UKHCDO

United Kingdom Haemophilia Centre Doctors' Organisation

7th September 2004

To UK Haemophilia Centre Doctors

Variant Creutzfeldt-Jakob Disease (vCJD) and Plasma Products

Dear Colleague,

We write to inform you that the Bio Products Laboratory (BPL) and Protein Fractionation Centre, Scotland (PFC) will shortly be releasing particular batch numbers for clotting factors (factor VIII and factor IX), antithrombin and other products manufactured using donations from individuals who subsequently developed vCJD.

These batches refer to plasma products, other than cryoprecipitate and fresh frozen plasma, sourced from UK donors until 1998, and include some batches that have been previously notified to consignees and some that have been traced subsequently. None of the implicated batches is within shelf life.

Previous notifications of UK donors who later developed vCJD, in 1997, 1999 and 2000, resulted in some recipients of implicated plasma products being traced but not put in an 'at-risk' group for vCJD. Following the announcement in December 2003 of a transfusion-associated case of vCJD, the situation regarding vCJD and plasma products has changed. Certain special precautions will need to be taken for some recipients of UK-sourced plasma products who may have been exposed to potential vCJD infectivity. This is in order to reduce any possible risk of onward transmission of vCJD.

Implicated batches

The basis for managing this notification is a detailed assessment of potential vCJD infectivity in implicated plasma products. This has been undertaken by the Health Protection Agency with the CJD Incidents Panel (CJDIP), an expert committee set up on behalf of the UK Chief Medical Officers to advise on the management of 'incidents' of potential transmission of CJD between patients. The Recommendations of the CJD Incidents Panel are enclosed.

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

Potential vCJD infectivity of plasma products

The potential risk of vCJD infection following treatment with any implicated plasma products, on top of the risk from dietary exposure to the bovine spongiform encephalopathy (BSE) agent, is very uncertain. However some patients treated with plasma products between 1980 and 2001 could pose a potential risk to others in defined circumstances.

The CJDIP advises that patients who are exposed to a 1% or greater potential additional risk of infection, should be considered 'at-risk' of vCJD for public health purposes (i.e. certain special precautions need to be taken to reduce any possible risk of onward transmission of vCJD).

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

These calculations are based on very cautious assumptions, and take a precautionary approach in an area of much scientific uncertainty. Therefore the 1% threshold is a tool for limiting the possible risk of transmitting vCJD between patients and should **NOT** be seen as a way of estimating an individual patient's potential additional risk of developing vCJD.

It is likely that many patients with bleeding disorders1 will have been exposed to a potential additional risk of 1% or greater. It is also likely that further batches of UK-sourced plasma products will be implicated in the future as more cases of vCJD arise. For these reasons UK Haemophilia Doctors and patient representatives believe that **all patients with bleeding disorders[1] who have been treated with UK-sourced pooled factor concentrates or antithrombin[2] between 1980 and 2001[3] should be considered 'at-risk' of vCJD for public health purposes and special precautions taken.** The CJDIP and UK Health Departments have endorsed this approach.

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

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

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

Information for patients

All patients with bleeding disorders should be made aware of whether they have received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001.

All patients who have received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001 should:

a) Be informed that they are at a potential additional risk of vCJD because they may have been treated with plasma made from donations from individuals who have subsequently developed vCJD, or who will do so in the future.

b) Be given the opportunity to find out whether or not they received known implicated batches. This includes both batches that are highly likely to expose patients to a 1% or greater potential additional risk, as well as batches for which this likelihood is so low as to be considered negligible[4]. They should also be made aware that with future recognition of implicated batches, any assessment of their individual exposure might change. Whatever their choice, this information will not affect their management as the same special public health precautions will be taken for **ALL** patients who have received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001.

c) Be informed that they are considered 'at-risk' of vCJD for public health purposes, and that their 'at-risk' status will be recorded in their hospital medical records and primary care notes. The extent of exposure to implicated batches, and whether or not a patient has asked to know if they have received implicated batches, will also be recorded on a Patient vCJD Exposure Assessment Form (see below) to be placed in their hospital medical records. Patients who have **NOT** received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001 should also have this fact clearly recorded on this form.

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

   - They should not donate blood, organs or tissues (many patients who have received plasma products may already be excluded from donation because of their underlying condition)

   - They should inform any clinicians and other healthcare professionals with whom they have dealings of their 'at-risk' status, so that special infection control precautions can be taken before surgery and other invasive procedures should they require future medical care. Patients should also be advised to inform their families, in case the patient needs emergency surgery in the future (see Clinical Information document).

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

[4] Refer to vCJD Implicated Batch Numbers Tables 1 and 3, accompanying the 'Recommendations of the CJD Incidents Panel'.

Parallel arrangements are underway with clinicians caring for patients with other conditions (see Summary of patient notification exercise attached).

For patients treated with single unit blood components (red blood cells, platelets, cryoprecipitate or fresh frozen plasma) donated by people who subsequently developed vCJD these steps are already in place. Patients treated with vCJD implicated single unit blood components are identified by the UK national blood services and the National CJD Surveillance Unit, Edinburgh. Local health teams are then advised to contact these patients so they can take special public health precautions.

Batch details

Details of the batch numbers of **ALL** known plasma products manufactured using donations from people who subsequently developed vCJD, including batches previously notified, are listed in the Tables attached (see vCJD Implicated Batch Numbers Tables 1 to 3). These include details of all implicated batches of factor VIII, factor IX and antithrombin, as well as other products used to treat other clinical conditions, stratified according to potential 'risk'.

A list of the specific **subset** of implicated plasma products that are known to have been supplied to your centre will also be forwarded from the plasma product suppliers (BPL), via the manufacturers' consignees. PFC has notified its implicated factor VIII and factor IX batches to Haemophilia Centre Doctors previously, there are no new batches to notify at present and therefore PFC will not be forwarding further information at this time.

In some cases this information may not be available for a number of weeks or may be incomplete, because other distributors may be involved in the supply chain and need to hand search paper archives.

What we are asking you to do now

We are asking you to help implement the notification process described above. In order for the notification process to run as smoothly as possible, it is suggested that each haemophilia centre now takes the following actions:

1) Informing your staff

This information should be communicated to clinicians and other staff in your centre as appropriate. It is suggested each haemophilia centre identifies a lead clinician responsible for liaison and managing this incident locally, and a deputy in the event of absence of the lead.

2) Contacting all patients

A letter should now be prepared for **ALL** patients with bleeding disorders[1] who are or have been treated with pooled factor concentrates or antithrombin. We have enclosed a draft patient letter that we recommend be used for all patients, including those who may not be considered 'at-risk' for public health purposes, with an accompanying 'Information for Patients' sheet.

Please try to ensure that all patients are given this information and the opportunity to discuss this with you. You may wish to give patients the option to attend a clinic to discuss their potential exposure with adequate time and support to discuss these issues.

3) Timing

The UKHCDO together with the Health Protection Agency, Scottish Centre for Infection and Environmental Health, Department of Health (England), Welsh Assembly Government, Department of Health, Social Services and Public Safety (Northern Ireland) and Scottish Executive Health Department ask you to prepare to send out your letter to patients on **Monday 20th September** by first class post, so that patients will start receiving their letters on Tuesday 21st September. A national announcement from the Department of Health is planned for shortly after this date. The Haemophilia Society will have written to its members and made a vCJD factsheet available on its website by the end of this week.

Coordinating the communication exercise in this way will help to ensure that the different patient groups who need to be contacted receive their information as far as possible at the same time. Clinicians who choose to make different local arrangements for informing and contacting their patients need to be prepared to manage enquiries from them if they become aware of the information from other sources.

It is possible that some enquiries may arise from members of the public and patients in the period before those affected by the notification receive their letters. We enclose an 'Enquirer Handling Protocol' that aims to set out information and arrangements for handling such enquiries. We suggest the level of information contained in this document should be adequate to handle these enquiries until most affected patients have received their individual letters.

All media enquiries should be referred to the relevant Government Press Office (see Media Handling Protocol attached).

4) Identifying patients 'at-risk' of vCJD for public health purposes

Please identify which of your patients have received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001. These will constitute the group 'at-risk' of vCJD for public health purposes, for whom special precautions should be taken. Patients' 'at-risk' status should be recorded in their hospital and GP medical notes (see points 5 and 6 below).

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

Patients who have died within the last year should also be assessed, and if identified as 'at risk', have their clinical history reviewed in order to identify and manage any recent surgical incident that may pose an infection control risk. Should centres identify 'at-risk' patients who are currently treated elsewhere, the centre doctor

should contact the clinician currently responsible for the patient's care, so they may manage the patient appropriately.

5) Patient vCJD Exposure Assessment

A Patient vCJD Exposure Assessment Form is attached to record the extent of exposure of individual patients to implicated products. You will need to identify which of your patients has received the implicated batches. Once completed, this form should be retained in the patient's hospital notes.

Population information on the extent of exposure of individual haemophilia patients is vital for public health monitoring and to inform public health precautions and future policy for this patient group. For this reason, a photocopy of each form should be forwarded as soon as possible after completion, in confidence to the UKHCDO National Haemophilia Database Co-ordinator in Manchester (address on form). This information is recorded anonymously, using only the patient's UKHCDO National Registration Number and date of birth. Therefore the patient's name should not be provided on the copy of the form that is forwarded.

6) Contacting GPs

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

- know that their patient is being informed about their 'at-risk' status,
- record the patient's 'at-risk' status and the special precautions required in their primary care records,
- include this information in any referral letters should the patient require surgery or other invasive medical procedures (see point 7.below)
- check information on the patient's recent surgical history at other hospitals and, if they have, liaise with their local Health Protection Team in order to ascertain whether any further action needs to be taken (see point 7.below)

We enclose a draft GP letter that we recommend be used for this purpose.

7) Infection Control

Please inform your Director of Infection Control (England) or Senior Infection Control Manager (HDL(2001)10) (Scotland) about any patients who are 'at-risk' of vCJD for public health purposes so that the appropriate special precautions may be taken. Guidance on infection control for any patient who is considered 'at-risk' of vCJD was published by the ACDP TSE Working Group in 2003: http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm.

As well as ensuring that infection control procedures are in place for any 'at-risk' patients who require surgery, the Director of Infection Control (England) or Senior Infection Control Manager (HDL(2001)10) (Scotland) should report relevant past surgical incidents to the CJDIP. If your patient has undergone surgery within the past 12 months please liaise with the local Infection Control Team in order to ascertain whether any further action needs to be taken.

Information on infection control issues is given in the Clinical Information document. The Clinical Information document gives background information on vCJD, the assessment of risk, special public health precautions, infection control issues for your patients and further advice.

Sources for Further information

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

Background information about vCJD with useful links is available from the following websites:

- HPA http://www.hpa.org.uk/infections/topics_az/cjd/menu.htm
- SCIEH: http://www.show.scot.nhs.uk/scieh
- National Public Health Service for Wales: http://www.wales.nhs.uk/sites/home.cfm?OrgID=368

It is planned that from 21st September 2004 information regarding vCJD and plasma products will also be available here. A national vCJD and Plasma Products advice line (0845 850 9850) will be operated by NHS Direct and its national colleagues for general public enquiries from this date.

If you, or your colleagues, have any questions regarding the content of this communication, the underlying rationale or the action to be taken, enquiries should be directed as follows:

- E-mail enquiries should be addressed to cjd@hpa.org.uk or SCIEHcjd@scieh.csa.scot.nhs.uk (Scotland) and will be answered as soon as possible.

- Health professionals needing to speak with someone directly should contact the following:

    1) Professor Frank Hill (Chairman, UKHCDO) on GRO-C

    2) The CJD Section (Health Protection Agency Communicable Disease Surveillance Centre (Colindale)) on GRO-C extension GRO-C

    3) (Scotland only) Dr Hester Ward (Consultant Epidemiologist, National CJD Surveillance Unit) on GRO-C or Dr Martin Donaghy (Clinical Director, Scottish Centre for Infection & Environmental Health) on GRO-C

    4) (Wales only) Dr Roland Salmon (Consultant Epidemiologist, National Public Health Service for Wales) on GRO-C

    5) (Northern Ireland only) Dr Brian Smyth (Regional Epidemiologist, Health Protection Agency Communicable Disease Surveillance Centre (Northern Ireland)) on GRO-C

Yours sincerely

GRO-C

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Professor Don Jeffries
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Enclosed documents

a) Recommendations of the CJD Incidents Panel
b) Tables of vCJD implicated batch numbers (with text insert)
c) Clinical information
d) Information for Patients
e) Patient vCJD exposure assessment form
f) Summary of patient notification exercise
g) Draft letter to patients with bleeding disorders
h) Draft letter to patients' GPs
i) Enquirer Handling Protocol
j) Media Handling Protocol