INFORMATION FACT SHEET

September 2004 **vCJD**

Summary

This factsheet has been written in response to a recent notification by haemophilia centres to all their patients. The letter has informed patients of recent developments intended to protect public health (ie transmission of vCJD to other people) and to make them aware that it is now known that more batches of haemophilia or von Willebrand's treatment have been made from the blood of donors who have been later diagnosed with vCJD.

People with a bleeding disorder who have been treated with 'implicated batches' are at a theoretical risk of been infected with this incurable disease. This risk is not proven and is an additional risk on top of the main risk from eating beef at the time when BSE was seen in British cattle.

vCJD is a recently identified disease of the brain. It is extremely rare – there have only been 157 identified cases in the world, mostly in the UK. It is thought to be caught from eating beef from cattle with BSE. There is no reliable test for the condition, but once symptoms have developed it quickly leads to neurological illness and death. There is no known cure.

Those who have only ever used recombinant Factor VIII or IX, imported plasma-derived products, or treatment made in Britain either before 1980 (when there was no risk of vCJD in the population) or after 2001 (by which time all the treatment being used was made from imported plasma), are **not** at any risk of developing vCJD from their treatment.

It is possible that a significant number of batches of Factor VIII or IX treatment made from UK blood donors may have been derived from blood from someone who was infectious for vCJD but was *never diagnosed*. For this reason all people who have had such British treatment between 1980 and 2001 will have to take certain precautions to prevent the unlikely event of passing on the infection. It is currently impossible to rule out this possibility, so such people will not be allowed to donate blood or other tissues and instruments used in certain forms of surgery will not be used on other patients. This requirement will also be included in their medical notes.

The theoretical risk which has led to these precautions must be put into perspective. The newness of the disease means that little is known about how it can be transmitted so that precautions are based on a worst-case scenario. It is very reassuring that no-one in the world with haemophilia has been diagnosed with vCJD, and that experts believe the actual risk to be very low.

This factsheet gives more detail about the risk assessment of transmission through factor concentrates and the background to vCJD. In addition to the help offered by haemophilia centres and the Haemophilia Society, it also lists other sources of support and information.

The Haemophilia Society September 2004

Introduction

There is much press, media coverage, and public debate about variant CJD (vCJD). Sometimes this can be confusing or even misleading. At the same time there is still much to be learned by scientists about vCJD. This means it is not possible to give definitive answers to all questions. We hope to explain what is known about the disease and in particular the current thinking about the theoretical risk that it can be transmitted in plasma products such as haemophilia clotting factor concentrates.

This fact sheet will try to answer some of the questions people with haemophilia and their families may have about vCJD. To date, before they became ill with vCJD, nine people are known to have donated blood and 23 donations used for blood products, including batches of Factor VIII and IX. The donations were made sometime before 1998. Haemophilia centres throughout the UK have been informed of the implicated batch numbers by the Bio Products Laboratory (BPL) and in Scotland and Northern Ireland by the Scottish National Blood Transfusion Service. This is because of the possibility that patients with haemophilia or von Willebrand's who have been treated with these products have been put at an additional risk of developing vCJD. The term 'additional risk' is used because it is a risk which is over and above that which potentially everyone in the UK is exposed to from eating beef. In turn, the centres have contacted patients about their potential exposure to vCJD.

More recently, the CJD Incidents Panel has advised that precautions need to be put in place to ensure that people put at additional risk of developing vCJD through blood products do not unwittingly pass on the infection. For this reason they are asked not to donate blood or other tissues, including semen, and if they need certain forms of surgery then extra infection control precautions will be taken with the instruments that were used, as this is another possible route of infection between patients at the same hospital. It is also recommended that they inform their medical, surgical and dental teams before invasive clinical procedures, so they can perform extra infection control procedures where appropriate. In September 2004 centres informed all their patients about these new precautions, and, as with previous notifications, they were advised to invite patients (or parents/carers of children) to know personally if they have used an implicated blood product. The precautions apply to all who have been treated with a product sourced from UK plasma between 1980 and 2001, whether or not it is *known* if they have been treated with an implicated batch.

A risk assessment will be done for each patient who has used one or more implicated batches of clotting factor to determine whether any such precautions should be taken. For example, some batches of Factor VIII have been manufactured with implicated albumin in order to stabilise the protein for storage. Albumin is a human blood product and if derived from the blood of a donor who may have been infectious at the time of giving blood then it is a potential risk. However, the CJD Incidents Panel advises that, as the risk of infection is minimal because of the small quantities involved, no precautions need be taken.

Patients who have only ever used the following types of treatment are **not** at any risk of vCJD:

- recombinant treatment
- plasma products imported from the USA, Germany or elsewhere
- British products made before 1980 (when BSE was not significant in the cattle population) or after 1998-2001 (the manufacturers switched from blood sourced from British donors to US plasma in 1998, but the shelf-life of UK-sourced products did not expire until 2001)

In order to protect public health, the risk assessment is done on a pessimistic basis, making various assumptions that the infectious agent (a prion) can pass through the fractionation process to produce clotting factor concentrates. Any of these may, in turn, be proved false. For example, it is assumed:

- that a donor later diagnosed with vCJD was *always* infectious and so at the time he or she gave blood, the plasma pool would have been contaminated
- that the recipient of the blood product was susceptible to the infection
- that the vCJD prion passes through all fractionation steps used to make Factor VIII and IX from whole blood

The actual risk is unknown and may turn out to be low, particularly as no-one with haemophilia in the world has yet been diagnosed with vCJD. These recommendations have been put in place to cater for the worst possible combination of scenarios which may mean that recipients of Factor VIII or IX have been infected and are therefore also potentially infectious to others. The conclusion of these

assumptions and calculations is that anyone who has had a single treatment with a product where the clotting factor has been derived from a donor later diagnosed with vCJD will be considered to be at a 1% or higher additional risk of developing vCJD on top of the risk from eating beef. However, because other haemophilia treatments may be identified in the future to have contained donated plasma from someone who developed vCJD much later, health protection measures will be applied to those who received British plasma concentrates between 1980 and 2001.In summary they are being asked:

- Not to donate blood or other tissues/organs
- To inform their medical/dental teams

What is vCJD?

Variant Creutzfeldt-Jakob Disease. It is a newly identified condition and was first described in 1996. It is one of four types of CJD; the others are sporadic, familial, and iatrogenic.

Sporadic CJD affects mainly the over 50s and is of unknown cause. It is marked by a rapid onset of dementia followed by neurological symptoms, which distinguish it from depression. Sporadic CJD was originally described by Dr Hans Creutzfeldt and Dr Alfons Jakob in the early 1920s and the course of the disease is measured in months. 90% of cases of CJD are of this type.
Familial CJD is inherited, with a younger onset and usually a longer duration than sporadic CJD.
Iatrogenic CJD occurs through contamination with infected tissues via medical procedures such as treatment with human growth hormone preparations.
Variant CJD (vCJD or nvCJD) is believed to be caused by exposure to Bovine Spongiform Encephalopathy (BSE or 'mad cow disease') and typically affects younger people.

How is vCJD transmitted?

Since the infection of British cattle with BSE there have been concerns that the infectious agent, a prion protein, has been transmitted to humans. It is believed that those individuals who have developed vCJD have acquired this fatal disease by eating infected meat at some point. At the time of writing (August 2004) there have been 147 people in the UK who are recognised by the CJD Surveillance Unit in Edinburgh to have contracted vCJD. It is not known how many more will develop the disease in the future, although the annual number of diagnoses appears to have peaked in 1999 and may now be in steady decline. There have been ten recorded cases outside the UK. Numbers of vCJD cases appear to be linked to the number of BSE cases in cattle and the UK has had far more cases of BSE (nearly 184,000) compared to the rest of the world (under 5,000).

What are the signs and symptoms of vCJD?

Early symptoms of vCJD are often psychiatric in origin, such as anxiety, withdrawal, behavioural changes, and depression. Persistent pain and odd sensations in the face and limbs are other early symptoms. More obvious neurological symptoms, such as unsteady gait and sudden jerky movements then develop, along with progressive dementia. All movement and speech is eventually lost and the patient will require 24 hour nursing care. Death occurs within an average of 14 months after the first onset of symptoms. vCJD typically affects much younger people than do other forms of CJD.

Evidence is emerging that some individuals may be genetically more likely to develop vCJD than others, as all of the cases in the UK have been found to have a particular gene pattern in common. However, it is not clear how significant this is as individuals who appear to be less susceptible to the disease may just be incubating it for a longer period of time before they develop symptoms.

How is vCJD diagnosed?

There is no routine screening test available yet and currently the disease is only identified when clinical symptoms appear. Scientists are working to develop a reliable blood test for vCJD and this may become available in the near future. However, vCJD has been found in organs such as the tonsils and the brain; small samples of either of these tissues can be taken to make a diagnosis, usually after the patient has died. Biopsies of tonsils are now undertaken regularly once a patient has

developed symptoms. MRI scanning can show certain changes which are highly suggestive of vCJD and can also be used to diagnose the condition in a living patient. However, these tests are intended to exclude causes of the symptoms other than vCJD, rather than establish whether or not a patient is free of vCJD.

Is there any treatment or cure?

Not at present. However, all patients diagnosed with vCJD are now offered the opportunity to take part in a clinical trial of quinacrine. Additionally, a recent high court judgement enabled some terminally ill British vCJD patients to be treated experimentally with a drug (pentosan). It is too early yet to know what the outcome of these experimental treatments may be.

How does this affect my family?

Those who have been classified as "at risk" need not take any special precautions in normal life. There is no evidence that vCJD can be passed to others by household contact, kissing or sex, or from mother to baby through childbirth or breastfeeding.

Can vCJD be transmitted in blood and blood products?

There is not enough scientific knowledge yet to be certain about whether vCJD may be transmitted in blood, because it is a relatively new disease. The risk is described as 'theoretical'. However, some animal experiments have shown that the infection can be passed through blood transfusion and there have been two probable cases of human-to-human transmission via blood in the UK.

In December 2003 the Department of Health reported the first case from anywhere in the world of possible transmission of vCJD from person to person via blood. A blood donor who was free of symptoms at the time donated blood to the National Blood Service in March 1996. Shortly after, packed red cells from this donation were transfused into a patient over the age of 60. The donor developed vCJD in 1999 and died in that year. The recipient developed vCJD and died in autumn 2003. It is important to note that in this case packed red cells were transfused (which are thought to contain the highest level of infectivity) and white blood cells had not been removed (also more likely to be infective). The process of removing white blood cells is known as leucodepletion. This intervention was not introduced until 1998 (see below).

In July 2004, the Department of Health reported the case of another recipient of blood (which had not been leucodepleted) which was donated by an individual who subsequently developed vCJD. The recipient had prion infectivity detected in his/her spleen and lymph node during a post mortem following death from a cause unrelated to vCJD. The patient had not yet become ill with vCJD and it is unclear whether he/she would ever have done so.

However, other evidence to date is more reassuring and experts still regard the risks of transmission by plasma derivatives (such as clotting factors for haemophilia treatment) as very low. No person with haemophilia has been found to have been infected with vCJD by the administration of any blood product, including plasma-derived Factor VIII and Factor IX.

The lower risk of infection from concentrates relative to whole blood is partly for two reasons:

The dilution of a contaminated donation by thousands of uncontaminated donations in a plasma pool
The collection and manufacturing process, from donation of whole blood to factor concentrate, includes steps such as precipitation, filtration, and column chromatography which are known from laboratory studies to reduce the quantity of similar infectious agents and may also achieve this for the vCJD prion

What steps have been taken to reduce risk?

1. Since 1997, the UK Government has taken measures to reduce any possible risk of transmission by human blood. In 1998 it discontinued the use of UK plasma in the preparation of clotting factor

concentrates. The National Blood Service imports plasma from the United States of America, where until recently there was no evidence of BSE to be found in cattle (the first case of BSE in the US was reported in December 2003). From the end of 1999, all British-produced plasma products were made from US plasma.

2. In December 2002, the Department of Health purchased the largest-remaining independent US plasma collector, Life Resources Incorporated to secure long-term supplies of non-UK blood plasma for NHS patients including people with haemophilia. The aim is to ensure that the current global plasma shortage will not reduce the availability to NHS patients of life-saving plasma products such as immunoglobulins and clotting factors. The plasma from Life Resources will be manufactured into plasma products by the NHS owned Bio Products Laboratory who supply 45% of NHS needs.

3. Blood donors are unable to donate blood if they have had, or suspect they may have had a blood transfusion in the UK from 1980.

4. Since 1998, as a precautionary measure, leucodepletion has been introduced by the National Blood Service. At donation, the white blood cells are removed from each unit of blood. The reason for this is the belief that if there should be any risk of transmission by human blood it would be most likely to take place via the white blood cells.

Why is recombinant recommended as the alternative to plasma products?

There is still not enough scientific evidence to eliminate the risk that vCJD might be transmitted in plasma products. The history of haemophilia treatment since the 1970s, with the transmission of hepatitis A, B, C and HIV, justifies extreme caution when considering appropriate treatment for people with haemophilia and related blood disorders. For these reasons, in 1997 the United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) recommended the use of recombinant clotting factor concentrates for all with haemophilia A or B.

In February 2003 Government announced £88 million to be made available to provide recombinant treatment for adults in England over three years. By 2006 it is hoped that the majority, if not all, adults will have had the opportunity to switch to recombinant Factor VIII or IX. Since 1998 all children in the UK and adults in Scotland and Wales have had access to recombinant.

What about the blood products that have been sourced to donors found to have vCJD?

The notification to patients of implicated batches of haemophilia treatment has been a source of concern for haemophilia centres and the Haemophilia Society. There was agreement between most doctors and nurses, and the Society, to ensure information on whether implicated batches had been used to treat individuals would be made available to patients (or their parents in the case of children), but only if they wanted to know. At the same time, we are aware that some patients and their families do not want to know and therefore the Society and UKHCDO recommend they be offered the choice of whether or not to be told. Hence the general policy now in communicating to patients about such incidents is to ask individuals whether or not they wish to know whether they have received the particular treatment product. It is important to note that whatever their decision about choosing to know this information, it will be placed in patients' medical records.

Is there monitoring of patients with haemophilia who may have been exposed to vCJD?

Following the earlier product notifications, the Department of Health is concerned to ensure that there is monitoring of haemophilia patients who have received plasma products that have been traced to a vCJD donor. This will help to provide more information to judge what, if any, risks there are that blood products may transmit vCJD. The Department is funding a joint study with the UKHCDO. This has involved setting up a confidential database of haemophilia patients who receive vCJD-implicated products. This database is linked to the national register of haemophilia patients kept by the UKHCDO.

Conclusions

While there are still many unanswered questions about vCJD it is important to focus on what we actually know about the theoretical risk of contracting the disease from blood products over and above the risk of infection that is believed to come from peoples' diet.

- None of the 157 people worldwide diagnosed with vCJD has been known to have haemophilia or any other related bleeding disorder
- The number of individuals in the general population so far diagnosed with vCJD is not the huge epidemic once feared
- There is no evidence to date of the transmission of vCJD by blood products, only a probable case of transmission through donated red blood cells and the finding of prion infectivity in the spleen and lymph node of a another recipient who died of causes unrelated to vCJD
- Any one of the many assumptions made by the risk assessment about infectivity of vCJD in blood products may be later proved unfounded and require the risk to be re-evaluated as much safer
- US plasma is now used for plasma-derived products manufactured in Britain for the NHS
- The most likely cause of vCJD is still believed to be eating beef products from cattle with BSE
- There are no validated screening tests to detect vCJD, although research is being done in this area
- Additional information can be gained from the staff at your haemophilia centre or the Society

Further Reading

- The Department of Health has commissioned an expert review of the possible risks of vCJD in blood and blood products. The final report *Risk assessment of exposure to vCJD infectivity in blood and blood products* was published in February 2003 and is available on the internet: www.dnv.com/consulting/news_consulting/RiskofInfectionfromvariantCJDinBlood.asp
- *UKHCDO 2003 Guidelines on Therapeutic Products to treat Haemophilia and Other Hereditary Coagulation Disorders* (*Haemophilia*, 2003, 9, 1-23). Available at: www.blackwell-synergy.com
- WFH Task Force – vCJD briefings (all available on www.wfh.org)

Useful websites and sources of support and information

The Haemophilia Society Volunteer Telephone Support Network "Need a listening ear? Talk in confidence to someone with similar experiences by ringing 0800 018 6068"
CJD Support Network www.cjdsupport.net helpline 01630 673973/673993 (24 hours)
Human BSE Foundation www.hbse.org helpline 0191 389 4157 (24 hours)
CJD Surveillance Unit www.cjd.ed.ac.uk
Department of Health www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/CJD/fs/en
Health Protection Agency www.hpa.org.uk/infections/topics_az/cjd/menu.htm
NHS Direct **www.nhsdirect.nhs.uk**
NHS vCJD and plasma products advice line 0845 850 9850 (24 hours)

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Contact the Haemophilia Society for a full list of publications and factsheets

This fact sheet can only give basic general information drawing on medical opinion and evidence available at the time of writing. Different people may give you different advice on certain issues and there may be some variations in the way care is managed in different hospitals and in different areas. It is important that you contact your own doctor(s) and nurses(s) for further information and advice on your own individual circumstances.