DRAFT –21/01/04

Interim report on incident involving blood components and vCJD and the patient notification exercise conducted from December 2003 to January 2004

Health Protection Agency
CJD Team

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1. Executive Summary

Still to write

2. Terms of reference of this report are:

- To inform the CJD Incidents Panel about the blood component incident and the patient notification exercise undertaken from December 2003 to January 2004.
- To identify issues for the CJD Incidents Panel to consider
- To identify issues for the HPA and others to consider and learn from in future incidents and notification exercises.

Throughout this report the terms "recipient" and "patient" have been used interchangeably. Individuals who have donated blood are referred to as 'donors'.

3. Introduction

The CJD Incidents Panel has proposed that people who received blood transfusions from donors with vCJD should be informed of their potential exposure and advised not to give blood or donate organs and tissues and that special precautions might be needed if they require surgery. The Panel has recommended that no one should be given this information until proper counselling and back-up facilities are made available.

In 2001, the Panel conducted a consultation exercise on a framework of proposals on the management of incidents. These proposals included contacting people put at risk of CJD, setting up a research database and quarantining contaminated instruments. Following the consultation exercise, these proposals were submitted to the four CMOs within the UK. In 2003 the CMOs accepted the proposals except for the database of 'at risk' patients. The Department of Health has asked the HPA to develop communications strategies and central expert support for local teams managing incidents.

3.1 Background

In March 1996, a blood donor, who was at the time free of the signs of vCJD, donated blood to the National Blood Service. Shortly after this the donated blood was transfused into a patient who underwent surgery for a serious illness. This recipient died in autumn 2003.

Although s/he was developing neuropsychiatric symptoms, prior to the time of death there was insufficient evidence to make a diagnosis of CJD infection. The local hospital carried out a *post mortem* and it was at that stage that they began to suspect CJD. Accordingly they sent tissue samples to the National CJD Surveillance Unit on 27th November. The Surveillance Unit established the presence of variant CJD on 9th December, and the Department of Health was informed.

On 15th December a group of national experts reviewed the evidence and concluded that the infection could be the result of a blood transfusion although there was no proven causal connection. This case is the first report from anywhere in the world of the possible transmission of vCJD from person to person via blood.

This incident came to light through the Transfusion Medicine Epidemiology Review (TMER) study. This research study identifies vCJD cases who have donated blood, and blood recipients who develop vCJD. By December 2003, 17 donors who subsequently developed vCJD had been identified through this study.

These 17 individuals had donated blood to 43 recipients. Of the 43, 26 were known to have died of unrelated illnesses, leaving 17 recipients thought to be alive in the whole of the UK. The Health Protection Agency was asked by the Department of Health to work with the National Blood Service to co ordinate the contacting, informing and supporting of the 15 individuals in England and Wales. The Scottish Health Department developed separate arrangements for informing two recipients living in Scotland.

3.2 Summary of main events

Between 8th and 15th December 2003 the Department of Health (DH) held a series of discussions with the Health Protection Agency (HPA). The HPA was asked to develop, to be ready in 4-6 weeks, the organisation and infrastructure required to notify recipients of blood components and plasma derivatives donated by people who subsequently develop vCJD.

On 16th December the HPA-CJD team was informed about the death of a blood recipient from vCJD, and that the Secretary of State was due to make a statement in the House of Commons at noon the next day (see appendix 10.1). The HPA was instructed that the exposed patients needed to be contacted as soon as possible.

On 17th December:

a The HPA received the list of recipients (name, date of transfusion and NHS number), draft House of Commons statement and DH Questions and Answers.

b The HPA-CJD team continued its work on a blood communications strategy and communications toolkit for exposed patients. This work built on and adapted the toolkit previously developed for surgical incidents.

c The HPA-CJD team held a teleconference with regional epidemiologists immediately after the statement had been made, asking them to identify a contact for each region for the purposes of the incident in the event of patients being resident in their region. The statement was disseminated to public health staff via public health link (see appendix 10.1).

d By the end of the day, a letter had been sent out to the regional contacts informing them about the incident and the HPA's role, with the communications toolkit attached: draft letters from CCDC/CPHM to GP and from GP to patient; patient information leaflet and information for clinicians (see appendix 10.2). Contacts for regions with patients to be informed were sent, in addition, details of the patient and their GP.

Daily teleconferences between the HPA, the Department of Health and the National Blood Service, were held until 23 December 2003.

On 22nd December, one new issue to emerge was that in situations where the GP had significant concerns about how the patient would receive the news because of underlying mental health problems, the GP might benefit from the support of the local mental health team as to when and how the patient should be informed. Discussions were also held concerning the issue of Christmas itself and the lack of support for the recipients and their GPs over this holiday period. It was decided that informing recipients should stop on 23rd December and resume on 5th January.

On 9th January 2004 HPA-CJD team was informed by the National Blood Service of a further donor who had subsequently developed vCJD. Two recipients of this blood were thought to be alive and were added to this notification exercise. One of these recipients is now know to have died from non-neurological causes.

In summary, as of 21 January 2004, the National Blood Service has reported to the HPA a total of 17 recipients in England and Wales. Fifteen of these were reported in December 2003, and 2 in January 2004. The NBS has also informed the HPA of 2 recipients in Scotland. Two of the English patients are known to have died from non-neurological causes prior to the notification process, leaving 15 living recipients in England and Wales.

4. Aims and objectives of the notification exercise

Aim

- To inform recipients exposed to blood products from donors who had subsequently developed vCJD. This would fulfil the ethical obligations of openness with respect to recipient's exposure risks, and ensure public health measures could be implemented.

Objectives

- To identify the recipients and verify their exposure to the implicated blood components
- To supply information and expert support to local health protection teams and local medical practitioners so that they could in turn give information and support to individual patients
- To ensure that recipients were notified with speed and sensitivity so as to minimise distress
- To protect public health by preventing secondary transmission as far as possible
- To maintain confidentiality and comply with Caldicott principles wherever possible in regard to patient data
- To coordinate the exercise throughout the Health Protection Agency
- To keep the Department of Health and others informed

5. Actions taken

Before being informed of the death of the index recipient, the DH and the HPA had been discussing the organisation and infrastructure required to notify recipients of blood components and plasma derivatives from blood donated by people who subsequently developed vCJD. At the outset of the incident, the HPA-CJD team developed a

communications strategy and drafted a communications toolkit for patients who had been exposed via blood components.

5.1 Information toolkit for local health practitioners

The toolkit was developed by modifying and redrafting information that had been prepared for patients exposed to vCJD via surgical instruments. The toolkit was disseminated to all health protection teams who had recipients residing in their local regions by the end of the first day of the notification exercise. The toolkit consisted of draft letters from CCDC/CPHM to GP and from GP to patient; a patient information leaflet; and information for clinicians. Because of the time pressure due to the initial aim to inform all the recipients before the Christmas holidays, the information could not be piloted and there was little time for consultation of professionals and others. As a result, the information toolkit underwent several revisions during the course of the notification exercise. The latest versions of the components are included in appendix 10.2.

5.2 Information for NHS Direct

Early discussions were also held with NHS Direct, which was to be the initial contact point and source of information for the public. The questions and answers, which had been prepared by the DH, were forwarded to the Communications Manager at the NHS Direct Intelligence Unit who reordered the information and disseminated it to the 23 NHS Direct call centres for use by the call operators. The local call centres also received the health alert notification of the incident and the CMO's public health link message. This information is attached in appendix 10.3. It was also agreed that NHS Direct would refer any questions their call centre supervisors could not deal with to the HPA CJD team.

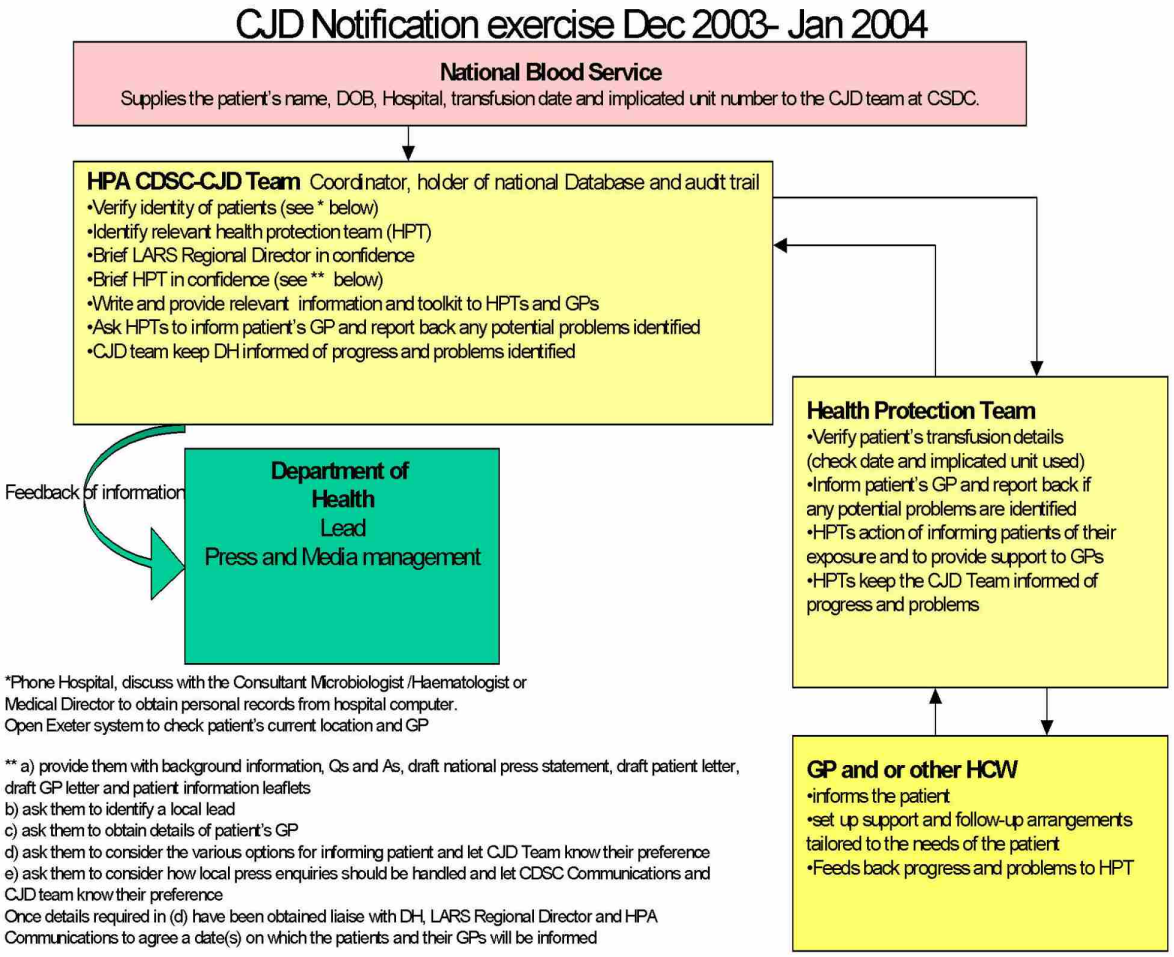
5.3 Notification exercise

The strategy for the conduct of the notification exercise was drawn up by the HPA CJD team in consultation with the DH immediately after the statement by the Secretary of State. This strategy evolved during the exercise as issues were identified.

The list of recipients compiled by the National Blood Service was derived from information held on local haematology laboratory computer databases. These record which blood units are issued to patients, but do not record whether a blood unit is actually transfused into a patient. When the CJD Team became aware of this discrepancy, local health protection teams were asked to cross-check with the patient's clinical notes to ensure that the implicated unit had been transfused, prior to informing GPs of their patient's exposure. In the event, all the implicated units had been transfused into the patients to whom they had been issued, although one recipient had received only 12 of the 14 units assigned to them.

It was decided that the clinical autonomy of local health doctors should be respected and that the GP, supported by the local health protection team, should decide on the most appropriate way to inform and support each recipient. At the same time, it was emphasised that where possible each patient should be informed during a face-to-face consultation and all the GPs involved agreed with this view. Where the local team felt uncomfortable with informing the recipient so soon before Christmas, teleconferences were held in order to discuss the issues with the HPA CJD team.

A summary of the steps taken in the notification exercise is shown in the diagram below:



5.4 Communications to support the notification exercise

Communications between the HPA and DH were conducted via telephone, electronic mail and teleconferences (initially on a daily basis) throughout the exercise. Exchanges of information, including patient details and progress updates between the HPA CJD team and local health protection teams were effected via telephone and electronic mail. These methods were efficient and timely.

5.5 Expert advice and support group

It was decided that support and advice, including counselling, for recipients should be provided locally. Access for local health professionals to advice and support from CJD experts and CJD counsellors was made available *via* the HPA CJD team.

5.6 Press and Media Management

In order to ensure a coordinated approach and to reflect 'ownership' of the incident, it was agreed at the outset that the DH should handle all press releases and queries in the first instance.

5.7 Feedback concerning the reaction of recipients

The initial reaction of recipients informed of their increased risk of developing vCJD was fed back informally from GPs *via* local health protection teams to the HPA CJD team. This provided an informal evaluation of the process and revealed potential problems early.

6. Results and local impact

17 recipients were identified in England and Wales

- 2 recipients were found to have died of non-neurological causes and no further attempts were made to inform their family of the possible exposure.
- All but one received red cells.
- The earliest transfusion was in 1993 and the latest in 2001.
- The oldest recipient was born in 1915 and the youngest in 1974.
- 11 were female and six were male.
- 11 lived in North England, 4 in East England and 2 in North Wales.

Patient data and progress with the notification exercise were documented in a variety of ways, as described below.

6.1 Individual patient log

Each recipient had an individual log, with brief clinical details. The log was revised as more information was collected. Daily updates from local health protection teams were collected each afternoon throughout the exercise. (See appendix 10.4)

6.2 Daily table

The progress made with the notifications was summarised in a daily table. This table was particularly useful in enabling rapid identification of the anonymised recipients and the HPA personnel at regional and local level when dealing with queries from colleagues. (See appendix 10.5)

6.3 Status Table

A daily status table was also constructed and revised each day. This allowed an overview of the situation. (See appendix 10.6)

6.4 Reason for transfusion

The reason for the transfusion of each implicated unit was collected by the local health protection teams. Most recipients received blood following post-operative procedures. There were four that had gastrointestinal surgery; four had orthopaedic surgery, two had cardiac surgery and four were emergencies. Three recipients had been transfused due to haematological disorders. This is summarised in the table below. This table does not include the two recipients who died shortly before the notification exercise.

Recipient Information			
Recipient ID	**Transfusion Date**	**Age Now**	**Reason for transfusion**
	16/01/1993	65	Gastro-intestinal bleed
	13/01/1995	47	Severe anaemia
	29/09/1995	31	Haematological problem-TTP
	13/09/1997	29	Post operative – colonic surgery
	23/12/1997	71	Road traffic accident
	24/04/1998	80	Post operative-total hip replacement
	30/12/1998	40	Gynaecological emergency
	21/10/2000	69	Severe anaemia
	08/06/2001	65	Post operative – cardiac surgery
	22/01/2001	30	Bleeding peptic ulcer
	20/03/2002	88	Post operative – total hip replacement
	09/04/1996	72	Post operative – colectomy for bowel cancer
	10/12/1997	74	Post operative – prosthetic knee
	27/02/1998	85	Post operative – total hip replacement
	15/02/1995	85	Emergency surgery- aortic aneurysm repair

6.5 NHS Direct

It was crucial that NHS Direct should be informed early on of the situation. NHS Direct adapted questions and answers prepared by the DH for their call centre staff. It was anticipated that many members of the public might ring NHS Direct on hearing the Secretary of State's speech or subsequent news items, but initial feedback from the NHS Direct Communications Manager was that there appeared to be a very low level of anxiety regarding this incident with fewer than 10 calls per centre.

6.6 Reaction of patients and local teams and support utilised

Initial informal feedback on the reaction of recipients on being informed of their exposure by their GPs was collected from the local health protection teams. The majority were informed by their GP; in some cases, the local CCDC was present at the local consultation. One recipient was informed by the local neurologist.

All but one of the recipients appeared to take the news calmly. This recipient became very anxious on being informed of the exposure. Because s/he had been at work on 23rd December when first contacted by the GP for an appointment, s/he asked to be seen on 24th December. S/he became very anxious over the Christmas holiday period, contacting the CJD Support Network, and subsequently expressed the view that s/he should not have been informed immediately before Christmas or, perhaps, at all. The GP arranged a referral to a

local neurologist. The CCDC is following up this recipient closely and has made arrangements to continue to support this patient locally.

The majority of recipients received information and support from their GPs and local health protection team. They have not as yet requested more consultations with neurologists or other experts.

A formal evaluation of the information and support provided to the recipients in this notification exercise will be undertaken in order to inform the planning for future vCJD incidents and patient notification exercises.

7. Issues identified from this incident and notification exercise

- The DH delayed telling the HPA for a week that a recipient had died of vCJD and of the imminent need to inform other recipients. This led to an avoidable rush to inform patients. The haste with which named information was transferred resulted in the necessity to use e-mail. Had the HPA been involved earlier, a higher level of confidentiality could have been achieved.
- The DH exerted great pressure on the HPA to ensure that patients were informed quickly in the week before Christmas. This urgency overrode the clinical care as patients were informed before Christmas, a stressful time of year for many, where support services may be limited. Local teams had little time to set up support services, and there was little time to brief counsellors. At least one patient felt insufficiently supported over the holiday period.
- The HPA had some difficulty in locating the current addresses of recipients. This made it difficult for the CDSC-CJD team to assign the relevant local health protection team to inform the recipient. The Open Exeter system can provide this information, but CDSC does not at present have access to it or its replacement system, the NHS Strategic Tracing service. Local health protection units can access Open Exeter but their access is limited to patients living in their locality. Although during this exercise it was fortunate that the Greater Manchester HPU had access via their host PCT to the NHS Strategic Tracing Service, which holds the national database. The details of most of the recipients were found and the printouts faxed to the CJD team within a

morning. HPA has applied for access to the new NHS Strategic Tracing service, but this has not yet been approved.

- Patient notification would be helped if the NBS could supply patients' NHS Number to the HPA.
- In addition to working with NHS Direct, the HPA needs to work with patient support groups who may also receive calls on incidents.

8. Issues for the CJD Incidents Panel to consider

Database

- The CMO has asked that a non-consented database of 'at risk' patients should not be set up at this stage. The Department of Health has asked the HPA not to develop a database of contactable patients involved in surgical incidents, for the time being.. As a result of the blood component incident reported here, CDSC now holds a *de facto* national database of contactable blood component recipients.
- This blood incident and future work on notifying patients who have received implicated plasma derivatives raise urgent questions on the database of contactable surgical patients; and how the database of contactable blood patients should relate to the TMER study run by the National CJD Surveillance Unit and the National Blood Service.

Surgical histories from recipients of implicated blood components

- It has been brought to the attention of the HPA CJD team that at least two of the recipients may have had major surgery following their transfusions of implicated blood components. Should these operations be assessed by the CJD Incidents Panel? Should surgical histories be obtained from all recipients (since the time of their transfusions) and past incidents assessed by the CJD Incidents Panel?
- If, so will the same be necessary for the hundreds, or possibly thousands of contactable patients exposed to plasma products?

Individual circumstances which made it difficult to inform the recipient

- During this notification exercise, there were occasions when the local health protection teams were reluctant to inform the recipient.
- These included instances where the GP had concerns about the patients' psychiatric state, ability to comprehend the information, or physical health. It was also evident that some local doctors may wish to make their own ethical decision on whether it is appropriate to inform patients about these exposures.
- While all of the patients in this notification exercise have now been informed, it is likely that many patients in the forthcoming plasma products notification exercise will not be informed, either following their own or their doctor's decision.
- In these cases what should be done to retain information about this risk group? What should be done to protect public health through blood, tissue or organ donations? What should be done to protect public health through future surgery?

9. Further work planned

Further work is already being planned by the HPA CJD team. This includes formal evaluation of the toolkit and information provided to the local health teams and NHS Direct as well as the process of the notification exercise itself.

It is planned that patient literature will be piloted and reviewed by the Plain English Campaign. Training workshops are being planned with patient groups and healthcare staff who may be involved in a plasma products notification exercise.

10. Appendix

10.1 CMO Cascade to Public Health practitioners and PCTs including the Secretary of State parliamentary speech

From: Sir Liam Donaldson - Chief Medical Officer - Department of Health
Date: 17 December 2003
Reference: CEM/CMO/2003/21
Title: BLOOD TRANSFUSION INCIDENT INVOLVING VCJD
This broadcast will be available online shortly at:
http://www.info.doh.gov.uk/doh/embroadcast.nsf/vwDiscussionAll/0301ECC6DF485EF880256DFF004DA063
To view the main website please go to:
http://www.info.doh.gov.uk/doh/embroadcast.nsf

To: Directors of Public Health of PCTs to forward to:

- All GENERAL PRACTITIONERS - please ensure this message is seen by all practice nurses and non-principals working in your practice and retain a copy in your `locum information pack'.
- Deputising services
- Project manager/Nurse lead in Walk in Centres
- PCT lead nurses
- Leads at nurse-led PMS Pilots

To: Medical Directors of NHS Trusts to forward to:
- Consultant Haematologists
- Consultant Neurologists
- Nurse Executive Directors of NHS Trusts
- Staff involved in blood transfusions

Cc:
- Regional Directors of Public Health
- Directors of Public Health of Strategic Health Authorities
- UK CMOs
- Chairmen of Professional Executive Committee

Dear Health Professional

Blood transfusion incident involving vCJD

Below is a statement announced by the Secretary of State for Health in Parliament today. I am sending you this for your information as you may get patients coming to you with questions relating to this. Anyone who is concerned can ring NHS Direct on: 0845 4647. NHS Direct are being advised on this issue by the Health Protection Agency.

Statement
"With permission Mr Speaker I wish to make a statement about a blood transfusion incident involving variant Creutzfeldt-Jakob Disease (vCJD).

It might assist the House if I begin by setting out the basic facts before coming on to discuss the implications.

In March 1996, a blood donor, who was at the time free of the signs of vCJD, donated blood to the National Blood Service. Shortly after this the donated blood was transfused into a patient who underwent surgery for a serious illness.

In continuing my description of these events to the House, I will from now on refer to these individuals as the 'donor' and the 'recipient' of the blood.

The donor showed no signs of vCJD at the time blood was given, but developed the disease three years later i.e. in 1999 and died from it.
The recipient of the blood died in the autumn of 2003. Initial post-mortem examination of the recipient of the blood showed changes in the brain indicative of CJD. Further examinations and tests of this patient's brain confirmed the diagnosis of variant CJD. The link between the donor and the recipient was first reported to

officials in my Department on 9 December 2003 at which time the diagnosis of vCJD in the recipient was still being confirmed.

I was first alerted to the developments on Friday 12 December and was briefed by the Chief Medical Officer on Monday and Tuesday this week. Today I am bringing this information to the House at the earliest opportunity. I have given the minimal clinical details of the recipient because the family has indicated that they wish to have their privacy respected.

In the light of the facts which I have outlined, it is therefore possible that the disease was transmitted from donor to recipient by blood transfusion, in circumstances where the blood of the donor was infectious, three years before the donor developed vCJD, and where the recipient developed vCJD after a six and a half year incubation period. This is a possibility not a proven causal connection. However, it is also possible that both individuals separately acquired vCJD by eating BSE (Bovine Spongiform Encephalopathy) infected meat or meat products.

This is a single incident, so it is impossible to be sure which was the route of infection. However, the possibility of this being transfusion-related cannot be discounted. That is the conclusion of the Chief Medical Officer and experts.

It is because this is the first report from anywhere in the world of the possible transmission of vCJD from person to person via blood that I thought it right to come to the despatch box to inform the House on a precautionary basis.

This incident was discovered by good surveillance. In 1997, the Department of Health funded a research study, the Transfusion Medicine Epidemiology Review (TMER) study to examine links between all vCJD cases and any form of blood transfusion. It is through this research study that the association between these two patients was identified. I should also point out that this emphasises the importance of post-mortem examination. Without it we would never have known about these matters. I would like to thank our NHS pathologists for their expertise and constant vigilance.

I can inform the House there is as yet no blood test for vCJD (or for that matter BSE) let alone one that could detect the disease years before symptoms develop. So, there is no way yet of screening blood donations for the presence of the CJD group of diseases.

Fortunately, however, a range of precautionary measures have been put in place by the Government since 1997, even though there was at that time no evidence of the risk of person-to-person transmission of the disease via blood. For the reassurance of the House, I will briefly set out the action that has been taken to date and the further action that we now propose.

Firstly, since 1997 all cases of vCJD that are reported to the National CJD Surveillance Unit and diagnosed as having 'probable' vCJD, result in a search of the National Blood Service blood donor records. If the patient has given blood, subsequently any stocks of that blood are immediately destroyed.

Secondly, on 17 July 1998 acting on expert advice, the Government announced a £70 million programme to remove most of the white cells from blood destined for transfusion. White cells were considered by experts at the time to be a potential source of infection. This process of so-called leuco-depletion was then a highly precautionary measure to reduce what was then a hypothetical source of infectivity. The process of leuco-depletion was implemented by the National Blood Service over time and completed by October 1999.

Thirdly, on 12 November 1998, again acting on expert committee advice, the Government announced a £30 million programme to phase out the use of United Kingdom-sourced plasma in the manufacture of blood products. This was at the time (in the absence of any defined risk) another highly precautionary measure. From the end of 1999 all blood products have been made using plasma sourced from the United States of America. To ensure continuity of supply the Department of Health purchased on 17 December 2002 the largest remaining independent US plasma collector, Life Resources Incorporated.

Fourthly, the National Blood Service has informed us that 15 people received donations of blood from donors who subsequently developed vCJD. Of the 15 individuals, we have been informed that five received blood after leuco-depletion had been implemented, the remainder before. The earliest such transfusion was in 1993 and the latest in 2001. Working with the
National Blood Service, the Health Protection Agency is in the process of contacting these individuals. All will be told about the circumstances of their case and have the opportunity to discuss the risks with an expert counsellor.

Many more patients of course, including haemophiliacs, will have received plasma products before plasma was sourced from the USA. They will have received products derived from large pools of plasma donated from many thousands of people and thus heavily diluted. The UK-wide CJD Incidents Panel considers the risks for this group to be even lower than for those who received whole blood. It is very difficult to trace all individual recipients of products made from these plasma pools. However, the CJD Incidents Panel will be advising on a case-by-case basis which recipients will need to be contacted as the necessary information becomes available.

This group of patients will also have the opportunity for a discussion with an expert on an individual basis. Any person with concerns may ring NHS Direct on 0845 4647.

Fifthly, before these events, expert groups were already deliberating on whether further measures were required in relation to vCJD and blood. In October of 2003 our expert committee on the Microbiological Safety of Blood and Tissues for Transplantation advised, on the basis of a risk assessment, that further action such as stopping people who have received a blood transfusion from giving blood was not necessary.

However, in the light of today's statement, we have asked this Committee to look comprehensively at whether further precautionary measures could be taken which would not adversely impact on the safety or availability of blood.

Sixthly, it is apparent that much more blood and blood products are used clinically, than need to be. There have been many past attempts to reduce the use of blood to situations where it is absolutely needed medically, but these have only been partially successful. I will be asking the National Blood Service to have urgent discussions with the medical Royal Colleges and NHS hospitals to address this area of clinical practice. More appropriate blood usage will reduce all the risks associated with blood and will make more effective use of our precious blood supplies.

A finding of this kind, albeit one whose full medical significance is still far from clear, inevitably will give rise to concern. It is therefore important to take account of the wider context in two respects.

Firstly, since the events in 1996, approximately 24 million units of blood or blood components have been given to patients in the United Kingdom.
Blood transfusion can be a life saving treatment but no medical treatment is free of all risks. Indeed it is an unfortunate fact that already each year approximately 12 die as a complication of blood transfusion. Many people receiving blood transfusion are already very ill, some in life and death situations. A wide range of measures are routinely used to reduce the risks of transfusion by screening for HIV/AIDS, hepatitis B and C and other infections. For specific high risk patients even more detailed screening takes place.

These wider measures should be seen in the context of the precautionary action already taken on vCJD, and a recognition that so far we have only one single report of a possible link between a single donor and a single recipient.

We are generally regarded internationally as having a very safe Blood Service, especially because of our precautionary approach to screening for infection, careful donor selection and the tradition of volunteering which means that our donors generally have a lower incidence of many viral diseases compared to those in other countries who are paid for their donations.

Secondly, as for the wider situation for vCJD, thankfully we have not so far seen the thousands of cases of vCJD that some projections suggested. As of 1 December 2003 there had been a cumulative total of 143 cases of vCJD in the United Kingdom. Over the last three years the annual number of new cases has fallen. However, there should be no complacency. It remains premature to conclude that the epidemic has peaked. Any case of vCJD is tragic for the patients and families concerned.

I hope that my statement has given the House a clear and accurate account of this finding in the full context in which it needs to be seen. I have asked the Chief Medical Officer to oversee the further work and investigation required and to keep me closely informed. I will of course keep the House informed of any major developments in this area."

10.3 Information prepared and sent to local Health practitioners

Draft letter for use in cases of difficulty setting up a face-to-face consultation between GP and patient (implicated blood components recipient)

[date]

[Patient name and address]

Dear [patient name]

I have been trying to contact you recently, but without success. As a result I am now writing to ask you to come and see me. This is in connection with a blood transfusion you had in hospital on [date]. As you may have heard on the news, a few people round the country have received blood donated by someone who subsequently developed variant Creutzfeldt-Jakob Disease (vCJD).

I regret to have to tell you that the blood transfusion which you had did include blood from one of the people who became ill with vCJD. It is thought that there is only a very small chance that you will develop vCJD.

However,I am sure you would like to come and see me to discuss this. I should also like to ask you to take some precautions which will not affect your everyday life, but may protect the health of other patients. Please could you make an appointment to see me so that we can talk about this and you can ask me any questions you might have.

There is only one case in the UK where someone may possibly have contracted vCJD from blood. It is not possible to say what your individual risk of developing vCJD is since there is very little known about vCJD and there is no screening test. I can, however, reassure you that there is no known risk of passing vCJD on to others through everyday contact or sexual contact.

As a precaution, however, I am asking you to do the following:

- Do not donate blood, organs or tissues;
- whenever you are going to have any surgery or invasive medical procedures, tell the doctor, dentist or nurse in charge of your care that you are in an 'at risk' group for vCJD. This will not affect the care you receive. It just means that the surgical instruments will be treated differently;
- tell your family (in case you might need emergency treatment in the future).

I apologise for any anxiety this may have caused. I enclose a leaflet which I hope you will find helpful and look forward to seeing you very soon in my surgery.

Yours sincerely,

[name of GP]

DRAFT letter: CCDC/CPHM to GP of a patient to be contacted (implicated blood component recipient)

[GP name and address] [date]

Dear Dr. [GP name]

Re [patient name, address, DOB] - risk of exposure CJD via blood components

Some blood donors (to date), asymptomatic at the time of donation, have subsequently gone on to develop variant CJD (vCJD). Now a patient has been diagnosed with vCJD possibly caused by a blood transfusion. This patient received blood from a donor who later developed vCJD. This affects your patient as s/he received implicated blood components from another of these donors.

The CJD Incidents Panel has assessed the risk of vCJD being transmitted to other patients via blood. Up to this time the risk had been theoretical, based on risk assessments and animal studies. Now the first case of possible transmission of vCJD via blood has been reported.

Fourteen patients in England who have been put at risk by receiving implicated blood components have been identified and this group includes your patient [name].

The CJD Incidents Panel advises that there is an ethical duty to inform this group of patients about their exposure. The Panel also advises that there is a public health duty to ask them to take precautions to limit possible further spread of CJD.

Your patient should be advised:

- not to donate blood, organs or tissues;
- to tell the doctor, dentist or nurse in charge of their care whenever they are going to have any surgery or invasive medical procedures that they are in an 'at risk' group for vCJD;
- to tell their family in case they require emergency surgery.

Your patient's exposure via blood to vCJD should be recorded in their medical notes.

I would be grateful if you would arrange to see your patient and tell him/her about the exposure, allowing sufficient time to explore these issues and your patient's concerns. Please provide him/her with information and support to help him/her understand the risk, and the precautions needed to limit any risk to others. Although the risk to your patient is very uncertain, and hard to quantify, it is important to reassure your patient that there is no known risk of passing vCJD on to others through everyday contact, sexual contact or from mother to child.

I enclose an information sheet with background information on vCJD and the risk of transmission through blood, as well as a patient information leaflet, to help you answer your patient's questions.

Please contact me if you would like further information or advice.

Yours sincerely

[insert name of CCDC]

Variant CJD and blood components: Information for clinicians

About CJD

Creutzfeldt-Jakob-Disease (CJD) is one of a group of fatal diseases which invade the brain through an 'infectious protein' known as a prion. CJD causes dementia and a range of neurological symptoms, including unsteadiness and jerky movements. The disease affects about one person in a million per year, giving rise to 50 or so new cases a year in the UK. At present CJD can only be diagnosed for certain by *post mortem* examination of the brain.

There are four main types of CJD: of these, sporadic accounts for 85% of cases, having no known cause. The other types are familial, iatrogenic and variant.

Sporadic CJD (sCJD) affects mainly the over 50s and is of unknown cause. The course of the disease is typically measured in months. Sporadic CJD is most common in the 45-75 year age group with the peak age of inset being 60-65 years. The number of cases of sCJD in the UK has increased since 1970, when figures first started being kept. In 1970-71 there were 21 deaths from sCJD and in 2002 there were 67 deaths. Most of the increase has occurred since 1990 and in the over 70 age group. It is not clear whether this is due to greater awareness of CJD among the medical profession, or whether it represents a genuine increase in the incidence of the disease. There is no evidence of any link between sCJD and BSE (bovine spongiform encephalopathy). 70% of patients die within six months of onset of symptoms. Rarely, sCJD lasts for several years.

Familial CJD is inherited, with younger onset and usually a longer time course than sCJD.

Iatrogenic CJD occurs through contamination with infected tissue via medical procedures such as treatment with human growth hormone.

Variant CJD (vCJD) is caused by exposure to BSE (bovine spongiform encephalopathy) and typically affects younger people. It has a relatively longer time course than most other forms, with an average of 14 months between onset of symptoms and death. Early symptoms are often psychiatric, such as anxiety and depression, and there may be persistent pain, with odd sensations in the face and limbs. More obvious neurological symptoms and progressive dementia follow. As at December 2003, 143 cases of vCJD have been reported in the UK. Eleven cases have also been diagnosed abroad. If the disease comes from exposure to infected beef products prior to the ban of specified offal in human food in 1980, as is now widely accepted, then there could be more cases if the incubation period is very long. However, without knowing the exact route of the infection, or who is most at risk and why, it is currently impossible to predict how many more cases of vCJD there will be.

In the UK all cases of suspected CJD are reported to the National CJD Surveillance Unit (NCJDSU) in Edinburgh. The number of cases is published on their website at www.cjd.ed.ac.uk/figures.htm

Abnormal prion protein

The infectious agent is thought to be an abnormal form of prion protein called PrP. In its normal form, PrP occurs in the brain and other parts of the body in humans and a wide range of animals. The function of the normal PrP protein is unknown. Unlike bacteria and viruses, prions are not inactivated by heat, ultraviolet light or other standard sterilisation procedures. When abnormal prions invade tissue containing normal PrP, they can convert it into the abnormal form, which leads to disease.

Vulnerability to this change can be inherited or it may occur for no known reason, as in sCJD. No firm link between the occurrence of CJD and risk factors such as sex, occupation or diet has been shown. It occurs in countries such as Australia not known to be affected by BSE or scrapie, the sheep prion disease. However, there is evidence that the majority of people with sCJD and all the people with vCJD have a PrP gene which is found in less than half the general population. This genetic variation may make normal PrP more vulnerable to conversion into the abnormal form associated with the disease.

Variant CJD

Variant CJD was first identified in 1996. It is caused by a new strain of prion protein. This is very similar to that seen in cattle with BSE, and is different from other strains seen in other human prion diseases such as sporadic CJD and kuru.

The symptoms of vCJD differ from those of sCJD. Initially there is typically anxiety, depression, withdrawal and behavioural changes. The patient may be referred first to a psychiatrist rather than a neurologist. The patient may also report persistent pain and odd sensations in the face and limbs. After several weeks or months, more clearcut neurological symptoms may set in including unsteadiness in walking, sudden jerky movements, progressive dementia and loss of mental function marked by symptoms such as memory loss. Death occurs on average around a year after the onset of symptoms. There is a different microscopic appearance at *post mortem*.

It is thought that vCJD is caused by neural tissue, including the spinal cord, from BSE infected animals in mechanically recovered meat used in the manufacture of sausages, meat pies and hamburgers. It is not known how many more people will develop vCJD.

Variant CJD differs from sCJD in several respects. The majority of cases reported to date have been in young people with an average age at onset of symptoms of 28.

Iatrogenic transmission

A few people have contracted CJD from brain operations using instruments previously used on someone with CJD. The prion agent survives the disinfection processes which normally destroy

bacteria and viruses. Intracerebral transmission of CJD has also occurred with corneal transplants and grafts of dura mater, the tough membrane which covers the brain. The incubation time for intracerebral iatrogenic CJD is between two and four years. There are no recorded instances of vCJD being spread through other types of surgery.

CJD has also been transmitted by treatment with human growth hormone. This is known as peripheral transmission because the route to the brain of the infective agent is through the circulation, not directly into the brain. Human growth hormone used to treat children with short stature was in the past prepared from human pituitary glands. The incubation time for peripheral iatrogenic CJD is longer than for the intracerebral form and is more like kuru (itself a peripherally transmitted disease) being in the order of around 15 years. There could therefore be more growth hormone cases to come. Growth hormone has not been made from human sourced pituitary glands since 1986. Peripherally acquired CJD may be more like kuru, with symptoms of ataxia (unsteadiness and lack of co-ordination) predominating and dementia being a rare feature.

There appears to be a genetic predisposition to contracting iatrogenic CJD.
Where transmission is intracerebral, the symptoms are like sCJD – initially depression, memory lapses, sometimes unusual fatigue. However, rapid progression to dementia and obvious neurological symptoms distinguish CJD from depression. Within weeks there can be unsteadiness and lack of co-ordination although sometimes these symptoms are the first to appear. Other symptoms may include sudden jerky movements, rigid limbs, blindness, incontinence and difficulty in speaking and swallowing. Eventually the patient loses the ability to move or speak and will need full time nursing care.

For iatrogenic transmission of vCJD via blood components please see next section.

5 Transmission of vCJD via blood components
Prion diseases are transmissible in certain circumstances, but they are not infectious in the usual way. They are not spread by airborne droplets or by sexual contact. Contact with a CJD patient does not lead to an increased risk of developing the condition and no special precautions are required.
In vCJD, the disease process involves many tissues, including the lymphoid tissue, but until now there has been no evidence that vCJD can be transmitted by blood components. Blood components are derived from a single blood or plasma donation or, in the case of platelets, a small pool usually of about four donations. These are labile products with a short shelf life. Blood components include whole blood; red cell concentrates; platelets; granulocytes; fresh frozen plasma; and cryoprecipitate (made by freezing and thawing plasma).
Most modern treatments use blood components rather than whole blood. Preparations of red cells, platelets and plasma contain varying amounts of the other components. Patients usually receive more than one unit in a transfusion, and may be transfused several times. However a patient is unlikely to receive more than one unit of a blood component from a particular donor with variant CJD. Even low

infectivity levels could be important because large quantities of blood and plasma derivatives are used to treat individual patients. These quantities greatly exceed the trace amount of protein remaining on surgical instruments after decontamination.

The National Blood Service (NBS) works with other organisations to determine whether there is any link between the development of vCJD and blood transfusions. When people are diagnosed with vCJD by the National CJD Surveillance Unit, the NBS is informed and a check made as to whether the patient donated blood. To date (December 2003) 16 individuals in England and Wales are known to have received components of blood donated by people subsequently diagnosed with vCJD. The dates of the transfusions were between 1993 and 2001. One of these recipients has recently died and had their diagnosis of vCJD confirmed. It is possible that vCJD was transmitted by the blood components. This is therefore the first documented probable case of vCJD transmitted by blood components.

6 Public health protection against CJD

Iatrogenic CJD is guarded against by destroying surgical instruments that have been used on people with CJD and by not accepting donations of blood, tissue or organs from people diagnosed with CJD or at increased risk of developing CJD. At present there is no way of protecting people from the sporadic or familial forms of CJD. A number of measures have been used by the government to minimise the risk of contracting variant CJD from BSE infected meat and meat products. These include a ban on specified offal in human food.

CJD and surgery

In all types of CJD most infectivity is present in the brain and spinal cord. Infectivity is also present in the eye and olfactory epithelium. In vCJD infectivity is also present in lymphoid tissue such as the tonsils or appendix. Instruments used on the brain or nervous tissues of someone with CJD are always destroyed after use. If the patient is suspected of having CJD then the instruments are quarantined and will not be used until an alternative diagnosis has been made. If the diagnosis is confirmed, the instruments are destroyed.

Advice for your patient

An information leaflet for patients exposed to risk of vCJD through blood components is available via your local Health Protection Unit.

A Infectivity

Routine contact with people who have CJD 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 by sexual intercourse.

In CJD most infectivity is present in the brain and spinal cord which are not exposed in routine situations. Infectivity in the eye has resulted in transmission via corneal transplantation. In vCJD

infectivity in the lymphoid tissue such as the tonsil or appendix could be a risk during surgery. There has been one possible case of vCJD transmission by blood donated by an individual subsequently diagnosed with vCJD.

B Donating blood, tissue and organs

It appears that vCJD may be spread through blood donations but there is no evidence that sCJD can be spread through blood. Patients with sCJD are no more likely to have received blood than other members of the population. We do not know the risk of spreading CJD by organ donations. In some cases CJD has been spread through donated eye tissue (corneas and sclera) and through dura mater grafts. Therefore, as a precaution, patients at increased risk of developing CJD should not donate organs, tissues or blood.

C Elective and emergency surgery

Patients at increased risk of developing CJD should inform the doctor or nurse in charge of their care about this in order that special arrangements can be made regarding the surgical instruments to be used. Their family doctor might also include this information in the referral letter.

D Dentistry

Patients at increased risk of developing CJD should inform their dentist about this. This will enable the dentist to ensure optimal standards of infection control are used and the inclusion of the information in referrals to specialists such as maxillo-facial surgeons.

E Can CJD be passed on from mother to child?

This has happened in some of the animal forms of prion disease. In sheep scrapie, for example, the disease has been known to pass from ewes to their lambs. Although it is theoretically possible that vCJD could pass from mother to child, to date there is no firm evidence that this has occurred in humans.

F Treatment for CJD

There is no cure at present for CJD, although scientists are researching into the causes of and potential treatments for the disease.

Further information

Management of possible exposure to CJD through medical procedures: a consultation paper. Department of Health, October 2001
Available at http://www.doh.gov.uk/cjd/consultation/cjdmanagement.pdf

Advisory Committee on Dangerous Pathogens and the Spongiform Encephalopathy Advisory Committee. *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. London: Department of Health, 2003. Available at http://www.doh.gov.uk/cjd/tseguidance/index.htm

Questions and Answers for patients exposed to risk of variant CJD through blood components
Health Protection Agency, December 2003

Why are you contacting me?

A patient has been diagnosed with vCJD (variant Creutzfeldt-Jakob disease), possibly caused by a blood transfusion. This patient received blood donated by a person who later developed vCJD. This is the first time that this has happened.

Some other people also donated blood before they became ill with vCJD. You have received blood donated by one of them.

What is variant CJD?

Variant CJD is a rare disease of the brain and nervous system. Variant CJD is thought to result from eating meat products from cattle with BSE (mad cow disease).

Variant CJD was first recognised in 1996, and over 130 people have died of the disease in the UK.

Do I need to know about this?

The risk appears to be very small, but it is important that you know, even though this may, regrettably, cause you anxiety. We must also do all we can to protect other patients.

How did you find out that I might be at risk?

When a patient is diagnosed with vCJD, checks are made to find out whether the patient has donated blood. More checks are made to look at who else could be affected, in this case people who have received blood from a donor who later developed vCJD.

Can I have a test to find out if I am going to get vCJD?

As yet, there is no screening test for people concerned that they may develop vCJD.

Am I a risk to other people?

There is a small possibility that vCJD could have been passed on to you. If this has happened, then likewise you could pass vCJD on to others in certain circumstances. This is why we are asking you to take some precautions.

What precautions do I need to take?

- Do not donate blood.
- Do not donate organs or tissues. Make sure that your immediate family knows about this.
- If you need any medical, surgical or dental treatment, tell whoever is treating you. They can then arrange any special procedures recommended for the instruments used in your care. Tell your family about this in case you might need emergency surgery in the future.

What about my family?

No special precautions are needed for family or other household members. 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.

Why do I have to inform people who treat me in the future?
It is possible that vCJD could spread between people having surgical operations. This is because the abnormal 'prion' proteins, which are thought to cause vCJD, are very hard to destroy. Surgical instruments could still have infectious prion proteins on them, even after they have been thoroughly washed and disinfected.

If this happens, then the prion proteins could infect someone else with vCJD, when the instruments are used in another operation.

When I inform the people treating me in the future, will this mean I won't get the treatment I need?

No, your care will not be affected. It is just that the surgical instruments will be treated differently.

If most of the UK population is at risk through eating meat, why do I have to take precautions?
While most of the people living in the UK have been exposed to vCJD from meat and meat products from cattle, you may have been put at an extra risk of vCJD because of this blood transfusion.

It is not possible to put an exact figure on your chance of getting vCJD, either from meat or meat products from cattle, or from this blood transfusion. Even so, it is important that you take precautions.

If I had been infected with vCJD because of this blood transfusion, when would I get ill?
As there has only been one possible transmission of vCJD by a blood transfusion, it is impossible to say whether you will develop vCJD or how long it would take.

How can I find out more about vCJD?
You can obtain more information about vCJD from the following organisations:

- CJD Support Network at http://www.cjdsupport.net/ (☎ 01630 673 973)
- NHS Direct http://www.nhsdirect.nhs.uk/ (☎ 0845 4647)
- National CJD Surveillance Unit at www.cjd.ed.ac.uk
- Department of Health at www.doh.gov.uk/cjd/index.htm

MRC Prion Unit at www.st-marys.org.uk/specialist/prion/index_prion.htm

10.3 Information prepared for NHS direct

HEALTH ALERT NOTIFICATION

variant CJD & Blood Transfusions

Alert No:	736	**Version number:**	V1
Date received:	17/12/03	**Date disseminated:**	17/12/03
Local/national:	National	**Site(s) affected:**	National
Status:	Information/awareness	**Type:**	Patient notification
Source:	Health Protection Agency/CDSC Collindale	**Author:**	Health Protection Agency/CDSC Collindale
Content:	Public Health Link Statement /Q&As (24 including this one)	**Skill set:**	HI/NA
Media issues:	Media interest today	**Advertising:**	
Contact at HIU:	Lee Johnson	**Other NHSD Contact:**	
Monitoring:			
Can Q&As be sent?	No	**Review Date:**	18/12/03

Dear all

Information follows concerning a blood transfusion incident involving variant Creutzfeldt-Jakob Disease (variant CJD)

The details include:

- Series of Q&A information
- CMO Public Health Link Message

NHS Direct has been given as a source of information for the worried well.

Kind Regards
Lee Johnson
HIU

Implications at site level for training/staffing:

Please raise staff awareness

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Q&A on Blood Transmission of vCJD

Q. I've had a blood transfusion. What's my risk?

A. Very small [see Safety of Blood questions below]

Safety of Blood

Q. **Is UK blood safe?**

A. The safety of blood and blood products used in the NHS is of paramount importance. Every reasonable step has been taken to minimise any risks during blood transfusion. The current high levels of safety are achieved by screening out potential high risk donors and then further testing of every unit of donated blood for the presence of infections before it is released to hospitals. Five major studies from SHOT (Serious Hazards of Transfusion) have demonstrated that blood transfusion in the UK is very safe and that it is becoming even safer with improving technology and clinical audit.

What are the UK Blood Transfusion Services criteria for excluding blood and tissue donors who have, or who could have had, contact with CJD?

- Permanently exclude individuals with CJD or other prion associated disorder.
- Permanently exclude anyone identified at high risk of developing a prion associated disorder. This includes:
  - Recipients of dura mater grafts.
  - Recipients of corneal or scleral grafts.
  - Recipients of human pituitary derived extracts such as growth hormone or gonadotrophins
- Individuals at familial risk of prion-associated diseases. This includes individuals who have had two or more blood relatives develop a prionassociated disease and individuals who have been informed they are at risk following genetic counselling.

(Exceptions: Individuals who have had two or more blood relatives develop a prion associated disease whom, following genetic counseling, have been informed that they are not at risk. This requires confirmation by the Consultant with responsibility for donors.)

Q. **What is being done to minimise the risk of vCJD being passed through blood?**

- Since 1998, plasma derivatives, such as clotting factors, have been prepared from plasma imported from the USA.
- Since October 1999, white blood cells (which may carry the greatest risk of transmitting vCJD) have been removed from all blood used for transfusion.
- In August 2002 we announced that fresh frozen plasma for treating babies and young children born after 1 January 1996 would be obtained form the USA.

- On 16 December 2002, the Department of Health completed its purchase of the largest remaining independent US plasma collector, Life Resources Incorporated. This secures long-term supplies of non-UK blood plasma for the benefit of NHS patients.

Q. **Will blood transfusion recipients be excluded from donating blood?**

A. The Government's Advisory Committee on the Microbiological Safety of Blood and Tissues (MSBT) has considered whether all blood transfusion recipients should be excluded from donating blood and has advised that this policy would have a damaging impact on blood supplies. We have asked this committee to look again, in the light of this incident, comprehensively at steps that could be taken without compromising the safety of patients in other ways.

Q. **Is Fresh Frozen Plasma (FFP) safe?**

A. As an added precaution against the theoretical risk of vCJD transmission, FFP will be obtained from the United States for new born babies and children born after 1 January 1996 who should not have been exposed to BSE through the foodchain. Each unit of FFP is made from plasma from a single blood donor and has [correct tense?] further viral inactivation treatment (with methylene blue) to reduce the risk of blood borne viruses. The National Blood service is continuing to look for sustainable supplies of imported plasma for other vulnerable groups.

Q. **How many people with vCJD have been blood donors?**

A. Nobody suspected of having vCJD at the time of donation has ever been a donor. 14 donors aysymptomatic at the time of donation have subsequently gone on to develop vCJD.

Q. **How many patients have contracted CJD through receiving blood or blood products**?

A. Worldwide, the suspected case announced this week is the first.

Q. **How do we know that blood donors go on to develop vCJD?**

A. vCJD cases are notified to the blood services by the CJD Surveillance Unit in Edinburgh so that a search can be made to identify any cases who were blood donors. In the event of a blood donor being identified, donation records are obtained and the fate of donations is traced.

Q. **Which countries don't accept donors who have visited/been resident in the UK?**

A. The US, Canada, Australia, Japan, New Zealand, Austria, Hong Kong, Germany, Italy, Switzerland. Finland, France and Israel do not accept blood donations from people who have visited or lived in the

UK for six months or more between 1980 and 1996. This is the period when Bovine Spongiform Encephalopathy (BSE) was epidemic in UK cattle and when the risk to the population of acquiring variant Creutzfeldt-Jakob Disease (vCJD) might be greatest.

Q. **Why is this?**

A. The basis for the ban is that this is the period when BSE was epidemic in UK cattle and those deferred from giving blood are likely to have been at risk of exposure to the BSE agent through eating beef. The ban on such potential blood donors, includes their own nationals.

Q. **Why isn't the UK taking the same measures?**

Introducing a regulation like this in the UK would in effect exclude the whole population. This is not, therefore, an option for the UK as we use 3 million units of blood every year. This blood cannot be replaced from any other source and there is no ready international market. Blood is needed in care of patients especially those who are critically ill, suffering severe accidents, patients with cancer and leukaemia, and those needing surgery.

Is there a blood test available for variant CJD?

Not yet. Several international groups of research workers are working to try to develop a blood test, but it is currently unclear how soon we shall have an effective test.

Can blood donors contract variant CJD from giving blood?

No. Blood donations are taken through sterile, non-reusable, disposable needles and equipment so it is not possible for anyone to contract variant CJD by blood donation.

Will universal leucodepletion reduce the risk of transmission of variant CJD?

Universal leuodepletion was announced by the UK government in July 1998 and implementation was completed by the Autumn of 1999. In patients with sporadic CJD and in animal models where infectivity has been found in the peripheral blood, a large proportion has been associated with the white blood cells. Leucodepletion removes all but a very few white cells, and it is hoped that leucodepletion will reduce the level of infectivity in the peripheral blood (if present) to below the threshold for transmission.

Are plasma derivatives likely to be infectious?

As of October 1999, all plasma products including Factor VIII and Factor IX, immunogloblins and albumin are derived from donors outwith the UK. Therefore, there should be minimal risk to patients receiving plasma products provided donors are from other countries with a known low risk for BSE. The risk to patients who received plasma products before October 1999 is uncertain. The UK BTSs have engaged in research on the ability of the plasma fractionation processes to remove prions. These experiments have shown that there are steps during each manufacturing process which remove prions though it remains unclear how closely these reflect how the natural infective agent behaves. The risk from UK plasma derived plasma products is likely therefore to have been very low, but we cannot yet assume that the risk was zero.

Should UK patients continue to accept blood components and tissues?

Blood and tissues should only be given when it is essential to the quality of life, health or survival of the patient. In these circumstances the benefits are carefully weighed against the uncertain risk of transmission of variant CJD. In some circumstances alternatives are available which could reduce the exposure to blood or tissue. BTS clinicians are continuing to work with colleagues throughout the National Health Service in establishing and implementing guidelines for the appropriate use of blood and tissues. It is a priority for the UK Chief Medical Officers and the medical community in the UK to ensure that patients are treated with blood or tissue only when there is a real need.

What is being done to ensure that blood is used only when there is a good clinical indication?

On advice of the UK Chief Medical officers national programmes for good transfusion practice have been established, supporting the work of local Hospital Transfusion Committees. Transfusion practitioners have been or are being appointed to many hospitals. Their roles include training staff in safe blood administration, assisting with clinical audit, the introduction of evidence based clinical guidelines and assisting with the investigation and reporting of adverse events to the national Serious Hazards of Transfusion reporting scheme (SHOT). There is increasing use in the NHS of techniques that can, for some patients, reduce the need for transfusion of donor blood or avoid it all together. Among these are: the use of regional and hypotensive anaesthetic techniques, good temperature control in the perioperative period, salvage and reinfusion of red blood cells lost during surgery and the use of antifibrinolytic agents. Transfusion may be unavoidable and life saving for patients who suffer massive blood loss. For those undergoing chemotherapy for leukaemia or being treated for cancer there may be no alternative to the use of donor blood components during periods when the bone marrow is not functioning normally.

What about autologous transfusion?

Red blood cells cannot be stored for very long, so pre-operative depositing of a patient's blood is not a possibility in the case of emergency surgery. In the case of elective surgery, only a small proportion of

patients meet the criteria for being Blood Transfusion Services donors. Autologous transfusion could be a possibility in those cases. Anyone who is interested in this approach should discuss it with their doctor. Pre-operative depositing of blood is only one aspect. Modern surgical techniques help to limit blood loss in the first place, and can also mean that when bleeding occurs, the red cells can be recovered and returned to the patient, reducing the need for donated blood. We are working to increase awareness of good surgical practice.

What are the new measures?

[See statement]

Why the delay in implementing the new measures?

We are introducing them as quickly as possible. We need to ensure that there is enough blood to meet patients' needs. We also need to give the Blood Transfusion Services time to change their procedures.

Aren't these new measures simply a panic reaction?

No. They represent a phased extension of initiatives already underway, based on a tight, but feasible, timetable for the NBS to implement further change. In taking a decision to give the go-ahead for these new measures I have been swayed by the view of the experts at Monday's meeting who were able to take account not just of the suspected case of blood transmission, but also of recent research evidence.

Can you say for certain that the blood used by the NHS is free of CJD?

No. [Repeat positive action taken to improve blood supply]

Do people having transfusions today run the risk of contracting vCJD?

Yes, unfortunately. But the risk is extremely small. [Repeat positive action taken to improve blood supply]

Is it not the case that hundreds/thousands of people who have had blood transfusions over the past few years could have been infected with vCJD?

We don't know. All we can say is that this is looking less likely as more information becomes available. This is because we don't know for how long in the incubation of the illness that a person's blood is infective. We don't know how infective that blood is. And we don't know for certain what effect the processing of blood has on infectivity. What we do know is that if blood were highly infective there would probably have been many more cases of blood transmission by now, and we

would have known about them because the NBS has a system in place for monitoring donors and recipients to investigate whether CJD or vCJD may have been transmitted by the blood supply. As it is this is the first suspected case.

Would you (SofS, CMO) allow your family members to have a blood transfusion tomorrow?

Yes, if there's a clear clinical need.

Can an NHS patient have US blood if they are prepared to pay for it?

US-sourced plasma is already given to children born after 1 January 1996. However, whole blood and blood components have a short shelf life, and it would not be possible to match supply of US products to clinical need.

Blood supply issues

Q. How many people are blood donors in the UK?

A. Over 1.7 million.

Q**. How many people receive blood transfusions and blood products each year?**

A. About 3 million units of blood are transfused to over a million NHS patients in the UK every year.

Will the new measures cause shortages of blood?

Winter is the time of year when the national blood supply comes under most strain. However we will work to avoid shortages. I would also encourage more people to become blood donors. The NHS relies on the regular pool of donors to ensure that much needed operations can go ahead.

Q**. What is the National Blood Service doing to ensure there are sufficient blood supplies?**

A. The National Blood Service has set up an Appropriate Use of Blood Working Group, formed in the light of the possible impact any vCJD testing may have on the NBS and their ability to maintain a safe and sufficient blood supply to meet all patients needs. The Group has four key tasks:

- How to minimise exposure to the unknown risk of transfusion transmitted vCJD by only transfusing blood when absolutely necessary.

- How to ensure the most effective and efficient use of an increasingly scarce resource – the available blood supply.

- Consider alternatives to blood transfusion programmes, all forms of blood substitute therapies including correcting anaemia with appropriate vitamin and iron supplements, feasibility of bloodless surgical units.

- Contingency planning for prolonged periods of blood shortages.

A report is to be produced by **Spring 2003[?]** for consideration by the Group and the CMO's National Blood Transfusion Committee. Appropriate recommendations for a future strategy will then be developed. This information will be made widely available on the Internet, to relevant individuals and organisations and promulgated through the Regional and Hospital Transfusion Committee structure.

Q. **Is there a shortage of blood supplies to the NHS?**

A. No. NHS Trusts are continuing to receive all the blood they need. Blood stocks have been maintained at a high level (currently 8 days supply is being held) for a number of months in the event that the demand for blood may increase in the near future.

The NBS has significantly improved its ability to meet the demands of hospitals in provision of blood red cells and have fully met all demand for blood over the past 2 years.

Q. **What is the Government doing to ensure there is a sufficient blood supply in the future?**

We are continuing to encourage the NHS to use less blood, which is why the Department published last year a Health Service Circular 2002/009 "Better Blood Transfusion - Appropriate Use of Blood" (available on www.doh.gov.uk/publications/coinh.html). This circular asks NHS Trusts and Primary Care Trusts to review and explore the use of effective alternatives to donor blood and also the appropriate use of autologous blood transfusion; pre-donation, peri-operative and post operative cell salvage by April 2003. We will be carrying out an audit to review the implementation of this guidance later this year.

The CMO's National Blood Transfusion Committee was also established to channel information and advice to hospitals and the NBS on best practice and performance monitoring with the aim of: improving the safety and appropriateness of blood transfusion practice, listening to and informing patient concerns about blood transfusion and promoting high quality and consistent transfusion practice.

[Membership is from the Royal Colleges, specialist organisations such as the British Society of Haematology, the National Blood Service a patient representative and the Department of Health]

CJD Background

What is CJD?

Creutzfeldt-Jakob Disease (CJD) is one of a group of diseases called Transmissible Spongiform Encephalopathies. All of these diseases have a very long incubation period, cause severe and irreversible damage to the central nervous system and there are so far no treatments.

Sporadic CJD, which was first described in the early 1920s, occurs throughout the world and affects around one person per million per year with an average age of onset of 65 years. Patients experience a rapidly progressive dementia with death within around six months. Other forms of the disease have since been described, including Kuru which was endemic in the Fore people of Papua New Guinea in the 1950s and transmitted through cannibalistic funeral rites. There are also rare familial forms of CJD due to inherited genetic abnormalities. In addition, transmission of CJD has occurred during medical care through neurosurgical instruments, corneal and dura mater grafts and cadaveric-derived pituitary growth hormone and gonadotrophins.

What is variant Creutzfeldt-Jakob Disease?

A different form of Creutzfeldt-Jakob Disease (variant CJD) was first identified in 1996. Unlike sporadic CJD, the new disease affects younger people (a median age of 29, range 14-74 years old). Clinical presentation is also different. Variant CJD patients show signs of behavioural disorder, depression and anxiety followed by problems with sensation and coordination leading to progressive dementia and death over a period of six months to two years. The clinical, epidemiological, neuropathological and experimental data all point to variant CJD being caused by the same strain of prion as Bovine Spongiform Encephalopathy (BSE) and a different strain of prion from those seen in sporadic CJD.

To date there have been just over 130 definite and probable cases of variant CJD in the UK, 1 case each in the Irish Republic, Italy, the US, Canada and Hong Kong and 6 in France. The eventual number of individuals within the UK population likely to develop variant CJD remains uncertain; current estimates range from current numbers up to 540.

How many people are currently incubating variant CJD in the UK?

Estimates of the number of people likely to develop variant CJD (and are therefore currently incubating the disease) vary widely but figures suggest that an upper limit of about 3,000. Recent reports from the CJD surveillance unit suggest that the increasing trend in variant CJD mortality peaked in 2000 (28 deaths) and has since fallen to 17 deaths in 2002. The observation that mortality has not continued to increase in the last 2 years is encouraging, however some caution should be exercised. Up to now all

cases of variant CJD have been in people who are methionine homozygous at codon 129 of the prion protein gene. Other genotypes may also be susceptible to variant CJD but have longer incubation periods (as has been seen in Kuru and peripherally transmitted iatrogenic CJD). In addition, it is possible that further cases could arise due to secondary human to human transmission via surgical instruments or blood transfusion.

Q. **Is there any way of telling how many people may be incubating vCJD?**

A. There is currently no way of telling how many people may be incubating vCJD nor to test whether instruments or blood donations pose a risk. Until there is a rapid simple test we are not going to be in a position to answer this. Research is in progress with the aim of developing a suitable test.

[There are still many uncertainties about vCJD, including important information on the incubation period, the route of infection, the infectious dose and the role of genetic susceptibility. Whilst so many uncertainties remain, the Department of Health is not in a position to make accurate predictions about the eventual number of people who might be affected by vCJD. Modelling work has produced estimates ranging from around 200 to as many as 150,000. The most recent analysis predicts of fewer than 3000 future cases of vCJD. The Department is funding work to enable more reliable estimates to be made.]

Q. **How many people have died from vCJD?**

A. 137 people have died (1 December 2003) (UK cases only)

Q. Why do we have a CJD Incidents panel?

A. The UK CJD Incidents Panel was set up in 2000 to advise on follow-up action where individuals who develop CJD are found to have had previous surgery, or to have donated blood, tissues or organs. Because the abnormal prion protein associated with CJD can survive the decontamination process used for surgical instruments, it means other patients may have been inadvertently and unknowingly infected.

Q. **What advice is there from the panel about treatment with contaminated blood products?**

A. In October 2001, the CJD Incidents Panel recommended that people who received blood from donors with vCJD should be informed of their potential exposure and advised not to give blood or donate organs and tissues and that special precautions might be needed if they require surgery. The Panel recommended that no one should be given this information until proper counselling and back-up facilities were made available. [However it is only recently that the Panel has been able to make an assessment of individual risk to determine who should be contacted.]

Why has it taken so long to publish the Incidents Panel's Framework document?

The Panel's draft Framework has been available on the HPA's website since they launched their consultation exercise, so the general thrust of the advice has already been available to clinicians and other interested parties. However the development and consideration of the blood Risk Assessment was prolonged because of the lack of information. It is only recently that the Panel felt sufficiently confident to propose a handling framework for blood incidents. We have moved quickly following the receipt of a definitive text of the Framework from the HPA.

Handling the Blood Incident

How are you going to tell the 15?

The HPA will be contacting the 15 people who were potentially exposed to vCJD once they have been traced. It is by no means certain that they will ever go on to develop vCJD themselves, but clearly this will be a source of distress to them. The Health Protection Agency will provide them with information and counselling to help them understand the position. The NHS will offer to monitor their health, and offer them a test for vCJD, should a proven test become available.

Will you pay the 15 compensation?

People who meet the conditions of the vCJD compensation scheme will get payment regardless of how they contracted vCJD.

[What if they don't develop vCJD. Will they still get payment?

Each case would have to be looked at on its merits.]

When will the 15 people exposed to contaminated blood be contacted?

The NBS will be contacting the 15 people who were potentially exposed to vCJD to once they have been traced. It is by no means certain that they will ever go on to develop vCJD themselves, but clearly this will be a source of distress to them. The [Health Protection Agency] will provide them with information and counselling to help them understand the position. The NHS will offer to monitor their health, and offer them a test for vCJD, should a proven test become available.

Will people who have been exposed to contaminated blood be able to get life insurance?

This is a matter for the Association of British Insurers and the individual insurance companies. The Department of Health will be working with the ABI to help insurers to understand the situation. [However at least some of the people exposed to contaminated blood are so old that they are highly unlikely to be seeking life insurance.]

Is there a helpline for people to call if they are worried?

[People should call NHS Direct if they are worried.]

Doesn't this prove that blood is unsafe?

Any medical procedure carries risks. The additional risk caused by a blood transfusion will be very slight for the vast majority of patients.

Has the family been told?

They are being told by the CJD Surveillance Unit.

Details about the donations to the 15 recipients from donors who developed vCJD?

There are 15 recipients of blood and blood components from the 14 donors. Of these all but one received red cells and one received plasma.
Of the recipients 5 received leucodepleted red cells.
The earliest transfusion was in 1993 and the latest in 2001.
The oldest recipient was born in 1915 and the youngest in 1974.
Of the recipients 10 were female and 5 were male.
Of the recipients 13 live in North England, 1 in North Wales and 1 in Surrey.

Are the 15 recipients alive and well?

We know that they're alive. However we need to trace them before we can know enough to give any more details in answer this question.

When did you hear about this?

We received the first tentative indications last week.

Why didn't you act sooner?

We needed to have the evidence confirmed by the relevant experts.

What is the timeline of the notification?

The patient who received vCJD from a blood transfusion died this Autumn. Although he was developing neuropsychiatric symptoms, prior to the time of death there was insufficient evidence to make a diagnosis of CJD infection. The local hospital carried out a post-mortem and it was at that stage that they began to suspect CJD. Accordingly they sent tissue samples to the UK CJD Surveillance Unit on 27 November. The Surveillance Unit established the presence of variant CJD on 9 December. On 15 December a group of national experts reviewed the evidence and concluded that the infection was most probably the result of a blood transfusion.

Does the fact that vCJD can be transmitted by blood meant that lean beef ie steaks could be infected with CJD as cow blood runs through it?

Controls have been introduced to reduce any risk to consumers from eating beef to an extremely low level. There is to date no evidence from ongoing studies that either blood or muscle from cattle can transmit BSE to uninfected cattle.

[In experiments by the Veterinary Laboratory Agency, lean muscle from different stages of incubation in BSE-infected cattle has been transferred to other cows, including muscle taken from animals at the prime age of slaughter for human consumption. No infection has yet transmitted, even though it is now 87 months after these experiments were initiated. To put this into context: cattle infected with infective material have died between 22 and 27 months post-infection, so infectivity in muscle is extremely low or negligible. Similar results have been obtained with blood.]

FRESH FROZEN PLASMA (FFP)

Q. **What is FFP?**

Plasma is the fluid in which the red and white cells and platelets are suspended and carried around the body. This fluid is separated from donated blood units by centrifugation and frozen. FFP contains clotting factors, antibodies, albumin and minerals.

Q. What is it used for?

It is used for instance to treat patients whose blood clotting is abnormal and in supporting some intensive care unit patients. It is also used for premature babies, and babies and children having heart surgery, liver transplants and after major accidents and injuries .

FFP is produced by the UK blood services using plasma from UK donors which has been leucodepleted to remove the white cells (which evidence suggests may carry the greatest risk of transmitting variant CJD). Each unit of FFP is also made from plasma from a single blood donor.

Q. Is FFP safe?

The safety of blood and blood products used in the NHS is of paramount importance. Every reasonable step has been taken to minimise any risks during blood transfusion. The current high levels of safety are achieved by screening out potential high risk donors and then further testing every unit of donated blood for the presence of infections such as HIV, Hepatitis B, Hepatitis C before it is released to hospitals.

Q. Why was it decided in August 2002 to import FFP from the United Sates for neonates and children born after 1.1.96?

The decision taken to import Fresh Frozen Plasma (FFP) from the United States for young babies and children born after I January 1996 was a precautionary step to protect the most vulnerable group who will not have been exposed to BSE through the food chain. The National Blood Authority (NBA) is currently involved in negotiating for supplies of FFP for this group of patients. This FFP will be virally inactivated by methylene blue viral inactivation, and its planned availability will be in the New Year. In addition, the NBA also implemented viral inactivation for UK FFP for this patient group in August 2002. Viral inactivation is designed to remove certain viruses that may be transmitted by transfusion.

Q. In view of the possible risks of vCJD why was there no consideration to import FFP before?

This was considered in 1998, but the Department was advised by the National Blood Service (NBS) that imported plasma for FFP could not be obtained for the large number of patients every year who require it.

The Spongiform Encephalopathy Advisory Committee (SEAC) and the expert Advisory Committee on Microbiological Safety of Blood and Tissues for Transplantation (MSBT) advised that UK FFP should continue to be provided but that the position should be kept under review.

Q. Why has it been decided to import FFP now?

MSBT has been reviewing the scope for importing FFP and has advised that it should be imported for newborn babies and young children as an added precaution against the theoretical risk of vCJD transmission.

Q. Why import FFP only for young babies and children born after 1.1.96?

This is the first step to protect the most vulnerable group. Children born after 1995 will not have been exposed to BSE through foodstuffs.

Q. Why doesn't NBS import enough FFP for all patients?

FFP is produced by the UK blood services using plasma from UK donors which has been leucodepleted to remove the white cells (which evidence suggests may carry the greatest risk of transmitting variant CJD). Each unit of FFP is made from plasma from a single blood donor. The NBS is continuing to look for sustainable supplies of imported plasma for other vulnerable groups.

METHYLENE BLUE AND SOLVENT DETERGENT FFP

Q. What is Methylene Blue treatment?

Plasma can be virally inactivated using methylene blue (MB) treatment. It is used, in conjunction with the application of light, to kill a range of transfusion transmitted viruses but not the vCJD agent. It is a registered medical device under the Medical Devices Directive and has a European safety (CE) marking. MB has been administered in medical practice since 1900, and in much larger doses (many thousand-fold) than the NBS will be using. The NBS will be removing more than 90% of MB before the FFP is issued to NHS hospitals.

Q. Does MB treatment of FFP destroy vCJD?

No. FFP is being imported from the US, a BSE free country. MB treatment is designed to kill certain viruses which can be transmitted by transfusion. It does not affect prions, the agent responsible for vCJD.

Q. Why is this being used when other countries are using Solvent Detergent (SD) treated FFP? Is this not a safer option?

A. Solvent detergent FFP is a product made by pooling several hundred donations, which means that there is a possibility that one infected donor could contaminate the whole pool. MSBT who are an expert Committee have recommended that single unit (not pooled) FFP from the US which is virally inactivated via MB treatment should be used.

Q. Some hospitals in the UK already use Solvent Detergent treated US plasma. Why not use this product?

Solvent Detergent FFP is a product made by pooling many hundreds of donations. Clinicians have a choice of which products to use but many prefer a product made from single donations, to avoid the possibility that an infected donor could contaminate a whole pool.

HAEMOPHILIACS – PLASMA DERIVED CLOTTING FACTORS

Q. Many haemophiliacs have already been infected with HIV and hepatitis C through NHS blood products and run the risk of contracting vCJD. When are you going to provide recombinant (synthetic) clotting factors instead of plasma derived clotting factors for all haemophiliacs?

A. It is generally accepted by United Kingdom clinicians that recombinant and plasma derived clotting factors are equally effective in treating clotting disorders. In guidelines produced by the United Kingdom Haemophilia Doctors Organisation, comparisons between the two types of product revolve around their relative safety, bearing in mind that no medicinal product can ever be completely free from risk.

An advantage of recombinant products, where they are entirely free of human albumin, is that they eliminate the risk from blood borne viruses and the unknown risk from vCJD. However, plasma derived clotting factors are tightly regulated by European and United States authorities to minimise the risk of viral transmission. This is achieved by the screening of donor blood and the anti-viral measures taken during manufacture. By ceasing to use UK plasma in the manufacture of blood products, the Government has already taken steps to reduce the theoretical risks from vCJD.

Q. On 12 February 2003 the Government announced investment of an extra £88m to provide haemophilia patients with synthetic clotting factors. When will the patients have access to these products?

We have been working with key stakeholders including the Haemophilia Society, clinicians, Primary Care Trusts and others to put in place a strategy to roll out access to recombinant products. We aim to begin the roll out as soon as possible. More information about the issues that the working group have had to consider prior to the roll-out can be obtained from www.doh.gov.uk/blood/rcfwg.

Recombinant clotting factors have been made available for all adult haemophilia patients in Northern Ireland, except for a small group of adult patients with severe haemophilia. It is expected that these patients will receive recombinant early in 2004.

vCJD COMPENSATION SCHEME

Bullet points

- In recognition of the special plight of those affected by vCJD the Government set up the vCJD Compensation Trust Fund. An independent Board of Trustees, chaired by Sir Robert Owen, administers the Fund.

- The terms of the Trust Fund were agreed with representatives of the families following a period of consultation. The Compensation Scheme provides for payments to be made in respect of 250 cases, up to a maximum of £55 million. As yet over half of the initial 250 cases have yet to present. If the number of cases exceed 250 an updated scheme would then be put in place.

- On top of the £55 million Trust Fund, the Government made provision in the scheme for payments of an additional £50,000 to each victim or their family in the first 250 cases.

- Additionally, within the overall scheme, there is a discretionary fund capped at £5 million. This is intended to provide the Trustees with some scope to meet exceptional cases of hardship. The use of this fund is at the Trustees' discretion.

Summary of the Scheme

The Scheme will provide for payments to be made in respect of 250 cases of vCJD up to a maximum of £55 million. In numbers exceed 250 cases, the scheme will be reviewed. Payments will be made under four headings, outlined below. **For the first 250 cases only, an additional sum of £50,000 will be paid** to each victim or family to take account of the legal and other difficulties the first families have had and the pressure they have had to bear.

i) The experience of vCJD for the patient.

The sum of £70,000 will be paid in all cases, together with a further £5,000 in those cases where vCJD was diagnosed before the publication of the Phillips Report.

ii) The experience of vCJD for the patient's immediate family and/or carers

Each family would receive a minimum of £5,000 plus a further £5,000 where members of the family have cared for the victim during his/her final illness, to be split between the carers and immediate family. In the case of those diagnosed before publication of the Phillips Report, a further £5,000 would be payable.

Where a member of the patient's immediate family has suffered psychiatric injury as a result of the patient having suffered vCJD, a further payment of £5,000 will be made. The Trustees have discretion to award further sums in cases where the psychiatric condition gives rise to particular hardship.

iii) Costs incurred by the patient and family as a direct result of the patient's suffering from vCJD.

Payments will be made to cover funeral expenses and capital expenditure reasonably incurred. Where care was provided either commercially or gratuitously before the implementation of the Care Package announced in Parliament in October 2000, a sum will be payable in respect of that care.
Where the patient and/or their carers have suffered loss of earnings and this has caused particular hardship, the Trustees will have discretion to make a further payment out of the Discretionary Fund.

iv) Future Losses caused to the patient's dependents as a result of his/her death from vCJD.

This category broadly reflects the common law approach but with the following important variations:-

a) Subject to a residuary discretion on the part of the Trustees, there will be no payment in respect of anticipated higher earning capacity in the future;

b) However, a minimum earning capacity of a net £7,500 per annum will be attributed to all victims, even those not working or earning less than that amount at the time of the onset of their illness. This is to reflect their future earnings potential;

c) Compensation in respect of pension loss will not be payable except to those aged 45 or over, for whom a discounted sum in respect of pension loss will be payable;

d) All figures are reduced by an overriding discount of 10%.

vCJD compensation scheme: Background Briefing

1. The compensation scheme will provide for payments to be made in respect of 250 cases. If the number of cases exceeded 250 the scheme will be reviewed and an updated scheme may then be put in place.

2. The overall estimated sum of £67.5m was agreed between the SofS for Health and the Treasury Chief Secretary. The figures were based on the advice of the Department's legal counsel, Justin Fenwick QC.

3. The Trust does not fall formally within the remit of the Commissioner for Public Appointments, nevertheless the principles of the Commissioner's guidance were followed in making appointments to the Trust Board.

4. The membership of the Trust Board is:

   Sir Robert Owen QC (Chairman), a senior member of the Judiciary and an experienced High Court Judge;

   John Melville Williams QC, leading Counsel with considerable experience in the personal injury field and past president of the Association of Personal Injury Lawyers;

   Ms Elaine Motion, a lawyer with extensive experience of personal injury claims and expertise in Scottish law;

   Mr David Churchill and Mr Malcolm Tibbert, both have been involved in the Human BSE Foundation for a number of years GRO-C GRO-C

   Dr David Stevens, a consultant neurologist with a distinguished medical career; and

   Ms Vicki Vidler, an experienced nurse with specialist expertise in the care of young patients with complex needs.

Potential treatments for CJD

1. Can people be treated to stop them developing CJD?

There is no treatment that has been proven to prevent the development of CJD.

2. Aren't some people already receiving treatment?

A small number of patients with clinical symptoms of disease have been treated with oral quinacrine, prior to the establishment of a clinical trial of this drug. A smaller group of symptomatic patients are being treated with pentosan polysulphate, administered directly into the brain.

Are these drugs licensed for use as treatments for any other diseases?

Quinacrine is licensed in the UK for use as a treatment for malaria. Adverse side effects include liver damage.

Pentosan is not licensed in the UK, although in the U.S. it is licensed for use as a treatment for interstitial cystitis and in Germany. Adverse side effects include bleeding and hypersensitivity.

3. What other potential therapeutic agents are there for CJD?

In addition to the above, several agents have been shown experimentally to inhibit the accumulation or conformational change of prion protein *in vitro*. Whilst providing a valuable experimental insight into prion chemistry these are, however, a long way from being considered as potential therapeutic agents.

Use of Pentosan Polysulphate in the treatment of, or prevention of vCJD

4. What is Pentosan Polysulphate? What is the evidence that it might be effective against vCJD?

Pentosan polysulphate is one of a group of compounds that has been shown to extend the incubation period or in some cases to prevent the onset of clinical disease when given prophylactically in animal models experimentally infected with TSEs.

Pentosan has in the past been used in the treatment of bladder and intestinal inflammations, but is not currently licensed for use within the United Kingdom.

5. If pentosan slows down or stops the onset of symptoms in animals, couldn't it be prescribed for the patients who may have received blood products from donors who subsequently developed CJD?

The most recent advice from the Committee on Safety of Medicines (CSM) is that there is some very limited evidence from animal studies that pentosan may be an effective prophylactic agent. However the CSM advises that there are currently insufficient data to form a basis for prescribing pentosan as a prophylactic or treatment. Pentosan is not licensed for use in the UK, and could only therefore be prescribed under a doctor's personal responsibility.

6. Has SEAC advised on the use of pentosan?

SEAC first considered pentosan in January 1999 and recommended more research should be undertaken. Specifically, studies on efficacy in rodent models and pharmacokinetics in mice and humans.

The Committee last considered the use of pentosan in the treatment of vCJD in October 2003. They noted research underway by the Neuropathogenesis Unit into this product which was being investigated in an animal study as a potential prophylactic for CJD, and the recent consideration of the product by the Committee on the Safety of Medicines - Biologicals Committee. They concluded that further work would be necessary to provide a rationale before any clinical use against CJD could be considered and added that it would be necessary, as a first step, to gain a much better understanding of its biological properties.

7. What followed?

Following the meeting in January 1999, DH funded and continues to fund work in the areas of efficacy in rodent models and pharmacokinetics in mice and humans at centres in Edinburgh and Manchester. Since the SEAC meeting in April 2001, the UK Health Departments have established a CJD Therapy Advisory Group. This and the Committee on Safety of Medicines now advise DH on matters relating to potential therapies for CJD.

8. What is the most recent expert scientific advice on pentosan?

The most recent advice from these two groups is:

Advice from the CJD Therapy Advisory Group published November 2003

- There are insufficient clinical data available to support the claim that Pentosan Polysulphate (PPS) is effective during clinical disease.
- There are insufficient safety data upon which to base a rational treatment regimen in humans.
- Further experimental study in animal models is warranted, including dose-finding studies in appropriate strains of human prion disease.
- Nevertheless at the dosage used (11µg/kg per day) in the one human patient treated to date, there have been no definite harmful effects attributable to the drug.

Advice from the Committee on Safety of Medicines published November 2003

- At present there are very limited data from animal models that may be relevant to vCJD indicating that PPS might be an effective prophylactic agent for this disease. There is no evidence in support of its use as a treatment in late stage disease.
- Although there is information on the basic pharmacology of PPS there is limited information relevant to these indications.

- There is insufficient information that could form a rational basis for prescribing PPS as a treatment or prophylactic agent for vCJD. In particular there is limited information on the route(s), dose(s), duration, or timing of the PPS administration in relationship to the receipt of or contact with potentially infectious material.
- The administration of PPS is associated with an adverse event profile which raises some concerns, particularly with regard to the potential for bleeding events and hypersensitivity reactions, neither of which have been adequately documented or quantified.
- In light of the limited information on PPS treatment of clinically established vCJD it is impossible to assess the risk/benefit relationship of PPS in these indications.
- There is a need to collect safety and efficacy data on PPS and also to establish robust methods for monitoring the effects of treatment on the disease and these should be achieved in the clinical trial setting.

9. What is DH's position on pentosan?

On the basis of the advice from our expert committees, DH does not endorse the use of pentosan. We are sympathetic to patients with clinical symptoms, who wish to try cerebroventricular pentosan, and continue to work to facilitate access to this experimental treatment through the NHS, where patients and their clinicians consider the risks to be acceptable and can be managed.

In this treatment, pentosan is administered directly into the brain. This method of administration is not suitable when trying to prevent disease.

DH research on potential therapeutics for CJD

10. What research is DH funding on pentosan?

DH funds a number of research projects on potential therapeutics for CJD. These include studies on the pharmacokinetics of pentosan in humans, to better understand the normal distribution of the drug in human tissue.

Supplementary Q&A on unlicensed medicines, if needed

11. Under what circumstances can a doctor prescribe an unlicensed medicine?

Medicines legislation allows a doctor or dentist to prescribe an unlicensed medicine to meet the special clinical needs of his individual patients, on his direct personal responsibility.

12. How can a doctor obtain an unlicensed medicine?

Legislation requires that an unlicensed relevant medicinal product (such as PPS) may only be imported by a licensed wholesale dealer. The importer may then supply the product in response to a bona fide unsolicited order of a doctor or dentist. The importer, as a condition of his licence, is required to notify the MHRA in advance of each importation. The maximum quantity that may be imported per

notification is defined by law as 25 doses, or 25 courses of treatment not exceeding 3 months duration. The MHRA may object to importation if an equivalent licensed product is available in the UK or if it has concerns about the safety or quality of the product. Also, if information emerges subsequently that raises concerns about the safety or quality of the product, the MHRA can instruct the importer to stop importation and supply.

13. Can a doctor or a patient import a medicine themselves?

A doctor or dentist may import a relevant medicinal product for his personal use or that of a member of his direct family. He may not personally import an unlicensed relevant medicinal product to treat his individual patients, unless he holds an appropriate wholesale dealer licence granted by the MHRA. A member of the public may also import a relevant medicinal product for his personal use or that of a member of his direct family.

Blood – non-TSE infections

Q. What is each blood donation screened for?

A. Every donation of blood is tested for HIV, Hepatitis B, Hepatitis C and Syphilis. Every donation is also tested for ABO blood group.

Q. Will the NBS screen for HTLV (Human Tcell Leukaemia virus) soon**?**

A. The NBS began introducing a screening HTLV test at the end of 2002.

Q. **When did the NBS start screening for HIV?**

A. The NBS started screening for HIV in October 1985. 1240 people were infected with HIV from blood before this date.

Q. **Since screening of HIV began, what are the chances of being infected with HIV through blood?**

A. Less than 1 in several million donations.

Q. **If All donations are screened for HIV, why is there still a chance of infection?**

A. No screening test is 100% effective. The tests may miss some individuals in the early stages of infection.

Q. **How many cases of HIV since screening began?**

A. There have been two cases (i.e. two donors are known to have transmitted). A total of five recipients were infected from these two donors. One case was in Scotland in 1986, and the other in the north of England in 1997.

Q. **When did the NBS start screening for hepatitis C?**

A. A screening test was introduced on 1 September 1991 in the UK

Q. **Since screening began what are the chances of being infected with hepatitis C through blood?**

A. Less than 1 in 2 million

Q. **Why?**

[as above for HIV question]

Q. **How many cases of hepatitis C since screening began?**

A. There have been 2 cases of transmitted hepatitis c infection (from anti HCV tested blood) reported since October 1995.

CDSC Collindale/Health Protection Agency December 2003

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10.4 Example of an individual patient log

X	X	
Transfusion conf.	GP consulted	Patient consulted

Patient Information

ID Number	1
Region	North West
Regional Contact	Martyn Regan GRO-C
Followed up by	Martyn Regan
Transfusion Date	21/01/01
Implicated unit	G095600450195A
Reason for transfusion	Bleeding peptic ulcer
First Name	xxxxxx
Surname	xxxxxxx
Date of Birth	**Xx/xx/xx**
Hospital Name	Arrowe Park Hospital
Hospital Number	xxxxxxxxx
Infection Control – Microbiology Consultant name and tel	Information obtained From Kathy McClarnon, Risk Management Coordinator Tel 0151 678 5111 ext GRO-C (Arrowe Park Hospital)
Brief Medical History	Have had surgery after the blood transfusion of the implicated unit.
GP Address	Dr Bates Devaney Medical Centre 4 Balls Road Oxton Birkenhead Tel 0151 652 4281
Patients Address	Xxxxxx xxxxx
Clinical Observations	xxxx
CCDC Address and tel	Dr. Nick Phin Cheshire and Merseyside Tel. 0124 366766
Comments	Transfused with 4 units including implicated unit and GP has been contacted
Reaction by the patient on being informed	xxxx

10.5 Example of the daily table

REGION	HPU	REGION CONTACT	REGION TEL	CCDC	CCDC TEL	DATE MATCH[1]	UNIT MATCH[2]	GP CONTACT?	PATIENT CONTACT?	COMMENT
NW	Cheshire & Merseysid e	**Martyn Regan**	GRO-C	Nick Phin	GRO-C	YES	YES	YES	Appt. made	Many attempts to contact Patient, Chaotic lifestyle. Appt. made Friday (09/01/04) pm.
WALES	SW Wales	**Meirion Evans**		**Sara Hayes**	GRO-C	YES	YES	YES	INFORMED 09/01/04	CCDC has met with GP on 30th Dec. 2003. Daughter is a health visitor at the practice. Pt. Had extensive leg surgery, also donated bone.
East of England	(Ipswich)	Richard Gair	GRO-C	**Torbjorn Sundquist**	GRO-C	YES	YES	YES	INFORMED 05/01/04	Consultant neurologist to tell patient at on 05/01/04.
NE	Gateshead & STyneside	Russell Gorton	GRO-C	**Bashir Malik**	GRO-C	YES	YES	YES	INFORMED 19/12/03	Patient and wife informed by GP and CCDC.
NW	Greater Mancheste r	Martyn Regan	GRO-C	**Lorraine Lighton**	GRO-C	DIED			PATIENT DECEASED	No neurological indications; transfusion unconfirmed (?TOP); IDDM and CRF
NW	Greater Mancheste r	Martyn Regan	GRO-C	**Lorraine Lighton**	GRO-C	YES	YES	YES	INFORMED 24/12/03	Patient informed on the 24th Dec at the request of the patient. C/o anxiety, depression and leg pains since transfusion. GP is referring to local neurologist.
NW	Greater Mancheste r	**Martyn Regan**	GRO-C	**Marco Petrovic**	GRO-C	YES	YES	YES	INFORMED 06/01/04	Patient informed on **6th Jan 2004**
East Midlands	Nottingha m	Martin Wale	GRO-C	**Richard Slack**	GRO-C	YES	YES	YES	INFORMED 02/01/04	cryo-depleted FFP.
Yorks& Humber	North Yorkshire	**Martin Schweiger**	GRO-C	Louise Coole	GRO-C	YES	YES	YES	INFORMED 23/04/03	GP informed the patient on the 23rd Dec 2003 and will visit again a week later.
East Midlands	Nottingha m	Martin Wale	GRO-C	**Richard Slack**	GRO-C	YES	YES	YES	INFORMED	GP will be contacting patient today (05/01/03) to arrange appt. this week.
Yorks& Humber	North Yorkshire	**Martin Schweiger**	GRO-C	Louise Coole	GRO-C	YES	YES	YES	INFORMED 23/12/03	GP informed the patient on the 23rd Dec 2003 and will visit again a week later.
Wales		Meirion Evans		**Richard Roberts**	GRO-C	YES	YES	YES	INFORMED 24/12/03	Patient was informed on the 24th Dec. The Patient's sister was

										present.
NW	Cheshire & Merseysid e	**Martyn Regan**	GRO-C	John Curnow	GRO-C	YES	YES	YES	INFORMED 06/01/04	Patient to be informed as part of regular consultation. Currently unwell with a heart condition.
NW	Lancaster	**Martyn Regan**	GRO-C	Nick Gent	GRO-C	YES	YES	YES	INFORMED 08/01/04	Patient informed on 8th Jan 2004. Took the news well. Has asked for an appt. to meet CCDC.
NW	Lancaster	**Martyn Regan**	GRO-C	Nick Gent	GRO-C	YES	YES	YES	INFORMED 09/01/04	Patient informed on 9/1/4. Was not overly concerned. Offered an appt. with CCDC.
East Midlands	East Lincolns	Martin Wale	GRO-C	Colin Brockway	GRO-C					
Yorks and Humber	Humber	**Martin Schweiger**	GRO-C	Terry Matthews	GRO-C					

End of play 12/01/04

10.6 Example of daily status table

CONFIDENTIAL

Daily status report vCJD blood incidents
CDSC – CJD Team

(NB – NOT for circulation beyond intended recipients)

Date: 20th Jan 2004

Classification	18/12/03	29/12/03	05/01/04	06/01/04	08/01/04	09/01/04	16/01/04	20/01/04
Total donors	**17**					**18**		
Total recipients	**43**					**51**		
Recipients died	**26**					**32**		
Recipients not known to be dead on 17/12/03	**17**					**19** 09/01/04	**19**	
All recipients	**17**	**17**	**17**	**17**	**17**	**19**	**19**	**19**
England – alive	13	12	12	12	12	14	13	13
England – dead –no further follow up necessary	1	1	1	1	1	1	2	2
Wales – alive	1	2	2	2	2	2	2	2
Scotland - alive	2	2	2	2	2	2	2	2
ENGLAND (& WALES)	E (W)	E (W)	E (W)	E (W)	E (W)	E (W)	E (W)	E (W)
Total patients under follow up	**13 (1)**	**12 (2)**	**12 (2)**	**12 (2)**	**12 (2)**	**14 (2)**	**13 (2)**	**13 (2)**
Hospital records checked – right day transfusion confirmed	10 (1)	12 (2)	12 (2)	12 (2)	12 (2)	12 (2)	13 (2)	13 (2)
Hospital records checked - specified unit accounted for	3 (0)	12 (2)	12 (2)	12 (2)	12 (2)	12 (2)	13 (2)	13 (2)
Total transfusion confirmed	**10 (1)**	**12 (2)**	**12 (2)**	**12 (2)**	**12 (2)**	**12 (2)**	**13 (2)**	**13 (2)**
Hospital records **not** checked	3 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0)	0 (0)	0 (0)
Total GP contacted	**5 (1)**	**12 (2)**	**12 (2)**	**12 (2)**	**12 (2)**	**12 (2)**	**13 (2)**	**13 (2)**
GP **not** contacted	8 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0)	0 (0)	0 (0)
Total Patient informed	**0 (0)**	**4 (0)**	**5 (1)**	**8 (1)**	**10 (1)**	**11 (2)**	**11(2)**	**13 (2)**
Patient **not** informed	13 (1)	8 (2)	7 (1)	4 (1)	2 (1)	3 (0)	2 (0)	0 (0)