

# **Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO)**

## **Summary of 1<sup>st</sup> Public Meeting – variant CJD and blood**

Tuesday 21<sup>st</sup> October 2008, 2pm-4pm  
New King's Beam House, London SE1

### **Introduction**

**Mr John Forsythe – University of Edinburgh/SaBTO Chair**

Mr Forsythe welcomed the audience, and outlined the background of SaBTO and the work of the committee. He explained that the committee feels that it is vital to share information used to make decisions and to invite comments from interested parties and the public. This explains the committee's decision to hold an annual public meeting on selected topic.

### **1<sup>st</sup> Presentation: Introduction to variant CJD**

**Dr Hester Ward – National CJD Surveillance Unit/SaBTO vCJD expert**

Dr Ward gave an introductory talk on the cause and epidemiology of variant CJD.

1. There are several different types of prion diseases in humans, which can be divided into idiopathic (e.g. sporadic CJD), acquired (e.g. variant CJD) and genetic (e.g. familial CJD). There is no evidence that sporadic CJD can be transmitted via transfusion.
2. Variant CJD emerged in 1996 with features distinct from those seen in sporadic CJD. It affects younger people, who survive longer, and there are also distinct clinical and neuropathological features.
3. 18 of those affected by vCJD are known to have been blood donors. 66 recipients of their blood have been identified, of whom 23 survive.
4. vCJD is infective in blood but there remain a large number of uncertainties. A self-sustaining secondary epidemic through blood transfusion may be possible.
5. Key to determining the size of a secondary epidemic is measuring how many people in the population may be carriers of vCJD (the 'population prevalence').
6. A study on stored appendix samples and one on tonsils have given estimates for carriers of between 1 in 1, 500 and 1 in 20, 000 of the UK population.
7. Possible further studies of this type could involve more appendix samples, a post-mortem archive or blood tests, which are not yet available but are in development.

### **2<sup>nd</sup> Presentation: Variant CJD and Blood: current safety measures and future options**

**Professor Marc Turner – University of Edinburgh and Scottish National Blood Transfusion Service/SaBTO Haematologist**

Professor Turner gave a presentation on the issues around variant CJD and blood, the current safety measures in place, and options that may be considered in the future.

1. The prevalence of sub-clinical infection amongst the population of blood donors was discussed. The best estimate for incidence of further clinical cases is 70 .

2. This represents a discrepancy with the retrospective tonsil and appendix study data which indicates that the prevalence of sub-clinical infection of vCJD is 1/4000 (range 1/1000 to 1/20000). This suggests that up to 3,000 members of the UK population may be infected but remain sub clinical (symptom free) in the longer term.
3. It is known that in rodent models the potential level of peripheral infection is around 10 infectious doses per ml of blood (range 1-300 ID / ml).
4. These data taken together with the known transmission of variant CJD by blood suggest the possibility of an ongoing risk of transmission of variant CJD through blood, tissues and organs.
5. In the face of uncertainty, the best risk management approaches are those that give at least some control of risk over a wide range of plausible scenarios. In the context of variant CJD and blood, there are four potential approaches; donor selection, donor screening, component processing and minimising exposure.
6. Although a number of donor deferral criteria have been introduced both in the UK and internationally, they represent a relatively blunt risk management approach and can undermine the supply of blood and tissues.
7. A future test for vCJD may detect the presence of the abnormal protein in blood which would help to control the risk of secondary transmission , but will not give definitive information on the likelihood of development of clinical disease and will pose problems around sensitivity and specificity, validation and the management of those who have tested positive. There are particular concerns around the impact of a 'poor' test on donors and the blood supply.
8. Blood component processing is used to further reduce risk from transfusion. Red cells are re-suspended in optimal additive solution rather than plasma, and all red blood cells undergo leucodepletion. Using prion reduction filters to filter out prions from leucodepleted red blood cells may further reduce infectivity and these are currently under evaluation.
9. Risk reduction by reducing exposure to blood represents an immediately available, low cost measure that is relatively straightforward to implement.

### **3<sup>rd</sup> Presentation – A Patient’s Perspective** **Mr Elwyn Nicol – SaBTO Patient Representative**

Mr Nicol, explained that some 5 years ago he underwent a heart transplant, hence his interest in becoming the SaBTO patient representative.

With no family connections or experience in, or background of, the medical profession. Mr Nicol represents the patient. He emphasised that his views are independent and well placed to express an opinion, based on his own experience.

To lay members in this audience he confirmed that the well-being of patients, on this committee, seems paramount.

There are 2.4m blood donors in the UK and it is claimed that the vCJD testing programmes being developed may be 99% effective. Mr Nicol said he considers that to be very good, but it could mean 1%, i.e. 24,000 donations or donors would be falsely told that they had tested positive for vCJD.

Until testing for vCJD in blood is 100% reliable, potentially 24000 blood donors, who 'do something special' without reward could be falsely told they have the disease every year. They could not know if they are truly threatened, not know if they will ever be able to get a life insurance policy, ever be able to get a mortgage or ever be able to buy a pension.

As a heavily transfused patient, Mr Nicol was and remains, content with the range of precautionary measures that exist. Until a 100% test exists Mr Nicol would prefer to rely on those existing measures rather than see potential distress and harm being caused to individual blood donors.

Those who will make the final decision have a very difficult choice to make – Mr Nicol said that we ask a lot from donors and asked if we can ask a society that their generosity be extended to submit to an unreliable test that could result in such anguish for so many?

### **Statements from family members of those affected by variant CJD**

Two relatives of individuals affected by vCJD spoke.

Mr Peter Buckland spoke on behalf of his family. His son died after contracting vCJD from contaminated blood. Mr Buckland made the following points:

- The devastating effect of vCJD on the families of those affected was huge.
- The tragic consequences of the disease have been made more acute by a lack of information available to his family at the time from government institutions.
- The processes around management of vCJD should be open and honest, and those responsible should be prepared to explain their decisions.
- Delays in notifying those at risk of the disease did those who went on to develop vCJD a great disservice. Lives would have been led differently if the future implications had been made clear.
- An earlier notification would at the very least have allowed families to explore potential treatments for the disease in the early stages.
- Any test for vCJD should be made available. It is not acceptable that “at-risk” individuals be kept in the dark, however low that risk may be.

Ms Christine Lord is the mother of Andrew Black, who died from vCJD in 2007 aged 24, and made the following points:

- Those making the decisions around management of vCJD should be supervised by independent sources that are not government funded or backed.
- The terrible risk and legacy of vCJD that the UK population now face should lay clearly at the door of those who Ms Lord considers responsible for her son’s death. Ms Lord believes that if those ministers and officials in the 1980s and 1990s had not put profit before lives vCJD would have never existed and SaBTO would not be faced with the terrible dilemmas it now has to wrestle with.
- Testing should be made available as soon as it is developed. Ms Lord believes that it may not be in the Government’s best interest to make such a test available. The doubts about prevalence mean that the likely number of positives is not known; ministers may be reluctant to allow the wider public to be made aware of the true prevalence of vCJD in the population, particularly if the situation was worse than is currently forecast.
- Testing for vCJD should be a personal choice allowing people to live their lives accordingly. Ms Lord believes that officials in the 1980s and 1990s played god with the UK populations lives resulting in vCJD and too many innocent people dying needlessly and she is mindful that government may

very well be playing god again by refusing the UK population the choice to test or not.

- As a mother who has lost her son to vCJD Ms Lord would take a test tomorrow and would like the opportunity to be able to do this in the near future.
- The devastation vCJD has wrecked on families, careers, futures and relationships cannot be described in mere words. As a bereaved mother, a qualified journalist and psychological counsellor Ms Lord is acutely aware of the huge impact and life scarring event that nursing a child through the most horrific disease has had on hundreds of family members and thousands of colleagues and friends. Ms Lord's website is [www.justice4andy.com](http://www.justice4andy.com).

### **Statement from Mr Andrew March**

Mr Andrew March is a haemophiliac who made the following points:

- As a haemophiliac, Mr March received 110 vials of Factor VIII which were later deemed to be vCJD-implicated in the 2004 HPA Product Recall notification. As with all patients with bleeding disorders who have been treated with UK-sourced pooled factor concentrates or antithrombin between 1980 and 2001, this means that he has been classed as “at-risk” of vCJD for public health purposes.
- Mr March and many other haemophiliacs are anxious to have their true vCJD status confirmed, and hope that any future blood test will be used for this purpose.
- Haemophiliacs are concerned that in the event of the development of a prion filter for blood components, the Government may choose only to implement this technology and neglect introduction of blood tests. This would not be acceptable to haemophiliacs who wish to know their true vCJD status.
- 4,000 people with bleeding disorders have been informed that they are at-risk of vCJD. Mr March asked that these people should be offered the opportunity to take any available blood test.
- Mr March requested that SaBTO remain mindful of the concerns of the haemophiliac community, given that they received large amounts of blood and blood products and were therefore more frequently exposed to risk of infection.

### **Summary of questions/open forum**

#### ***Q. What developments have there been since 2004 aimed at reducing the risk of vCJD transmission by blood transfusion?***

SaBTO is considering other potential options for mitigating the risk of vCJD, including importation of red cells for the children, double-dose red cell collection, extension of platelet apheresis and importation of plasma for all recipients.

Several manufacturers are developing filters aiming to remove prion protein from red cells for transfusion. One of these filters is CE marked which means that it can legally be used in the UK. This filter is under active assessment by the UK and Irish Blood Services. It is important that any new technology used to produce blood components is assessed to make sure that it is effective and will not cause any harm to patients. A pathway for assessing prion removal filters has been established by the UK Blood Services and endorsed by SaBTO. The Spongiform Encephalopathy Advisory Committee (SEAC) have advised that the UK Blood Services should obtain an

independent assessment of the ability of these filters to remove prion protein. The first of these studies is well underway with early results expected to be reported in 2009. The UK Blood Services are also undertaking a clinical study of prion-filtered red cells in surgical patients and then transfusion dependent patients, designed to assess whether the filter results in an increase in adverse events to patients. These clinical studies were endorsed by SaBTO's predecessor, the Advisory Committee on the Microbiological Safety of Blood, Tissues and Organs (MSBTO). SaBTO will review this subject further in spring/summer 2009 when data from the independent evaluation and clinical studies of prion-filters are likely to become available.

***Q. What are the panel's views on the potential for embryonic stem cells to be used to produce blood components for transfusion?***

Although there has been considerable progress in this area, we still have a lot to learn about how the growth of stem cells is controlled, and also how to produce specific cell types from stem cells. There are significant challenges in being able to produce sufficient amounts of cells for transfusion or transplantation from stem cells and it is likely to be some years before such cells can be used clinically.

***Q. How long is the incubation period for vCJD transmitted by blood transfusion?***

We do not know, but in the 4 cases where vCJD infection is thought to have been transmitted by blood transfusion, the incubation period between receiving the implicated transfusion and development of symptoms of disease was 6-8 years in the 3 symptomatic cases. In animals, the incubation period following infection can be influenced by genetic factors and in other human prion diseases, such as Kuru, the incubation period can be up to 40 years. It is possible, therefore, that some people have been infected but have not yet (and maybe will never) develop clinical disease.

***Q. When is a test for vCJD in blood likely to be available?***

There is currently no validated diagnostic test that can be used to determine whether blood is infected with vCJD. Several companies are developing tests for vCJD in blood and are making good progress. As for prion removal filters the UK Blood Services have developed a pathway for assessing tests that may be applied to blood donors. We currently do not know how accurate these tests will prove to be. There are concerns around telling asymptomatic people, for example blood donors, that they may be infected with vCJD when the significance of the test result is uncertain, when it is unknown whether infection would necessarily result in disease, and when there is no proven treatment.

The impact of a screening test on the blood and tissue supply could be profound depending on how accurate the test is due to the direct loss of donations due to false positive results and the indirect impact in deterring people from donating., In addition there would be a need to carry out lookback studies and both donors and past recipients may need to be designated as "at risk of vCJD for public health purposes" leading to significant impact on the wider NHS.

It was noted that the development of a diagnostic test for vCJD was highly desirable for groups of patients who have been identified as 'at risk from vCJD for public health purposes'. However, SaBTO's remit is restricted to consideration of tests in the context of blood, tissue and organ donation.

***Q. With regards to screening tests for vCJD in blood, what level of specificity and sensitivity do SaBTO regard as acceptable?***

Currently the UK Blood Services screen blood for several viruses. Donors that have a positive result then undergo further testing with one or more confirmatory tests before being informed that they are positive. The acceptable performance of a vCJD screening test would depend, in part therefore, on whether a secondary screening test or confirmatory test was available.

***Q. Why is blood labelled "Risk of adverse reaction/infection, including vCJD" but other infectious agents such as HIV not included on the label? Why is plasma that is imported not labelled the same way?***

The labelling of blood components has been changed to bring it in line with labelling of tissue products. Other infectious agents such as HIV do not appear on the label as blood donations are currently tested for these; there is no screening test for vCJD available. Plasma is imported from a country with low risk of vCJD and therefore not labelled in the same way as blood components from the UK. SaBTO are currently examining the possibility of recommending full written informed consent for transfusion, which would include information on the risks involved and whether there are any suitable alternatives.

***Q. Why aren't platelets imported? Is importation of red cells feasible?***

Plasma components have a 2 year shelf-life and can be transported frozen. Platelets have a shelf-life of 5 days and must also be transported and stored in a very specific way to preserve them. It would therefore be highly unlikely that sufficient platelets could be imported from outside the UK with these limitations. NHS Blood & Transplant are currently conducting a feasibility study to assess options for importing red cells. Importing red cells for all patients in the UK will not be possible (over 2 million units of red cells per year are required). It may be possible to import red cells for selected patient groups, for example for children. Importation of special red cell products with a short-shelf life of 5 days or less is not likely to be feasible however. It is important to also consider other risks that may be increased in possible source countries, such as viral risk, since systems are not available to treat red cells to kill viruses.

***Q. If a test for vCJD is available, should it be used to screen egg and sperm donors?***

So far SaBTO have only considered the possible use of a vCJD screening test for blood donors. In due course the committee will also have to consider the application of such a test to donors of tissues, organs and gametes.

***Q. Would prion filtration prevent the need to import red cells? And unlike screening for vCJD, prion-filtration would not have any negative impact on the donor.***

Prion-filtration or importation of red cells would reduce the cost-effectiveness of the other. SaBTO are considering a number of possible options to reduce the risk of vCJD transmission by blood. The cost-effectiveness and advantages/disadvantages of each option have been considered at the April and July 2008 meetings of SaBTO. The committee will be considering these measures further in 2009 when further data on prion filtration and testing are available.

***Q. Has there been a case of vCJD transmission by blood transfusion of leucocyte depleted blood?***

No. So far all 4 possible transmissions of infected prion protein have all been from non-leucocyte depleted red cells and there have been no known infections from blood since this time. Leucocyte depletion was implemented in the UK in 1998/1999. Animal studies suggest that leucocyte depletion only removes about 40-50% of infectivity in blood. We also do not know what the maximum period of incubation between transfusion of infected blood and development of vCJD could be, and therefore leucocyte-depleted blood could be capable of transmitting infection but there may not have been sufficient time for any of the recipients to develop clinical disease as yet.

***Q. Have SaBTO sought advice from the Association of British Insurers regarding vCJD tests?***

The Association of British Insurers have been consulted previously with regard to patients who have developed CJD following treatment with growth hormones. Their response indicated that such recipients would not have any issues relating to insurance policies. SaBTO will obtain further information from the Association of British Insurers when more information is available on the performance of vCJD screening tests.

***Q. SaBTO requested a feasibility study on the use of double-dose red cells at their July meeting. When will this be available?***

NHS Blood & Transplant have been asked to perform a feasibility study on the use of double dose red cells for selected patient groups. This will be presented to the committee in Spring 2009 along side other options for risk-reduction of vCJD by transfusion.

***Q. Why does SaBTO still use estimates of prevalence from the Hilton study published in 2004 and not the later National Anonymised Tonsil Archive (NATA) study?***

This has been reviewed by the Spongiform Encephalopathy Advisory Committee (SEAC) not SaBTO. The Hilton study was on both appendices and tonsils (but mainly appendices). There are differences between the studies in terms of the tissue studied, the period in time the study was performed since the initial BSE epidemic and the sensitivity of test methods used. SEAC therefore do not consider it to be appropriate to combine data from the two studies. The estimates of prevalence from the two studies are currently consistent with each other, and the confidence intervals of the NATA study are within those of the Hilton study.

At the end of the meeting it was generally agreed that this exercise had been very useful – both to spread important information on this issue and also to open dialogue with all those involved. SaBTO intend to hold a similar public meeting next year.