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Blood Matters

Quarterly information for hospitals served by the National Blood Service

NATIONAL BLOOD SERVICE

NHS

Editorial

This fourteenth Edition of *Blood Matters* is themed around some of the blood safety issues highlighted in the latest SHOT Report (Serious Hazards of Transfusion), a summary of which is presented in the first article. There is a marked increase in reports of TRALI in this year's SHOT Report, so it seemed appropriate to provide an update on how the National Blood Service (NBS) is addressing this problem. Bacterial contamination of blood components, particularly platelets, remains a serious issue; so again it seemed appropriate to provide NBS updates on what is being considered concerning bacterial reduction in blood components and the possibility of extending the shelf-life of platelets.

Often there are misunderstandings about blood donor selection policies, so in this edition, there is an article describing the principles underlying these policies. Position statements from the UK Blood Transfusion Services describing how and why the Services are handling potential threats, such as West Nile Virus, can be found on the Joint Professional Advisory Committee website. *(http://www.transfusionguidelines.org.uk).*

There is now close collaboration and co-operation between the National Blood Transfusion Committee (NBTC) and the NBS. Nevertheless, one of the roles of the NBTC is to monitor the performance of the NBS in its provision of services to hospitals, and the final article in this edition illustrates some of the performance measures that are reviewed regularly by the NBTC.

As launched in the previous edition of *Blood Matters*, a CPD questionnaire relating to the contained articles has again been devised for this edition, followed by two Frequently Asked Questions, and a 'handy hint' to add to the toolkit for implementation of Better Blood Transfusion 2. If you have any questions that you would like answered, please remember to write in to the Editor and we will try to respond in this format to benefit all our readers. Any more 'handy hints' to share with others to help tackle BBT2 will also be welcomed. Readers will be pleased to note that the new Patient Information Leaflet is available in ten other languages on the NBS Hospital website via the Library section *(http://www.blood.co.uk/hospitals)*.

Finally, I would like to thank all the respondents to our *Blood Matters* Questionnaire. Feedback suggests that 70% of recipients read it and only 3% rarely or never read it; 93% thought the breadth of content was good or even excellent. The information contained was rated good or better by 92%. Adverse responses were few (which of course we will take note of) but the majority of respondents felt that *Blood Matters* registered at an appropriate technical level and contained relevant material. In other words, the Editorial Board need to try and maintain the current standards and breadth of coverage. To do this, please continue to provide us with your feedback, comments and suggestions for any hot topics, or even better, volunteering authorship would be more than welcome.

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vCJD – an update

On the 17th December, the Secretary of State for Health made a statement to Parliament concerning the UK blood supply and the possible risk of vCJD being transmitted by blood.

A patient who recently died with vCJD had received a blood transfusion six years previously, prior to precautionary measures being implemented. The patient received blood from a donor who developed vCJD three years after making the donation.

It is possible that vCJD was transmitted from the donor to the patient by the blood transfusion, although it is also possible that both individuals separately acquired vCJD by eating BSE infected meat or meat products.

This is only a single incident, so it is impossible to be sure of the route of infection. However, the possibility of this being transmitted by blood cannot be discounted.

By the end of December 2003 there have been 145 cases of vCJD in the UK. The eventual number of people who will develop vCJD is uncertain and we cannot tell how many current or past blood donors may develop vCJD.

Since 1998 the National Blood Service (NBS) and other UK Blood Services have introduced a number of measures as a precaution against the possible risk of vCJD being transmitted by blood. These have included:

- Importation of US plasma for manufacture into plasma products (such as Albumin) since the end of 1999.
- Leucodepletion of all blood components (the removal of the white cells) since October 1999.
- Withdrawal and recall of any blood component or plasma product made from a blood donation since 1997 from any individual who later develops vCJD.

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- Encouraging the appropriate use of blood by promoting the take up of the Department of Health's Better Blood Transfusion 2 by working with the National Blood Transfusion Committee and the Regional Transfusion Committee network.

The NBS is also about to start to source US Fresh Frozen Plasma (FFP) for babies and young children born on or after 1st January 1996.

The Health Protection Agency is in the process of contacting the 15 people who have received donations of blood from donors who subsequently developed vCJD. The intention is for all to be told about the circumstances of their case and have the opportunity to discuss the risks with an expert counsellor.

Many more patients will have received plasma products before plasma was sourced from the USA. They will have received products derived from large pools of plasma donated from many thousands of people and thus heavily diluted. The CJD Incidents Panel considers the risk for this group to be even lower than for those who received whole blood. It is very difficult to trace all individual recipients of products made from these plasma pools. However, the CJD Incidents Panel will be advising on a case-by-case basis which recipients will need to be contacted. Any persons with concerns should ring NHS Direct on 0845 4647.

The Department of Health (DH), along with the NBS and other blood services, and other medical and scientific experts are continuing to review the current precautions against vCJD and any other precautions that could be implemented. As more information becomes available we will keep you informed.

First BSE case reported in the USA

The United States has reported its first case of BSE (also known as mad cow disease) in Washington state just before Christmas. BSE has been linked to variant Creutzfeldt-Jakob Disease (vCJD). Further investigations are ongoing in the USA into this first case of BSE.

It is important to remember that this is a single case. In the UK, there have been over 180,000 reported confirmed cases of BSE in British cattle.

6th Shot Report 2001-2002

The 6th SHOT report was published on July 17th and has been distributed to all hospitals. It can also be found on the SHOT website *(www.shotuk.org)*. This year's report contains a wealth of data which should now be used by hospital transfusion teams to educate staff and to impress clinical governance groups with the importance of ensuring transfusion safety in their organisations.

The first key message from the report is that, whilst almost all hospitals are now participating in SHOT, less than 50% submitted incident reports last year, suggesting that transfusion errors and hazards are still under-recognised and under-reported. Nevertheless there was a 21% increase in the numbers of reports of incorrect blood component transfused (IBCT), which constitute 72% of total reports received.

The following findings from IBCT reports deserve special emphasis:

- 40% of IBCT events involved multiple errors
- Two thirds of errors occurred in clinical areas, the commonest error being failure to check 'right blood to right patient' at the bedside.
- Patient misidentification was the predominant finding in 'near-miss' events
- One third of errors occurred in hospital laboratories, 25% of these were grouping errors.
- There were 32 reports of ABO incompatible red cell transfusions resulting in the deaths of 2 patients and major morbidity in 4. A further 2 patients suffered major morbidity due to ABO incompatible FFP or platelets.
- Twenty-one patients received unnecessary transfusions on the basis of a wrong full blood count result. In 2 cases it was considered that the transfusion contributed to the patient's death.
- 19 RhD negative patients (including 3 young females) received unintentional RhD positive transfusions, 13/19 as a result of laboratory errors.
- Special transfusion requirements were not met in 83 patients, 60 of whom were put at risk of transfusion associated graft-versus-host disease (TA-GvHD). Failure or inability to access patients' transfusion records and lack of communication in shared care were contributory factors.

Notable findings from other sections of the report were:

- A marked increase in reports of TRALI, suggesting increasing clinical awareness. Whilst the degree of diagnostic certainty was variable, TRALI is emerging as the most important

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serious complication of transfusion, contributing to the deaths of 7 patients and major morbidity in 18. 'Plasma-rich' components were implicated in 28/33 cases.

- FFP was implicated in the majority of anaphylactic and allergic acute transfusion reactions - in some cases the indication for transfusion appeared dubious. Many cases of acute transfusion reaction (ATR) were inadequately investigated.

- Bacterial contamination of platelets continues to occur, causing major morbidity in 5 patients this year. In 4/5 cases the platelets were 5 days old and in 3/5 cases the organism was *Staphylococcus epidermidis*.

- There were no confirmed reports of transfusion-transmitted viral infection.

- There were no reports of TA-GvHD, and only 3 of post-transfusion purpura. This reduction in incidence since 1999 suggests that leucodepletion of all blood components may have a protective effect.

- Five patients died following haemolytic transfusion reactions, 2 acute and 3 delayed. Contributory factors were: failure to seek specialist advice for patients with complex transfusion problems; failure to recognise delayed haemolytic reactions, resulting in an unnecessary laparotomy in one fatal case; critical delays in providing blood and lack of availability of patients' previous transfusion history.

As a result of these findings, SHOT makes a number of recommendations. Whilst some of these are directed at government and the blood services, those summarised below are aimed at reducing the incidence of 'wrong blood' events in hospitals.

- All institutions where blood transfusions are administered must participate in SHOT.

- An open learning and improvement culture must be developed in which SHOT reporting is a key element.

- Adequate resources must be made available for improvements in transfusion safety in hospitals.

- Hospital transfusion teams must be established and supported.

- SHOT recommendations must be on the clinical governance agenda.

- Appropriate use of blood components must be strenuously promoted.

- Training in blood administration should be implemented and competency testing developed to ensure an effective outcome.

- Blood transfusion should only be prescribed by authorised clinicians.

- Hospital blood bank laboratory staffing must be sufficient for safe transfusion practice.

- Clear policies should be developed for communicating special transfusion needs of patients to other hospitals or units which share their care.

The SHOT Annual Meeting was held jointly with the National Blood Transfusion Committee on 26th September in the Royal College of Physicians and chaired by Professor Ted Gordon-Smith. Dr Archie Prentice, President of the British Society for Haematology, pledged the support of the society for SHOT and for biomedical scientists working in transfusion laboratories. Difficulties and stresses faced by laboratory staff, particularly when working 'out-of-hours', were further emphasised by Debbie Asher in her excellent presentation on reducing errors in the laboratory. Judith Chapman outlined the Blood Stocks Management Scheme and how it contributes to knowledge about how blood is used.

The audience heard from Mike Pearson and Fiona Regan on the preliminary findings from the RCP/NBS National Comparative Audit, to be reported soon, and were left in no doubt that there is much to be done to improve the safety of the transfusion process at the bedside. Emily Okukenu, of Bart's and the London Hospital Trust, gave an inspirational account of what can be achieved by an enthusiastic Specialist Practitioner of Transfusion (SPOT), and Maggie O'Donovan from the National Patient Safety Agency (NPSA) described the collaborative project between SHOT and the NPSA using root cause analysis to investigate transfusion errors. Benefits and pitfalls of IT solutions were described by Derek Norfolk, Joan Jones, Claire Mellors and Mike Murphy; Fraser Fergusson told us how better blood transfusion is being implemented in Scotland.

Following talks by Lorna Williamson and Sam Machin on plasma safety and the problems of plasma replacement in TTP, the day concluded with an open forum discussion, introduced by Hannah Cohen, who told the audience of SHOT's future plans. Priorities for this year are: to ensure that 'participation' is truly active, to improve the IBCT questionnaire in collaboration with the NPSA, making it more user-friendly and incorporating some root cause analysis tools, and to explore confidential sharing of information with other databases together with some projects to obtain denominator data on transfusion practice.

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The SHOT scheme, though independent, is funded by the UK Blood Transfusion Services, and hence indirectly by hospitals as users of blood components. Only by active and complete participation will hospitals derive full benefit from the scheme. This means all staff being alert to failures in the transfusion process, both actual events and also "near-misses", where the error is detected in time to avoid the wrong blood being given. In addition to reporting all such events to SHOT, the hospital transfusion team should ensure that they are investigated fully and openly, and reviewed by the hospital transfusion committee and risk management/clinical governance committee or equivalent.

Finally, it should not be forgotten that there will be two 'victims' of clinical error; the healthcare worker who is at the 'sharp end' of a system failure may be devastated by having committed an error resulting in harm to a patient. Support is needed, rather than threat of disciplinary action, if positive lessons are to be learned from such experiences. Underlying causes of system failures must be teased out, acknowledged and corrected – only then will we improve the safety of blood transfusion in our hospitals.

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Update on TRALI - Reducing the Risk

In *Blood Matters* Issue 9 (January 2002) we published an article on TRALI and recommended that clinicians and nurses who administer transfusions should be aware of the condition so that it can be appropriately investigated and managed. The increase in the number of cases reported in the SHOT Report 2001-2002 suggests that awareness of the condition has increased.

However TRALI still remains a severe potentially life threatening complication of transfusion, and the evidence that the presence of donor leucocyte antibodies plays a major role in the aetiology of the syndrome is strong.

TRALI Risk Reduction Project

In March 2003, a National Blood Service Project was set up to consider how we could reduce the risk of TRALI from transfusion of blood components. In order to decrease the transfusion of leucocyte antibodies contained in plasma, the strategies considered included either reducing the amount of plasma (and therefore antibody) transfused in cellular components, or minimising the risk that plasma contains leucocyte antibodies. Leucocyte antibodies are produced mainly as a result of pregnancy – a history of transfusion is thought to be a lesser stimulus to antibody development. Different strategies are likely to be more appropriate for some component types than others, and therefore options for each component were considered separately.

The option appraisal has been performed in conjunction with the Economic and Operational Research Department of the Department of Health.

The Project is still underway, but it became clear early on that the cheapest, most 'do-able' operationally, and probably the most effective option with regard to decreasing TRALI risk overall, would be to select only male donors to manufacture FFP. FFP transfusion accounts for up to a half of all TRALI cases. The main challenge for implementing this involved putting in mechanisms to identify the sex of the donor once blood had arrived in processing departments. This has now been successfully piloted at one NBS site, and it is planned to roll out this change to all sites by the end of 2003. It was felt that asking male donors about a history of transfusion would add little to the overall safety, as transfused males suitable to continue as donors would be likely to have had only 'one-off' transfusions, with only a low risk of generating persistent leucocyte antibodies. The requirement for extra donor questioning is an important consideration, given the extra questions that have recently been added to donor questionnaires regarding SARS and West Nile Virus.

Some work has also been done to decrease the amount of plasma remaining in red cell components (in additive solution). Red cells are implicated in only a small number of TRALI cases and this measure should reduce the risk from this component still further.

Options for other components such as platelets (both pools and apheresis-derived) are still under assessment – they include removal of some plasma and resuspension in platelet additive solution, using male plasma to resuspend platelet

pools, and screening female apheresis donors for the presence of leucocyte antibodies. The impact on other services (e.g. HLA matched platelets) and processes (e.g. possible ability to extend the shelf-life of bacterially screened platelets) has to be carefully considered in conjunction with reducing the TRALI risk so that the added benefits do not have detrimental effects on other aspects of the Service.

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Though much more work remains to be done, we should soon hopefully begin to see the benefits in a reduction in the number of TRALI cases reported, and we will continue to report progress on this Project.

Please continue to report any suspected cases, however, to both SHOT and your local Blood Centre, so that we can perform appropriate investigations.

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The National Blood Service (NBS) Approach to Bacterial Reduction in Blood Components

What is the problem?

The SHOT report[1] continues to highlight the fact that one of the most frequent serious hazards of transfusion results from bacterial contamination of blood components, particularly platelets. Since surveillance began in 1995 there have been 22 reported episodes of post transfusion infection as a result of bacterial contamination of platelets, of which 5 were implicated in the death of a recipient whilst other recipients suffered major morbidity. These bacterial contaminants are largely due to skin flora entering the pack at the time of collecting the donation, but may also occur during processing into blood components and rarely may be associated with a (symptomless) bacteraemia in the donor. Platelet components must be stored at room temperature (± 22°C) to maintain their activity, however these are conditions that actively promote the growth of any bacteria present and it is of note that the majority of the implicated platelet packs (21 out of 22) were 3 or more days old at the time of transfusion. See table 1.

In addition the NBS National Bacteriology Laboratory have been monitoring bacterial contamination rates in expired blood components since 1999. Results show that the overall rate of bacterial contamination is approximately 0.5% (1 in 200 platelet packs). The rate is higher in platelet pools (0.6%) than apheresis packs (0.3%). These are in keeping with reports from other countries.

In response to these ongoing reports of bacterial contamination of blood components the NBS has reviewed all procedures and processes to identify

Table 1 Transfusion-transmitted bacterial contaminations reported in UK between 01/10/1995 and 31/12/2002 by species and component type and age (N=26).

	Platelets Age (in days) at use							Red cells
	1	2	3	4	5	NK[b]	All	
All species	***0***	***1***	***3***	***6***	***8***	***4***	***22***	***4***
Bacillus cereus				3[a]		1	4	
Coagulase negative Staphylococci					1		1	1 (23 days)
Enterobacter aerogenes			1[a]				1	
Escherichia coli			1[a]			1	2	
group B Streptococcus			1	1		1	3	
Morganella morganii					1		1	
Serratia liquifaciens								1
Staphylococcus aureus					1	1[a]	2	
Staphylococcus epidermidis		1[a]		2	5		8	1 (32 days)
Yersinia entercolitica								1[a] (33 days)

[a] *Infection was implicated in the death of a recipient*

[b] *NK=not known*

the sources of possible contamination. There are three key stages:

- Firstly, during collection procedures, either due to ineffective cleansing of the donor arm pre-insertion of the needle, or due to a contaminated skin plug entering the donation.
- Secondly, the donor may have a symptomless bacteraemia, contaminated blood being directed straight from the donor into the blood collection pack.

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- Lastly, contamination may occur during processing of the blood donation into its constituent components, or during storage. Effective GMP, the use of sterile, integral processing systems and effective cleanliness minimise the risk of contamination during processing. New processes and systems have been developed that are designed to reduce as far as practically possible the potential for infection of blood occurring during the collection procedure.

What is the NBS doing about the problem?

IMPROVING THE EFFECTIVENESS OF ARM CLEANSING

A significant amount of work has been carried out to assess new methods of cleansing the donor arm prior to venepuncture. Both the chemical agents used to clean the venepuncture site and the method of swabbing are important factors. An effective system has been identified for national implementation and is already being piloted in apheresis departments but full implementation across all donor sessions has been delayed by the need to complete the licensing requirements of the MHRA (Medicines and Healthcare products Regulatory Agency).

DIVERSION OF THE FIRST FEW MILLILITRES OF THE BLOOD DONATION

It has been shown that bacterial contamination can be reduced by diversion, into a sample pouch, of the first few millilitres of the donation after venepuncture. This effectively removes the skin plug, formed during the insertion of the venepuncture needle, together with any potentially harmful bacteria associated with the surface of the donor arm. New blood collection systems, which incorporate this diversion system, have been in routine use throughout the NBS for over a year.

Both of these are simple procedures designed to prevent as far as possible the initial contamination of blood donations. They do not fully protect the donation from the potential of contamination but together have been estimated to reduce the risk by approximately 70%.

What more could the NBS do to reduce the risk of bacterial contamination of platelets?

New systems are available which can provide additional assurance on the bacterial safety of blood components, particularly in consideration of platelet components. These include systems to test for bacterial contamination in manufactured components and pathogen reduction mechanisms that are claimed to inactivate bacteria (viruses and other pathogens) during the manufacturing process.

TESTING FOR BACTERIAL CONTAMINATION

A variety of testing methods can be used to detect bacterial contamination of blood components but the most sensitive and until now probably the best suited to routine donation screening is Bactalert™, a fully automated blood culture system which can be interfaced with main blood centre computers. There is extensive experience, world-wide, with Bactalert™ and its use has been shown to significantly reduce the incidence of transfusion transmitted infections of bacterial origin. It is currently being used by other UK blood services, Irish and Dutch services. Manufacturers are actively working to develop other bacterial detection systems which are operationally more efficient but will offer the same or improved levels of specificity and sensitivity. At present only the Bactalert™ and Pall (BDS) systems are both CE marked and FDA approved. A third mechanism, Scansystem (Hemosystems) is currently only CE marked.

There are a number of specific issues relating to bacterial testing which may have significant impact on when and how testing could be carried out, whether components would be released prior to testing, shelf-life of platelets, and the use of either plasma or plasma/additive solution for suspension of platelets. This is also directly impacted on by other project work, specifically that relating to transfusion-related acute lung injury (TRALI) and the use of Platelet Additive Solution (PAS). Accordingly, the NBS has formed a project group to actively consider all these issues and recommend the most appropriate course of action.

Typically, platelets are tested on day 1 or 2 of their shelf life and the result read 24 hours later. Clearly, it is safer to release platelets once the result is known to be negative but this delays their release to stock and may result in shortages. It would be feasible and useful logistically to extend the shelf life of platelets to 7 days however current data suggests that platelets are better maintained when suspended in plasma. For TRALI, however, the possibility that PAS may significantly reduce the incidence of this condition is also under investigation. Thus there are competing safety initiatives and the Economics and Operational Research (EOR) division of the Department of Health are working with the project group to assess the relative risks of these options. Additional work on extended platelet storage with or without additive solution, and with a variety of platelet storage packs is currently being carried out by the NBS Component Development Laboratory and is reported in this edition of *Blood Matters*.

It is proposed to begin phased implementation of bacterial testing of platelet components during 2004/5. This would commence with an extended assessment of appropriate technologies which would be designed to compare sensitivity and

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specificity and determine the most appropriate testing process for routine use (also in consideration of cost and space).

PATHOGEN REDUCTION SYSTEMS

There is currently only one licensed system available, Baxter Intercept, which is a photochemical process using a psoralen-based compound (S59 or amotosolan) and UV light to inactivate nucleic acid. It is CE marked and is at present undergoing investigation by the FDA. There are restrictions to this system as it is currently suitable only for the inactivation of recovered platelets, although work is ongoing to complete licence applications for apheresis platelets. Clinical trials have been conducted in the US and Europe and the product appears to be safe and efficacious. However, additional work is underway to examine clinical effectiveness and to increase the inactivation data on a range of additional pathogen markers. Other manufacturers are developing similar systems both for platelets and other blood components, although it is not expected that these will complete clinical evaluation before 2005/6.

The NBS has already undertaken a limited evaluation of the Baxter Intercept system. However, given the stage of development of these technologies it would be premature for the NBS to make any decisions with regard to their implementation at this time. This is a new and untried system, which although potentially offering significant advantages in the inactivation of bacteria and other pathogens, would benefit from a fuller assessment of its capabilities in an operational context, including space, staff and resource requirements and acceptability from a clinical perspective. The NBS is mindful of the need to consider the future role of pathogen reduction within the overall scope of its longer-term blood safety strategy and will ensure that it is prepared to conduct more extended evaluation in due course

Summary

The NBS has adopted a number of approaches to reduce the risk to patients of bacterial contamination of blood components. These include improved arm cleansing methods, diversion of the first few millilitres of the blood donation and plans to commence bacterial testing of platelets. These form part of the Service's continued commitment to an overall blood safety strategy in which consideration will be given to the future role of pathogen reduction technologies.

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1. Serious Hazards of Transfusion Annual Report 2001-2002, ISBN 0 9532 789 5 6
http://www.shot-uk.org

Extending the Shelf-life of Platelet Concentrates

In the NBS we currently prepare platelet concentrates (PC) by two methods:

- Collection of PC by apheresis technology; this accounts for 40% of platelet production.
- From whole blood donations - buffy coats from four donors are pooled together with one unit of plasma from one of the donations and red cells are centrifuged out; this accounts for 60% of production.

Currently all PC are leucocyte depleted at source and stored in plasma at 22 +/- 2°C with agitation, with a shelf-life of 5 days. There are no clinically significant differences in platelet numbers or quality between apheresis and pooled platelets.

Why are we considering extension of platelet shelf-life?

The primary reason for considering extension of platelets shelf-life is to facilitate the implementation of tests to screen platelets for bacterial contamination, which is being considered as a risk reduction option. As the risks of viral transmission have become vanishingly small, this risk is now high on NBS' safety priorities. Because of the need to hold platelets for 24-48 hours while bacterial screening tests incubate, extension of shelf-life would be necessary to maintain the number of days for which issued platelets would be available for patients. A fringe benefit would be greater flexibility of stock during 4-day bank holidays and other periods when stocks can become very low.

Storage of PC to 7 days is not new – it was permitted in the USA in the 1980's until 1986 when the FDA restricted storage to 5 days. This was not related to loss of platelet efficacy but because of concerns over the increased risk of bacterial contamination with increasing storage time. With increased interest and implementation of bacterial screening, some European countries have already extended the shelf-life of PC to 7 days. This has been facilitated by pre-storage removal of leucocytes, and by modern storage packs with better gas diffusion; both factors contribute to better platelet viability and function during storage.

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How does extending platelet shelf-life effect platelet function?

Assessing platelet function in platelet concentrates is not as straight forward as you may think, since no in vitro tests have been fully validated in patients after transfusion, and some functions which decline during storage can be restored following transfusion.

There are four basic levels of evidence for assessing the efficacy of PC:

- in vitro analysis
- Animal models of thrombocytopenia
- Recovery and survival of radio-labelled autologous PC in normal volunteers
- Platelet increment studies in thrombocytopenic patients.

In vitro testing: ***Tests in vitro that show a degree of correlation with viability following transfusion to healthy volunteers are:-***

- HSR - hypotonic shock response (poor viability <40%)
- extent of shape change (ESC)
- adenosine tri-phosphate (ATP) levels (poor viability <4 mol/10^{11} platelets)
- pH (poor viability <6.2 and >7.6)

pH is well maintained in PC stored in plasma for at least 7 days, with most studies showing pH >7.00<7.60 at day 7. Likewise most studies show that there is good preservation of platelet ATP and HSR scores of 40-65% at day 7 compared with 50-85% at day 1.

As the storage time increases, platelets become more activated. At day 7 around 30-50% of platelets express P-selectin compared with 20-30% at day 4/5. We don't fully understand the clinical implications of this. Some studies have suggested that increased platelet activation is associated with a decrease in platelet recovery following transfusion. But using animal models, others have shown that activated platelets are able to circulate and function in the recipient.

The expression of key platelet glycoproteins GPIb and GPIIb/IIIa are also well preserved during storage in plasma for 7 days, although there is a 40% decrease in the amount of fibrinogen binding to platelets stimulated with thrombin. In flowing blood models, platelet adhesion to fibrinogen and collagen is good at day 7/8 with values >85% of those at day 1.

Animal studies. Data from animal models of thrombocytopenia suggest that platelet recovery, survival and function are not significantly different after 7 days storage compared with 5.

Volunteer studies. There are no autologous transfusion studies on extended storage of PC conducted using buffy coat platelets because they are made from more than one donation. With apheresis PC, two studies have shown a decrease of 15-30% recovery and 15-20% survival between day 7 and day 5. In the USA, studies using PC prepared using the platelet-rich plasma methods show little difference in recovery and a decrease of 0-25% in survival over the same time period.

Patient studies. Corrected count increments 1-24 hours following transfusion of buffy coat PC to thrombocytopenic patients are similar whether they are stored for 5 or 7 days.

In summary, therefore, the data on platelet storage beyond 5 days suggest there may be a degree of loss of viability and function. For more details of the data, please see our recent review (Cardigan & Williamson, 2003).

What about platelet additive solutions?

Currently, platelets in additive solution are produced only for patients with severe reactions, but it would be possible to produce all platelets in additive solution. Provided 30% of the plasma is left on the platelets, viability to day 5 is unaffected as assessed in the laboratory. Some clinical studies, though not all, have shown slightly lower corrected count increments. Removal of 70% of the plasma is likely to have benefits in reducing the risk of reactions, and of transfusion-related acute lung injury. The NBS is therefore conducting laboratory studies on licenced additive solutions to look at storage of platelets in them to day 7. Newer solutions being developed internationally have the potential to offer storage to day 9 and beyond!

Where do we go from here?

The fundamental question is whether platelets at day 7, either in plasma or additive solution, are good enough to prevent and control bleeding in thrombocytopenic patients. It is not feasible to conduct large, highly expensive multicentre trials of every modification to platelet storage. There are currently no internationally agreed standards for what constitutes acceptable platelet viability, something the Biomedical Excellence for Safer Transfusion (BEST) working party of the International Society for Blood Transfusion is developing. We are actively involved in these discussions, and will be participating in a study of 7 day platelets in volunteers next year.

We are currently compiling data on platelet function in PC prepared and stored with methodology currently used by the NBS. This will enable UK

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advisory committees to take a view on whether platelets at day 7 of storage are acceptable. The issue will also be discussed with users through the National Blood Transfusion Committee.

Extended shelf life platelets again raise the issue of striking the right balance of safety versus efficacy. Many safety initiatives in use or under consideration involve some detriment to the product, whether through physico-chemical means to kill pathogens or by extension of shelf life. Ongoing discussions with users will be an important part of achieving the correct balance.

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Principles of Blood Donor Selection Policies

Blood Transfusion Services such as the NBS have to collect enough blood which is also safe for transfusion. These conflicting requirements need constant attention. Safety is even more of an issue following Mr Justice Burton's legal ruling in 2001 which makes the NBS liable for any defective blood product it issues for patient use. This was in the wake of transfusion-transmitted hepatitis C.

In principle, three main strategies can be used for reducing the risks of infecting patients with blood collected from people harbouring transfusion-transmissible diseases – careful donor selection; mandatory testing of collected blood for markers of infection; and treating the final product with microbial-inactivating agents. All three strategies are now used in the UK – the most recent development is the treatment of plasma for babies and young children with methylene blue and UV light while processing it into FFP. This kills lipid-coated viruses and bacteria to several orders of magnitude (6.5 logs in the case of West Nile Virus). However, none of these approaches can be absolutely foolproof. Not all microbes can be tested; no test can be 100% specific and 100% sensitive and microbial inactivation procedures are still in their infancy (although they hold much promise, even perhaps eventually for prion inactivation). For these reasons it would not be appropriate to lower selection standards simply because we appear to have a better testing or inactivating system.

This article focuses on donor selection procedures, however, these are also vulnerable. They depend crucially on donor honesty, which is best sustained in an atmosphere of trust and understanding by the community at large – something to which, arguably, we still aspire rather than achieve. However, even the most honest and apparently healthy donor can harbour a condition which may kill a recipient – which is why the hunt is still on for a vCJD test. Sadly the NBS can be a victim of public attitudes which illustrate a distrust of 'authority'; we have some distance to go in attaining universal respect. A recent survey has revealed that some people assume that donor selection rules are written by 'a committee of professors in a back room' – implying secrecy and unfamiliarity with behavioural and societal norms. Of particular concern are the frequent accusations of unfair discrimination by advocates of the gay community. These sometimes centre on perceptions of human rights. Our view is that although everyone has a right to be considered for blood donation, the rights of recipients (to get blood which is as free as possible from the risk of transmitting any disease) take precedence. However, any prospective donor who is deferred has the right to an honest and full explanation (although they do not have to be convinced). These explanations must be based as far as possible on relevant epidemiology (such as current incidences of sexually transmitted infections - STIs) and on factors such as the pharmacodynamics of potentially teratogenic medications. All are regularly reviewed and updated in light of new information – based as far as possible on good evidence.

Donors must weigh at least 50 Kg (7st 12lb) as the amount of blood collected – usually about 490ml – should not exceed 13% of their circulating volume. To exclude anaemia before donation all donors have an Hb estimate from a finger-stick blood sample. At the session donors are handed an Information Pack and complete a health questionnaire in a 'tick-box' format. To help speed up the donation process, donors now receive the health questionnaire by post and can bring the completed signed form to the session. This addresses their lifestyle (including sexual), medical history (medication, recent surgery, etc), other infection risks (including vaccinations and family history of CJD), and travel history (relevant mostly to malaria). The Pack also contains two leaflets: 'Keeping Blood Transfusion Safe' describes in more detail some of the conditions which cause temporary or permanent deferral; and 'Important Information on Blood Donation' gives basic advice on the donation process. All first time donors are also given a face-to-face interview to clarify answers and to answer further questions including any history of STI.

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Recent risk estimates (the chance that a product manufactured from a single donation – in spite of being marker negative – will pass an infection on to a recipient) are: for hepatitis B, 1 in 0.9 million; HIV 1 in 8.3 million; and HCV 1 in 30 million. Repeat donors (whose last donation was less than two years ago) have a lower incidence of conventional markers of infection, and as certain products (red cells for neonatal transfusions, FFP and platelets collected by apheresis) are prepared only from blood from repeat donors, they are relatively safer. Such low figures crucially depend on continuing the current donor selection policies. Risk estimates for methylene blue-treated FFP are confounded by the virus inactivation procedure, but are even lower. FFP imported from countries with a low incidence of BSE has the additional theoretical advantage of being risk-free from vCJD transmission.

Donor selection procedures are still needed. They have to be fair and justifiable as – being of necessity discriminatory – they can attract great public interest. Although there is always room for improvement, they are constantly being refined and improved.

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NBS Performance Measures for the National Blood Transfusion Committee

The NBS measures its performance in a number of ways, both internally and with the Department of Health. The National Blood Transfusion Committee (NBTC) also has a remit to "Review the performance of the services provided by the National Blood Service." At each NBTC meeting a set of previously agreed performance measures are presented by the NBS for consideration and comment by the committee. These agreed performance measures are also reproduced regionally for Regional Transfusion Committees. The measures do not currently represent the full range of NBS services and are likely to develop with time.

The latest set of performance measures (covering April – June 2003) were presented to the NBTC on 29th September. These covered aspects of performance such as the red cell and platelet stock levels held by the NBS, the age of stock and the number and category of compliments received as well (see table 1).

How is the NBS performing?

The area of NBS performance, which has drawn the most comment, has been the age of blood upon arrival at hospitals. This was caused by an increase in NBS stocks during 2002/03. Figure 1 shows that the average age of blood at issue had dropped from about 14 days old to approximately 10 days old by the end of June. This followed comments from hospitals regarding the age of blood and the resultant wastage in hospitals. The total red cell stock held by the NBS has now fallen from approximately 8 days to approximately 4 days. It is planned to hold the total stock cover at approximately 5 days for the remainder of the financial year.

Customer complaints

Delivery problems continue to be the largest area of concern, although many of the most frequent areas for complaint have been falling. All centres received some complaints during the quarter, with eleven compliments received as well. (See table 1).

Customer satisfaction

The first national satisfaction survey was issued to hospitals in June 2003 and full results are available on our website *www.blood.co.uk/hospitals*. A total of 309 surveys were sent through the post to all Transfusion Laboratory Managers. 206 completed surveys were returned. This represents an excellent return rate of 67%. Thank you to everyone who completed a copy of the survey.

The survey was designed following in-depth interviews with selected Transfusion Laboratory Managers to determine what was important to them regarding the service provided by the NBS. It is planned to conduct this survey three times a year.

The areas of greatest satisfaction identified were: safety, quality, labelling & packaging of blood and blood components and the service provided by NBS drivers. The areas of least satisfaction identified were: quality of invoicing, age of products, Red Cell Immunohaematology reporting and the service from courier drivers.

Respondents were also asked to identify the areas of greatest importance to them. These were recorded as: safety of products, quality of products, time taken with urgent orders and accuracy of orders.

The areas considered to be of least importance were: frequency & content of communications, time taken with routine orders, service provided by drivers, quality of invoicing and complaints handling.

The results of this and future surveys will be used by the NBS to target areas for improvement.

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Frequently Asked Questions (FAQs)

What does the NBS do to ensure that donations with an unusual appearance are safe for transfusion?

Significant differences in the appearance of units of blood or plasma often attract comment from visitors to blood processing laboratories, especially those expecting to see a textbook dark red or straw coloured liquid!

Much of this is due to normal physiological variation in the concentration of metabolites such as bilirubin and lipid in the donor's blood. A few donors have Gilbert's syndrome (associated with persistently raised bilirubin) and some have lipaemia which may indicate dietary or hereditary factors. Taking some oral tanning agents or contraceptives can impart a characteristic orange or green colour respectively to plasma. Raised carboxy haemoglobin in heavy smokers can look like arterial blood! Rarely, an unusually thick buffy coat highlights an abnormally high leucocyte count and blockage of the leucodepletion filter can indicate cold agglutination of donor red cells or sickle cell trait. In some cases advice from an NBS clinician is required in order to resolve the situation for the donor and potential recipient. However, the above variation in appearance, although prompting an occasional rejected unit, would generally be expected to have little bearing on the outcome of transfusion.

Nevertheless, an abnormal appearance is sometimes the hallmark of a bacterially contaminated unit which could, if undetected, lead to a serious or even fatal transfusion reaction. This can include the presence of haemolysis (especially if the blood is permanganate coloured), a flocculent precipitate or clotting. Detection (and differentiation from the trace of haemolysis associated with the red cell storage lesion) requires the utmost vigilance on the part of all involved in the preparation, handling and administration of blood components and an appreciation of their normal range in appearance.

In the absence of international standards, it is essential for the NBS to set standards for visual inspection of blood and to apply these during blood collection, processing and at issue. Historically such standards have been developed and applied by individual blood centres. They have taken the form of colour charts, comparators and photographs. Included are standards for lipaemia, icterus, haemolysis and for red cell contamination of plasma and platelet products. In some cases, their use has been rigorously enforced through incorporation into SOPs with training of staff and involvement of local hospitals. All of this has helped to make decision making in this area more objective.

The establishment of an NBS strategic function for the processing, testing and issue of blood has provided an excellent opportunity to review and agree the use of such standards nationally and this process has now started in earnest.

What are the recommendations for investigation and management of patients who suffer non haemolytic febrile, allergic or anaphylactoid reactions to plasma or platelet transfusions?

If the patient suffers a serious reaction, stopping the transfusion, if appropriate, and immediate resuscitation is obviously paramount. All such serious reactions must be reported to the hospital Haematologist. The duty Consultant at the local Blood Centre should be contacted and depending on the case history, will advise about investigations to exclude transfusion transmitted bacterial infection, TRALI and IgA deficiency.

Prior to universal leucodepletion of blood and blood components in the UK, a frequent cause of both severe and less severe febrile/allergic transfusion reactions to platelet transfusions, was the presence of HLA antibodies in the patient's plasma reacting with leucocytes in the transfused dose of platelets. Now that all components are leucodepleted, the presence of HLA antibodies in the patient is not a likely cause of a febrile or allergic transfusion reaction.

Once infection, TRALI and IgA deficiency have been excluded for severe reactions, the most likely cause of febrile, allergic and anaphylactoid reactions to plasma or platelet transfusions is a reaction to plasma proteins. Whilst it is possible to test for some plasma protein antibodies, such investigations are not undertaken since management of the case would be the same whether plasma protein antibodies are detected or not. Mild plasma reactions can often be prevented in subsequent transfusions by the prophylactic use of piriton and hydrocortisone. If reactions to plasma proteins become severe, for example if there are extensive rashes, rigors or swelling of the throat or facial tissues causing shortness of breath, then further transfusion of any plasma containing products should be avoided. This can be achieved for platelets by using platelets in 100% additive solution (PAS) and for red cells by using washed cells. If a patient who has suffered a severe allergic reaction of this nature requires a further source of clotting factors, then the hospital Haematologist may need to discuss the individual case with the Blood Centre Consultant.

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Table 1: Complaint by Category

	February	March	April	May	June	July
Clinical/scientific advice				1		1
Comment	3	3	1	5	1	1
Compliment	2		2	4	5	1
Damaged pack	5	2	1		1	5
Delayed reporting – DDR	1	3	1		2	
Delivery	8	11	15	10	15	16
Delivery failure – DDR	1	2	1	2	4	3
Faulty product	11	4	6	8	4	8
Incorrect delivery	1	1	1	2	4	2
Incorrect expiry date supplied	1	3	6	4	3	4
Incorrect/no product supplied	3	3	4	9	1	3
Incorrect packaging	2	2	1	1		1
Incorrect reporting	2	1				1
Invoicing		2		1		2
NBS response/ communication	1	3	3	3		4
Product & delivery problem		2				3
Product labelling	3	5	4	7	4	7
Product unavailable	3					
RCI Reagents	5	10	24	12	17	7
RCI Reference	4			2	2	1
Staff attitude		1		1	1	2
Unclassified						2

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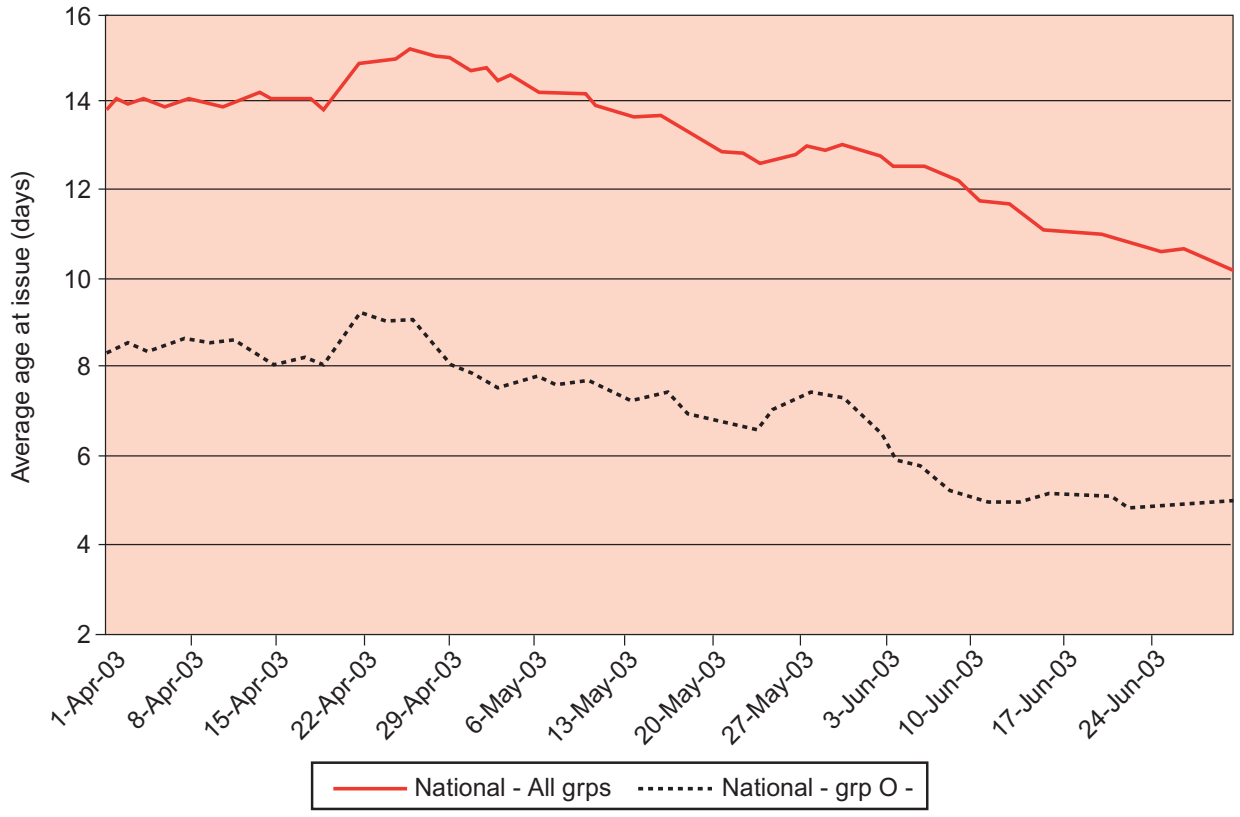
Figure 1: Red Cells Average Age at Issue - All Groups & Group O -



Handy Hints

All doctors at some stage in their clinical practice are involved in the transfusion of blood and blood components. Here is a suggestion to ensure that newly qualified doctors are aware of the Hospital Transfusion Policy:

- Ensure your Transfusion Practitioner is included in the New Doctors Induction Day
- Include a visit to the Transfusion Laboratory as part of their induction
- Give them a list of useful numbers they can ring for advice
- Follow up in a few weeks auditing information given to see if they have found this helpful.

Thanks to Wrexham Maelor Hospital for providing this 'Handy Hint'.

Have you any 'Handy Hints' to add to a Better Blood Transfusion Tool Kit? We are looking for examples that have made a real difference to blood usage and better blood transfusion that we can share across the whole blood transfusion community. Please send your example to the Editor for possible inclusion in the next edition of Blood Matters.

2004 Diary of Events

MONTH	EVENT	ADDRESS / WEBSITE
FEBRUARY: 19 - 21	EHN (European Haemovigilance) Zurich	www.EHN-org.net
MARCH: 18 - 19	NATA (Network for Advancement of Transfusion Alternatives) *Greece*	www.nataonline.com
APRIL: 1 - 2	TRALI Consensus Conference *Toronto*	Blajchma@mcmaster.ca
19-21	BSH – Annual Scientific Meeting *Cardiff*	www.b-s-h.org.uk
21 – 22	BBTS Apheresis & Blood Collections SIG *Birmingham*	www.bbts.org.uk
20 - 21	British Association of Tissue Banking Annual Scientific Meeting *Edinburgh*	www.snbts.org.uk

Blood Matters is prepared and issued by the National Blood Service, Oak House, Reeds Crescent, Watford, Herts WD24 4QN (Telephone 0208 258 2700)

CPD Questionnaire

Q1 Overall rate of bacterial contamination of platelet packs is
a) higher in apheresis packs
b) higher in the UK
c) approximately 1 in 200
d) approximately 1 in 100

Q2 Use of a diversion sample pouch at donation
a) will reduce risk of initial contamination of blood donations by 70%
b) effectively removes the skin plug, together with any potentially harmful skin flora
c) acts as a reservoir to pool blood in a donor with asymptomatic bacteraemia
d) will be used soon

Q3 Extended shelf-life of platelet packs
a) to 7 days is not currently practised anywhere
b) to 7 days would result in significant deterioration in the function of the transfused platelets
c) to 7 days will require routine testing for bacterial contamination
d) to 7 days will reduce the incidence of TRALI

Q4 Pathogen reduction systems
a) will remove the need for donor selection policies
b) will eliminate infection risks of transfusion
c) are not yet in routine use
d) are routinely in use for some FFP

Q5 Amount of whole blood collected from a donor should not exceed
a) 10% of circulating volume
b) 12% of circulating volume
c) 13% of circulating volume
d) 14% of circulating volume
e) 15% of circulating volume

Q6 Pathogen inactivation of FFP by methylene blue and U-V light
a) kills lipid-coated viruses
b) is effective against prions
c) is ineffective against bacteria
d) kills all viruses

Q7 Recent risk estimates for Hepatitis B are
a) 1 in 90,000
b) 1 in 900,000
c) 1 in 9,000
d) 1 in 900

Q8 Stored platelet viability to day 5 is unaffected
a) if 30% of the plasma is left
b) if 10% of the plasma is left
c) if 20% of the plasma is left
d) if all plasma is removed

Q9 As reported in the 6th SHOT report 2001-2002
a) All transfusions are clinically indicated
b) 25% of errors occurred in hospital laboratories
c) 40% of errors are due to a single factor
d) 66% of errors occur in the clinical area

Q10 As reported in the 6th SHOT report 2001-2002
a) there have been no reports of TA-GvHD since 1999
b) all participating hospitals reported incidents last year
c) most anaphylactic and allergic acute transfusion reactions are adequately investigated
d) reports of TRALI have reduced