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Blood Matters

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Editorial

This edition of Blood Matters is concerned with appropriate use of blood components and some of the strategies that can be used to avoid allogeneic red cell transfusion. It is often difficult to target the best areas of practice for implementation of "alternatives" to transfusion unless there is baseline data giving some idea of how much resource could be saved. Limited data regarding who is being transfused, and why, can reduce the effectiveness of guidance about appropriate use of blood and when to invest resources in alternatives.

Traditionally the NBS has been rich in data on donor demographics, as well of course as on all aspects of blood safety, processing and R & D and yet questions about exactly which patients are using blood components have been harder to answer. Thanks to development in the NBS within the last few years, patient facing activity is now much more prominent, in particular through the Hospital Liaison function and the Patient's Clinical Team (PCT). Crucial information is now being gathered which allows effective targeting of appropriate interventions to reduce unnecessary blood component use.

The Trent audit of appropriate use of red cells is one such example of the work of a member of the PCT, Dr Hafiz Qureshi, and his colleagues. This work acknowledges the reduction in red cell use in the UK in the last few years and is now aiming to identify further any areas where there might still be improvement in practice. Nineteen hospitals have participated, with data on over 1200 transfusion episodes being analysed using the current BCSH guidelines (2001) as the audit standard for red cell transfusion. Up to 20% of transfusions of red cells may be deemed to be inappropriate from this analysis. However, in order to reduce this figure, detailed data on the decision making process (i.e. who is making the decision, how and why) would allow education, and if necessary competency assessment, to be targeted to the right clinical groups, limiting those who are allowed to prescribe blood to those who have been fully trained and educated. I am sure that the Trent data will spark off further studies into whether it is a certain kind of prescriber that prescribes blood inappropriately or whether it occurs in a particular patient group or at specific phase of the patient's pathway through hospital. The study also highlights the variance between different hospitals in terms of the amount of inappropriate transfusion going on - as does the article by Carol Cantwell on use of group O RhD negative red cells. Many questions are still unanswered as to exactly why – but I am sure that further sleuthing by members of the HL team will lead to effective strategies to improve appropriateness of transfusion.

The EASTR study goes a step further towards understanding who uses the blood components and how transfusion decisions are made. It has gathered national data on blood use in England for twelve months and includes long-term follow up of all the patients with survival data. This study looks not just at red cell transfusion but also at FFP and platelet use.

Analysis of the use of other components is becoming more and more critical – as red cell use has declined, platelet use has continued to increase with several implications for the blood services in terms of maintaining the supply, and the logistical decisions surrounding collection and processing. In SW England in particular platelet use has increased and this edition of Blood Matters contains a summary of a one-month audit instigated by another member of the PCT, Dr Janet Birchall, and colleagues. It shows a majority of platelets being used in haematology patients and most of these for prophylaxis. Once again, in order to fully understand why a platelet component should be prescribed inappropriately more questions need to be asked regarding who the prescriber is, the exact clinical scenario and whether the decision is a medical one or a logistical one.

Once areas of high red cell (or platelet) usage are identified alternative practices may be considered to be suitable ways of cutting down on unnecessary transfusions. Alternatives to red cell transfusion include pre-operative autologous deposit (PAD), erythropoietin (EPO), and intra operative cell salvage (ICS).

Dr Frank Boulton, another PCT member, has written a helpful synopsis of the new BCSH guidelines for pre-deposit autologous blood donation. This process is now only permitted in Blood Establishments within the EU and the indications are also much more restricted than previously. In the UK PAD is only available to patients with complex constellations of antibodies undergoing certain types of surgery (including paediatrics).

The use of EPO in cancer-associated anaemia has been evaluated recently by NICE and an outline of these decisions and the reasons behind them has been written by Dr Simon Stanworth and Dr Hazel Tinegate, of the PCT. Although the initial recommendation from NICE was that EPO should be used in very limited circumstances, this is being extended following an appeal. The article discusses the evidence of effectiveness of EPO in this setting and makes the point that the patient's perspective is hugely important in successful cancer management. However the role of EPO as a serious contender as a blood saving device remains to be proven and there is a need to weigh up absolute effectiveness with cost effectiveness – EPO may well be able to save blood as a resource, in absolute terms, but there is a major cost implication as things stand at present.

Intra-operative cell salvage has a proven track record for reducing allogeneic blood usage and saving resources and money in an increasing range of surgical procedures. However its implementation in NHS Trusts and private hospitals across the UK has been patchy partly because of a lack of know-how. A training framework has now been developed and a competence assessment workbook is available – this very welcome development is described in an article

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by Catherine Howell and Joan Jones respectively head of the Transfusion Liaison Nurse scheme in the NBS and of the Hospital Transfusion Practitioner scheme in the WBS.

I am sure you will find this addition of Blood Matters very thought provoking. In particular it shows the essential role of the HL Team and the Patient's Clinical Team in informing decision making and policy within the NBS. Further development of their relationship with the users and prescribers of blood will help to define the structure of NBS services and guide appropriate use of limited resources in the future.

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Who Uses Blood? Introducing the EASTR Study

Blood transfusion is an important part of modern medical care but in the last few years there has been a steady decline in red cell demand from hospitals. Like all other parts of medicine, transfusion practice in hospitals is constantly evolving as clinicians begin to unravel who does and who does not require transfusion. At this time it therefore seems particularly important to understand how blood is being used and which diseases and operations require transfusion. This article has been written to illustrate how hospitals and blood services can benefit from information on who uses blood and to introduce the first national English study of blood transfusion.

Why do we need data on blood use?

Blood services have closely followed trends in blood collection and hospital issues for many years. At the other end of the transfusion chain, understanding who uses blood is an equally important part of planning an effective transfusion service in blood centres and hospitals. These data can be used to:

1. Calculate more accurate estimates of future blood use. Knowledge of the patient groups that are being transfused means that changes in medical and surgical practice can be assessed and calculations altered as necessary.
2. Improve planning for blood shortages. The National Blood Service and hospitals have prepared an integrated contingency plan for blood shortage. A better understanding of which patients are being transfused will help to ensure these plans remain relevant and their goals are achievable.
3. Assess the potential of blood saving techniques between different patient groups and allow these to be targeted to those surgical procedures or diagnostic groups where their benefit will be greatest.
4. Provide denominator data to interpret haemovigilance reports. For example 10% of SHOT reports up to 2004 were for patients aged less than 18 years. A regional study of blood use in the North of England in 2004 reported that these patients received only 4.2% of all red cells. This disparity suggests that errors are more likely to occur with paediatric transfusion (although a difference in reporting patterns could account for some of this difference as well).
5. Estimate the uptake and cost of developments in blood components, including safety initiatives. Information on blood use is particularly important when a new component is only intended for a limited number of recipients e.g. Methylene Blue treated FFP for children.
6. If data on the survival of transfused patients is available, these can inform the analysis of costs and benefits of safety initiatives. This is particularly true with diseases thought to have a long incubation period such as vCJD.

How can hospitals benefit?

At first glance it may seem that only blood services will gain from this sort of information. In the first instance data can be used to challenge traditional views of which clinical specialities or diagnoses use blood. For example several British studies have now reported that medical transfusions are more common than those given to surgical patients. Hospital transfusion teams can use regional or national data to prioritise and focus their work by identifying clinical areas for blood saving, further study or clinical audit and education. Blood saving measures typically target elective surgery patients, but common medical indications for transfusion such as gastrointestinal bleeding and non-haematological cancer should also be considered.

Some countries and regions (e.g Scotland or Sweden and Denmark) have established population based registers of all transfusion episodes linked to clinical coding information. This approach allows comparison of transfusion rates between hospitals and benchmarking of blood use per specified procedure (e.g total hip replacements).

The EASTR Study

Until now there has been no national data on blood use in England. Regional data has been collected in the North of England and in London and the South-East. The NBS/MRC Clinical Studies Unit established the EASTR (Epidemiology and Survival of Transfusion Recipients) study to meet the need for up to date national information on NBS transfusion recipients. 29 representative hospitals across England participated in the study. Complete blood bank records for the twelve months to September 2002 were obtained from each hospital and a monthly quota system was used to select over 14,000 red cell, FFP and platelet recipients. Details of the indication for transfusion have been extracted from hospital information systems which record diagnostic and procedure codes for all hospital admissions or day case attendances. The survival of transfusion recipients will be followed for 10 years using the National Health Strategic Tracing Service, a central register of all NHS patients.

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There were initial delays to the study because of concerns around the use of patient identifiable information. However data collection is now complete and analysis is underway. The study group hopes to publish initial results within the next twelve months.

Conclusions

The EASTR study is the first national study of blood recipients in England. It aims to provide important information to inform transfusion medicine at both national and local levels.

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Acknowledgements
Thanks to all staff at participating hospitals who assisted with data collection for the EASTR study.

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Trent Regional Audit of the Appropriate Use of Red Cells

During the last few years there has been a significant reduction in the use of red cells. This has been achieved by educating clinicians, adapting restrictive transfusion thresholds, and introducing transfusion alternative strategies such as intra- and post-operative cell salvage.

Whilst these measures have been effective in reducing the inappropriate use of blood to an extent, recent audits of blood use suggest that there is considerable room for further improvement. The Trent Regional Transfusion Committee commissioned a regional comparative audit of the appropriate use of red cells in a variety of clinical settings in 2005. Data was collected on 1204 red cell transfusion episodes from 19 hospitals in the region. The audit findings and recommendations are summarised in the following sections.

The aim of the audit was to gain an awareness of red cell transfusion triggers, taking account of relevant clinical information and co-morbidities, at which Medical, Haematology, ITU, Primary Hip and Primary Coronary Artery Bypass Graft (CABG) patients were being transfused in the Trent region. Red cell transfusion data was collected for 20 consecutive transfusion episodes for each of the above clinical categories.

Audit Standards

The audit standards used to assess the appropriateness were based on the current BCSH guideline - 100% indicates the patients would almost always be expected to receive red cell transfusion, 0% indicates that the patient(s) should not be transfused at the given haemoglobin levels.

Table 1 - Audit Standards

Indicator	Expected Compliance	Exceptions
Hb>10 g/dL	0%	• Active Bleeding • Haematology patients undergoing chemotherapy or disease related marrow failure
Hb<7 g/dL	100%	
Hb between 7-9.9 g/dL **AND** no further blood loss anticipated	0%	• Elderly patients (>70 years) • Ischaemic heart disease • Respiratory disease • Significant symptoms of anaemia present (e.g. dyspnoea, angina, worsening heart failure) • Haematology patients undergoing chemotherapy or disease related marrow failure. Transfusion at Hb 9g/dL or less considered appropriate.
Transfusion should aim to sustain Hb levels of 8 to 9 g/dL	100%	• Elderly patients (>70 years) • Ischaemic heart disease, heart failure • Respiratory disease

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The appropriateness of each transfusion episode was reviewed by six medical consultants, four haematologists, one anaesthetist and one orthopaedic surgeon. Each clinician initially reviewed the entire audit data individually, and those episodes where all six clinicians did not completely agree were subsequently reviewed by the clinicians as a group and a consensus was reached for all transfusion episodes.

Results

19 out of 21 hospitals in Trent participated in the audit, providing data for 1204 transfusion episodes. Mean pre-transfusion Hb for all categories was 8 g/dL (2.8-15.9), and mean post transfusion Hb was 10.2 g/dL (5.6 – 16.4, SD=1.5).

- 246/1204 (20.4%) patients were transfused when Hb was less than 7g/dL.
- 862/1204 (71.6%) patients were transfused when Hb was between 7 and 10g/dL.
- 87/1204 (7.2%) patients were transfused when Hb was greater than 10g/dL.
- Overall, 911/1204 (76%) transfusion episodes were considered appropriate according to the audit standards described above
- An additional 49/1204 (4%) transfusions were considered appropriate, but the number of units transfused was inappropriate. In all such cases it was considered that the patients were over-transfused.
- 145/1204 (12%) transfusion episodes were considered entirely inappropriate
- 99/1204 (8%) transfusion episodes could not be assessed due to insufficient information or poor quality of data.

Figure 1 – Comparative data on % appropriate transfusions for participating hospitals

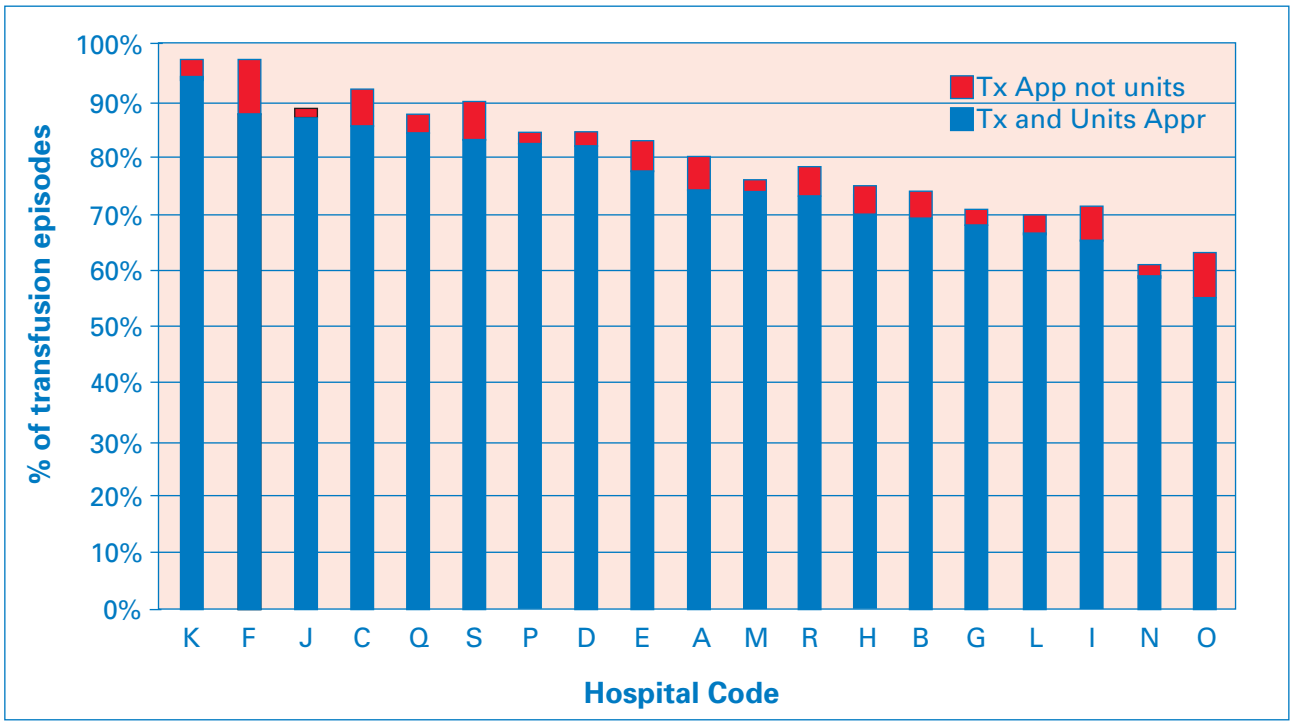

Figure 2 - Mean Pre and Post Transfusion Hb Levels for each speciality / procedure

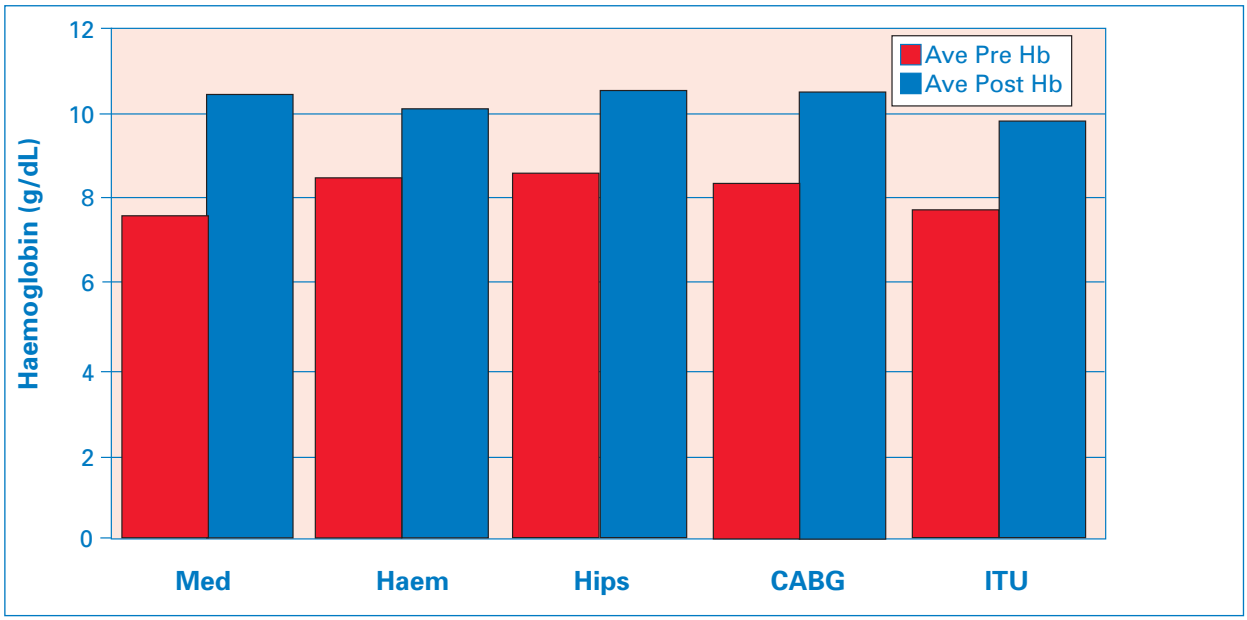

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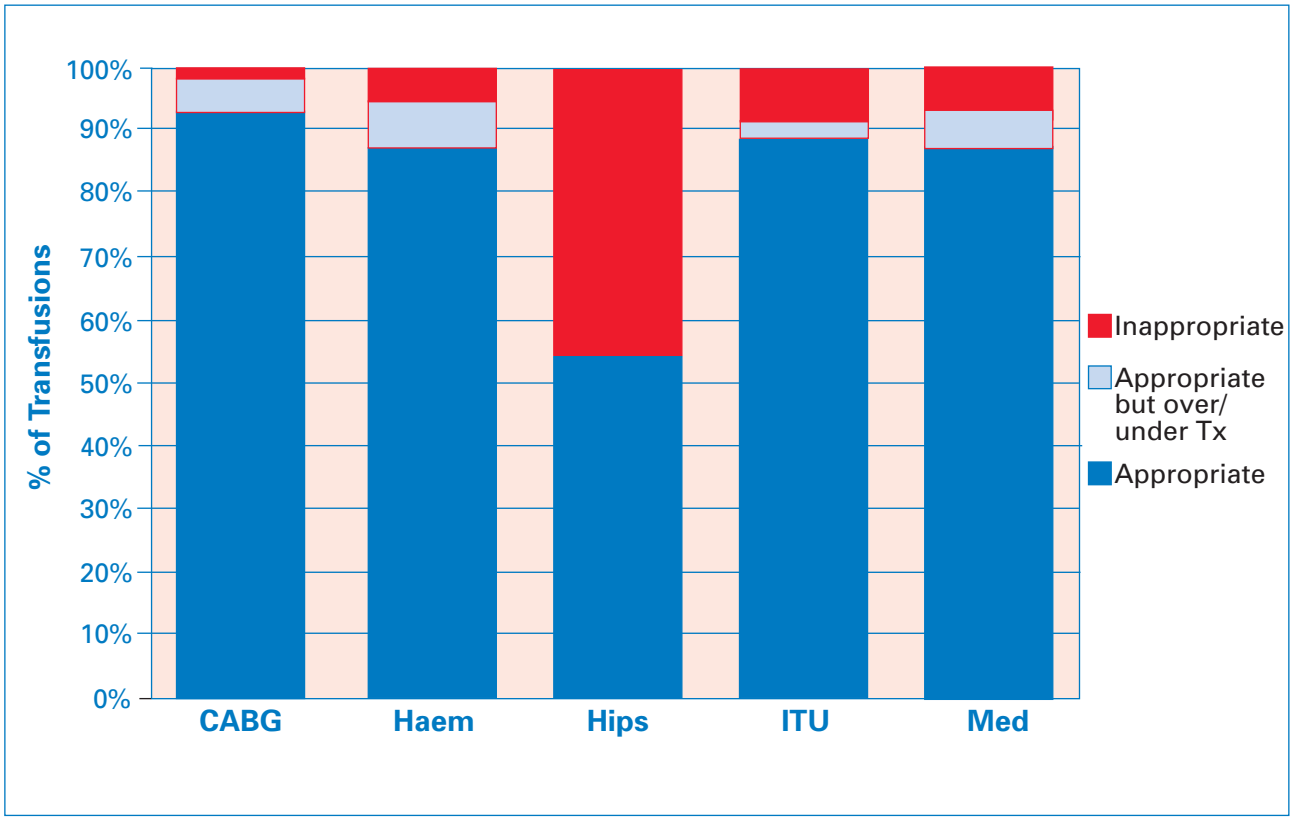
Figure 3 – Appropriateness of Transfusion for each speciality / procedure



Overall, the majority (911/1204, 74%) of red cell transfusion episodes were considered appropriate and in accordance with the current BCSH guidelines. An additional 4% of transfusions (49/1204) were considered appropriate in terms of indication to transfuse but the number of red cell units given was thought to be inappropriate, all such cases were considered over-transfused.

Among the remaining 20% (244/1204) transfusion episodes, 12% (145/1204) were considered clearly inappropriate. In addition, in 8% (99/1204) of episodes, the appropriateness could not be determined because of insufficient information provided. Taking this into account, it is possible that up to 20% transfusion episodes may have been inappropriate. This is a similar level to that reported in other recent audits (Northern Ireland RTC, 2006).

The highest level of inappropriate transfusions was observed in patients undergoing primary hip replacement surgery whereas most patients undergoing primary CABG were transfused appropriately. This audit also highlights considerable inter-hospital variation in the level of inappropriate transfusions recorded (10% to 38%).

The results from this audit have been widely disseminated with the recommendation that all hospitals should develop and follow red cell transfusion protocols based on the current BCSH guidelines. A re-audit is planned during 2007.

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Acknowledgements

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O RhD Negative Use and Abuse

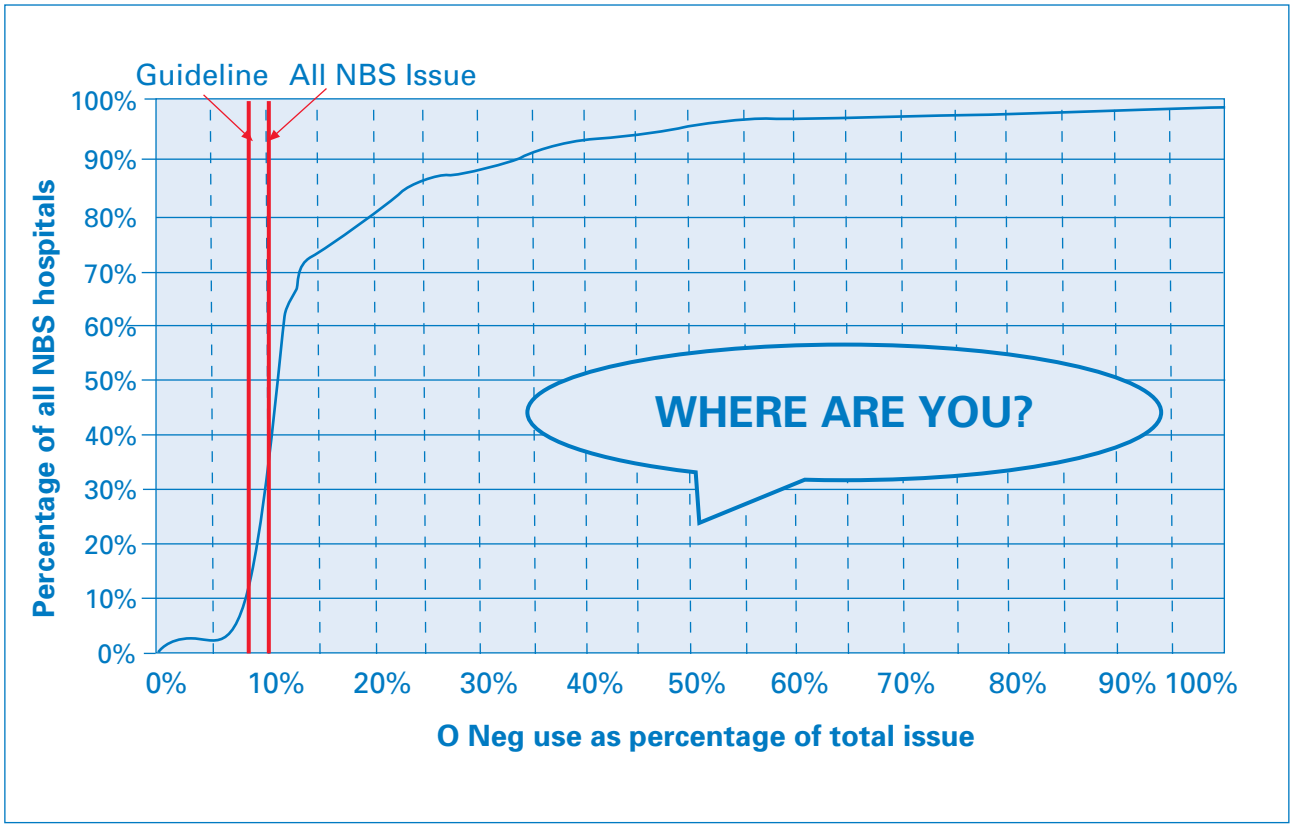
In the UK, dependent upon geographical location and ethnic mix, between 6.7% and 8.3% of the population are O RhD Negative. In 2005-2006 the National Blood Service (NBS) issued 197,880 units of O RhD Negative; 10.2% of all NBS issues. The NBS therefore needs to collect almost 2 percentage points more O RhD Negative than expected comparing actual issues with the population expression. Fulfilling this demand for O RhD Negative poses a significant challenge. However, the NBS Clinical Policies Group has suggested that usage should be around to 8 to 8.5% of overall blood usage. In the past year there have been two new investigations into the reasons for the discrepancy between actual and expected usage. Their findings are summarised below.

In May 2006 UK NEQAS issued an emergency situation simulation to determine what pre-transfusion testing was performed prior to release of blood. Patient 1 was an O RhD Positive male needing blood in 10-15 minutes. Although they had already grouped the patient as O RhD Positive 50 out of 414 laboratories selected O RhD Negative. This finding correlates with the 2003 UK NEQAS report which investigated emergency testing and Flying Squad (FS) showing little change since then. It would appear that at least 10% of hospitals are, because of inherent risks associated with (manual) urgent testing, issuing O RhD Negative irrelevant of the patient's group. The NBS Clinical Policies Group recommend use of O RhD Negative in emergency situations, only **until** the patient's blood group has been determined, with a limit of two units, if possible.

In June this year the Blood Stocks Management Scheme (BSMS) open meeting included a workshop facilitated by Maggie Pailing and Dr Craig Taylor, on the use of O RhD Negative red cells with the aim of understanding the variables associated with practice. In their report they identified many areas contributing to the observed wide variation in stock levels, rotation and ordering. The stockholding of O RhD Negative was clearly influenced by the proximity of the laboratory to the Blood Centre. Unsurprisingly, laboratories that were further away from Blood Centres carried more stock. They also found that at weekends and at night hospital staff ordered more O RhD Negative as a "security blanket". The workshop also identified that laboratories with small blood requirements had particular problems with stock rotation and units expiring and that they had difficulties in setting up arrangements for larger laboratories to take their older stock.

The use of FS was also discussed. There was extensive variation in practice with some hospitals holding 2 FS and others 6. This variation is backed up by the 2003 UK NEQAS review which reported that the availability and use of FS blood varies enormously: the number of sites within each institution varies from 1-8 (median 2, mode 1) and its use ranges from 0 to 100 times/year (median 5). It is therefore obvious that at any time there is a lot of O RhD Negative blood reserved for possible FS use just sitting in blood banks decreasing in shelf life. It was recognised that laboratory staff and clinicians do not always agree on the number of FS made available.

Data shown is hospitals' O RhD Negative as a percentage of total issue in 2005/06.



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The workshop felt that the NBS itself contributed to the higher usage of O RhD Negative due to the infrequency of deliveries and their timings and the use of O rr blood for sickle cell patients when there are no group O Ro units available.

The workshop group were unsure whether the 8 to 8.5% recommended usage of O RhD Negative is achievable for all laboratories given the varying issues and constraints but they felt it was clear that practice in many areas could be improved.

Review of the BSMS data on O RhD Negative red cells shows clearly that some hospitals are able to manage their stocks at this level. However, in a few cases O RhD Negative issues were over 20% of total; in real terms this translates to 1 in 5 or more units issued by the NBS is O RhD Negative. In hospitals where the demand for group O RhD Negative red cells is higher than recommended in the guidelines, there is generally a resulting high expiry and/or inappropriate usage. The median percentage issue of O RhD Negative is 11% and 85% of hospitals are issued more than the recommended guideline percentage of O RhD Negative.

The NBS has developed an O RhD Negative donor base greater than the percentage naturally occurring in the population. Any additional increases in O RhD Negative requirements would be difficult and expensive to achieve. If all hospitals reviewed their stock and usage of O RhD Negative with an aim of trying to achieve the recommended 8 to 8.5% O RhD Negative red cells, it would allow reserves for neonatal or complex phenotype units. As a start each of us can find out our own laboratory's percentage O RhD Negative issue using the BSMS VANESA system.

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Acknowledgements:

Clare Milkins, UK NEQAS, Judith Chapman & Rob Hick, BSMS, Maggie Pailing, NBS Hospital Liaison.

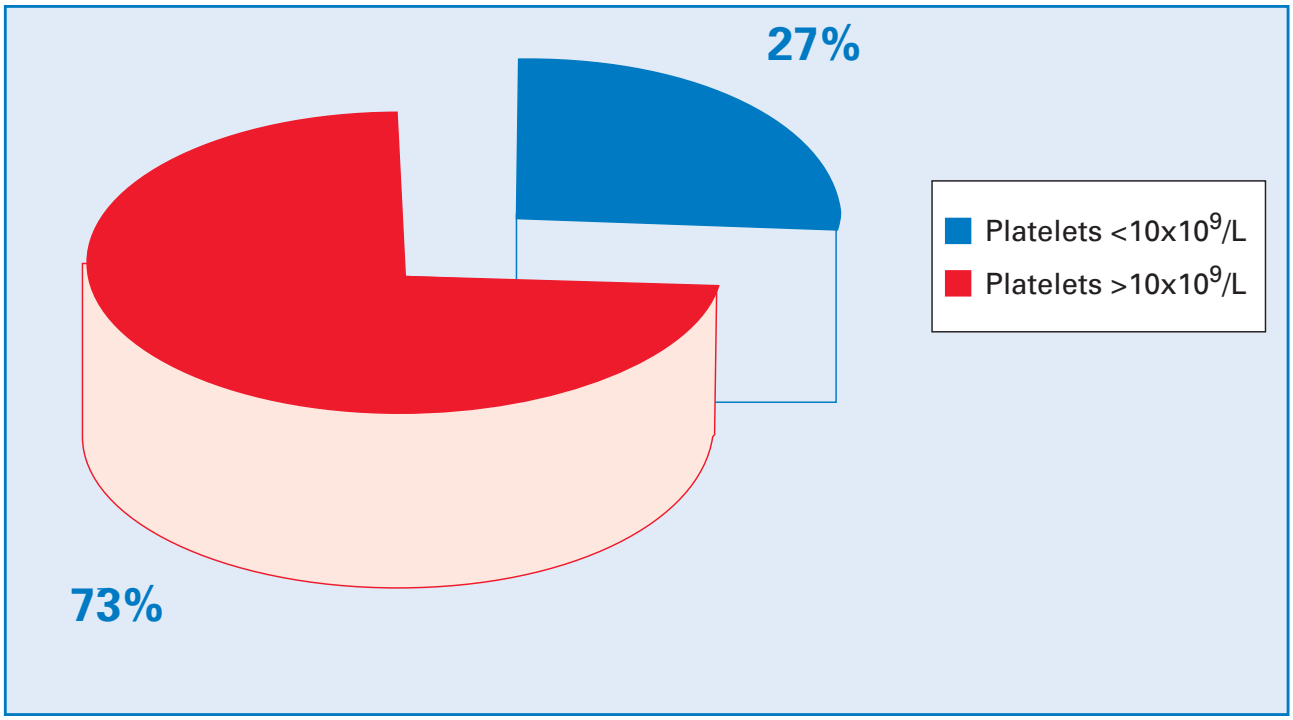
Reference:

Guidelines For The Use Of Group O RhD Negative Red Cells. NBS Transfusion Medicine Clinical Policies Group.
http://www.blood.co.uk/hospitals/library/clinical_guidelines_and_advice_internal/index.asp

Platelet Use in the South West Region

Although the use of red cells in England has declined steadily since 2000, platelet transfusions have continued to increase. This rise has been more pronounced in the South West, with issue figures between April 02 and March 05 identifying a 22.5% increase compared with 7.5% nationally. To investigate this the South West Regional Blood Transfusion Committee initiated a baseline audit to determine which patients were being transfused platelets and why.

Units requested for prophylactic use



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To try and achieve maximum participation from Trusts/hospitals a simple data set was used to identify – the age of the recipient, the requesting directorate/specialty, whether the platelets were for prophylaxis or bleeding, the type of operation (if relevant), the platelet count prior to issue, the number of doses requested and the number used. This information was collected for one month, during November and December 2005, by transfusion laboratory staff.

Results

The participation was excellent with 21 out of 28 hospitals in the South West region returning satisfactory information. Only one NHS Trust did not contribute data and all other non participating hospitals were within the private sector and did not require platelets. Overall 1,323 units were requested and 1,226 (93%) units used for the initial request. Comparison with NBS issue data to participating Trusts/hospitals during the study period identified that this represented 86% (1323/1535) of all platelets issued. Variation in usage between hospitals was large with 4 hospitals requesting more than one hundred and 2 hospitals requesting more than two hundred units. Platelet use increased with age and over five hundred units were requested for patients 65 years or over. 59% of all platelets requested (779 units) were for haematology patients. Oncology and cardiac surgery were the next highest users each requesting about 11% of total (149 units and 139 units respectively). When prophylactic or therapeutic use was known, 74% (904 units) were requested for prophylaxis. 75% of these were for haematology patients and 73% when the preceding platelet count was greater than $10x10^9$/L – see diagram *(previous page)*.

26% of platelets were requested for bleeding (310 units). 30% of these were for cardiac surgery and 53% when the previous count was more than $50x10^9$/L. This study indicates that the main users of platelets are haematologists (59% of total). Oncologists and cardiac surgeons were the next highest users, however combined they used around a third of those used by haematologists. 74% of all platelet use was to prevent rather than treat bleeding. Despite BCSH guidelines which recommend a platelet threshold of $10x10^9$/L or less for this purpose, 73% of prophylactic use was associated with a previous count of greater than $10x10^9$/L. Individual analysis of prophylactic requests from the 4 Trusts who used most platelets showed a large variation in practice, with requests when the count was more than $10x10^9$/L ranging from 49% to 80%. It is probable that in many cases BCSH guidelines were not followed and platelets were unnecessary at the time of transfusion. However other explanations include use in patients with additional risk factors for bleeding, or in outpatients in whom an additional visit to monitor the count may have been significantly inconvenient. Although more than half of platelets were given to control bleeding when the last recorded count was higher than $50x10^9$/L, only 26% of all platelets were requested for therapeutic use. Dysfunctional platelets, lack of an immediately available platelet count, a desire for a higher threshold count or availability of platelets are likely to be significant factors for requests in this category. The use of near patient testing should be considered when quantitative or qualitative platelet problems are suspected.

In conclusion, haematology patients are responsible for the majority of platelets used. The increasing age profile of the population is likely to put greater demands on the National Blood Service to collect platelets with a resulting high financial burden on Trusts/hospitals unless platelet use alters. Short term, the current British Society of Haematology guidelines should be followed and the recent National Comparative Audit looking in more detail at the reasons for platelet transfusion should help to understand why so many prophylactic transfusions are given above a count of $10x10^9$/L. Longer term further work to assess the need for prophylactic platelet transfusions should be performed.

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Recombinant Human Erythropoietins in Patients with Anaemia Associated with Cancer

Background

The action of erythropoietin, whether physiological or pharmacological, is to increase red cell production in the presence of a functioning bone marrow. Its role in the management of anaemia associated with chronic kidney disease is well recognised, but its use in other groups of patients that are transfusion dependent is more uncertain. The Health Service Circular BBT2 encourages us to explore alternatives to donor blood, and therefore if erythropoietin were to prove a useful and safe treatment, the National Blood Service, far from considering it to be a competitor, would encourage its use.

The Blood Services of England and Wales are stakeholders in the National Institute for Health and Clinical Excellence (NICE) appraisal determination for the use of erythropoietin in cancer treatment-induced anaemia. In this article, we review both the current state of this on going assessment exercise and some related issues from a Blood Transfusion perspective. As part of the NICE procedure, an appraisal assessment was commissioned and produced by the West Midlands Health Technology Assessment (WMHTA) collaboration. This document provided much of the background and framework for the subsequent discussions (Wilson 2005). Since then the NICE committee have been evaluating comments and feedback from a range of stakeholders including patient groups and pharmaceutical companies.

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Summary conclusions to NICE appraisal document

The current final appraisal determination indicates that erythropoietin is recommended for use in the management of anaemia only as part of ongoing or new clinical trials to generate robust and relevant data for the following purposes:

- To address the gaps in the currently available evidence, notably its effects on health related quality of life and fatigue.

- To confirm the benefits and risks associated with erythropoietin in the management of anaemia induced by cancer treatment (specifically mortality benefits and risks) and to identify patients sub groups (including those with different tumour types) in which possible risks are acceptable.

This conclusion might at first seem rather restrictive as an 'endorsement'. However, various stakeholders have successfully appealed on the following grounds:

- reconsideration of the guidance in the light of the national priority of conserving blood and avoidance of unnecessary exposure to donor blood, and use of intravenous iron.

- special consideration should be given to patients who refuse blood on whatever grounds, patients who cannot be crossmatched, for example because of multiple antibodies and patients with ovarian cancer who are receiving platinum-based therapies.

The Evidence for Efficacy and Safety

Most of us in transfusion practice are familiar with erythropoietin and aware of its potential benefits, in terms of reducing red cell transfusion requirements and in increasing levels of haemoglobin. Although there are potential concerns about safety and sufficiency of the alternative therapy (i.e. blood transfusion), it is very difficult to 'quantify' how real this risk of diminished supply is, and indeed there have been no real shortages of blood components to date in UK.

The WMHTA Collaboration updated the original Cochrane systematic review and then undertook an economic evaluation of the different forms of erythropoietin. A recent update to the Cochrane review (Bohlius 2006a; Bohlius 2006b) included data from 57 trials and 9353 cancer patients in which the effects of three different forms of recombinant human erythropoietin were evaluated. Patients treated with erythropoietins had a lower risk of transfusion than control subjects and were more likely to achieve haematological response - in this case a haemoglobin increase of 2 grams.

However, on the basis of 6769 patients in 35 trials, adverse events such as thrombotic events and worsening hypertension were observed in 229 of 3728 (6%) patients treated with erythropoietins but in 118 of 3041 (4%) untreated control patients. This was reported to indicate that the relative risk of adverse events was increased by 67% in the treated group compared to the control group (Bohlius 2006b).

Overall survival was also analysed in the combined studies for 8167 patients from 42 trials. The meta-analysis showed that survival was not improved by treatment with erythropoietins. However, with the inclusion of more recent clinical studies, there was a (worrying) possibility that erythropoietin treatment might adversely affect survival. In this case it should be noted that only 7 included trials were specifically designed to look at overall survival, rather than as a secondary outcome. Although adverse events such as those mentioned above may contribute to reduced survival in patients treated with erythropoietins, other mechanisms might be mediating this, for example effects of erythropoietins on tumour growth.

But how reliable are these results? Several methods can be applied to try and address this. For example, we can inspect the forest plots and use a statistical method (reporting I2) to assess heterogeneity -i.e. determine whether the differing results reported by the trials can be explained by chance alone. We can also review whether all relevant publications were identified, i.e. publications that did not report adverse events have not been missed (publication bias), using methods such funnel plot analysis. The reader is referred to the individual articles for these analyses, although as a generalisation, these findings were not considered of major consideration for the overall conclusions.

Alongside evidence for effectiveness and safety, health related quality of life (QoL) assessed from a patient's perspective is also important. The WMHTA review utilised a "vote count" method to summarise QoL. This classifies studies as showing a positive, negative or neutral effect. The data suggested a trend towards erythropoietin having a beneficial effect on health related QoL. The importance of changes in QoL was not easily interpretable from the available data, so although anecdotal evidence suggests individual patients report improved QoL whilst taking erythropoietin, it was difficult to quantify these findings from data included in any of the available systematic reviews.

Conclusion

The reviews and NICE guidance have raised the important issue of survival and side effects for erythropoietins in the management of cancer treatment-related anaemia. There seems little doubt that their use is associated with reduced red cell transfusion requirements and increasing levels of haemoglobin, but what is not clear is how exactly to balance benefit against risk. With this uncertainty in mind, the NICE determination has indicated that further clinical data is urgently required in the first instance.

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Studies of blood use in the Northern region, and in London and the South-East, show that over 14% of all blood (300,000 units) is used by patients with malignancy. Factors such as an ageing population, a steady increase in the incidence of some malignancies, and higher intensity of cancer treatments may increase this figure. Blood use in these groups may be moderately reduced by application of the National Blood Transfusion Committee's indication codes for red cell transfusion, and by investigation for treatable causes of anaemia, but many patients will remain transfusion-dependent. If concerns about blood conservation and BBT 2 requirements to consider alternatives to donor blood are given heavier weighting in the future, these factors may also influence any final judgements on recommendations for use of erythropoietin.

One lesson that does clearly emerge from the NICE appraisal determination, is the importance of understanding levels of risk for patients. In general we have a very good baseline level of risk associated with blood transfusion – but is comparable and accurate data available for other drugs including erythropoietin? Will the role of erythropoietin in other clinical areas (such as management of chronic anaemia or blood conservation in surgery) be treated to similar rigorous appraisal? We await the final NICE decision with interest.

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Guidelines on Pre-deposit Autologous Blood Donation and Transfusion

The British Committee for Standards in Haematology (BCSH) has put onto its website (*www.bcshguidelines.com*) the latest guidelines on the use of Pre-deposit Autologous Blood Donation and Transfusion (PAD) which will form the first part of a set of guidelines on Alternatives to Allogeneic Blood Transfusion. The abstract is given below:-

Decades of clinical application demonstrate that it is quite feasible to auto-transfuse blood which has been collected and stored for an interval of up to six weeks in standard storage media, and that up to three standard collection volumes (approximately 500ml) can be collected from normal sized adults (over 50Kg) during that interval. Furthermore, systems have been developed to reduce risk to participants, and to boost haemoglobin production during and after the procedure. However, such "Preoperative Autologous (Blood) Donations" (PAD) are not without risk, are of low clinical efficacy and are poorly cost-effective for the vast majority of patients in the UK. These Guidelines update those previously issued by the BCSH and do not recommend the practice and use of PAD unless the clinical circumstances are exceptional.

After summarising the 1993 Guidelines, and defining the stakeholder involvement (which includes patients) the text has three parts.

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Part 1 summarises the BSQR (Blood Safety Quality Regulations) legislation of 2005 which requires any facility undertaking PAD to be a licensed Blood Establishment. The BSQR Quality Regulation, which came into force in August 2006, requires separate storage of autologous from allogeneic blood and that autologous units must not be used for allogeneic transfusion. The donation process is subject to strict legislation, including traceability. The transfusion process itself is regulated by Good Professional Practices. Definitions are given, and also the need for testing as required by law. It details the information to be provided by and given to PAD donors. An adverse event register for PAD is also emphasised. The guidelines recommend processing as for allogeneic donation, including leucodepletion although leucodepletion failure is more frequent in PAD.

Part 2 shows that there have been very few Randomised Controlled Trials of PAD. Those available are not encouraging. For example, Billote et al (2002) concluded that PAD provided no benefit for non-anaemic patients undergoing primary total hip replacement surgery. The Guidelines also refer to the NHLI 'Transfusion Alert' of a decade ago (still on the web), the useful SIGN (Scottish Intercollegiate Guidelines Network) report of 2001 and the Cochrane reviews and those from the International Society of Perioperative Transfusion (ISPOT). Brecher and Goodnough (2001) conclude that PAD is mostly a form of chronic haemodilution, but also state that "should another risk of transfusion-transmitted infection (TTI) be identified, or if blood collections fail to keep pace with demand for blood, the pendulum (in favour of PAD) may swing back again". Reports on the use of EPO (+/- iron supplements) are cited and also the generally disappointing effect of iron supplementation during PAD, especially if EPO is not given. A brief cost-analysis indicates the relative expense of EPO-plus-iron regimes in PAD. The general difficulties of conducting PAD in children are highlighted (psychological stress and venous access). In contrast, successful regimes for the elderly are reported.

In the third part, it is held that current conditions in the UK (especially the low-risk of TTI from allogeneic transfusions) discourage PAD unless the circumstances are exceptional. The process must take place in licensed blood establishments and for each case there should be a clear reason for why PAD is preferred. However, if conducted the following must apply:-

- Patients must be candidates for elective surgery where transfusion is likely.
- The admission and operation days must be guaranteed.
- Sufficient time must be allowed for collection, but no more than that allowed for storage.
- Sufficient time should be given from the date and time of the ultimate PAD collection prior to surgery for the patient to make a full circulatory recovery.

Potential candidates

- should be clinically judged to tolerate repeated blood loss at each collection
- should be told eligibility criteria
- should be considered for supplementation with EPO
- should have the following Hb concentrations before PAD
  - men, 110-145 g/l
  - women, 130-145 g/l

The limited indications include:

- Rare blood groups
- Children with scoliosis (special provisions required[1])
- Patients with serious psychological aversion to donor blood
- Patients refusing consent to allogeneic transfusion

PAD is not recommended for children under 10 years old.

Candidates who are positive for markers of TTI present issues of staff safety, and are a greater threat to other recipients if administrative and other errors occur. The Task Force **does not** recommend that PAD be offered to such patients unless clinical circumstances are exceptional.

Given the costs of EPO, its economic value must be regarded as doubtful. The Task Force **does not** recommend that EPO be used unless clinical circumstances are exceptional. The Task Force **does not** recommend prophylactic iron to iron replete individuals undergoing PAD, and further recommends that PAD be denied to persons who are iron deficient and receiving iron therapy until they have been effectively treated.

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Reference:

Morley, S. Should children be offered predeposit autologous transfusion? *Blood Matters*, Issue 20, 12-13.
http://www.blood.co.uk/hospitals/library/pdf/bm20.pdf

Development of a Competency Assessment Workbook for Use in Intra-Operative Cell Salvage

A concerted drive for the appropriate use of blood must continue if the demand for red cells is to be further reduced. If the impetus is lost, the demand for red cells will drift upwards. Intra-operative cell salvage is an alternative to blood transfusion which is not used to its full potential; there is a wide variation in activity across England and Wales.

A barrier to implementation has been the lack of a consistent approach to the training and competency assessment of operators. National Occupational Standards for cell salvage, developed by Skills for Health, specify the standards of performance that operators are expected to achieve and the knowledge and skills required to perform these functions effectively. Skills for Health are part of the NHS but have their own board and management committee. Their main aim is to help the whole health sector by working with employers and stakeholders to ensure that they are equipped with the right skills to support the development and delivery of healthcare services.

To support these standards, a competency assessment workbook for cell salvage operators has been developed and is now available to hospitals. The training framework has been developed on behalf of the National Blood Service Appropriate Use of Blood Group and the Welsh Assembly Clinical Advisory Group, in consultation with cell salvage "champions" and other national groups with blood safety and conservation as part of their remit.

It is essential that all staff involved in operating cell salvage machines are trained to the level at which they are expected to operate. Training should include both theory and practice. Operators need to develop a broad understanding of the appropriate use of cell salvage including the contra-indications and implications of administration and reinfusion of salvaged blood. It is recommended that learners complete the UK cell salvage e-learning package available on the following website prior to commencing this workbook: *www.transfusionguidelines.org.uk*

A co-ordinated drive is needed to facilitate the wider implementation of cell salvage. A UK Cell Salvage Action Group has been established to develop a variety of tools to help hospitals set up this service locally. Information and outputs from this group will be available on the DH Better Blood Transfusion Toolkit website: *www.transfusionguidelines.org.uk.*

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DIARY DATES

- 12 - 15 April 2007, **BGS Reading 2007**, Reading University. For more information: www.bgsreadubg,org or email: *jane@bgsreading.org.*
- 14 April 2007, **Introduction to Pre-Transfusion Testing**, *Colindale Blood Centre*. For more information: Wendy Sewell, Tel: 020 8258 2734, *email: wendy.sewell@nbs.nhs.uk*
- 19 - 20 April 2007, **Sanquin Spring Seminar, Amsterdam**. For more information: *www.sss.sanquin.nl* or Seminar Secretariat Tel: +31 20 679 3411 or *sanquin@eurocongres.com* or *www.eurocongres.com*
- 21 - 22 April 2007, **8th Annual NATA Symposium on Transfusion Medicine & Alternatives**, *Budapest, Hungary*. For more information: *nata.secretary@lms-group.com*
- 30 April - 2 May 2007, **British Society for Haematology - 47th Annual Scientific Meeting**, *Bournemouth International Centre*. Flyer & information: *http://www.transfusionguidelines.org.uk/docs/pdfs/diary_20070430_Flyer.pdf*
- 9 May 2007, **Microbiology SIG,** *NIBSC, South Mimms, Herts*. For more information: Morag Ferguson Tel: 01707 641 314
- 9 - 10 May 2007, **Apheresis & Blood Collection SIG**, *Crown Plaza Hotel, Central Birmingham*. Draft Programme: *http://www.transfusionguidelines.org.uk/docs/pdfs/diary_20070509_programme.pdf*
- 10 May 2007, **Blood Stocks Management Scheme Open Meeting**, *Paragon Hotel, Birmingham*.
- 17 May 2007, **Hospital Based Transfusion Practice SIG**, *Manchester Conference Centre*. Submission information: Flyer: *http://www.transfusionguidelines.org.uk/docs/pdfs/diary_20070517_Flyer1.pdf*
- 5 - 6 June 2007, **IBMS Portfolio Knowledge**, *Brentwood Blood Centre*. For more information and application form contact: Wendy Sewell, 020 8258 2734 or *email wendy.sewell@nbs.nhs.uk. Web: www.blood.co.uk/hospitals/training*
- 13 - 15 September 2007, **BBTS 25th Annual Scientific Meeting**, *The Exhibition & Conference Centre, Glasgow*. Flyer: *http://www.transfusionguidelines.org.uk/docs/pdfs/Diary_20070913_flyer.pdf*

NEWS

Website Education Update

Have you recently visited the DH Better Blood Transfusion Toolkit website?
www.transfusionguidelines.org.uk.
There is lots of new information on this site, and following the establishment of an Editorial Board, all materials have recently been reviewed and updated.

Did you know that an intra-operative cell salvage e-learning package is now available? It is a useful reference point for all those wanting to gain a bit of background knowledge and is invaluable for new cell salvage operators.
Visit the website *www.learncellsalvage.org.uk*.

Feedback on either of these websites is welcome and can be submitted directly from each website homepage.

If you wish to promote these websites within your organisation, promotional materials are available from the NBS Hospital Liaison Administration Office. Please contact Alena Slodicakova:
Alena.Slodicakova@nbs.nhs.uk

CPD

Objective

After evaluating specific articles published in 'Blood Matters', participants in the CPD Questionnaire should be able to demonstrate an increase in, or affirmation of, their knowledge of Transfusion Medicine.

Credits

Each participant can earn CPD credits, as reflective learning - as designated by the participants scheme (for example 1 credit per hour of reflective study in the RCPath scheme). Each participant should claim only those credits that he or she actually spent in the activity and should write reflective notes in the relevant section of his/her portfolio.

Blood Safety and Quality Regulations (BSQR) – Where Are We Now?

Sixty-seven "for cause" hospital blood bank inspections were identified by the MHRA following submission of compliance forms. Inspections are now being carried out by the MHRA and it is not surprising that major deficiencies have been identified in the following areas:

Quality systems - training, self-inspection, incident reporting and change control.

Equipment issues - validation, calibration and verification

The MHRA have commented that Blood Bank activities are considered safe, staff are well motivated and technically proficient.

Further information on inspections is available at:

http://www.transfusionguidelines.org.uk/index.asp?Publication=REGS&Section=23&pageid=952

If you have been inspected and are prepared to write an account of your experience please send to joan.jones@wbs.wales.nhs.uk (Chair of the Operational Impact Group).

The NBS is part of NHS Blood and Transplant.
Blood Matters is prepared and issued by NHSBT, Reeds Crescent, Watford, Herts WD24 4QN (Telephone 01923 486818)

CPD Questionnaire

Select one correct answer for each question.

Q1 **Intra-operative cell salvage**

a) Is used to its full potential

b) Shows even distribution of activity across England and Wales

c) Training is only practical

d) E-learning package is available

Q2 **Use of Red Cells: *In a recent regional audit***

a) Up to 20% of transfusion episodes may have been inappropriate

b) Up to 90% of transfusion episodes may have been inappropriate

c) Less than 4% of transfusion episodes were considered entirely inappropriate

d) Less than 6% of transfusion episodes had insufficient data

Q3 **Use of Red Cells: *In a recent regional audit, recommendations included:***

a) No requirement for a transfusion trigger policy

b) Patients should usually have haemoglobin checked a maximum of 24 hours prior to transfusion

c) Decision to transfuse should be based on haemoglobin alone

d) Documentation of transfusion episodes is perfect

Q4 **Recombinant Human Erythropoietin**

a) Is recommended for the management of anaemia

b) Is recommended for the management of anaemia only as part of ongoing or new clinical trials

c) Relative risk of adverse events was increased by 2% in the treated group compared to the control group

d) Meta-analysis showed that survival was improved by treatment with Erythropoietin

Q5 **Recombinant Human Erythropoietin**

a) Inclusion of more recent clinical studies, showed a possibility that Erythropoietin might adversely affect survival

b) Use of Erythropoietin is not associated with reduced Red Cell transfusion

c) Less than 10% of all blood is used for patients with malignancy

d) Levels of risk for patients are fully available for the use of Erythropoietin

Q6 **Who Uses Blood: EASTR Study**

a) Will only aid the planning for blood collection

b) Should aid with the focusing clinical areas for blood saving

c) Will not include survival of transfused patients

d) Initial results will not be available for 10 years

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Q7 Platelet Use

a) Both platelet and Red Cell usage has reduced since 2000

b) Platelet use decreased with age of patient

c) Over half of all platelets used were for Haematology patients

d) Over 80% of platelets requests were for prophylaxis

Q8 Platelet Use

a) Most requests for prophylactic use were made when patient platelet count was less than 10 x 10^9/L

b) Nearly ¾ of requests for prophylactic use were made when patient platelets count was greater than 10 x 10^9/L

c) Over ⅓ of platelet requests were for actual bleeding episodes

d) There was a concordance in the use of platelets between trusts

Q9 O RhD Negative Use and Abuse

a) Less than 9% of UK population are O RhD Negative

b) Less than 10% of all NBS issues during 2005-06 were O RhD Negative

c) Stocks of Flying Squad blood is constant between all hospitals

d) Less than ¾ of hospitals are issued with more that the recommended guidelines percentage of O RhD Negative

Q10 Pre-deposit Autologous Blood Donation and Transfusion Pre-deposit Autologous Blood donation

a) Requires prophylactic iron

b) Can be performed on iron deficient patients, while receiving iron therapy

c) Conclusive randomised controlled trials have shown benefit over allogenic blood transfusion

d) Is not recommended for children under 10 years old