MAY 2002
ISSUE 10

Blood Matters

Quarterly information for hospitals served by the National Blood Service

NATIONAL BLOOD SERVICE

NHS

Editorial
How Much Does Blood Matter?

Despite the high public profile of 'Bloody Matters' through media exposure and publication of vCJD incidents, SHOT reports, the CMOs' 'Better Blood Transfusion' seminar, the EU Blood Safety Directive and CNST Clinical Risk Standards, improving hospital transfusion practice still appears to have a low profile amongst competing priorities within hospital Trusts. This is illustrated by the fact that during the last 5 years of SHOT reporting, transfusion of the wrong blood remains the commonest adverse event and accounts for 61% of the incidents reported, with 11 deaths probably attributable to these errors. During this time, only 50 Transfusion Nurses/Practitioners have been appointed in the 413 SHOT-participating hospitals and Consultant Haematologists with dedicated sessional time for hospital transfusion practice remain a select minority.

In an attempt to undertake a national audit of the appropriate use of FFP, as reported in this edition, it is noteworthy that only 49% of hospitals were able to respond as the remainder had no means of obtaining details on usage, and of these, only 53% had policies in place for the use of FFP. Unless adequate allocation of resources are made available within hospital Trusts, the NBS joint initiative with the MRCP Clinical Effectiveness and Evaluation Unit to undertake national benchmarking and comparative audit in blood transfusion will not be able to achieve its objective of improving hospitals' transfusion practice.

Meanwhile, political and regulatory pressures are building up to ensure effective and safe blood transfusion provision to all patients. The possible shortage of blood due to the implementation of precautionary measures for vCJD has helped to accelerate the drive to promote the appropriate use of blood. The CMOs' 'Better Blood Transfusion II' initiative will be providing another important driver to improve clinical blood transfusion practice. This time, the outcome recommendations will include guidance and tools to enable implementation of better practice. The EU Blood Safety Directive is likely to be adopted later this year and this will include some mandatory requirements impacting on the hospital blood transfusion process, such as training and updating of staff, implementation of quality systems, documented SOPs and guidelines, traceability (from donor to recipient and vice versa), centralised reporting systems for adverse events, blood component recall mechanisms, standards for storage, transport and distribution, and data protection and confidentiality. There will be a nine-month period of grace for each EU member country to implement this Directive once it has been adopted.

It is also noteworthy that the Clinical Negligence Scheme for Trusts (CNST) has introduced amendments to their Clinical Risk Management Standards with compliance to commence from 1st April 2002. These Standards relate to the safe administration of blood and blood products, and to meet these standards, Trusts need to have a Blood Transfusion Policy which includes protocols and training for all staff who request and/or collect blood products. The CNST will want evidence to show that appropriate systems are in place for the request, safe storage, collection and administration of human blood and blood products. Compliance with the CNST Clinical Risk Management Standards enables a Trust to claim a discount on their 'premium' and as the article on the Hospital Transfusion Practitioner in this edition points out, such a discount would be sufficient to fund one of these posts within a Trust.

To deliver and implement 'Better Blood Transfusion' there needs to be a heightened profile of blood transfusion practice within Trusts. It needs to be on the Governance and Risk Management agenda, with advocacy from the Chair of the Hospital Transfusion Committee. The framework of a National Blood Transfusion Committee reporting to the CMO, linking into regional and local Hospital Transfusion Committees, is in place to aid the process. What is needed now is an effective clinical infra-structure, including dedicated consultant sessional time and the appointment of more Transfusion Nurses/Practitioners. Many Consultant Haematologists have little time left to become involved in transfusion matters, as they are overwhelmed with other clinical work. Haematology consultant manpower planning needs a collaborative approach from the BSH, BBTS, the Colleges and the NBS to tackle this issue and factor in the additional sessional time and leadership required to make 'Better Blood Transfusion' happen, otherwise SHOT 5 years on will show no change.

Dr Angela Robinson
NBS Medical Director
Contact email: *angela.robinson@nbs.nhs.uk*

Specialist Training In Transfusion Medicine

Blood transfusion continues to have an ever-increasing public profile, partly as a result of the emergence of new pathogens which have posed a threat to the safety of the blood supply and partly as a result of major scientific developments. There has been enormous progress in transfusion medicine, which has developed into a specialist area of its own. Transfusion medicine now encompasses many important areas of medicine including haematology, immunology, transplantation science, microbiology, epidemiology and clinical practice. Therefore there is a need to have an

contin..ed on page 3

appropriate training for future Transfusion Medicine specialists; this article outlines the present requirement in Transfusion Medicine for Haematologists and proposed training requirement for a specialist in Transfusion Medicine.

Box 1 details the requirements for training in blood transfusion as laid out by the Joint Committee on Higher Medical Training (JCHMT) for Higher Specialist Training in Haematology.

Box 2 details the requirement for training in Transfusion Medicine as proposed by the JCHMT for Higher Specialist Training in Transfusion Medicine. This represents much more specialist training than generally given to Haematology SpR posts, so there is a proposal that the NBS will establish two training "fellowships" available at any NBS Centre for one year and designed to turn otherwise suitably trained specialists into transfusion medicine specialists. In the main the NBS expect haematologists to be interested, but other backgrounds, such as immunology, virology, and perhaps public health, might also fit the bill for a career in certain areas of the service. The posts are intended for candidates on the specialist register or within three months of CCST, but conversion within post-part 1 haematology training could be contemplated.

Posts will be paid at an appropriate point on the SpR scale.

This missed the 2000/2001 business plan, but the NBS may be able to fund one from half way through this year. Once the NBS have identified funding, the opportunity for this training will be advertised each year.

For further information, please contact Dr Tim Wallington on *tim.wallington@nbs.nhs.uk* or phone 0117 991 2099 or fax 0117 991 2186.

Dr Rob Webster
Consultant Haematologist

Box 1

BLOOD TRANSFUSION FOR HIGHER SPECIALIST TRAINING IN HAEMATOLOGY

Subject

Understand the principles of blood transfusion laboratory practice including:-

- The identification of antibodies
- The identification of autoantibodies
- Crossmatching techniques
- Automation in blood transfusion
- Use of computers in the transfusion laboratory.

Basic principles of donor selection and the preparation of blood components including:-

- Donor selection
- Donor safety
- Preparation of blood products including viral safety.

Acquire principles of clinical blood transfusion practice including:-

- Appropriate use of blood transfusion
- Use of blood components
- Hazards of blood transfusion
- Management of complications of transfusion
- SHOT report and the role of the Hospital Transfusion Committee
- Management of warm and cold auto-antibody problems.

Box 2

TRANSFUSION MEDICINE FOR HIGHER SPECIALIST TRAINING IN TRANSFUSION MEDICINE

Scientific Basis

Subject Matter

- The development and co-operative nature of the immune system and the basis and application of immunological techniques in transfusion medicine.
- Gene structure, function and inheritance.
- Inheritance patterns of blood groups (red cells, white cells and platelets) and their biochemical basis.
- The principles and applications of molecular biological techniques in transfusion medicine.
- The basis of immune-mediated transfusion reactions.
- Risks of transfusion-transmitted infections (viral and bacterial) in immunocompetant and immunocompromised recipients.
- Basic knowledge about virus types, detection systems and modes of transmission.
- Component preservation (including cellular storage injury), plasma fractionation and viral activation.
- Physiology of oxygen delivery and the response to acute blood loss in neonates, children and adults.
- Therapeutic applications of mononuclear cell transfusions.

contin..ed on page 4

Laboratory Experience
Red Cell Immunohaematology
Subject Matter

- Techniques for antigen typing.
- Methods of antibody detection, identification and assessment of clinical relevance.
- Requirements for screening cells and antibody detection panels.
- Donation testing.
- Pre-transfusion testing
  - (i) sampling procedures and documentation
  - (ii) blood grouping requirements
  - (iii) antibody screening techniques
  - (iv) compatibility testing
  - (v) electronic issue
  - (vi) provision of red cells for allo-immunised recipients
- Investigation of complex incompatibilities and transfusion support in:
  - (i) multiple red cell alloantibodies
  - (ii) high titre low avidity antibodies (HTLAs)
  - (iii) antibodies against high and low frequency red cells antigens
- Diagnosis and investigation of immune mediated haemolysis
  - (i) haemolytic transfusion reactions
  - (ii) autoimmune haemolytic anaemia (AIHA)
- Antenatal and perinatal screening procedures
  - (i) antibodies causing severe HDN
  - (ii) serial titrations
  - (iii) quantitation of anti-D and anti-c, and assessment of clinical significance
  - (iv) role and clinical significance of biological assays
  - (v) place of molecular typing in fetal medicine
  - (vi) quantitation of feto-maternal haemorrhage

Laboratory Experience
White Cell Immunology
Subject Matter

- HLA typing procedures.
- Techniques for HLA antibody detection.
- Methods for final selection of donors for haematopoietic stem cell and solid organ transplantation.
- Investigation of immunological refractoriness to platelet transfusions
  - (i) provision of an HLA typed panel and selection of HLA compatible platelets
  - (ii) selection of crossmatch-compatible platelets
- Principles of investigation of TA-GvHD
- Principles of investigation of TRALI

Platelet Immunology
Subject Matter

- Platelet antigen typing procedures
- Methods of platelet antibody screening and identification
- Investigation of conditions caused by allo-immunisation to platelet antigens (NAITP, PTP)

Transfusion Microbiology
Subject Matter

- Mandatory screening for markers of diseases transmissible by transfusion:
  - (i) Rationale for selection of mandatory tests and the international perspective
  - (ii) basis of screening and screening methodologies
  - (iii) assessment and selection of testing kits
  - (iv) confirmatory assays
- Selective donor screening for other transmissible infections
- Bacteriological monitoring in blood procurement, processing and storage

Blood Component Production
Subject Matter

- Methods of component preparation
- Methods of leucodepletion
- Methods of pathogen inactivation;
  - Methylene blue
  - Psoralens and other systems
- Irradiation of blood components

Clinical Transfusion Medicine
Subject Matter

- National criteria for the selection and care of blood and tissue donors, including confidentiality

contin..ed on page 5

- Methods to identify 'high risk' donors
- Donor counselling
- Effects of blood donation; adverse and positive

Clinical Transfusion Medicine
Apheresis
Subject Matter

- Automated apheresis techniques
- Criteria for donor selection and safety
- Indications and use of therapeutic apheresis
- Hazards of apheresis

Clinical Transfusion Medicine
Transfusion Microbiology
Subject Matter

- Surveillance and Look-back procedures
- Investigation of post-transfusion infection
- Donor epidemiology; non-remunerated versus paid donors

Clinical Transfusion Medicine
Use and Management of Specialist Panels
Subject Matter

- HLA typed platelet donor
- HPA typed platelet donor
- Bone marrow and cord blood registries

Hospital Clinical Practice
Subject Matter

- Indications, administration and use of blood components
- Transfusion support for;
  - (i) haemoglobinopathies
  - (ii) bone marrow transplantation
  - (iii) acute massive blood loss
  - (iv) fetal/neonatal allo-immune cytopenias
  - (v) auto-immune haemolytic anaemia
  - (vi) premature neonates
  - (vii) elective surgery in children and adults
  - (viii) solid organ transplantation
- Prevention of Haemolytic Disease of the Newborn
- Familiarization with hospital blood bank practice and the provision of a routine hospital immuno-haematology service
- Clinical liaison in transfusion medicine; transfusion policies and ward procedures, including strategies to prevent 'wrong blood to patient' episodes
- Bloodless surgery; the main management of Jehovah's Witnesses
- Autologous transfusion and other means of reducing allogeneic exposure
- The management of untoward effects of transfusion
- The principles of systematic reviews, evidence-based medicine and randomised controlled clinical trials

Management and Quality Assurance
Subject Matter

- The principles of quality systems and clinical governance
- The regulatory framework pertaining to Good Manufacturing Practice
- Good Laboratory Practice and accreditation
- Current relevant guidelines and product specifications
- Audit systems and audit methodology
- Product recall
- Use of information Technology within the transfusion service and in a hospital blood bank
- Clinical governance in hospital transfusion practice:

  including HTC
- Haemovigilance and SHOT

The "Hospital Transfusion Practitioner"

There is increasing recognition - in transfusion circles at least - of the need for hospitals to appoint staff frequently called 'Hospital Transfusion Nurses'. Unfortunately, transfusion practice still has too low a priority in the overall plans of many hospital Boards, and fewer new posts have been established in the UK than needed, even though many business cases have been submitted or are being prepared. There are now 50 such posts in the 413 hospitals eligible to take part in the 'SHOT' scheme. Hospitals are under pressure to deliver a multitude of clinical services, and transfusion is just one of many 'competing' priorities. This state of under-representation of Transfusion Practitioners may be partly because the hospitals have rarely had serious shortages of blood. Paradoxically, however much we protest that this state of 'plenty' is a delusion, successive

contin..ed on page 6

SHOT reports indicate continuing poor practice in many hospitals, particularly with regard to bedside checking. Furthermore, universal leucodepletion has made a new generation of ward staff less familiar with previously recognised common 'downsides' such as febrile non-haemolytic reactions, perhaps perpetuating an impression of safety. It is even conceivable that technical developments such as 'electronic blood issue' (a new and subtly different term from 'electronic cross-match') may compound such delusions if ward staff feel that they can just 'take blood off the shelf'.

The majority of transfusion 'mistakes' are entirely avoidable. Good transfusion practice must be advocated efficiently, competently and correctly. In five years, during which over 15 million blood components have been transfused in the UK, the SHOT scheme has had 1148 events reported, of which 699 (61% - or about 1 transfusion in 20,000) were of wrong blood component, all of which were avoidable. These figures suggest that imperfect understanding will probably be revealed by a scheme which assesses how much is known about blood groups by current hospital staff (including doctors), what is in a blood pack or platelet pack, storage requirements, procedures in the event of adverse reactions, etc. It was said by a newly appointed transfusion nurse that all he knew about blood was that it was red, and important to get into the patient whose name was on the label. At least the identification needs were appreciated. Similarly, a review of existing hospital transfusion practices will probably reveal depressingly frequent deviations, such as checking the blood pack label details away from the patient's bedside or theatre table.

An audit of essential features of transfusion practice may well prove helpful in establishing the business case for appointing a Transfusion Practitioner. These should include accuracy of patient identification, details of transfusion episodes in patients' notes, monitoring of all adverse events over a fixed period, use of blood in emergency, storage and transport conditions, as well as the clinical indications for any transfusion including the identity of the prescriber. Whereas a financial analysis - that is, would the money saved by ensuring good practices be able to pay for a Practitioner? - is not necessarily the most relevant approach (as the prime justification must be to improve transfusion safety), having such analyses available would be helpful. The 'Clinical Negligence Scheme for Trusts' requires a section on Blood Transfusion Policy, and education programmes for all hospital workers involved in the transfusion process. If this standard is met it can save Trusts up to £75,000 per year, more than enough for a Transfusion Practitioner's salary, plus equipment, plus secretary.

The title of this article is meant to encompass appointees from various health professional backgrounds; but the most appropriate are nurses, with biomedical scientists running a close second place (some would say equal). Although pharmacists, physiotherapists, occupational therapists, etc could undertake this role after suitable further training, a nursing background has undoubted advantages; biomedical scientists (and - with luck - doctors) also have a basic understanding of the transfusion process; but those other health care professionals will probably lack experience or knowledge of the process as a whole and would need a high degree of training to make them competent and able to educate and influence the practice of others 'on the ground'.

Ideally, transfusion nurses should already have significant senior nurse experience, and have taken specialist courses in their current specialism. Indeed, those in acute disciplines may have gained some extra insight into transfusion; for example, the ENB 100 Intensive Care for Specialist Nurses - which takes six months to acquire - has special detailed lectures on haemostasis and is reinforced by lectures from intensivists and anaesthetists. Rachael Rowe, of the RCN Faculty of Emergency Medicine (rachael.rowe@rcn.org.uk), is also championing the cause of good transfusion practice in that setting. Further skills such as communication, organisation and teaching are also required. Although it is certainly possible to apply such extra teaching to non-nurses, it may be more difficult to do so. However, without extra training in transfusion, most Registered Nurses have insufficiently detailed understanding to be a Transfusion Practitioner. A recurring theme at meetings of the BBTS SIG on Hospital-Based Transfusion Practice is the lack of undergraduate teaching in transfusion in most Schools of Nursing in the UK, as it can be hard to find adequate mention of transfusion science or practice in their curricula. Great attention is (rightly) paid to the dispensing of medications, including positive patient identification; and the administration of intravenous medications requires certification. Education for nurses at undergraduate level in 'transfusionology' needs addressing urgently, as it is more difficult to develop good practice otherwise.

Extra in-hospital training of ward and theatre nurses can be difficult to apply where schedules are heavy. There are instances where the initial transfusion-nurse-led enthusiasm among the Directors of Nursing in clinical areas for standardising hospital transfusion policies 'trails-away' after cascading to staff, such as those working at night. It is particularly important to get such training to these staff; experience shows that they are always very appreciative of trainers visiting them during *their* working time.

The British Blood Transfusion Society's Special Interest Groups in Autologous Transfusion, and in Hospital-Based Transfusion Practice, advocate increasing awareness and training for practitioners of transfusion in hospitals and for them to gain credibility among their peers. The BBTS website (www.bbts.org.uk) is currently carrying on its forum a dialogue with Brian

continued on page 7

Jackson at Manchester (BJACKSON@labmed.cmht.nwest.nhs), and Ruth Melchers of the Specialist Practitioners of Transfusion Group (r.melchers@rbh.nthames.nhs.uk), both of whom offer help in preparing job descriptions and business cases for appointing Transfusion Practitioners. One important aspect is to encourage awareness among patients. With Sandra Gray, Project Manager of the 'Effective Use of Blood' group in Scotland, Ruth has written an excellent chapter in the Fifth Annual Report of the SHOT group, which covers the period 2000 - 2001. In their last paragraphs they state *"The role of the Hospital Transfusion Specialist is still in its infancy (but) their contribution is just beginning to be realised. By breaking down inter-professional boundaries ..... and by acknowledging that the neglect of transfusion education for all professional groups can perpetuate mistakes and bad practice, the existing culture can be changed. ..... To meet government directives ..... all hospitals should consider employing a Transfusion Nurse Specialist."*

Such Specialists will get significant support from the NBS, particularly from its Hospital Liaison Managers who, while often working with hospital blood bank staff, have the same aims as the practitioners and the blood bankers - safe blood transfusion in hospital wards and operating theatres. Furthermore, the NBS is appointing a National Transfusion Liaison Nurse Manager who will lead a team of nine nurses spread across England. Their role will be the provision of support, education and information to help drive forward best practice and principles of Better Blood Transfusion.

The CMOs' second meeting on Better Blood Transfusion on 29th October 2001 (see www.doh.gov.uk/bbt2) referred in some detail to the positive role which could be played by hospital transfusion practitioners. Among other things, this gives attention to the training of staff and of the need for positive patient identification by bar-code identity-readable wrist bands. Ending with a quote from the CMOs' conference which, although made over 80 years ago (the quote, that is!) seems more relevant than ever:

"Every hospital should follow every patient it treats long enough to determine whether or not the treatment was successful and to inquire 'if not, why not?' with a view to preventing similar failures in future."

Frank Boulton
NBS Southampton and Dept of Haematology,
Southampton University Hospitals Trust
Chair BBTS SIG on Hospital-Based
Transfusion Practice
Contact email: frank.boulton@nbs.nhs.uk

The author acknowledges with thanks the help received from Jan Gordon, Sandra Gray, Catherine Howell, Brian Jackson and Ruth Melchers during discussions while writing this article.

Audit Of The Appropriate Use Of Fresh Frozen Plasma

A full report of this audit has been sent to all hospitals. Further copies may be obtained on request from Dr D Stainsby, NBS Newcastle Centre (0191 2194436)

Introduction

A national audit of the use of FFP and related components was initiated in June 2001 because of concerns that

- demand is rising (7% since 1998/9) and previous audits have reported inappropriate use.
- there is a need to avoid uneccessary exposure, following reports from SHOT of a relatively high incidence of adverse reactions.
- options regarding future provision are being considered in the light of concerns regarding vCJD.

The aim of the audit is to study the clinical use of FFP and make recommendations about measures to encourage its appropriate use.

The objective of the first phase was to find out where and why plasma components are used, and how inappropriate use can be reduced by implementation of policies and protocols, educational strategies, control of issue from blood banks, audit and monitoring

The next phase will be to develop national benchmarking and comparative audit of FFP use.

Summary of Findings

- 317 questionnaires were issued of which 156 were returned, a response rate of 49%. A third of participating hospitals were unable to provide detailed information on usage.
- There was a disappointing level of implementation of policies for the use of plasma components and for management of the clinical situations in which they are used (Fig 1) Only 53% of responding hospitals had a policy in place for the use of FFP. Many hospitals place the onus of responsibility on blood bank staff to challenge inappropriate requests.
- Most FFP and related components are used on general medical and surgical units and in cardiothoracic surgery (Fig 2), typical clinical scenarios being rapid reversal of Warfarin anticoagulation and massive transfusion. Use of FFP in cardiothoracic surgery requires further study, particularly as indications for use in this situation are unclear. FFP use in liver units appeared low, however liver transplant surgery was under-represented.

contin..ed on page 8

- Six local audits of FFP use against BCSH guidelines[2] were submitted, in which 493 patients were studied. Compliance ranged from 62% to 92%. Clinical notes and blood bank requests were noted frequently to be inadequate for assessment of appropriateness of transfusion. Inappropriate use was effectively reduced in one hospital by education of prescribers.
- Although 70% of hospitals aimed to use the BCSH recommended dose of 12 to 15 ml/kg, reported audit data indicated that this is not always achieved.

Recommendations

- It is the responsibility of every HTC to ensure that a local strategy is in place to reduce inappropriate use of plasma components. Transfusion nurses or co-ordinators have an important role. Effective strategies include
- Implementation of policies supported by educational programmes.
- Audit and monitoring.
- Educational request forms, including dosage guidance.
- Appointment of transfusion co-ordinators with a remit for education, monitoring and audit.
- Underdosage exposes patients to risks of adverse events for little therapeutic benefit. The use of a dose/weight chart is recommended.
- Use of FFP in 'conditional' indications such as massive transfusion and cardiothoracic surgery should be guided by tests of coagulation. The use of near-patient coagulation tests merits consideration if a rapid turnaround cannot be achieved by the haematology laboratory.
- Clinical audit requires good information and resource in hospitals. Accurate documentation of indications for FFP is essential.
- The use of FFP for immediate reversal of Warfarin anticoagulation can be limited by
  - better availability of Prothrombin Complex Concentrate for the treatment of life-threatening bleeding
  - judicious use of Vitamin K
  - better planning of elective procedures

Examples of a dose/weight chart and an educational request form may be obtained from the NBS Clinical Audit Department.

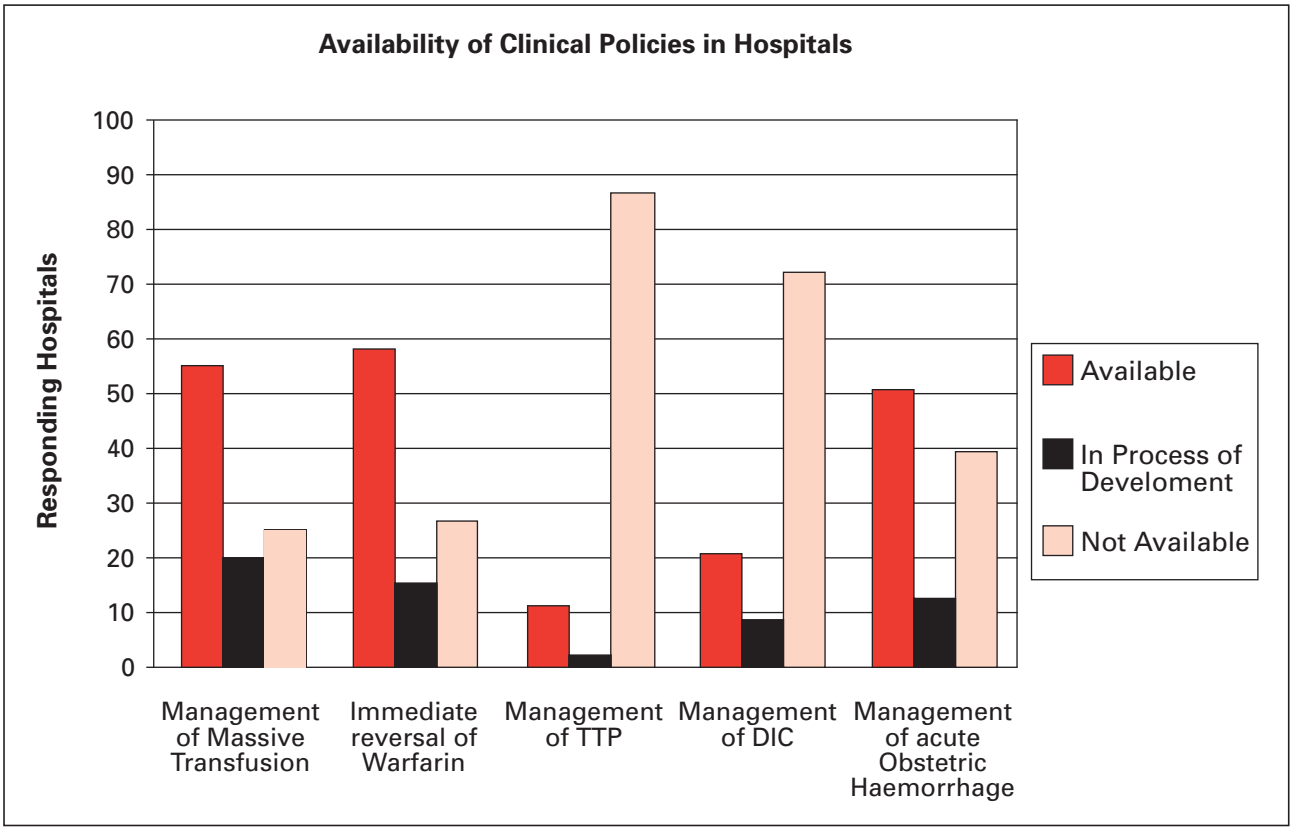
A standard audit tool is being developed as part of the next phase of the audit.

References:

1. Appropriateness of the use of Fresh Frozen Plasma. H Eagleton, S Benjamin, M Murphy. Transfusion Medicine. 2000, **10**, 6
2. British Committee for Standards in Haematology (BCSH) Guidelines for use of Fresh Frozen Plasma: Transfusion Medicine 1992, **2**, 57-63

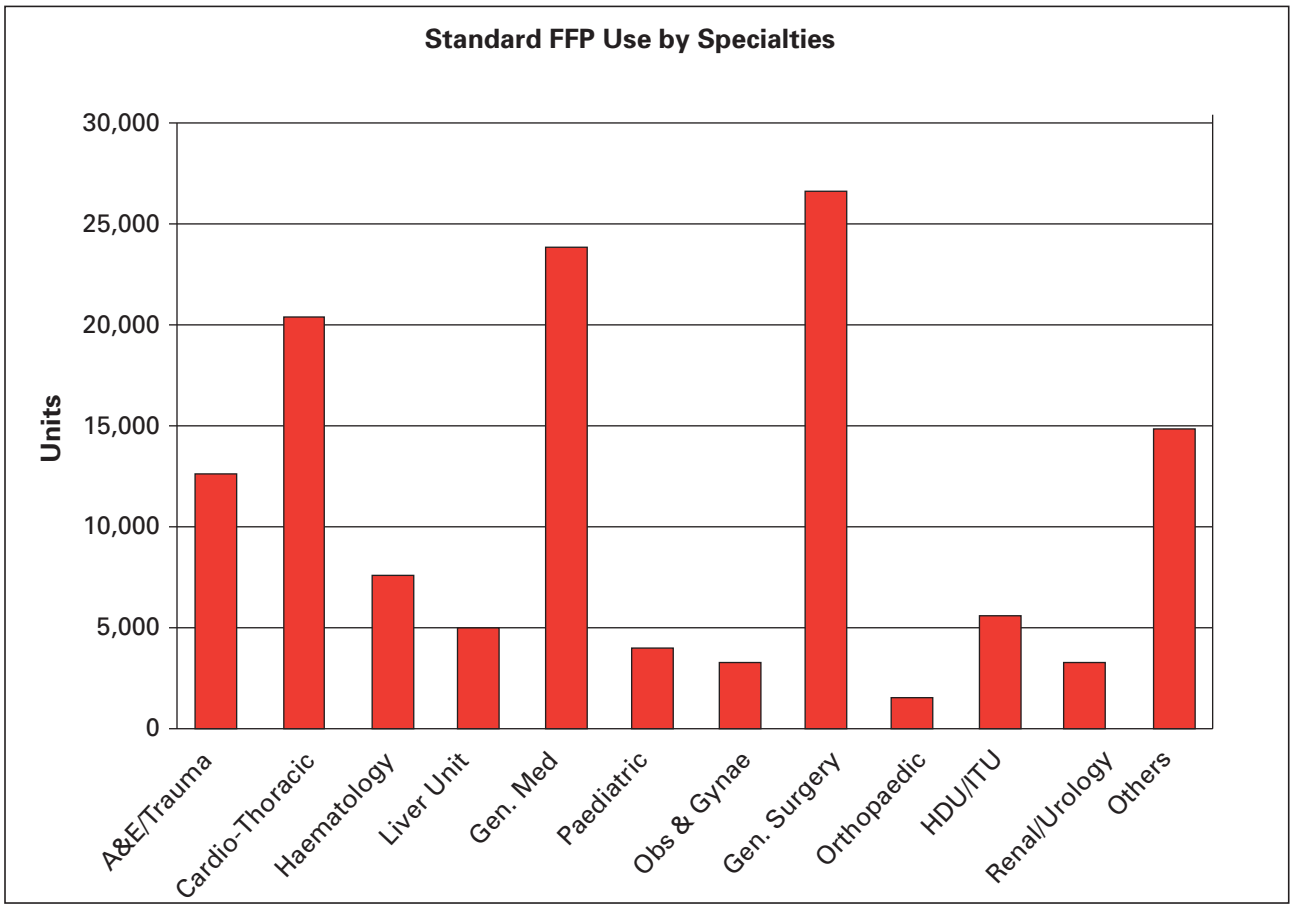
Dr Dorothy Stainsby & Valerie Burrowes-King
NBS Clinical Audit & Effectiveness Department
Contact email: *dorothy.stainsby@nbs.nhs.uk*

Figure 1



contin..ed on page 9

Figure 2



Therapeutic Apheresis in the National Blood Service (NBS)

Background

Cell separator machines for the collection of plasma from volunteer donors were introduced into the NBS in the 1970's. Initially they were used for the collection of plasma containing anti-D antibody for immunoglobulin production. In the 1980's large amounts of normal plasma from volunteer donors was collected as part of a national programme for self-sufficiency in blood products, particularly factor VIII concentrate and albumin. At about the same time, cell separators were introduced for the collection of platelet rich plasma.

Developments in apheresis technology have resulted in improvements in product quality, particularly in platelet yields. Now, 40% of adult therapeutic doses (ATD) of platelets collected by the NBS are collected by apheresis. Moreover, the vast majority of plateletpheresis donors are selected to donate double or triple ATDs and all plateletpheresis products are leucodepleted during the collection procedure. The collection of platelets by apheresis enables the provision of HLA and HPA matched platelets for patients who are refractory to platelet therapy. Platelets for neonatal and paediatric patients are also provided by apheresis from a small pool of regular and frequently tested donors. As plasma for fractionation is now imported, little plasma is collected by apheresis, but apheresis plasma is still collected for the preparation of FFP for paediatric and neonatal use from regularly tested donors, for specialist plasma products such as IgA deficient plasma and plasma for reagent use.

NBS staff continue to maintain and expand their expertise in the field of apheresis. New machine techniques are investigated and validated. One of the more recent developments is the collection of double doses of red cells in SAG-M solution (Saline Adenine Glucose Mannitol) using apheresis technology. The advantage of red cells collected by this method is the greater consistency and component quality that can be guaranteed on every occasion and the reduction in donor exposure that can be achieved for regularly transfused patients if they are given two red cell units from the same donor.

Therapeutic Apheresis

The experience and expertise gained by the NBS over many years, is now being used to great advantage in the field of therapeutic apheresis, which involves the physical removal of abnormal blood constituents for the purpose of alleviating or controlling disease symptoms. Nine of the nineteen NBS apheresis units in England, undertake some or all of the following types of therapeutic apheresis procedures.

contin..ed on page 10

Red cell exchange: This is a type of procedure in which abnormal red cells are removed and replaced with normal red cell components.

Leucapheresis: In this procedure, leucocytes are selectively removed from a patient/donor using a cell separator. This procedure could be undertaken to reduce the number of circulating white cells in patients with chronic myeloid leukaemia, before definitive myeloablative treatment is started. It is also used to collect cells from the mononuclear cell layer for storage for use as a "rainy day" peripheral blood stem cell harvest in patients with chronic myeloid leukaemia. The term cytapheresis or removal of cells is sometimes used synonymously with leucapheresis.

Plasma exchange: This involves removing plasma and replacing it with suitable colloid solution or plasma. The therapeutic procedure removes intravascular constituents and repeated small volume exchanges are more efficient than large volume and less frequent exchanges. Table 2 below shows the percentage of intravascular constituents removed depending on the volume of plasma exchange undertaken.

Table 2 Plasma exchange volume and percentage of intravascular contents removed

Volume of exchange	*Percentage removed*
1 volume exchange	66%
2 volume exchange	85%
3 volume exchange	95%

The replacement fluid for plasma exchange is usually 4.5% human albumin solution, saline or a mixture of these. Albumin is not suitable as a replacement fluid in cases of TTP (thrombotic thrombocytopenic purpura) and cryopoor FFP or solvent detergent treated FFP is used.

Photopheresis: This is a procedure in which ultraviolet light is targeted for the treatment of a desired component in the patient (for example, T cells in patients with cutaneous T cell lymphoma), while other untreated blood components are returned to the patient.

LDL Apheresis: Low density lipoprotein (LDL) apheresis is a procedure in which a special immunoadsorption column removes the excess cholesterol in patients with homozygous hypercholesterolaemia and returns the cholesterol depleted plasma to the patient.

Peripheral Blood Progenitor Cell Collection by Apheresis

Blood progenitor or stem cells from the mononuclear cell layer can be collected from the peripheral blood by apheresis. Allogeneic or autologous peripheral blood progenitor cell collection requires a specialist team linked to a Bone Marrow Transplantation Unit to ensure co-ordination of all the procedures involved: preparation of the patient/donor, timing of the cell collection, appropriate laboratory processing , cryostorage and preparation of the stem cells for reinfusion. There is a detailed clinical guideline published by the BCSH (see further reading).

OTHER CLINICAL ISSUES
APHERESIS GRANULOCYTES

Some apheresis units collect granulocytes from screened unrelated volunteer donors by apheresis technology for treatment of patients undergoing intensive chemotherapy who are severely neutropenic and unresponsive to second or third line antibiotics. The evidence for the use of granulocytes in this way is not strong and because the numbers of patients requiring these treatments are exceedingly small, it has been very difficult to organise controlled randomised clinical trials to assess the efficacy of this component. Pooled buffy coats are occasionally being used when apheresis granulocytes are not available.

In May 2002, a one-day meeting is planned under the auspices of the UK BTS's Standing Advisory Committee on Blood Components (SACBC) to discuss this issue. This should have an impact on provision of this component by apheresis and it is hoped that this meeting will determine the way forward for granulocyte provision within the National Blood Service.

Service Provision by the NBS

To date, the development of therapeutic apheresis services within the NHS has been somewhat ad-hoc, either developing in association with specialist units in some Trust Hospitals, e.g. Renal Units (plasma exchange), BMT Units (PBSC collection), or within some NBS apheresis units. Currently the NBS is a major provider of the whole spectrum of therapeutic apheresis services and as a result of increasing demand for PBSC collections and the re-emergence of a demand for granulocyte transfusions, NBS resources are being stretched beyond their current capacity. In the past, resource planning has been difficult because of the unpredictability of demand. Over the next few months the NBS will start to address this by exploring optimum collaborative partnerships with Trust Hospitals to ensure agreed, adequately resourced and appropriate service level provision is delivered when and where required. The objective will be to engage key users of the service in meaningful discussions to determine the best way forward for the future.

One of the issues to clarify is the boundaries of responsibility for patient care and management of problems directly related to the therapeutic apheresis procedure being performed, but the overall care of the patient remains with the referring clinical team. This has not always been clear in the past and has occasionally led to misunderstandings on both sides.

contin..ed on page 11

One of the issues to clarify is the boundaries of responsibility for patient care and management of problems directly related to the therapeutic apheresis procedure being performed, but the overall care of the patient remains with the referring clinical team. This has not always been clear in the past and has occasionally lead to misunderstandings on both sides.

It is therefore becoming important to standardise policies and procedures for referral, consultation and handover of patient care between the NBS apheresis team and the referring clinical team. For example:

No apheresis procedure is possible without patient vascular access and this remains the primary responsibility of the referring clinical team. Establishing clear principles and policies should provide a clear framework in which the mutual interests of NHS hospitals and the NBS are combined to provide an efficient management of this service to patients.

FUTURE PLANS

There is no doubt that the NBS will be playing an important role in the procurement of peripheral blood stem cell services by apheresis for hospitals. Issues of accreditation mean that the NBS, fully versed in principles of good manufacturing practice, is in a position to provide this service where hospitals wish us to do so. Over the next few months, discussions will be taking place with those hospitals that have approached the National Blood Service for help with provision of this service.

For the future, we will continue to evaluate new therapeutic strategies. The increasing use of immunoadsorption techniques in the treatment of diseases is an area of development likely to expand.

Standardisation of protocols for therapeutic apheresis has already begun. During this process, we will address ethical and safety issues with the objective of providing the safest possible service for both donors and patients.

Further Reading on Apheresis

1. Apheresis: Principles and Practice. AABB press. Editors, Bruce C. Mcleod, Thomas H. Price, Mary Jo Drew. Copyright 1997.

2. Clinical Applications of Therapeutic Apheresis. Journal of Clinical Apheresis, Vol 15, Issue 1-2 (Special Issue), 2000.

3. Guidelines for the Clinical Use of Blood Cell Separators, Clin. Lab. Hae, 1998, **20**, 265-278.

4. Guidelines on the provision of facilities for the care of adult patients with haematological malignancies (including leukaemia and lymphoma and severe bone marrow failure). Clinical & Laboratory Haematology, 1995, **17**, 3 - 10.

5. Collection, processing and storage of human bone marrow and peripheral stem cells for transplantation. Transfusion Medicine, 1994, **4**, 165-172.

Dr Moji Gesinde
Lead Consultant Apheresis
Contact email: *moji.gesinde@nbs.nhs.uk*

Cold Reacting Antibodies And The Selection Of Blood For Transfusion

Not all red cell antibodies cause *in vivo* cell destruction and there is sufficient evidence to show that alloantibodies that fail to react *in vitro* at 37°C i.e. "cold reacting" alloantibodies, can be regarded as being not clinically significant.

The 1996 BCSH Guidelines on pre-transfusion testing state that 'for patients with clinically significant antibodies blood should be selected which has been tested and found negative for the relevant antigen. If the antibodies are not clinically significant, it is not necessary to select antigen negative blood.' Blood of the same ABO and D type as the patient should be selected for compatibility testing and *IAT cross-match compatible blood* supplied for transfusion.

Despite these recommendations many blood banks continue to use antigen negative units for patients with antibodies that are not clinically significant. The aim of this article is to give further guidance on the selection of blood for patients with antibodies.

Firstly, there is no evidence that cold-reactive antibodies cause clinically significant *in vivo* destruction of red cells that carry the corresponding antigen even when patients are subjected to hypothermia during surgery.

If anti-P_1, -A_1, -Le^a, -Le^b, -Lu^a or -N reacting by an indirect antiglobulin technique is detected, it is unlikely that it will be reactive at strict 37°C. In this situation, if units of the same ABO and D type of the patient are selected, compatible units can be found without difficulty by using a pre-warming crossmatch technique (i.e. warming the serum and cells to 37°C prior to mixing them together and incubated at 37°C. At the end of the incubation period, the cells should be washed, or the gel centrifuged immediately). If you have difficulties with undertaking these tests please seek advice from your local RCI laboratory manager.

Even those antibodies that react weakly in prewarmed *in vitro* tests, rarely cause problems in finding suitable blood. For example, the P_1 antigen expression on red cells varies, and potent examples of anti-P_1 will often only react at 37°C with cells with a strong P_1 antigen. In addition, many examples of anti-Le^b that react by IAT

continued on page 13

with group O screening or panel cells will fail to react with group A, B or AB cells as they are in fact anti-Le^{bH}, requiring both Le and H to be present on the red cells. Therefore if units of the patient's own ABO blood group are selected no incompatibility will be found on crossmatching.

The BCSH Guidelines permit the use of anti-IgG in the IAT, for routine antibody screening and cross-matching. The use of anti-IgG in routine screening will reduce the number of 'unwanted' cold reacting antibodies detected; and even if anti-IgG is not used routinely, its use in crossmatching where a cold-reacting antibody is known or suspected to be present, will markedly reduce the likelihood of problems. Finally, it should be noted that if the routine cross-matching method incorporates a room temperature or immediate spin direct agglutination method, substitution of this with a pre-warmed 37oC direct agglutination method will alleviate cross-matching problems in this phase. Crossmatching at 37°C will not affect the detection of ABO incompatibility.

Anti-C^w and anti-Kp^a are sometimes found in the absence of other allo-antibodies. As these antibodies are of doubtful clinical significance and the incidence of the corresponding antigens low, about 2% for both antigens, there is no need to select C^w or Kp^a negative blood. For anti-C^w selecting RhC negative blood is sufficient but for Kp^a it is only necessary to select blood of the same ABO and RhD type as the patient for crossmatching by IAT.

The table below is based on the BCSH Guidelines and forms the basis of the policy the NBS has adopted for the supply of antigen negative blood. We are increasing our efforts to ensure there are sufficient stocks of blood phenotyped for the important antigens but stopping routine and expensive typing for those antigens whose antibodies are considered not to be clinically significant.

If there is any doubt about the reactivity of an antibody or its clinical significance, samples can be referred to your local NBS RCI reference laboratory for testing. RCI staff will be pleased to advise you about selection and testing of appropriate units for crossmatching and transfusion.

Dr Mahes de Silva
Lead Consultant
Red Cell Immunohaematology
Contact email: *mahes.desilva@nbs.nhs.uk*

Robin Knight
Service Development Manager
Red Cell Immunohaematology
Contact email: *robin.knight@nbs.nhs.uk*

System	Antibody	Recommendation
ABO	Anti-A_1	ABO & D matched blood compatible by 37°C IAT*
H	Anti-H1 (in A_1 and A_1B patients)	Own ABO group compatible by 37°C IAT*
Rh	Anti-D, -C, -c, E, -e	Antigen negative
Rh	Anti-C^w	RhC negative, D matched, IAT crossmatch compatible
Kell	Anti-K, -k	Antigen negative
Kell	Anti-Kp^a	ABO & D matched blood compatible by 37°C IAT*
Kidd	Anti-Jk^a, -Jk^b	Antigen negative
MNS	Anti-M (active 37°C)	Antigen negative
MNS	Anti-M (not active 37°C)	ABO & D matched blood compatible by 37°C IAT*
MNS	Anti-N	ABO & D matched blood compatible by 37°C IAT*
MNS	Anti-S, -s, -U	Antigen negative
Duffy	Anti-Fy^a, -Fy^b	Antigen negative
P	Anti-P_1	ABO & D matched blood compatible by 37°C IAT*
Lewis	Anti-Le^a, -Le^b, -Le^{a+b}	ABO & D matched blood compatible by 37°C IAT*
Lutheran	Anti-Lu^a	ABO & D matched blood compatible by 37°C IAT*
Diego	Anti-Wr^a	ABO & D matched blood compatible by 37°C IAT*
All	Others active by IAT at 37°C	Seek advice from Blood Centre

* select blood of the same ABO and D type as the patient; antigen negative blood is NOT required
The above guidance is also suitable for patients undergoing hypothermia during surgery.

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