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Blood Matters

Quarterly information for hospitals served by the National Blood Service

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NATIONAL BLOOD SERVICE

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Editorial

This special Spring edition has been deliberately developed to focus on the possible link between transfusion and the transmission of vCJD and the impact the precautionary measures recently announced by the Minister might have on the sufficiency of the blood supply. It includes an article on the Transfusion Microbiology Epidemiology Review, the existence of which enabled rapid notification of possible "at risk" blood recipients to be undertaken once the CJD Incidents Panel's recommendation to do so had been ratified by the Department of Health *(http://www.hpa.org.uk/infections/topics_az/cjd/inc_panel.htm).*

There is also an update article on the experience so far of HTLV testing of blood donations in England and Wales, followed by a description of how the HTLV Lookback will be undertaken. Phase I of this exercise will commence shortly. This will involve tracing the fate of previous donations from a donor who has been confirmed positive for HTLV so that action can be taken to notify and offer testing to any living recipient(s).

It is too early to accurately predict what the short and longer term impact will be on the blood supply once the exclusion criteria for donors who have previously been transfused is implemented in April. However, the Health Minister in both his December and March statements to the House of Commons emphasised the need to drive forward the UK CMO's *Better Blood Transfusion (BBT)* initiatives, aimed at improving the safety and effectiveness of transfusion practice in hospitals so as to minimise unnecessary patient exposure to the risks of blood transfusion and to minimise the impact of potential blood shortages. The CMO's initiatives *BBT1* (1998) and *BBT2 (HSC 2002/009)* set the framework for action, key points being the avoidance of unnecessary transfusion and the use of alternative strategies. Progress in the implementation of the recommendations in HSC 2002/009 was assessed by a questionnaire survey in 2003. The response rate was disappointing (45%) and the implementation of many of the recommended measures had not gone far enough.

Serious discussions are now underway between the CMO's National Blood Transfusion Committee (NBTC) and the DoH to determine possible ways forward to ensure that all hospitals have a clear policy on appropriate use and alternative strategies, and that this policy is underpinned with adequate resources to provide for:-

- dedicated consultant sessions
- appointment of Blood Transfusion Practitioners
- access to audit tools
- implementation of blood conservation measures
- blood shortage contingency planning
- high profile performance management at Executive level.

Whilst this further drive to implement *BBT2* gets underway, it is equally important to get into a state of preparedness in the event of possible blood supply shortages. A lot of collaborative work has been done between the NBTC and the NBS to develop an integrated plan for the management of blood shortages, the planning principles of which are to ensure that blood is available for all essential transfusions to all patients equally across the country and that overall usage is reduced to ensure the most urgent cases receive the supply which is available. Details of the proposed plan are being issued to hospitals as both the NBS and hospitals need to develop their emergency blood management plans now so they are ready to be put into action in any future shortage situation.

Finally, a summary of the UK Blood Services/NIBSC position statement on Creutzfeldt-Jakob Disease is included to provide readers with the background to the precautionary measures that so far have been implemented to mitigate against the possible risk of transfusion transmission of vCJD and for those of you who wish to gain a few more points, there is a CPD Questionnaire at the end.

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vCJD and The Blood Supply – NBS Response to the Ministerial Announcement

On 16th March, the Secretary of State for Health announced further measures designed to reduce the possible risk of vCJD transfusion transmission from donor to patient. The National Blood Service (NBS) has been working closely with the Department of Health and the other UK Blood Services since December 2003, when the first possible case of transmission of vCJD through blood was widely reported.

Following the reporting of this case in December, the Chief Medical Officer asked the expert Advisory Committee on the Microbiological Safety of Blood and Tissues for Transplantation (MSBT) to consider whether there was a need for any further precautionary measures to be taken to mitigate against the possible risk of vCJD being transmitted by blood and blood products.

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The further precautionary measures announced by the Minister require the NBS to implement the following initiatives:-

- Whole blood donors who know that they have received a transfusion in the UK since 1st January 1980 will no longer be able to give blood after 5th April 2004. The best estimate is that the NBS will lose 3.2%, or 52,000, of its donors.

- The NBS will work to increase the proportion of platelet donors bled by apheresis from the current level of 37% (March 2004). In addition, further research will be conducted into the benefits of platelet and red cell donation by automated collection.

- There will be an increase in emphasis on the "appropriate use" of blood and components. In particular, and in conjunction with the Department of Health, it is planned to drive forward the **Better Blood Transfusion** initiative.

- Arrangements are also being put in place for a national contingency plan in the event of blood supply shortages. There will be an integrated process for managing any shortages across the NHS, using a partnership approach between the NBS, Department of Health, and Hospital Trusts.

- Options will be considered by the NBS regarding the reduction of the plasma content in red cell components.

- Options for the additional procurement of US-sourced Fresh Frozen Plasma, to be used in the treatment of certain high-risk patient groups will be investigated by the NBS for further consideration by the MSBT.

- The NBS will develop a vCJD Test Assessment Facility, based at the Manchester Blood Centre. The Facility should open in March 2005. This facility will be used to validate any potential blood test for vCJD. In the background, the NBS will maintain a close watch on current research projects designed to produce a vCJD test, which could be applied to blood donations.

As of 31st January 2004 there have been 146 definite and probable cases of vCJD in the UK. The eventual number of individuals within the UK population likely to develop vCJD remains uncertain. It is therefore not known what number of current or past blood donors may develop vCJD in the future. The UK Blood Services have already implemented a number of precautionary measures against the possible risk of vCJD being transmitted by blood:

- Withdrawal and recall of any blood components, plasma derivatives or tissues obtained from any individual who later develops vCJD (December 1997).

- Import of plasma from the US for fractionation to manufacture plasma derivatives (October 1999).

- Leucodepletion (removal of white cells) of all blood components (Autumn 1999).

- Importation of clinical Fresh Frozen Plasma from the US for patients born on or after 1st January 1996 (introduced Spring 2004).

- Promotion of appropriate use of blood and tissues and alternatives throughout the NHS.

What does this mean for the blood supply?

The loss of 3.2%, or 52,000, of NBS blood donors could have a substantial impact on our ability to keep blood stocks healthy. Over the coming months, the NBS will be launching a range of marketing, advertising and other initiatives. These initiatives will be aimed at replacing those lost donors and encouraging regular donation amongst existing donors.

What does this mean for patients?

The NBS' prime concern is always the safety of patients through maintaining the quality and sufficiency of the blood supply. Whilst it is acknowledged that blood transfusion can never be 100% safe, the introduction of these additional precautionary measures are further steps to mitigate against the possible risk of vCJD transfusion transmission, carefully balanced against the risk of failing to maintain adequacy of supply. However, it is also important to put the current situation into context. Since the first cases of vCJD were recognised and reported in 1997, the NBS has issued 24 million blood components for use and through the TMER study, it can be confidently stated that, to date, only one possible vCJD transfusion transmission link case has been identified.

Nevertheless, in the light of these developments and the impact these initiatives might have on the blood supply, it is increasingly important to recognise that the decision to give a blood transfusion to a patient should only be made after careful consideration. In making that decision, it is important to balance the risk of having a blood transfusion against the risk of not having one.

Patients still concerned can ring NHS Direct on 0845 46 47.

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Notification Exercise For Recipients of Donations Given By Individuals Who Later Developed vCJD & The Transfusion Microbiology Epidemiology Review

Transfusion Medicine Epidemiology Review (TMER)

This research study was set up in 1997 to investigate the possibility of a link between CJD and blood transfusion. It is a joint study between the four UK Blood Services and the national CJD Surveillance Unit (CJDSU). The study involves the provision of data in relation to blood donors and blood recipients who develop CJD (all types), and control donors and recipients, to a confidential database. The information is provided by CJDSU and blinded to the Blood Services (and hence the hospitals) so that neither the Blood Services nor the hospitals know whether the tracing exercise involves a CJD case or control. The study was purposely set up to try and avoid the possibility of inadvertently revealing the status of the donor (case or control, vCJD or sporadic CJD) to hospital staff, as this could put those staff in a difficult situation. We were aware that some Clinicians felt that recipients should be informed if the donor later developed vCJD, even at the time the study was set up in 1997. Ethical approval for this study was granted on the basis that recipients should not be informed.

The CJD Clinical Incident Panel was set up by the Department of Health in 2000, with a specific remit to advise Health Authorities and Trusts on the management of incidents where patients might have been put at risk of CJD through clinical interventions. The Blood Services asked the Panel for advice on the management of recipients of blood components donated by individuals who later developed vCJD. This advice was requested on a "generic" basis without any indication of the personal details of those recipients. A risk assessment was commissioned, updating a previous assessment prepared in the late 1990s. Information from that risk assessment was used to formulate the advice of the Panel and incorporated in the Panel's Framework Document [1]. The advice indicated that these individuals should be notified of the situation with respect to their blood transfusion. Certain other matters were to be addressed; in particular the mechanism for notification and the provision of support for these individuals. That work was progressing when the TMER, for the first time, demonstrated a link between a donor and recipient in the study, both of whom had developed vCJD.

Patient Notification Exercise

As a result of the case demonstrating a link between a donor and a recipient in the TMER, an announcement was made in the House of Commons by the Secretary of State in December 2003, indicating that other individuals identified as recipients of donations donated by individuals who later developed vCJD would be notified (as per the Clinical Incidents Panel's advice). What had been part of a research study had now become a public health issue. The Blood Services were now required to carry out a "lookback" into the recipients of donations from donors who had later developed vCJD. The first stage of any lookback process is for the NBS to notify the hospital blood transfusion laboratory of a blood component that requires tracing, and for the laboratory to search records for the fate of the component. That first stage had already been carried out and the information could be extracted from the TMER database. There was no consideration of repeating this step (thus clearly distinguishing the work carried out in relation to the TMER with the work carried out in relation to a lookback/notification exercise). The risks of repeating the exercise as part of the lookback are as follows: -

- Information might no longer be retrievable from hospital records, as some relates to donations made more than ten years ago.
- Information revealing the status of the blood component (i.e. the association with a case of vCJD) to hospital staff could at worse jeopardise patient confidentiality, and would certainly unnecessarily increase the number of individuals involved in what is a very sensitive issue. Such involvement would be totally unnecessary, as the information had already been obtained on a previous occasion.
- Duplication of effort in repeating a task already performed is not a sensible option. Furthermore, this could have substantially lengthened the time taken to contact the recipients, when information was in the public domain and undertakings had been made in Parliament with Christmas fast approaching.

The fact that recipients have now been notified of their situation is an issue outside the TMER. If the TMER had not existed, we would have been embarking on a lookback exercise from the start. As it was, responsibility for the notification exercise was given to the CJD Unit at the Health Protection Agency, who carried this forward through local Health Protection Teams (HPTs). These teams are well used to dealing with incidents of many sorts. Local Consultants in Communicable Disease Control (CsCDC) worked with others as necessary to satisfy themselves that the correct recipient had been identified (usually by reviewing medical records at the Trust) before contacting General Practitioners with a view to ensuring that the recipient was notified. In many cases, the verification process was straightforward. In others, where verification was not straightforward, the local Haematologist may have been involved.

The notification exercise which took place in December 2003 was unusual for many reasons. In future, cases of vCJD arising in donors will be

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managed according to the standard lookback protocol that the Blood Services have developed over the years, but linking that with the Clinical Incidents Panel advice. This protocol will involve contact with the local Consultant Haematologist in charge of the blood transfusion laboratory for the initial tracing exercise. Thereafter, the primary responsibility for future management of the "incident" will rest with the CCDC. It is vital that the CCDC is always involved, since there may be other issues (such as subsequent medical or surgical interventions) which will require investigation and management.

We are aware that some Haematologists would have liked to have been informed of a notification exercise involving a patient treated within their Trust. On the other hand, it was important to ensure clear lines of communication and responsibility and the task of notification was given to the Health Protection Agency. The only involvement of the NBS was to provide the information needed to confirm that the correct recipients had been identified. Great efforts were taken to try and ensure that the identity of recipients (and, indeed, the identity of hospitals) was not inadvertently made public. Restricting the number of people who had access to this information was an integral part of those efforts. We hope that these reasons are understood, and apologise if any Haematologists were put in a difficult position by not being "in the loop".

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Reference
1. CJD Clinical Incidents Panel Framework Document *(http://www.hpa.org.uk/infections/topics_az/cjd/inc_panel.htm)*

HTLV Matters

HTLV testing of blood donations in England and Wales – the experience so far

In August 2002, the English and Welsh blood services began testing all blood donations for anti-HTLV. By December 2003, 0.0002% of donations tested were found positive for HTLV. Prior to routine testing, seroprevalence rates among blood donors in London and Birmingham had been reported to be 0.0013% and 0.055%, with higher rates among Afro-Caribbean donors. Some of the anti-HTLV positive donors identified through routine testing of blood donations had donated before, and as a result a lookback has begun to identify any recipients of these potentially infectious donations. In addition, the HTLV National Register has been established to provide a facility for future monitoring and long-term assessment of HTLV infection detected through testing of asymptomatic blood donors, recipients and their families.

HTLV

Human T cell Lymphotropic Virus type I (HTLV-I) is endemic in Japan, the Caribbean, southeastern United States and parts of South America and Africa. Here, seroprevalence is between 1% and 4%, although can be as high as 15% in parts of Japan. In non-endemic areas such as Europe, HTLV-I is less common and most infections are identified in immigrants [1].

HTLV-I can be transmitted through sexual intercourse, breast-feeding, intravenous drug use and blood transfusion of whole and cellular components (rarely plasma and never in plasma products)[2]. *Leucodepletion* (carried out by the NBS since 1999) along with increased age of components, is known to reduce transmission[3]. The epidemiology of HTLV-II is different, being predominantly found among indigenous American-Indian populations and among IVDUs, but the routes of transmission are the same[1].

People infected with HTLV have a low (5%) risk of developing disease, however the natural history has not been fully described. In the UK, HTLV-I has been most often associated with either an aggressive malignancy (adult T cell leukaemia/lymphoma, ATLL) that characteristically appears after a long latent period, or a chronic neurological disorder (tropical spastic paraparesis also called HTLV associated myelopathy) that can develop months or decades after infection[4;5]. Other undiagnosed forms of these malignancies or neurological diseases may occur along with other HTLV associated diseases. Each year, approximately 60 cases of HTLV symptomatic disease in UK are reported to the Health Protection Agency Communicable Disease Surveillance Centre (data available at *http://www.hpa.org.uk/default.htm*); this is likely to be an under-estimate of the burden of HTLV associated disease because of infrequent reporting due to under-diagnosis.

HTLV in Blood Donors

Between August 2002 and December 2003, 66 HTLV infections (55 HTLV-I, 7 HTLV-II and 4 untypable) were confirmed among three and half million donations tested in England and Wales. Since December 2002, the number of infections identified each month has declined as previously tested donors are re-tested and HTLV infected donors are excluded from the donor pool (fig). Donors attending centres in London (NBS Colindale and NBS Tooting) account for 45% of all infections, although infections have been identified across England and Wales with reports from donors attending most (9 of 11) blood centres.

Of the 55 HTLV-I infections identified, 16 were among new donors and 39 were in donors known to have donated before. Information was available on age, sex and probable exposure for 53. Of these, 28 were among older (over 40 years) female donors, and the rate among female donors was 3 times higher than in males. Most (28 of 42) HTLV-I infections where

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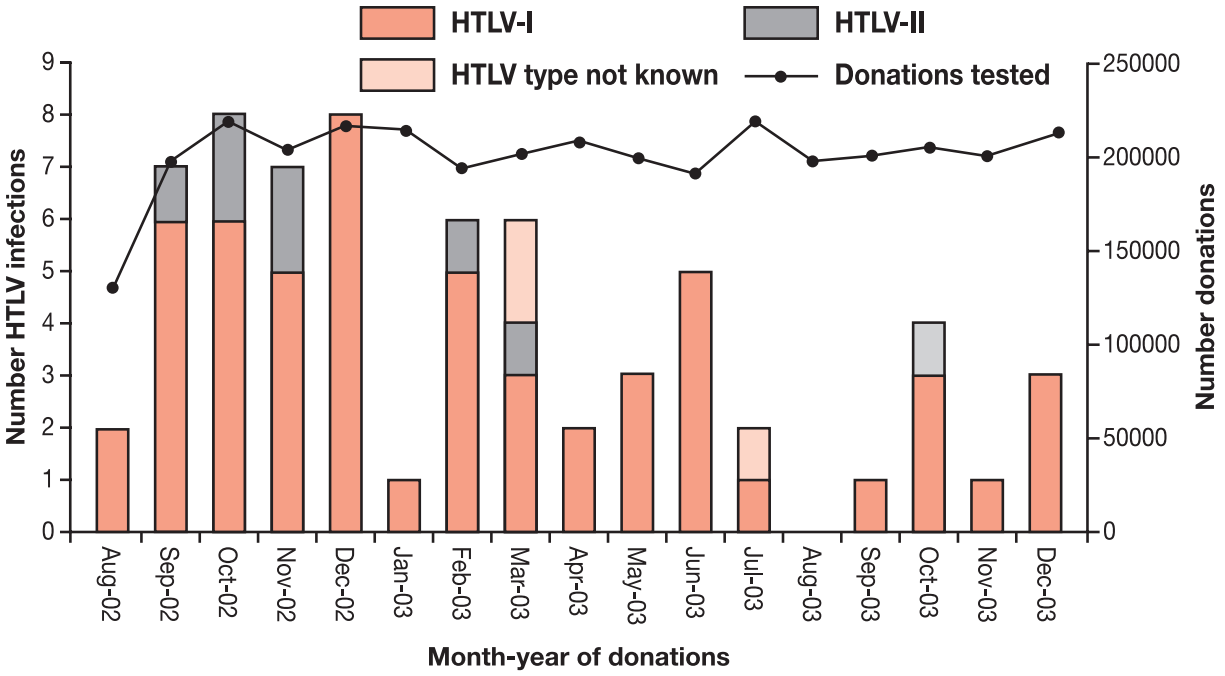
Figure: HTLV infections in blood donors in England and Wales, August 2002 to December 2003 by month of donation



a probable exposure had been identified were associated with an endemic country - 11 had probably been exposed in the UK through heterosexual intercourse with a partner from an endemic country, 16 were either born in or to parents from an endemic country and one patient had had a blood transfusion in an endemic county. No exposure had been identified for 9 HTLV-I infections and two cases were awaiting interview.

All of the seven HTLV-II infections identified in blood donors were among donors known to have donated before. Nearly all (6 of 7) were among female donors, and most (4 of 6) of these were over 45 years of age. Injecting drug use was associated with two infections; no probable source of infection was identified for the remaining six.

Overall, anti-HTLV seroprevalence levels among blood donors, a group known to be at low-risk for blood-borne infections, in England and Wales are low. Levels are similar to those seen among donors in other European countries such as Germany, France and the Netherlands when routine testing commenced. Since testing has been introduced, there have been no cases of seroconversion of HTLV in blood donors in England and Wales.

Monitoring and analysis of data contributes to understanding the epidemiology of HTLV and helps to ensure donor selection criteria are optimal.

The HTLV National Register

Since some of the infected donors identified through routine testing will have previously donated blood, the NBS has begun a lookback to trace all cellular blood components derived from these donations. The recipients identified, along with the HTLV infected donors, provide a rare opportunity to recruit a cohort of individuals to observe the clinical course of HTLV infection, treatment and final outcome. To do this the HTLV National Register has been established. The register is based on the HCV National Register set up in 1996 and infected donors, recipients of potentially infectious donations and family members of infected recipients/donors (along with other asymptomatic HTLV infected individuals presenting at specialist centres) are invited to take part. In addition, factors associated with transmission, disease and survival of recipients of potentially infectious donations will be investigated with non-infected recipients as a comparative group.

The register is a collaboration between the NBS, Health Protection Agency and Imperial College Medical School and is the first prospective study of its kind in Europe. Both the HPA and Multi-centre Research Ethics committees have approved it.

For further information on the HTLV National Register please email htlvregister@hpa.org.uk.

HTLV Lookback

Lookback is defined as tracing the fate of previous donations from a donor who has been confirmed positive for a microbiological marker, so that action can be taken to notify and offer testing to any living recipient(s). It should not be confused with the investigation of possible transfusion transmitted infection, which is triggered by identification of infection in a blood recipient, but which in most instances is shown not to be related to transfusion.

Lessons learned from the HCV lookback have been taken into account when planning the HTLV lookback. The documentation has been revised but will be largely familiar. A national database for the HTLV lookback has

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been set up by the NBS Transfusion Microbiology Surveillance section, based at NBS Colindale, and component details will be transferred directly from this database onto the forms (LBF1) sent to the Consultant Haematologist with responsibility for the relevant hospital blood transfusion laboratory. These forms will be used to identify the fate of the component from hospital records. When completed, forms will be returned to Dr Patricia Hewitt at NBS Colindale, where details will be transferred onto the database. The fate of components which have been transfused will need to be confirmed by reference to the patient's medical records, and the Consultant Haematologist will be asked to notify the clinician who was caring for the patient at the time of transfusion, and ask whether that clinician would want to notify the patient. This step is particularly important for patients who are under continuing hospital care. A sample standard letter is provided. If the clinician chooses not to notify the patient him/herself then the local NBS Consultant with responsibility for Transfusion Microbiology will proceed to contact the recipient through the General Practitioner. For those who wish to notify recipients, full guidance notes are available and the NBS is able to provide testing (including HTLV PCR where necessary) for all recipients.

A staged approach is planned for the HTLV lookback, with donations held on the current NBS (Pulse) computer system being investigated in phase 1. Pulse holds records from 1998/99 onwards, and these are most likely to be traceable at hospitals and the recipients most likely to be contactable (if still living). Phase 2 will include donations held on Blood Centre Heritage archive systems. It is unlikely but possible that components on Blood Service paper records will then need to be traced as phase 3. The 'yield' of traceable recipients will be reviewed at the end of each phase before moving to the next.

The NBS introduced screening for HTLV during the summer of 2002. In the first year of testing 55 HTLV positive donors have been identified, of which 11 have no previous donations to trace. Since August 2003 all the newly-identified infected donors had given blood for the first time. Many of the regular donors have a long donation history. However, the numbers are much smaller than for the HCV lookback, and as the virus is intracellular, the risk of transmission from frozen components is considered negligible so these are not included in the lookback. It is estimated that in the order of 800 components will need to be traced nationally.

For comparison, the HCV lookback programme covered the years from the early 1980s and resulted in a total of 9222 blood components entering lookback (although small numbers continue to be added, as lapsed donors return), but only 65% of these were established as transfused[6]. The fate of 32% of components was not identified[7]. Of components issued for transfusion, 41% had been transfused to recipients known to be dead and for 10% the recipient was not tested, either because the recipient was not traced, or the clinician advised that the recipient was unsuitable for testing. In all, 76% of the 4432 components linked to identified recipients did not result in a tested recipient. The number of HCV infections detected was 669, Overall, approximately one **living** recipient was identified per 4 transfusable components entering lookback, and one **infected** recipient was identified per 12 components entering lookback, per 8 recipients identified, and per 2 tests performed. Restricting lookback to components issued in the 5 years before testing would have identified 75% of the infected recipients. These figures cannot be extrapolated to the HTLV lookback, as leucodepletion was introduced before HTLV screening commenced, and leucodepleted components would be expected to have a reduced risk of HTLV transmission. The most recently transfused recipients, (who will also be the easiest to trace) will, therefore, have the lowest risk of infection!

Any questions about HTLV lookback should be addressed to Dr Patricia Hewitt, Lead Consultant in Transfusion Microbiology (020 8258 2720).

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References

1. Taylor GP. The epidemiology of HTLV-I in Europe. *J Acquir.Immune Defic.Syndr.Hum.Retrovirol*. 1996;13 Suppl 1:S8-14.
2. Tajima K, Tomanaga S, Suchi T, Kawagoe T, Komoda H, Hinuma Y. Epidemiological analysis of the distribution of antibody to adult T-cell leukaemia virus. *Japanese Journal of Cancer Research* 2002;73:893-901.
3. Okochi K, Sato H, Hinuma Y. A Retrospective Study on Transmission of Adult T Cell Leukemia Virus by Blood Transfusion: Seroconversion in Recipients. *Vox Sanguinis* 1984;46:245-53.
4. Osame M, Izumo S, Igata A, Matsumoto M, Matsumoto T, Sonoda S *et al*. Blood transfusion and HTLV-I associated myelopathy. *Lancet* 1986;2:104-5.
5. Tosswill JH and Parry JV. HTLV-I in English patients. *Lancet* 1989;2:328.
6. Soldan K, Ramsay M, Robinson A, et al (2002). The contribution of transfusion to HCV infection in England. *Epidemiol. Infect*. 129, 587-591.
7. The English National Blood Service HCV Lookback Collation Collaborators (2002). Probability of receiving testing in a national lookback program: the English HCV experience. *Transfusion*. 42: 1140-1145.

Development of An Integrated Plan for Management of Blood Shortages

There has not been a significant blood shortage in England and North Wales since January 1999. The current plan for managing shortages had not been developed in conjunction with hospitals and on the occasions when it has been put into action, it has not operated as effectively as planned, primarily because a set of actions across the NHS has not been agreed. Since October 2001 a group of Transfusion Laboratory Managers from around the country has joined with NBS staff to develop a plan which will include specific actions for hospitals and the NBS to ensure an integrated, uniform response to a shortage. The group has recently been expanded to include medical colleagues and the plan is now "owned" by the National Blood Transfusion Committee (NBTC).

The plan has been developed to manage shortages in all situations such as:

- Short term shortages, caused by, for example, bad weather or an influenza outbreak;
- Very acute shortages, caused by, for example, security issues which stop donors coming forward;
- Prolonged shortage, perhaps caused by the deferral of donors.

Planning principles

The plan is designed to ensure that hospitals and the NBS can work within a consistent, integrated framework across England and North Wales. The key issue is to ensure that those patients who need blood can receive a transfusion regardless of their geographical location. The plan is designed to ensure that:-

- blood is available for all essential transfusions to all patients equally across the country;
- overall usage is reduced to ensure the most urgent cases receive the supply which is available.

Also, the plan is designed to build on actions taken by hospitals to improve transfusion safety and effectiveness in line with the *Better Blood Transfusion*[1] initiative. Within the framework, hospitals which have taken actions to reduce the usage of blood will, at times of shortage, contribute less to a general reduction in blood usage to manage the shortage. It follows that those hospitals which have not implemented these actions will contribute more to a general reduction in usage. The Department of Health will be developing a performance management framework which will be used to determine the relative level of reduction in blood use required of each hospital. Details of this framework will be issued shortly.

The plan is designed to operate at all times, even when there is no shortage. In most cases, shortage can be avoided by reducing the current usage of blood through appropriate use programmes. To support hospitals to implement *Better Blood Transfusion* initiatives, the NBTC has collated guidance on these programmes and is further developing a toolkit to support hospitals in this work. This will be available in the near future.

Plan structure

The plan is structured to provide a framework of actions for the NBS and hospitals at three stages:

- Green: "Normal" circumstances where supply meets demand
- Amber: Reduced availability of blood for a short or prolonged period
- Red: Severe, prolonged shortage

It is envisaged that the NBS and each hospital will produce an Emergency Blood Management Plan (EBMP) for each of the above stages, agreed in advance by a high-level hospital team. A generic EBMP will be sent to all hospitals to assist with the production of individual hospital plans. By ensuring that all hospitals have EBMP's for shortage it is expected that, on declaration of a shortage, all hospitals will invoke these plans at the same time.

The Amber and Red phases will include actions to:

- reduce the stockholding of red cells at each hospital to ensure the maximum availability of the national "pool" of blood. This will mean reducing stockholding to pre-defined levels.
- reduce usage to ensure blood is available for those patients who need it most urgently.

During shortages the usage at all hospitals will be monitored by measuring the reduction in issues from the NBS. Hospitals who are not making the required reductions in usage will be contacted and options to reduce usage further will be discussed.

When a shortage is declared it is planned that all hospitals will activate their EBMP's. If the shortage is likely to occur for only a short period, the plan may require only a reduction in hospital stocks to release blood for use by all patients.

If the shortage is expected to be for a prolonged period, a reduction in usage may be required to prevent stocks falling further. Wherever possible blood will be moved around the country to ensure the transfusion needs of all patients are met. It is anticipated that in most cases the reduction in usage will be achievable through appropriate use initiatives. However, where these have not been implemented some hospitals may have to consider the cessation of procedures for patients. The generic EBMP which will be issued to all hospitals has categorised patients into

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three groups in order of urgency, to help decision making regarding those patient groups which will not receive blood. Category 1 contains the most urgent cases and category 3 the least urgent. Should a hospital be unable to reach the target reduction in usage it may have to consider the cessation of procedures for patients in category 3 of the generic EBMP shown below. In a prolonged shortage this will have an impact on waiting time targets.

Category 1	Category 2	Category 3
Active Major Bleeding	Cancer Surgery	Elective Surgery which is likely to require transfusion support
Emergency Surgery	Urgent Cardiac Surgery	Post op top up transfusion
Life-threatening anaemia	Anaemia with Major Symptoms	Elective top up for anaemia

In a major shortage where 50% or more of the current supply becomes unavailable, it is likely that only patients in category 1 would be treated.

Both the NBS and hospitals need to develop their Emergency Blood Management Plans as soon as possible so they are ready to be put into action in any future shortage situations. It is anticipated that by ensuring the NBS and all hospitals are able to take action as soon as a shortage is declared the available blood can be targeted for those patients who need it most, wherever they may be.

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1. Health Service Circular HSC 2002/009; *Better Blood Transfusion – Appropriate Use of Blood*, Department of Health, 2002.

UK Blood Services/NIBSC Joint Professional Advisory Committee Position Statement on CJD: a summary

(http://www.transfusionguidelines.org.uk/index.asp?Publication=DL)

The "Transmissible Spongiform Encephalopathies" can affect many mammals. The human forms, of which there are several types, are called "Creutzfeldt-Jakob Disease (CJD)". All have very long incubation periods and severely and irreversibly damage the central nervous system. To date there is no treatment. The most common type, sporadic CJD (sCJD) affects about 50 people a year in the UK, and has no obvious cause. However, surgery on the brains of affected people may contaminate instruments and spread the disease to the next patient even though the instruments have been sterilised in the normal way. The putative transmissible agents are called 'prions'. Although there is no evidence of transfusion-transmission so far in humans the UK Blood Services some time ago introduced a number of precautionary measures against this possible risk. Therefore the following selection criteria (in line with WHO recommendations) are applied to exclude anyone in a risk category from donating blood, tissues or stem cells.

- 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 (two or more blood relatives developing a prion-associated disease), and those who have received genetic counselling and been told that they are at risk.

Variant Creutzfeldt-Jakob Disease (vCJD)

This was identified in 1996. Unlike sporadic CJD, it affects younger people and its clinical presentation is also different. Affected patients show behavioural disorder, depression and anxiety, then get problems with sensation and co-ordination, and then show progressive dementia. They die after six months to two years. All investigations point to vCJD being caused by the same prion which causes Bovine Spongiform Encephalopathy (BSE) and not that which causes sCJD. To date there have been just over 146 definite and probable cases of vCJD in the UK, 6 in France and 1 each in the Irish Republic, Italy, the US, Canada, and Hong Kong. The eventual size of the epidemic is uncertain. Therefore, we cannot tell how many current or past blood, tissue or stem cell donors may be incubating vCJD. In December 2003, the first possible transmission of variant CJD by blood transfusion was described[1]. The transfusion occurred in 1996, the blood donor at the time was well, but went on to develop symptoms of vCJD in 1999 and died the following year. The recipient was diagnosed with vCJD in 2003. Having already adopted a number of precautionary measures, as a result of this case, the UK Blood Services have recently agreed on further action and these are listed together below.

For blood:

- Since 1998, withdrawal and recall of any blood components or plasma derivatives made from a blood donation from any individual who later develops vCJD.
- Since 1999, import of plasma from countries other than the UK for fractionation into plasma derivatives.

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- Since 1999, leucodepletion of all blood components.
- Since 29 March 2004, introduction of importation of clinical FFP for patients born on or after 1st January 1996.
- Promotion of appropriate use of blood and tissues and alternatives throughout the NHS.
- From 5 April 2004, donors who know they have received a transfusion since 1st January 1980 in the UK will be excluded from donating blood themselves.

For tissues:

- Improved washing and blood removal techniques for processed sterilised bone grafts.
- The use of disposable instruments for some types of tissue retrieval and processing.
- Improvement in decontamination procedures prior to sterilization of instruments.
- Batching of retrieval and processing of instruments to allow for the tracking of their use.
- Dura mater grafts are not provided.

Questions and Answers

HOW MANY PEOPLE ARE CURRENTLY INCUBATING vCJD IN THE UK?

The eventual size of the epidemic is uncertain. The number of cases may have peaked in the year 2000 but caution must still be exercised. All affected people have been homozygous for methionione at position 129 in the prion protein (about 30% of the UK population have this genotype); other genotypes may simply have a longer incubation period before they get symptoms. In addition, further cases may arise due to secondary human to human transmission via surgical instruments or blood transfusion or by cell or tissue transplantation.

HOW MANY PATIENTS HAVE BEEN EXPOSED TO BLOOD COMPONENTS OR PLASMA PRODUCTS FROM DONORS WHO WENT ON TO DEVELOP vCJD AND WILL THEY BE INFORMED?

There are currently 15 living recipients (England and north Wales) of blood components from donors who went on to develop vCJD. These have already been informed. The CJD Incidents Panel is currently calculating which groups of patients will need to be contacted following receipt of plasma products from batches contributed to by a donor who went on to develop vCJD. Some groups of patients have already been contacted. The others will be contacted as soon as their risk of exposure has been clarified.

ARE THERE ANY ADDITIONAL DONOR SELECTION CRITERIA THAT CAN BE APPLIED?

From 5th April 2004, only whole blood donors who know that they have received blood transfusions in the UK since 1 January 1980 are excluded from blood donation. It is estimated that this will affect 3-5% of UK blood donors . So far this exclusion has not been extended to platelet apheresis donors (where the loss of donations is likely to be greater because of their high frequency of attendance) or to tissue donors where the loss is likely to be higher still due to the different demographic features of this donor population.

WHAT ABOUT DONORS WHO ARE NOT SURE IF THEY HAVE RECEIVED A TRANSFUSION?

For the time being the new exclusion criterion for whole blood donors will apply only to those who are confident that they have received a transfusion since 1 January 1980. For the U.K. this is estimated to result in the loss of up to 60,000 whole blood donors, which will have a significant impact on the UK Blood Services' ability to maintain adequate supplies. The new measure is a precautionary one and extending the exclusion to those who are not sure if they have been given a transfusion could result in as many lost donations again. Any decision to extend the exclusion criterion will take into account the balance of risks i.e. the risk of disease transmission versus sufficiency of supply.

IS A BLOOD TEST AVAILABLE FOR vCJD?

No. Several international groups are trying to develop a test, but it is unclear how long this will take.

WILL UNIVERSAL LEUCODEPLETION REDUCE THE RISK OF TRANSMISSION OF VARIANT CJD?

It is hoped that leucodepletion will reduce infectivity (if it is present in the blood) enough to stop transmission. However this is unproven.

ARE THERE ANY OTHER COMPONENTS PROCESSING STEPS, WHICH COULD REDUCE THE RISK OF TRANSMISSION OF vCJD BY BLOOD, TISSUES OR STEM CELLS?

Consideration is being given to the following possible measures:

- Sourcing a greater proportion of platelet concentrates from individual donors using apheresis.
- Reducing the volume of plasma on red cells and platelet concentrates through the greater use of optimal additive solutions.
- For tissues, further measures are under consideration.

ARE TISSUE OR CELL PRODUCTS LIKELY TO BE INFECTIOUS?

The UK Blood Services Tissue Services are undertaking a formal review together with the Department of Health's Economic and Operational Research Department (EOR) to consider the risks of transmission of vCJD by tissues and cells.

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ARE PLASMA DERIVATIVES LIKELY TO BE INFECTIOUS?

As of October 1999, all plasma fractions including Factor VIII and Factor IX, immunoglobulins and albumin are derived from donors outside the UK. Therefore, there should be minimal risk. The risk to patients who received plasma products before October 1999 is uncertain. Fractionation does appear to remove some prions, so the risk from UK plasma-derived plasma products may have been very low, but we cannot assume that the risk was zero.

SHOULD UK PATIENTS CONTINUE TO ACCEPT BLOOD COMPONENTS?

Blood, tissues and stem cells should only be given when essential to the health or survival of the patient. The benefits of these treatments should be carefully weighed against the risk of transmission of vCJD. Sometimes, alternative approaches can be used to reduce exposure to blood components. UK Blood Services' clinicians are working with hospital colleagues to establish guidelines for the appropriate use of blood, and tissues.

IS ANY TREATMENT AVAILABLE FOR CJD?

There is no treatment currently available for CJD. Ongoing research suggests that several drugs could help prevent transmission or treat early disease. These include monoclonal antibodies and pentosan sulphate. However, much work still needs to be done.

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 practice have been established. Transfusion practitioners are being appointed to many hospitals, to help to educate and train staff and to conduct audit. Other developments in anaesthetics and blood salvage during surgery can also help reduce transfusion need; but transfusion may be unavoidable for patients suffering heavy blood loss, or for patients with cancer receiving powerful drugs which suppress bone marrow function.

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Reference

1. C A Llewellyn et al, Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. Lancet 2004, 363:417-421

Diary Dates

- 6 May, BBTS Meeting "Febrile Transfusion Reactions" and "Choose Your Plasma: FFP, MBFFP or SDFFP?", Birmingham. Email: Emily.Colquhoun@nuth.northy.nhs.uk
- 5-9 May, ESH-EBMT Training Course, Haemopoietic Stem Cell Transplantation, Budapest. Email: ghyslaine@esh.org or msimon@chu-stlouis.fr
- 7-10 May, International Society for Cellular Therapy 10th Annual Conference, Dublin. Website: www.celltherapy.org
- 13-16 May, 8th European Symposium on Platelet & Granulocyte Immunology, Austria. Website: www.interconvention.at/rust2004/
- 9 June, EU Blood Directive, Royal College of Obstetricians & Gynaecologists, London. Email: Events@bbts.fsnet.co.uk
- 10-13 June, 9th Congress of the European Hematology Association, Geneva. Email: eha2004@eurocongress.com
- 14-15 June, 9th International Paediatric, Haematology & Oncology Update Meeting, Edinburgh.

  Email: icms@indexcommunications.com
- 6 July, SHOT, Royal College of Physicians, London. Email: hilary.jones@nbs.nhs.uk or marie.jones@nbs.nhs.uk
- 11-15 July, XXVIII Annual Congress of the ISBT, Edinburgh. Email: info@in-conference.org.uk

NEWS & SNIPPETS

Malaria

The NBS now has a malaria test, which looks for antibodies to the parasite in the blood. This test is now available across the NBS and so anyone who has visited a malarious area of the world, or who has had malaria, can now donate blood 6 months after their return to the UK.

Blood Matters is prepared and issued by the National Blood Service, Oak House, Reeds Crescent, Watford, Herts WD24 4QN (Telephone 01923 486800)

CPD Questionnaire

Q1 NBS response to the Ministerial announcement

a) NBS will reduce proportion of platelet donors bled by apheresis

b) Discourage regular donation amongst existing donors

c) Consider increasing plasma content in red cell components

d) After 5 April, whole blood donors who know that they have received a blood transfusion in the UK since 1 Jan 1980 will no longer be able to donate blood.

Q2 vCJD

a) Only has been reported in the UK

b) Affects similar age group as sporadic CJD

c) Lookback studies have revealed a possible transmission by blood transfusion

d) Continues to be an increasing trend in mortality.

Q3 Integrated Plan for the Management of Blood Shortages

a) Only operates at times of blood shortages

b) Owned by National Blood Transfusion Committee

c) Obviates need for hospital Emergency Blood Management Plan

d) Category 3 contains the most urgent cases.

Q4 Transfusion Medicine Epidemiology Review (TMER)

a) This study demonstrated a link between a donor and a recipient, both of whom developed vCJD

b) Involves the provision of data in relation to blood donors and blood recipients who develop vCJD only

c) Provides the same information as the CJD Clinical Incidents Panel

d) Notification of recipients was a feature of TMER

Q5 HTLV in blood donors

a) All HTLV-1 infections were associated with an endemic country

b) In the first year of testing for HTLV - 0.002% of donations tested were positive for HTLV

c) Intravenous drug use was a very common source of HTLV-II infection

d) Since testing has been introduced, there have been no cases of seroconversion of HTLV in blood donors in England and Wales

Q6 HTLV in blood donors

a) Number of HTLV infections identified among blood donors each month is constant

b) The rate of HTLV-1 infection is higher in females

c) Donors attending centres in London account for over half of all infections

d) The UK has a higher seroprevalence rate than other European countries

Q7 HTLV lookback

a) It is estimated that in the order of 800 components will need to be traced

b) Frozen components will be included in the lookback

c) In the first year of testing 555 HTLV positive donors have been identified

d) As a comparison, the HCV lookback programme resulted in a total of 922 blood components entering lookback.