advise on incidents of possible transmission of CJD through medical procedures. These include treatment with blood or plasma products. When people are diagnosed with vCJD, any blood donations they have given are traced. The Panel has reviewed in detail all batches of plasma products known to date to have been made using plasma from donors who later developed vCJD. We refer to these below as 'implicated' products and batches.

What is the risk from these implicated products?

The Panel has used scientific evidence and expert opinion, together with information from the plasma product manufacturers, to examine the possible risks to health from having received implicated plasma products. This risk is on top of the general risk from eating beef and beef products that may have been contaminated by the agent causing Bovine Spongiform Encephalopathy (BSE or 'mad-cow disease').

The potential additional risk to health depends on the type of plasma product and how each batch was manufactured.

For most batches of implicated products the potential additional risk is so low as to be considered negligible. For example some batches of factor VIII, where only the albumin (which is used to stabilise factor VIII in the vial) has

been sourced from a donor with vCJD, are extremely low risk. However, batches of factor VIII where the clotting factor (and not the albumin) has been sourced from a donor with vCJD, and other implicated products, which include factor IX and antithrombin, carry a higher risk.

What does this mean?

The potential additional risk of actually developing vCJD from receiving any implicated plasma product, on top of the general risk from eating beef, is unknown, but the chances of it happening are likely to be very low.

Some patients who have received certain implicated products do, however, have a greater chance of passing the agent that causes vCJD to others through surgical operations and some other medical procedures. For public health purposes steps need to be taken to prevent spread this way.

Unfortunately, it is likely that further cases of vCJD will occur in people who previously donated blood. This means that more batches of UK-sourced plasma products may be implicated in the future.

Who is affected?

It is likely that special public health precautions will need to be taken for many patients with bleeding disorders or congenital antithrombin III deficiency, because they will have received clotting factors or antithrombin that either are currently implicated (which include particular batches of factor VIII, factor IX and antithrombin) or that may be implicated at a later date. Therefore, **ALL patients with bleeding disorders or congenital antithrombin III deficiency[1] who have received clotting factors or antithrombin derived from UK-sourced plasma[2] between 1980 and 2001 are considered 'at-risk' of vCJD for public health purposes.**

This time period of 1980 to 2001 has been chosen as the most cautious: it runs from when BSE is thought to have entered the human food chain to the last possible expiry date of any product manufactured in the UK that was sourced from UK donors until 1998. Since 1998, plasma for manufacturing plasma products has been imported from the United States.

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[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.

Am I 'at-risk' of vCJD for public health purposes?

If you have received any UK-sourced plasma derived clotting factors or antithrombin between 1980 and 2001, even if you have not received a currently implicated batch, you are 'at-risk' of vCJD for public health purposes.

If you are not sure whether you [your child] have [has] received UK-sourced plasma derived clotting factors or antithrombin between 1980 and 2001, and therefore whether you [your child] are [is] 'at-risk' of vCJD for public health purposes, please contact your Haemophilia Centre. You can do this using the reply form at the end of this letter.

What special precautions should I take?

If you are 'at-risk' of vCJD for public health purposes:

- you should not donate blood,
- you should not donate organs or tissues,
- you should tell whoever is treating you before you undergo medical, surgical or dental treatment, so that they arrange any special procedures for the instruments used in your care.
- It would be best if you tell your family about this in case you might need emergency surgery in the future.

If you are 'at-risk' of vCJD for public health purposes then a note of this will be made in your hospital medical records and will be recorded on the National Haemophilia Database. We will also tell your GP of your 'at-risk' status who will record this in your GP medical notes.

Does this affect my care?

If you are 'at-risk' of vCJD for public health purposes, your clinical care should not be compromised in any way. Healthcare professionals need to know you are 'at-risk' so that if any surgical instruments are used in your care they can be treated differently.

How does this affect my family?

If you are 'at-risk' of vCJD for public health purposes you do not need to take any special precautions in normal life. There is **NO** evidence that vCJD can be passed on between people by:

- living in the same house,
- sharing utensils,
- kissing,
- sexual contact,
- from mother to baby through childbirth or breastfeeding.

Can I find out if I have been treated with an implicated batch?

We are currently checking our patients' records to determine who was treated with UK-sourced clotting factors or antithrombin between 1980 and 2001, which of them have received implicated batches and the extent of their exposure. We will record this in patients' hospital medical notes.

If you would like to find out whether you [your child] have [has] received any of the implicated batches, or you wish to discuss this further with us, please indicate this on the reply sheet. We expect the process of identifying who has received those batches to take some time, as it may involve hand-searching records from many years ago, and liaising with other Centres. We are sorry for this unavoidable delay. We will arrange an appointment for you once we have the information.

If you do not wish to find out whether you [your child] have [has] received one of the implicated batches, please be aware that this information needs to be recorded in the hospital notes. Despite our best intentions, it is possible that this information may become apparent to you [your child] inadvertently, when, for example, looking at your [your child's] medical records.

Whether or not you have received any of the implicated batches or choose to discuss this with us should **NOT** affect your care, as the same special precautions will be taken for **ALL** patients with bleeding disorders or congenital antithrombin III deficiency who received UK-sourced clotting factors or antithrombin between 1980 and 2001.

How can I decide whether to find out if I have received implicated products?

At present there is no known case of a patient with haemophilia developing vCJD through treatment with blood products. There is no diagnostic blood test for vCJD and there is no treatment or cure for this condition. In addition, the same special precautions will be taken for **ALL** patients who have received UK-sourced plasma derived clotting factors or antithrombin between 1980 and 2001, whether or not they have received an implicated batch.

In the light of the above, you may wish to consider carefully whether or not you wish to know if you have received any of the implicated batches.

How can I find out more?

I enclose an information sheet about vCJD developed by the Health Protection Agency alongside the Scottish Centre for Infection and Environmental Health, clinicians' representatives and patients' groups, which I hope will go some way to answering your first questions.

I do appreciate that this information creates uncertainty that may worry and concern you. Do contact the Haemophilia Centre on +44 (0) 207 830 2068 if you wish to talk about this.

Yours sincerely

GRO-C	GRO-C	GRO-C	GRO-C
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Enc.

Information for patients
Patient reply form
Prepaid envelope for return of patient reply form.

Variant Creutzfeldt-Jakob Disease and Plasma Products
Patient Reply Sheet

Name of patient/child*:
Date of birth:
National Registration Number (if known):
Telephone:
Address:

1. I would like confirmation of whether I/my child* received UK sourced plasma derived clotting factors or antithrombin between 1980 and 2001. These include: factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complexes as well as antithrombin.

IN PERSON / IN WRITING

2. I would like to know if I/my child* received an implicated batch.

YES/NO/DON'T KNOW

3. I would like to have a specific consultation with [the team] to discuss the implications of this issue. Please contact me to make an appointment.

YES/NO

4. I understand that my/my child's exposure to an implicated batch will be recorded in my/my child's hospital and GP notes, and on the National Haemophilia Database.

Signature _____ Date _____

Print name _____

Health Protection Agency

Scottish Centre for Infection and Environmental Health

NHS National Services Scotland

National Public Health Service for Wales

Health, Social Services and Public Safety

VARIANT CREUTZFELDT-JAKOB DISEASE and PLASMA PRODUCTS

INFORMATION FOR PATIENTS

1. What is variant Creutzfeldt-Jakob disease?

Creutzfeldt-Jakob Disease, or CJD, is one of a group of rare and fatal diseases in humans and animals that affect the structure of the brain.

There are four main types of CJD: of these, sporadic CJD (arising spontaneously) is the most common and accounts for 85% of cases. The other types are familial, iatrogenic (through medical treatment) and variant CJD (vCJD). In animals the best-known TSE is bovine spongiform encephalopathy (BSE or 'mad-cow disease'). Variant CJD is believed to be the human form of BSE.

Many people living in the UK have been exposed to BSE (Bovine Spongiform Encephalopathy or 'mad-cow disease') from eating infected beef and so are at a possible risk of developing vCJD.

2. What's this about?

Late last year the death of a person from vCJD who died some years after receiving a blood transfusion from a donor who themselves died of vCJD, was announced. This was the first case of transfusion-associated vCJD infection and increased concern about the possible infectivity of blood. A second probable case was reported in July 2004.

When a patient is diagnosed with vCJD, the UK Blood Services are informed and checks are made to find out whether the patient ever donated blood. Blood products include blood components, which are derived from a single donation of blood, or pools of up to six donations; and plasma products, which are prepared from the pooled plasma of several thousand blood donations in a process known as 'fractionation'.

To date, nine people are known to have donated blood before they became ill with vCJD, and their donations were used to make plasma products. Thus a number of patients may have been exposed to vCJD infection in the course of their past medical care.

This information sheet about vCJD has been developed with doctors' and patients' groups for patients who have been informed by their doctor that they are considered 'at-risk' We hope it will go some way to answering your first questions.

3. Why am I being contacted?

Patients who have received implicated plasma products may be at an additional risk of vCJD. This risk is 'additional' since it is on top of the general risk for many people in the UK from eating beef in the past.

It is impossible to put an exact figure on the chances of getting vCJD, either from BSE-infected beef and beef products, or the possible additional risk from receiving implicated plasma products. So far there have been no cases of vCJD amongst recipients of plasma products sourced from blood donors who later developed vCJD, and the risk of this happening is likely to be very low.

If you received implicated plasma products there is a small possibility that vCJD could have been passed on to you. If so it might be possible for you to pass vCJD on to others in certain circumstances, in which case you and the people providing your healthcare need to take some special precautions to avoid putting other people at potential risk. This is why it is important that you know, even if this causes you anxiety.

4. What measures are already being taken for vCJD?

A number of measures have minimised the risk of getting vCJD from eating BSE-infected meat and meat products. These include banning the feeding of animal protein to other animals, and removing certain parts of animals from the food we eat.

In the healthcare setting, the abnormal 'prion' protein, the infective agent that causes vCJD, is very hard to destroy. Using surgical instruments only once, or destroying those that have been used on patients diagnosed with vCJD, is one way to guard against passing on vCJD. In recent years much effort has also gone into ensuring that the decontamination of all surgical instruments is to the highest standards. The aim is to remove as much potentially infected material as possible.

5. And in relation to blood?

Because it is uncertain whether vCJD can be transmitted by blood the United Kingdom blood services have taken a number of precautionary measures:

- Withdrawal and recall of any blood components, plasma products or tissues obtained from any individual who later developed vCJD (December 1997),
- Importing plasma from the US to manufacture plasma products (1998),
- Removal of white blood cells (leucodepletion) from all blood components (Autumn 1999),
- Importing fresh frozen plasma from the US for patients born on or after 1st January 1996 (Autumn 2002),
- Not accepting donations from people who have received a blood transfusion since 1980 (April 2004),
- Promoting appropriate use of blood and tissues and alternatives throughout the NHS.

6. And in relation to patients?

In 2000 an expert advisory committee called the CJD Incidents Panel (CJDIP) was set up to advise on the handling of 'incidents' of possible transmission of CJD, including vCJD, in a healthcare setting. The CJDIP assesses the risk to other patients, and advises whether patients should be contacted and informed about their possible exposure.

The CJDIP has agreed that, in general, where patients may have been exposed to a 1% or greater possible risk of infection[1], they may have an additional unknown risk of developing vCJD, on top of the general risk from eating beef in the past, and should be contacted. These patients should be given advice about what they should do to avoid putting other people at risk. This advice includes not donating blood, tissue and organs, and informing healthcare professionals so that extra precautions can be taken if they require invasive medical or dental procedures, for example a surgical operation.

There are a lot of uncertainties in estimating the risk of infection with vCJD and a very cautious approach has been taken. The CJDIP has chosen this 1% threshold for informing patients of their exposure so that special precautions can be taken to limit the possible risk of transmitting vCJD between patients. This is considered the best balance between protecting the public from further spread of vCJD and causing excessive anxiety regarding a risk which is uncertain, but thought to be low.

7. So what's new?

Since the CJDIP was established it has been considering policy towards recipients of blood from donors who later developed vCJD.

When people are diagnosed with vCJD, any blood donations they have given are traced. The CJDIP has estimated the potential additional risk of vCJD from treatment with plasma products sourced from all donors known to have later developed vCJD. This risk depends on the type of plasma product and how each batch was manufactured, as well as the amount a patient may have received.

For certain plasma products (e.g. intramuscular immunoglobulin used for travel vaccinations against hepatitis A, or anti D for Rhesus negative pregnant women) the amount of estimated infectivity in the implicated products is so low that the possibility of reaching the 1% threshold can realistically be ignored. Patients who have received these products do not need to take any special precautions.

For other products (e.g. clotting factors and antithrombin, intravenous immunoglobulin, albumin 4.5%) the infectivity may be higher, depending on how the product was made. Once one of these plasma products has been identified the next step is to try to identify those patients who are likely to have had sufficient product to reach the 1% threshold and who need to take special precautions. These patients are considered to be 'at-risk' of vCJD for public health purposes.

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[1] A 1% risk of infection means that there is a 1 in 100 possibility that vCJD can be transmitted.

8. Who is affected?

Patients who are considered 'at-risk' of vCJD for public health purposes will be informed by their doctor. The people who may be affected are in three main groups:

- some patients with bleeding disorders (including congenital and acquired haemophilia (haemophilia A and haemophilia B), Von Willebrand Disease, other congenital bleeding disorders) and congenital antithrombin III deficiency,
- some patients with primary immunodeficiency (PID), and
- some patients with other illnesses who might be considered 'at-risk'. These may include, patients with secondary immunodeficiencies; certain neurological conditions and autoimmune illnesses (such as idiopathic thrombocytopaenic purpura), plasma exchange recipients and patients with severe burns. Patients with certain other conditions requiring critical care (including acquired antithrombin deficiency or patients requiring rapid warfarin reversal) may also be affected.

9. How does this affect me?

If you have been informed that you are 'at-risk' for public health purposes, you are being asked to take the following actions 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 then arrange any special procedures for the instruments used in your care.**
- **It would be best if you tell your family about this in case you might need emergency surgery in the future.**

A note of this will be made in your hospital medical records and your GP notes. Your care should not be compromised in any way – it will be just the surgical instruments that will be treated differently. Nor will you need extra medical follow-ups because you are 'at-risk' for public health purposes. However, your doctor will always be willing to see you if you have any worries about your health.

10. So if I'm 'at-risk' for public health purposes - what happens now?

You need do nothing other than follow the advice given above (see Section 9).

Normal social contact and household activities do not spread the infection. Your family and friends are not at risk from you and you do not need to take any special precautions in your normal life.

Variant CJD is not infectious in the usual ways. There is no evidence that it can be passed on between people by sneezing or coughing (like colds and flu), sharing utensils, by skin contact, or through kissing or sexual intercourse.

There is also 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 for public health purposes should also not donate sperm.

11. Does this mean I'm going to suffer from vCJD?

Having reached the 1% threshold does not mean you will actually develop vCJD. This risk is unknown, but the chances of it happening are very low.

There is no evidence for transmission of vCJD by plasma products. Although the process of estimating risk is based on the best evidence available, there is much uncertainty about many aspects. As a result a cautious approach has been taken and may have over-estimated the potential additional risk of vCJD from receiving the various implicated plasma products. Despite these limitations it is still important to take extra public health precautions to provide the best protection for the population in general.

12. Can I be tested to see if I am infected?

No. Scientists are working very hard to develop a test, but as yet there is no test available that can be used to identify someone who may have been infected. Variant CJD can only be reliably diagnosed by brain biopsy or through examining the body after death.

13. What happens if I develop strange symptoms?

CJD causes dementia and a range of other symptoms, including difficulty with balance and extreme clumsiness. Unlike the other forms of CJD, vCJD often starts with psychiatric symptoms like depression and anxiety.

Go and see your doctor. It is unlikely that 'strange symptoms' will be the start of vCJD but your doctor will be able to arrange for you to see an expert if appropriate.

14. Will this mean I won't be able to get life insurance?

The Association of British Insurers have informed the CJDIP that their members will not refuse insurance just because someone is categorised as 'at-risk' for public health purposes.

15. General information about vCJD

What is the cause of vCJD?

Infections like influenza and pneumonia are caused either by viruses or bacteria. Some stomach infections are caused by microscopic parasites. Variant CJD, and the other TSEs, are different from these common infections. The cause is an abnormal infectious protein known as a 'prion'.

There is no test, treatment or cure for vCJD at present and the disease is always fatal. Scientists are researching the causes and possible tests and treatments for the disease.

How do you catch vCJD?

Variant CJD is believed to be caused in the first instance by exposure to the abnormal prion protein that causes BSE. Many of the UK population have been exposed through eating BSE-infected beef and beef products in the 1980s and early 1990s.

Variant CJD may also be transmitted between patients in the healthcare setting. So far there are no recorded instances of vCJD being spread through surgery, nor have there been any cases amongst recipients of plasma products sourced from individuals who later developed vCJD.

How many cases of vCJD are there?

So far, almost 150 cases of vCJD have occurred in the UK and a handful in other, mainly European, countries.

It is thought that the UK epidemic may have reached a peak. However no one knows how many people will contract this disease in the future.

16. Sources for Additional information

The process of informing patients about their possible additional risk status, and the special precautions they may need to take is being coordinated by the Health Protection Agency (HPA) in England, Wales and Northern Ireland, and in Scotland by the Scottish Centre for Infection and Environmental Health (SCIEH).

More information about vCJD with useful links is available from their websites
HPA: http://www.hpa.org.uk/infections/topics_az/cjd/menu.htm
SCIEH: http://www.show.scot.nhs.uk/scieh

Further information is also available from:

The Haemophilia Society http://www.haemophilia.org.uk
The Primary Immunodeficiency Association http://www.pia.org.uk
CJD Support Network http://www.cjdsupport.net
Human BSE Foundation http://www.hbsef.org
National CJD Surveillance Unit http://www.cjd.ed.ac.uk
Department of Health http://www.doh.gov.uk/cjd/index.htm
National Prion Clinic
http://www.st-marys.org.uk/specialist/prion/index_prion.htm
National Public Health Service for Wales
http://www.wales.nhs.uk/sites/home.cfm?OrgID=368
NHS Direct Online http://www.nhsdirect.nhs.uk

NHS Direct and its national colleagues are also operating a 'vCJD and Plasma Products' advice line for general enquiries (telephone: 0845 850 9850).

VARIANT CREUTZFELDT-JAKOB DISEASE (vCJD) and PLASMA PRODUCTS

CLINICAL INFORMATION

Health Protection Agency

Scottish Centre for Infection and Environmental Health

NHS National Services Scotland

National Public Health Service for Wales

Health, Social Services and Public Safety

1. Introduction

In 2000 an independent expert advisory committee, the CJD Incidents Panel (CJDIP), 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.

The CJD Section of the Health Protection Agency (HPA), based at Colindale, North-West London, provides the secretariat to the CJD Incidents Panel. It is coordinating the notification of patients who may have been exposed to variant CJD (vCJD) through implicated plasma products, in liaison with clinician and patient groups in the UK. The HPA is handling this notification in England, Wales and Northern Ireland. The Scottish Centre for Infection and Environmental Health (SCIEH) is handling this notification in Scotland.

This booklet is aimed at clinicians and other staff at local level who may be involved in notifying those patients who have received vCJD-implicated plasma products. This may also be used to supplement the accompanying Patient Information Sheet.

2. Background

In 1997, 1999 and 2000 the UK national blood services were advised of donors who later developed vCJD. The implicated products that had been manufactured from plasma donated by these donors were identified and consignees were notified according to guidance at the time. These earlier notifications did not involve placing patients in a group 'at-risk' for vCJD. However some recipients were traced and informed by their clinician.

The situation has changed. Regarding plasma products, the CJD Incidents Panel currently advises that certain special public health precautions need to be taken for some recipients of UK sourced plasma products who may have been exposed to potential vCJD infectivity. This is in order to reduce any possible risk of onward transmission of vCJD. These new recommendations were not available at the time of previous notifications. In December 2003 a case of transfusion-associated vCJD was announced, increasing concern regarding the potential vCJD infectivity of blood. A second probable case of transfusion-associated vCJD infection was reported in July 2004.

To date, nine UK plasma donors are now known to have developed vCJD. Collectively, they have made 23 plasma donations. The donated plasma has been used to manufacture factor VIII, factor IX, antithrombin, intravenous immunoglobulin G, albumin, intramuscular human normal immunoglobulin and anti-D.

3. Public health precautions against vCJD

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 from the human food chain.

Other public health measures are aimed at minimising any possible risk of transmitting vCJD between people. These include:

- Measures to protect the blood supply,
- Improving decontamination standards for surgical instruments, and
- Taking special infection control precautions when operating on patients with, or 'at-risk' of, vCJD.

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

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 include:

- Not donating blood, tissue and organs, and
- Informing their medical carers so that extra infection control precautions can be taken should they require future medical care. This subject is considered in more detail in Section 9.

4. Public health precautions in relation to blood

The risk of transmitting vCJD through blood remains uncertain. The Department of Health (England) commissioned an assessment of this risk by Det Norske Veritas (DNV) Consulting, which was assessed by the Spongiform Encephalopathy Advisory Committee (SEAC) and accepted in early 1999.

As a result 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 (August 2002).
- 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 had previously had a blood transfusion (August 2004).
- Promotion of appropriate use of blood and tissues and alternatives throughout the NHS.

5. CJD related healthcare incidents

CJD incidents occur when there is a possibility that patients could have been exposed to CJD, or vCJD, either through exposure to contaminated instruments, through transplantation, blood transfusion or treatment with plasma products. This includes situations in which people have received blood transfusions or plasma products derived from donors who have subsequently developed vCJD.

The CJDIP advises on the handling of these incidents, which includes advice on the management of patients who could have been exposed to vCJD. Local infection control teams and health protection teams should seek advice from the CJDIP on how to manage these incidents. The CJDIP assesses the risk to these patients, and advises whether patients should be contacted and informed about their possible exposure. These patients are then advised whether special public health precautions need to be taken to prevent possible transmission to other patients.

More information on the CJDIP is available on the HPA website at: http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm. This includes the CJDIP Framework document, which sets out the principles of managing CJD incidents and also describes the risk assessment models that underpin the risk management of surgical and blood incidents.

6. Calculation of potential vCJD infectivity in plasma products

The CJDIP has considered the risk to people who have received originating from donors who subsequently developed vCJD. Det Norske Veritas Consulting have carried out a risk assessment to inform the management of these incidents. This uses published experimental data to model the potential vCJD infectivity in blood, its various components, and in plasma products. In Autumn 2003 this risk assessment was accepted by SEAC, the Committee on the Microbiological Safety of Blood and Tissue, and the Committee on Safety of Medicines. This DNV risk assessment is available at:

[http://www.dnv.com/consulting/news_consulting/RiskofInfectionfromvariantCJDinBlood.asp].

The CJDIP has used the Risk Assessment together with information on how batches of plasma products are manufactured, to assess the potential levels of infectivity in different plasma products that would be used to treat patients, as follows:

- Plasma that had been donated by people who subsequently developed vCJD was traced through the National CJD Surveillance Unit, Edinburgh and national blood services to identify the specific batches of plasma products made from these patients' blood.
- Plasma product manufacturers supplied the relevant data on each implicated batch, so that the infectivity in each could be estimated.
- The CJDIP then applied the infectivity estimates in the DNV report to the detailed circumstances involved in the manufacture of these batches. (For each of the major assumptions underlying the risk assessment, the most precautionary option was chosen.)

The final calculations indicate the potential level of vCJD infectivity in different plasma products that were used to treat to patients

7. Recommendations of the CJD Incidents Panel

The potential risk of vCJD infection following treatment with any implicated plasma derivative, on top of the risk from dietary exposure to the bovine Spongiform Encephalopathy (BSE) agent, is very uncertain. However, some patients treated could pose a potential risk to others in certain circumstances.

The CJD Incidents Panel advises that patients who have been exposed to an estimated 1% or greater potential additional risk of vCJD infection, whether from contaminated instruments, through transplantation, or by blood transfusion or treatment with implicated plasma products, should be contacted and advised that they are 'at-risk' of vCJD for public health purposes and should take special public health precautions.

The likelihood of patients being 'at-risk' of vCJD for public health purposes following exposure to implicated plasma products, should be categorised as follows:

- **High:** the amount of potential vCJD infectivity in product batches is high enough for patients to be considered 'at-risk' of vCJD for public health purposes following the administration of a very small dose (e.g. one treatment with Factor VIII, Factor IX or antithrombin where one vial used has been implicated).

- **Medium:** the amount of potential vCJD infectivity in product batches is not low enough to be ignored but substantial quantities of the material in question would need to be administered for patients to be considered 'at-risk' of vCJD for public health purposes (e.g. several infusions of intravenous immunoglobulin, or large doses of albumin 4.5%).

- **Low:** the amount of potential vCJD infectivity in product batches is so low that the likelihood of a patient being considered at potential additional risk of vCJD infection can realistically be ignored (e.g. albumin 20%, factor VIII products where the albumin excipient (which is used in the manufacturing process to stabilise the factor VIII concentrate in the vial) and not the plasma concentrate itself, has been implicated, intramuscular human normal immunoglobulin (used, for example, for travel prophylaxis against hepatitis A), and anti-D.)

The uncertainties underlying the assessment of risk are great, and several precautionary assumptions are involved. **The 'at-risk' threshold is a guide for implementing special public health precautions to limit any possible human-to-human transmission of vCJD. It should NOT be used as a precise guide for advising individuals about their potential additional risk of developing vCJD.**

8. Identifying recipients of implicated plasma products

8.1 Patients with bleeding disorders[1]:

Treatment with UK-sourced factor VIII (where the plasma concentrate used in the manufacturing process has been implicated), factor IX or antithrombin is highly likely to expose patients to this potential additional risk. This is because a single dose of these products, as used in clinical practice, is estimated to contain sufficient potential vCJD infectivity to cross the 1% threshold. Treatment with factor VIII where only the albumin excipient used in the manufacturing process, and not the plasma concentrate, has been implicated, is very unlikely to expose patients to a 1% or greater potential additional risk. This is because several thousand vials of the implicated product would be needed, and this is not likely to occur in clinical practice.

It is likely that many patients with bleeding disorders will have been exposed to a potential additional risk of 1% or greater. It is also likely that further batches of UK-sourced plasma products will be implicated in the future as more cases of vCJD arise. For these reasons UK Haemophilia Doctors and

[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.

patient representatives believe the Panel Recommendations should be that **all patients with bleeding disorders[1] who have been treated with UK-sourced pooled factor concentrates or antithrombin[2] between 1980 and 2001[3] should be considered 'at-risk' of vCJD for public health purposes and special precautions taken.** The CJDIP and UK Health Departments have endorsed this approach.

If there is uncertainty about whether a patient has received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001 (eg due to incomplete records), then the patient should **NOT** be considered at risk of vCJD for public health purposes.

Patients who have died within the last year should also be assessed, and if identified as 'at risk', have their clinical history reviewed in order to identify and manage any recent surgical incident that may pose an infection control risk (see section 9). When centres identify 'at-risk' patients who are currently treated elsewhere, the centre doctor should contact the clinician currently responsible for the patient's care, so they may manage the patient appropriately.

All patients with bleeding disorders are to be informed about the situation. The clinical care of the patients identified as 'at-risk' for public health purposes should not be compromised in any way.

All patients with bleeding disorders who are 'at-risk' of vCJD for public health purposes are to be given the option of finding out whether or not they received known implicated batches. This includes batches that are highly likely to expose patients to a 1% or greater potential additional risk (factor VIII where the plasma concentrate has been implicated, factor IX and antithrombin) as well as batches for which this likelihood is so low as to be considered negligible (factor VIII where the albumin excipient has been implicated). Patients should also be made aware that with future recognition of implicated batches, any assessment of their individual exposure might change. Whatever their choice this information will not affect their management as **ALL** patients who have received UK-sourced pooled factor concentrates and antithrombin as described above will be managed in the same way, i.e. as 'at-risk' of vCJD for public health purposes (see Section 9).

Patients 'at-risk' of vCJD for public health purposes should be informed that their 'at-risk' status will be recorded in their hospital medical records and primary care notes. The extent of exposure to implicated batches, and whether or not a patient has asked to know if they have received implicated

[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.

batches, will also be recorded on a Patient vCJD Exposure Assessment Form to be placed in their hospital medical records. This assessment is important for public health monitoring and to inform public health precautions and future policy for this patient group. If further batches of plasma products are found to have been sourced from donors who have developed vCJD (as a result of trace-back from new vCJD cases), the exposure record of 'at-risk' patients will need to be updated.

Haemophilia centres should use the Patient vCJD Exposure Assessment Form in response to the UKHCDO/Department of Health vCJD Surveillance study, which collects data on patients with bleeding disorders who have been exposed to implicated plasma products, and monitors their outcomes. The form is anonymous; a copy should be sent in confidence to the UKHCDO National Haemophilia Database Coordinator. The information will also be used when public health policy for this patient group is reviewed.

8.2 Primary Immunodeficiency (PID) Patients:

Eleven batches of Vigam (intravenous immunoglobulin G) released by BPL, are known to have been manufactured from donations from people who later developed vCJD. Nine of these batches may have been used to treat patients with primary immunodeficiency between December 1996 (the first release date) and February 2000 (the last expiry date)[4]. Substantial doses would need to be administered before a patient is classified as 'at-risk' of vCJD for public health purposes, and special precautions taken (Section 9).

Intravenous immunoglobulins manufactured by other manufacturers, in particular, the Protein Fractionation Centre (PFC) of the Scottish National Blood Transfusion Centre, have **NOT** been implicated to date.

The CJDIP advises that all patients with primary immunodeficiency who have received implicated batches of Vigam manufactured by BPL and **who have been assessed as having been exposed to a 1% or greater potential additional risk of infection** should be considered 'at-risk' of vCJD for public health purposes. Patients who have not received implicated batches, or who have received an insufficient dose of an implicated batch to be considered at a potential additional risk of 1% or greater, are **NOT** affected.

All patients with PID are being informed of the situation. Because most of these patients will not have had sufficient exposure to be classified as 'at-risk' of vCJD for public health purposes, an individual risk assessment will be carried out on **ALL** who received Vigam between December 1996 and February 2000 and who therefore may have been exposed. This risk assessment can be completed locally using a Patient vCJD Exposure Assessment Form provided by the HPA for PID patients.

[4] The remaining two batches were used as part of a clinical trial for ITP (trial coordinators are being contacted directly and these batches followed up separately)

The Patient vCJD Exposure Assessment Form will record the patient's known exposure to the implicated products; include an uncomplicated method for calculating whether the 'at-risk' threshold has been reached; and provide a record of the patient's current 'at-risk' status to be placed in their hospital medical records. It will also record whether or not a patient has asked to know if they have received implicated batches (see below). All patients should be informed of this fact. If further batches of plasma products are found to have been sourced from donors who have developed vCJD (as a result of trace-back from new vCJD cases), the exposure record and risk assessment of all patients will need to be updated.

Collation of individual assessments is important for public health monitoring and to inform public health precautions and future policy for this patient group. For this reason for each patient who is assessed to be 'at-risk' of vCJD for public health purposes a copy of the Patient vCJD Exposure Assessment Form should be sent in confidence to the Consultant Head of the CJD Section at the HPA-Communicable Disease Surveillance Centre in Colindale (via SCIEH in Scotland), where all clinical 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.

Patients' individual risk assessments should be based on the implicated batches of immunoglobulin that a patient is known to have received. Where there is doubt, e.g. because of gaps in a patient's treatment record, then the patient should **NOT** be included in the 'at-risk' group.

Patients who have died within the last year should also be assessed and, if identified as 'at-risk', have their clinical history reviewed in order to identify and manage any recent surgical incident that may pose an infection control risk (see section 9). When centres identify 'at-risk' patients who are currently treated elsewhere, the centre doctor should contact the clinician currently responsible for the patient's care, so they may manage the patient appropriately.

Those patients who received Vigam between December 1996 and February 2000 who are assessed to be 'at-risk' of vCJD for public health purposes will be informed after consultation with their current GP. They should be informed that their 'at-risk' status will be recorded in their hospital medical records and primary care notes. The clinical care of the patients identified as 'at-risk' for public health purposes should not be compromised in any way.

Patients who did not receive Vigam between December 1996 and February 2000, or who did but are assessed to be not 'at-risk' of vCJD for public health purposes, will also be contacted. Patients who received Vigam between December 1996 and February 2000 should be informed that the extent of their exposure will be recorded in their hospital medical records. These patients should be advised they are not currently considered 'at-risk' of vCJD

for public health purposes, although the extent of their exposure might change if other product batches are implicated in the future. They should also be given the option of finding out if they received any of the implicated batches of Vigam, even though this would be insufficient to place them 'at-risk' of vCJD for public health purposes.

8.3 Other patients who may be at potential additional risk:

In addition to patients with bleeding disorders and primary immunodeficiency there are a variety of other patients whose treatment may have involved sufficient quantities of implicated plasma products for them to be considered 'at-risk' of vCJD for public health purposes.

It is not possible to give an exhaustive list but examples include:

- conditions requiring several infusions of intravenous immunoglobulin G (including secondary immunodeficiencies; certain neurological conditions and autoimmune illnesses such as idiopathic thrombocytopaenic purpura),

- conditions requiring large volumes of albumin 4.5% (including plasma exchange recipients and patients with severe burns)

- patients with certain other conditions requiring critical care (including acquired antithrombin deficiency or patients requiring rapid warfarin reversal).

Blood Transfusion Laboratories, Hospital Blood Banks and Hospital Pharmacies are being asked via their Medical Directors to assess the traceability of the implicated batches back to particular patients.

The CJDIP advises that patient notification should be considered only where records are readily accessible and patients can be easily identified as having received implicated batches. Only in such circumstances is the trace-back effort likely to be proportionate to any possible public health benefit.

If patients are identified as having received implicated batches, the responsible clinician is asked to forward a copy of the Patient vCJD Exposure Assessment Form in confidence to the Consultant Head of the CJD Section, at the HPA-Communicable Disease Surveillance Centre in Colindale (via SCIEH in Scotland), who will undertake an individual risk assessment to decide whether the patient should be considered 'at-risk' of vCJD for public health purposes. The clinical data forwarded will be managed in accordance with Caldicott guidance, the requirements of the Data Protection (1998), and the Health and Social Care (section 60, 2001) Acts.

Patients' individual risk assessments should be based on the batches of implicated product that a patient is known to have received. Where there is

doubt, e.g. because of gaps in a patient's treatment record, then the patient should **NOT** be included in the 'at-risk' group.

Patients who have died within the last year should also be assessed and if identified as 'at-risk' have their clinical history reviewed in order to identify and manage any recent surgical incident that may pose an infection control risk (see section 9). Patients whose care has been transferred elsewhere should be followed up if they are assessed to be 'at-risk' of vCJD for public health purposes.

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

9.1 Advice to patients and their general practitioners

Patients considered 'at-risk' of vCJD for public health purposes[5] are asked to take certain special public health precautions: not to donate blood, organs or tissues and to inform their clinician if they need medical, surgical or dental treatment, so that extra infection control precautions can be taken to reduce any possible risk of spreading vCJD.

All patients who are considered 'at-risk' of vCJD for public health purposes should be advised to inform clinicians of this fact so that extra infection control precautions can be taken should they require future medical care. They should be asked to inform all healthcare professionals, for example, in private clinics, not just those working in the NHS. Patients should also be asked to inform their families, in case the patient needs emergency surgery in the future.

Patients who are considered 'at-risk' of vCJD for public health purposes should also have their 'at-risk' status recorded in their hospital medical records and primary care notes.

The clinician responsible for a patient who is 'at-risk' of vCJD for public health purposes should contact their patient's general practitioner so they may:

- know that their patient is being informed about their 'at-risk' status,
- record the patient's vCJD 'at-risk' status and the special precautions required in their primary care records,

[5] These include patients who are considered 'at-risk' of vCJD for public health purposes because of their exposure to implicated plasma products, as well as patients treated with implicated single unit blood components, such as fresh frozen plasma, cryoprecipitate, red blood cells or platelets, donated by people who subsequently developed vCJD. For recipients of single unit blood components these steps are already in place. Patients treated with vCJD implicated single unit blood components are identified by the UK national blood services and the National CJD Surveillance Unit, Edinburgh. Local health teams are then advised to contact these patients so they can take public health precautions.

- include this information in any referral letters should the patient require invasive medical or dental procedures, for example a surgical operation (guidance on infection control for any patient who is considered 'at-risk' of vCJD was published by the ACDP TSE Working Group in 2003 [http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm],
- check if the patient has undergone any surgery within the past 12 months at other hospitals, 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 the patients identified as 'at-risk' for public health purposes should not be compromised in any way.

9.2 Future donation of blood, tissue and organs:

Patients who are considered 'at-risk' of vCJD for public health purposes are advised not to donate organs, tissues or blood. Many patients who have received implicated plasma products and who may be at a potential additional risk of 1% or more, e.g. those with bleeding disorders or primary immunodeficiency disease, are already excluded from donation because of their underlying condition.

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 for public health purposes should be advised not to be sperm donors.

9.3 Future surgery and invasive medical procedures:

Revised guidance on infection control for any patient who is considered 'at-risk' of vCJD was published by the ACDP TSE Working Group in 2003: http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm. This document describes the infection control measures that should be taken in hospital care, in surgery, and community healthcare including dentistry. A new 'endoscope' annex to this guidance is to be published imminently. This TSE Infection Control Guidance should be followed.

When patients who are 'at-risk' of vCJD for public health purposes need to undergo an invasive medical procedure, they should inform the doctor or nurse in charge of their care about this so that special infection control precautions can be taken.

This information might also be included in the referral letter. Patients should also be asked to inform their families, in case the patient needs emergency surgery in the future.

9.4 Dentistry:

Patients considered 'at-risk' of vCJD 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 may also include the information in referrals to specialists such as maxillofacial surgeons.

The 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 vCJD] 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 [as 'at-risk' for public health purposes] or their relatives should be refused routine dental treatment. They can be treated in the same way as any member of the general public."

9.5 Previous surgery, invasive medical procedures and donations:

Many patients considered 'at-risk' of vCJD for public health purposes may have undergone surgery in the time that has elapsed since their possible exposure to vCJD. If this is the case, surgical instruments that have come into contact with medium or high risk tissues[6] could pose an infection risk to other patients. This is because the infective agent for vCJD, the abnormal 'prion' protein (PrP^{Sc}) is not completely removed by routine decontamination processes.

Any risk of transmitting vCJD on such surgical instruments will decrease each time they are used and decontaminated. After going through approximately ten cycles of use and standard decontamination, the instruments are unlikely to pose a significant risk of infection to other patients.

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[6] High risk tissues in vCJD are currently defined as the central nervous system and posterior eye. Medium risk tissues in vCJD are currently defined as: the olfactory epithelium, anterior eye and cornea, gastrointestinal lymphoid tissue (including tonsil, appendix and rectum) and peripheral lymphoid tissue. Tissues of concern include the spleen, lymph nodes, thymus and adrenal gland. (see the ACDP TSE Working Group guidance http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm (section 4.41)

Recent procedures on medium or high risk tissues in which instruments may not have undergone ten cycles of use and standard decontamination since being used on an 'at-risk' patient should be reported promptly to the CJDIP by the local hospital infection control team as described at :
http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm.The incident should be reported using the reporting form available on this website.

Surgical units vary in how often different instruments are re-used and decontaminated. A review of each 'at-risk' patient's surgical history over the previous 12 months should reveal any instruments that still pose a potential risk to other patients.

The surgical records of patients 'at-risk' of vCJD who have died within the last year should be reviewed in the same way.

The CJDIP may advise that instruments used in these procedures should be quarantined immediately or destroyed. The CJDIP 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 that have been undertaken on these 'at-risk' patients do not need to be investigated further or reported to the CJDIP.

Donations of blood, tissues or organs made by 'at-risk' patients since they were possibly exposed to vCJD, should be reported to the CJDIP. The CJDIP advises that patients who have received blood, tissues or organs donated by any of these 'at-risk' patients do not need to be contacted. This advice will be reviewed as new scientific evidence emerges in this field.

10. Advice and care for 'at-risk' patients

The information that has to be given to patients who may be 'at-risk' of vCJD for public health purposes through exposure to implicated plasma products may be devastating.

It is quite likely that your patient will want you to give them an absolute guarantee that they will not develop vCJD. This is clearly not possible, as many in the UK will have had possible dietary exposure to the BSE agent responsible for vCJD, and the potential additional risk of actually developing vCJD from receiving any implicated plasma product, on top of the general risk from eating beef, is unknown. However the chances of it happening are likely to be very low. Everyone also has a very small but measurable risk of developing sporadic CJD (see Section 11).

Providing this information will require careful consideration and preparation, including making arrangements for follow up discussions with appropriate health care staff.

Infectivity:

Routine contact with people who have CJD, including vCJD and those considered 'at-risk' of vCJD, does not pose a risk for relatives, healthcare workers or the community at large. CJD 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 pass between people from mother to child.

Treatment for vCJD:

There is no test, treatment or cure for vCJD at present, nor is there likely to be in the foreseeable future although research is underway into the causes, tests and potential treatments for the disease.

Discussion of implications:

Decisions will need to be made locally regarding how patients will be informed about their potential additional risk of developing vCJD. Many patients are likely to require more than one session to discuss the implications of the news if they are to come to terms with the impact of what they have been told. Advice on managing this process may be sought from a trained counsellor.

11. About CJD

11.1 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 or '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 CJD, can only be reliably diagnosed by the histological examination of central nervous system tissue following a brain

biopsy or after a post mortem. There is no test for CJD, no treatment and the disease is universally fatal.

11.2 Types of CJD

Sporadic CJD

Sporadic CJD is most common in the over 50s, and affects about one person per million per year worldwide. It is thought 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 occurs through inoculation with infected tissue either via surgical procedures or transplant 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 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 associated with blood transfusion in the UK (announced late 2003 and 2004) to date.

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.

Almost 150 cases of vCJD have occurred in the UK and a small number in other countries. It is thought that the UK epidemic may have reached a peak and the latest estimates 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. 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.

11.3 Abnormal prion protein (PrPSc)

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. The patient had died from a cause unrelated to vCJD. This was some years after a transfusion of non-leucodepleted 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.

11.4 Transmission of vCJD

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.

In vCJD the consumption of BSE-contaminated beef or other bovine-derived products remains the most likely means by which vCJD was acquired, and 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 sourced from individuals who later developed vCJD. However the recent (July 2004) announcement of the second case of transmission of vCJD infection after receiving a blood transfusion from a donor who themselves died of vCJD increases concern about the possible infectivity of blood.

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, and some cases could have occurred without this source 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.

12. Sources for Additional information

The process of informing patients about their possible additional risk status, and the special precautions they may need to take is being coordinated by the Health Protection Agency (HPA) in England, Wales and Northern Ireland, and in Scotland by the Scottish Centre for Infection and Environmental Health (SCIEH).

More information about vCJD with useful links is available from their websites
HPA: http://www.hpa.org.uk/infections/topics_az/cjd/menu.htm
SCIEH: http://www.show.scot.nhs.uk/scieh

Further information is also available from:

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

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/

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

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

National CJD Surveillance Unit, Edinburgh http://www.cjd.ed.ac.uk/index.htm

National Prion Clinic www.st-marys.nhs.uk/specialist/prion/index_prion.htm

CJD Support Network http://www.cjdsupport.net/

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

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

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