

# Blood Matters

Quarterly information for hospitals served by the National Blood Service

## INTRODUCTION

Dr Angela Robinson, Medical Director, National Blood Authority introduces this edition of *Blood Matters*

Page 2

## NATIONAL BLOOD STOCKS PROJECT UPDATE

Page 2/3/4

## THE RED BOOK: PAST, PRESENT AND FUTURE

Page 4/5

## CJD/vCJD RESEARCH WITHIN THE NBS AND ITS PARTNERS

Page 5/6/7

## UPDATE ON ANTI-D

Page 7

## WEIGHING THE ISSUES AROUND CLINICAL FFP

Page 8/9

## NATIONAL CALL CENTRE

Page 9/10

## A NEW DIRECTION

Page 10

## RED CELL STOCK LEVELS DURING 2000-2001

Page 11

## ISBT CODE 128 PROJECT

Page 11

## ISBT 128 DIARY PLANNER FOR HOSPITAL BLOOD USERS

Page 12



Welcome to the third national issue of Blood Matters. I am delighted to say that we have been getting very positive feedback about the style and content of this newsletter, such that we have had to increase the print run to meet demand. Good suggestions for articles and updates are being put forward together with 'volunteer' authors, which makes the task of the editorial board relatively easy. Thank you to those readers who have given us feedback and thank you to all our 'volunteer' authors so far. Please continue to keep the suggestions for articles coming as this helps to convince busy individuals that their time and effort spent putting pen to paper is worthwhile.

In this edition there is the fourth update from the National Blood Stocks Project which reports on the latest achievements of this enormous collaborative effort between hospitals and the NBS. Forty six hospitals are now participating and some real progress has been made in understanding the blood supply chain between blood centres and hospitals. Thanks to this tremendous cooperation and the remarkable honesty between all participants, some real guidance and benchmarks are emerging which should lead to improved stock management nationwide. For those of you who have not yet come across 'The Red Book', this article will apprise you of how these guidelines and standards came into being and how they are continuously maintained and updated. They now serve as a really valuable tool for UK experts sitting in EU working parties where new directives on blood safety are being considered. Unfortunately, despite the UK's excellent blood safety track record the shadow of vCJD still hangs over it. A brief report is therefore included in this issue on what research the NBS is involved in to try and help resolve some of the remaining unanswered questions. It was also thought timely to provide an update on the use of anti-D to prevent Rh haemolytic disease of the newborn, where full compliance with the new guidelines should further reduce the incidence of what is now a rare disease. On another topic there has been a constant and ongoing debate about the use of clinical FFP in its various formats. The article 'Weighing the Issues around clinical FFP' is an attempt to explain this difficult conundrum. To maintain a regular and constant supply of blood it is vitally important for the NBS to be as responsive as possible at all times to any queries raised by blood donors. You may therefore be interested to read about our National Call Centre (NCC), which is a relatively new and highly successful venture greatly improving NBS communications with the general public. Finally there is a short update article about the current NBS reorganisation entitled 'A New Direction'.

Please do not hesitate to contact my colleague Hilary Hampson on 01923 486800, fax 01923 486801 or e-mail [angela.robinson@nbs.nhs.uk](mailto:angela.robinson@nbs.nhs.uk) if you have any comments or ideas about this newsletter

**Dr Angela Robinson**  
Medical Director, National Blood Authority

## **National Blood Stocks Update**

### **INTRODUCTION**

Welcome to the fourth update of the National Blood Stocks Project. This is the second regular information sheet in Blood Matters to help keep key hospital staff aware of the developments that are being made in this important project.

The two major aims of the project are;

- continual improvement in the relationship between hospitals and blood centres based on trust and mutual cooperation;
- improvement in the physical management of blood stocks and effectiveness of the whole supply chain.

The development of both of these areas is seen as essential to the long-term success of an optimal demand/supply relationship between blood centres and hospitals.

Those who are not aware of this project will find background information in the second issue of Blood Matters together with a resume of the findings from phase 1.

Phase 2 of the hospital blood stocks project commenced in April 1999 using the same benchmarks as in phase 1, with the addition of 'allocated stock data' and specific data from 'case studies'. Phase 2, was a two month data collection exercise of stockholding levels, request and issue practices and wastage rates. This phase involved 21 of the same 22 hospitals in phase 1 and all NBS blood centres.

Having completed phase 2, the project is moving rapidly and is now into phase 3, with an additional 24 hospitals taking part.

As a consequence of participation in this project, some important changes in hospital working practices have already been implemented.

A successful phase 2 conference of both current participants and the new hospitals has been held, with unanimous agreement that the project is proceeding in the right direction.

Terry Male  
Project Chairman

## **Data Collection**

### **ISSUABLE STOCK**

Centres were faced with a shortage of issuable stocks during phase 1, particularly O POS. Sufficient stocks were available during phase 2 for all groups. The average NBS stockholding for O POS in phase 1 was 1.5 days compared with 8.5 days in phase 2. In contrast hospital stocks showed little change in issuable stock levels, average 4.36 in phase 1 compared to 4.48 in phase 2. A number of hospitals were holding lower stocks, possibly a reflection of increased confidence in the centres ability to supply or due to the shorter shelf life of some stocks received from centres.

### **ALLOCATED STOCK**

During phase 2 some hospitals were able to collect a further data set, 'Allocated Stock'. Allocated stock is stock which is not available for immediate issue. Some of the large hospitals with several off site satellite fridges and ward fridges did not have the resource to supply this information. The ratio of issuable/allocated stock was compared to the crossmatch/transfusion ratio. Similar values were obtained for both sets of data for some of the groups, and this will be investigated further.

*continued on page 3*

## BLOOD WASTAGE

The hospital wastage categories from phase 1 were further refined in phase 2. The major cause of wastage at both centres and hospitals was time expiry and a sizeable number of these units were group AB. The higher NBS stock levels resulted in time expiry rates in excess of those seen in phase 1, with the expected variation between zones. At hospitals there was again significant wastage *out of temperature control outside the hospital transfusion laboratory.*

## IMPACT ASSESSMENT

Due to the higher stock levels in phase 2 the incidence of both centre and hospital impact assessment scores was very low, in marked contrast to phase 1.

The need for an impact assessment to address issues arising from higher stock levels at centres has been identified and will be tested in phase 3.

## Case Study data

### ABO/RH MISMATCHES

Analysis of the data showed that the use of compatible, but ABO mismatched blood was widespread. The mismatching of O RhD negative units is of particular interest given the recurrent supply problems with this group. Overall, 26% O RhD negative units given to non-O RhD negative recipients were considered to be clinically justified. A further 12% were supplied by the NBS where phenotyped units of the patients group were not available.

### ABO MINOR GROUPS

Three smaller hospitals who did not hold stocks of minor groups in phase 1, began to hold stocks in phase 2. Most of the blood appears to have been used, however, the results are still being followed up.

### RETURNS

There were a few instances where hospitals wanted to return blood, mostly B Pos and AB POS, to the centre for reissue. These returns will continue to be monitored as an ongoing issue, although the overall impact of any change in this area would be very small.

### RESERVATION TIMES

All hospitals agreed to use a maximum 48 hour reservation time where possible. Some hospitals already operated this policy and those changing to these new times have found the change to be beneficial.

### HOSPITAL TRANSFERS

The group initiated this study because there was little data available on the wastage resulting from blood being transferred with patients to another hospital. Research has shown there was relatively little wastage overall.

### HOSPITAL QUESTIONNAIRE

A questionnaire was distributed to all 22 participating hospitals in an attempt to understand the potential factors contributing to stock-holding policies, blood stock management and the constraints existing within local systems. 19 hospital responded to this questionnaire.

### Questionnaire Findings:

- The distance from the Blood Centre influenced stock levels only in hospitals issuing less than 5000 units annually.
- 10 out of 15 hospitals, using more than 5000 units annually had a high confidence in deliveries being fulfilled.
- During shortages, 12 out of 19 hospitals increase orders or make repeated orders to maintain ideal stocks.
- The size of satellite stocks appeared not to influence total group O stock-holding.
- 15 out of 19 hospitals have Hospital Transfusion Committees, and the 8 hospitals monitoring wastage have lower time expiry wastage.
- 11 out of 19 laboratories receive less than 24hrs notice for a significant proportion of their cross-matching work and in 5 out of 19 laboratories, less than 25% of the patients for elective surgery have been grouped in advance. As a result these hospitals tended to hold larger stocks of ORhD Negative.
- 10 out of 15 hospitals dealing with emergency transfusions are constrained in providing group specific units owing to delays in receipt of patient samples.
- When faced with specific problems the most common solutions suggested by hospitals were:
  - for reducing stock levels - more deliveries and electronic issue;
  - for reducing wastage - education of ward staff;
  - for equity in stock holding - the use of the stock indices.
- 13 out of 19 hospitals have introduced changes in stock management as a result of involvement in the project.

The findings above show that effective hospital blood stock management is dependent upon good intra-hospital communications. With minor modifications, this questionnaire will be a very useful tool to assess those areas of national practice which cannot be quantified from data collection.

### CENTRE CASE STUDY

Six NBS Centres were nominated to take part in a case study designed to examine those areas of operational practice which may influence red cell time expiry rates. A detailed evaluation of validation, stock lodgement and rotation procedures indicated a broad similarity in approach by all centres. However more specific aspects of stock management associated with segregation of product lines and rotation of phenotyped stock indicate the potential for improvement. The case study has resulted in a number of recommendations for consideration and ultimate implementation e.g. the use of stock management tools such as age profiling techniques need to be more accessible.

### Next steps

Phase 3 of the project commenced on November 1st and will run until February 29th 2000, with 4 weeks break over the holiday period for millennium issues. This phase is to consolidate the work carried out in phases 1 & 2 and

primarily to establish the benchmarks to be used when this project makes the transition to national mainstream activity.

These benchmarks form the basis for the development of new national guidance that will help ensure that best practice is adopted throughout all points of the blood supply chain across the country.

The benchmarks will not only be data based e.g. stock levels, wastage, impact assessments, request/issue levels, but will also feature key organisational aspects e.g. presence of active transfusion committees, use of MSBOS, crossmatch techniques etc.

## USEFUL CONTACTS

Anyone requiring more information should contact his or her respective representatives on the project group:

### Northern zone

- Adrienne Harper, National Blood Service, Sheffield, 01 14 203 4892
- John Revill, Leicester Royal Infirmary, 0116 258 6604

### Midlands and South West zone

- Mary Cutts; National Blood Service, Bristol, 01179 912055
- Stephan Bates, Cheltenham General Hospital, 01242 274055

### London and South East zone

- Stuart Penny, National Blood Service, Colindale, 0181 258 2805
- Bill Chaffe, William Harvey Hospital, Ashford, 01233 616017

## The Red Book: Past Present and Future

The Red Book is the common name for The United Kingdom Blood Transfusion Services/ National Institute of Biological Standards Guidelines for the Blood Transfusion Services in the United Kingdom. The book has always had a red cover and will continue to do so. The familiar and loved common name will therefore continue to be appropriate and summarise a rather cumbersome title.

The Red Book was conceived in 1987. The National Institute of Biological Standards (NIBSC) and the then United Kingdom Blood Transfusion Services, with great foresight, formed a Liaison Group to formulate guidelines and provide standards which a Government licensing Authority could use to accredit Transfusion Centres. Crown Privilege, introduced in 1968, was to end as new regulations emanated from the European Economic Community.

The minutes of the first meeting of this Liaison Group state ... "the formulation of guidelines... would be timely in view

of the EEC Directive on Product Liability, due to be introduced in the UK in July 1988, and a possible future Directive to remove Crown Immunity from NHS establishments. The guidelines were to be formulated on a purely professional basis by independent expert advisory groups within the red book committee structure. It was also clear that joint work in many fields would benefit both organisations. Crown Immunity was finally removed from NHS establishments in 1990.

## Production of the Red Book

In 1987 the Regional Transfusion Directors (RTDs) and NIBSC set up three Standing Advisory Committees (SACs) consisting of doctors and scientists nominated for their expertise in different aspects of transfusion. The SACs reported to the Executive Liaison Committee consisting of the chairmen of the SACs, Directors of NIBSC and chairmen of RTDs and representation from the Medical Control Agency. Early meetings were attended by observers from the DoH. Right from the start it was a UK wide undertaking. Each of these SACs was responsible for producing the appropriate chapter for the Red Book. These chapters reflected best professional practice and advice. The work of the SACs was discussed at the meetings of the Executive and only fully agreed guidance appeared in the Red Book.

Over the years Standing Advisory Committees have increased reflecting increasing complexity of transfusion practice, and with the creation of the four National Blood Transfusion Services in the United Kingdom all four Medical Directors are now part of the Executive. The basic ethos however has not changed: these are professional guidelines reflecting best practice in a rapidly changing environment, based on available evidence. Obtaining such evidence where it does not exist is also part of the remit of the organisation.

There are now eight Standing Advisory Committees consisting of about 8-10 members, nominated for their individual expertise.

Donor Care and Selection

Transfusion Transmitted Infections

Blood Components

Immunohaematology

Information Technology

Tissue Banking

Plasma for Fractionation (continuing its monitoring role even though currently UK plasma is not fractionated).

1999 also saw the creation of a new SAC: Clinical Transfusion Medicine

Some SACs have standing subcommittees and ad hoc working parties may be created to deal with specific issues. Wide consultation with professional groups and organisations outside the Transfusion Services, and also outside the NHS, is necessary. Scanning the horizon for new developments is an important remit of all SACs. The parent body remains the UKBTSs/NIBSC Joint Liaison Executive Committee and meets three times annually.

## **Editions of the Red Book**

The first edition of the Red Book appeared in 1990 and was so enthusiastically received that in the introduction to the second edition in 1992 Dr Bill Wagstaff, the then chairman of the Liaison Group wrote "a great deal of satisfaction was engendered in the hearts of those involved in its formulation." The book was issued as a loose leaf Controlled Document free to all Hospital Blood banks and all Transfusion Centres. Further copies could be purchased from the publishers, the HMSO. It is no exaggeration to say that the Red Book has become a respected classic set of guidelines and minimum standards adhered to by all in the transfusion field, hospitals and Services alike. It is indeed a set of minimum standards against which Transfusion Centres are audited by the MCA.

A third edition appeared in 1996 with several new chapters. Further 'amendments and a whole new section on Tissue Banking were issued in early 1999. 1000 copies are normally printed of which approximately 800 are distributed free of charge. We are currently preparing the fourth edition which will appear in the Spring of 2000. It will be a bound copy, published by The Stationary Office, issued free as before, also available for purchase and available on the internet with password protected printing facilities. It is no longer possible to maintain the formal Controlled Document status and therefore we aim to publish annual versions and use developing IT technology to ensure that all available copies are always up to date.

Two separate sections of the Red Book: Medical Assessment of Donors and Medical Assessment of donors of tissues (MAD or A/Z and MAD-T) will remain fully controlled documents and will be issued separately to named interested parties, in electronic format if required. The contents of these two documents are liable to numerous changes throughout the year and it is essential that only one version is in circulation at any one time.

## **Influence of Europe**

The European Union has evolved from the EEC established in 1957 with the treaty of Rome. Gradually it has taken a greater interest in health related issues and has become involved in the safety of blood and blood products in EU countries. EU directives in this area as in all others have to be abided by and the Red Book needs to be consistent with these. Since the European Union has taken many of its recommendations from the longstanding work of Council of Europe in this area the Red Book needs to be consistent with the Council of Europe guidelines. This is achieved by representation on the Council of Europe working parties. The Council of Europe is a totally distinct political entity from the EU, currently consists of 41 European pluralist democracies and dates from 1949 when it was originally set up to deal with human rights problems post two world wars. It has also gradually taken on a limited health remit, including safety of blood and tissues.

## **Conclusion**

The Red Book is alive and well, both red and read. It is under constant review. As technology advances out of date guidelines are abandoned and new guidance and standards, based as much as possible on evidence and

not opinion, introduced. We all have a part in maintaining its vitality and usefulness.

All suggestions for improvement and amendment will be gratefully received by myself and directed for appropriate consideration.

**Dr Virge James**

Chairman -

UKBTS/NIBSC Joint Executive Liaison Committee

## **CJD / vCJD research within the NBS and its Partners**

### **INTRODUCTION**

Blood safety is a prime concern of blood services around the world. I do not need to remind you of why the transmissibility of spongiform encephalopathies is of particular concern to these services in the UK. At the moment our working hypothesis is that the agent of a vCJD can be transmitted by all blood components. UK plasma is no longer fractionated. All blood components are leucodepleted before issue. Collaborating with the Research and Development Division of the Department of Health and the National Institute of Biological and Serological Control, the UK Blood Services have research programmes relevant to this problem. This short article will outline this activity.

### **RELEVANT ASPECTS OF TSE PATHOLOGY; PRION LOCALISATION**

The precautions taken so far against blood transmissibility are based on current knowledge of the pathology of relevant transmissible spongiform encephalopathies (TSEs) and the small amount of published work in animals, (1) making the assumption (with considerable justification) that structurally altered prion protein (PrP<sup>sc</sup>) is the infectious agent then fundamental questions related to transmissibility can be asked for vCJD. Where is this protein located? We already know that it is in brain, tonsil and appendix, but what about blood? Collaborative research based in Bristol (Bristol Institute of Transfusion Science, BITS), Cambridge (University Department of Transfusion Medicine), Edinburgh (Academic Transfusion Unit, SNBTS) and Compton (Institute of Animal Health) is addressing this issue. So far studies are confined to native prion protein (PrP<sup>c</sup>) and it is becoming clear that this is found as a membrane bound glycoprotein on and in platelets and leucocytes (2) and free in plasma. The red cell data is less certain but the preliminary result is that it is found associated with these cells as well. More relevant would be the presence of and distribution of PrP<sup>sc</sup>. It is a big step to assume that it is similarly distributed and animal work suggests that in blood it is mostly found in the cells of the buffy coat until disease is symptomatic when it is also found in plasma (3). The scarcity of clinical material, reagents and technology are at present barriers to answering these questions directly for vCJD. The present programme is developing techniques needed to meet that objective.

### DOES LEUCODEPLETION USING CURRENT METHODS CLEAR PRPSC?

The premise that PrPsc can be removed from blood by removing a cell population (leucodepletion) would be upset if the technology used were to leave behind microvesicles or fragments derived from those cells, or release PrPsc from them. This is being investigated by collaborative research based in Bristol, Cambridge, Edinburgh and Compton running alongside the prion distribution project. This research is at an early stage.

### DISTINGUISHING NORMAL FROM PATHOLOGICAL PRION (POSSIBLY DEVELOPING A BLOOD TEST)

A fundamental problem is to distinguish PrPc from PrPsc using methods applicable to clinical material and with the potential to eventually provide a blood test for transmissible PrPsc if it is present to be detected. Monoclonal antibodies to prion are the discriminators most likely to be useful. There are knock out mouse strains that can be immunised against prion. Much effort is being invested into the development of mouse monoclonals particularly through collaboration between Bristol and the MRC Prion Unit, St Mary's Hospital, Paddington. This is enjoying some success, as is work in Bristol and Edinburgh on high sensitivity

### THE EFFECTS OF PLASMA FRACTIONATION ON PRIONS

PrPc is a relatively small glycoprotein, MW in the range of 35 KD. The alteration in conformation of this protein which results in PrPsc leads to changes in physical properties amongst which is a tendency to aggregate. In addition to being of high MW these molecules present both hydrophilic and hydrophobic domains and are membrane sticky. It is reasonable to assume that they will partition in plasma fractionation and be retained at certain stages of the process such that some blood products will be free of PrPsc even if it is present in the plasma pool from which they are derived and there is data from around the world that can be used to support this assumption (3). This problem is being approached by spiking start plasma with model prions (hamster scrapie is usually used). The read-out of infectivity is based on the inoculation of susceptible mice with fractionated material. Work is based at the PFU and National Science Laboratory SNBTS in collaboration with the Institute for Animal Health Neuropathogenesis

### WHAT CAN BE LEARNT FROM TSE EPIDEMIOLOGY?

If TSEs transmit by blood transfusion then there might be epidemiological evidence of that for CJD. A collaborative study between the CJD Surveillance Unit (CJDSU) Edinburgh and NBS transfusion microbiology specialists is in progress. A group of patients with CJD and matched controls who are known to have donated blood were identified and a single blinded look-back exercise is in progress. The details of all recipients who received components are now held on the CJDSU register so there can be a check whether any subsequently develop CJD.

This process has been extended to vCJD cases which at present are much less numerous. So far 30 patients have been identified in the CJD study and 12 in the vCJD study. None has, as yet, appeared on the register. The reverse process is also underway. The study group consists of patients who have received blood and controls. The donors are being traced and then linked to the CJDSU register. So far 282 donors have been traced, none appear on the register. Only one vCJD patient is known to have received blood but a lot of it, 103 components, none of the donors who have all been identified appear on the register.

### IS IGA DEFICIENCY SIGNIFICANT TO CATCHING VCJD?

IgA deficient persons are relatively common between 1:600 and 1:800 of the population. They are known to absorb more undigested protein and it was suggested they might be more susceptible to infection by BSE. Studies on the limited amount of clinical material available have not supported this hypothesis.

### SOLVING LEUCODEPLETION IMPLEMENTATION PROBLEMS

The implementation of leucodepletion has presented practical problems which require research to solve them. Critically important, and a considerable challenge, has been quality control. Progress to workable procedures has required the evaluation of methods and introduction of protocols for the accurate counting of very low numbers of leucocytes in component specimens. EQA schemes have been developed for the external control of this counting. Presently laser based technologies are used to count individual labelled cells but are not ideal. Work is in progress on novel approaches designed specifically to cope with counting the large number of specimens involved, allow automation and computer control of the work in line with the high standards of GMP that are required. Several groups based at NBS Birmingham, Brentwood and Bristol in the Haematology department at the Northern General Sheffield who are providing EQA are collaborating in this work.

### WILL UNIVERSAL LEUCODEPLETION HAVE OTHER BENEFITS?

Thus far the main impact of vCJD on transfusion practice in the UK is the introduction of universal leucodepletion. This has been implemented as a precaution to reduce potential transmission of vCJD but may have other very significant benefits for patients who require transfusion, particularly perioperative blood transfusion. Perioperative blood transfusion has been identified as an independent predictor of post-operative infection. There is considerable evidence to suggest this is the result of the allogeneic leucocytes transfused. It was important to take the opportunity that leucodepletion offered to examine this possibility and a multicentre study is in progress. This is recording postoperative infection and length of post-operative hospital stay in two cohorts each of 1200 patients undergoing elective orthopaedic and cardiac procedures in eight UK hospitals. Data from the first cohort who received standard blood has been collected. The study of the second cohort receiving leucodepleted blood is underway. Two untransfused cohorts of 750 patients are included to account for other variables.

## SUMMARY

I hope this short article illustrates just how important this area of research has become to the UK Transfusion Services. That is not surprising as blood safety is, and will remain, a top priority to them. This effort is minute in world-wide terms, for a very useful review see (4).

T B Wallington for the NBS R&D Strategy Group

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## Update on Anti-D

Before 1968, there was a high fetal and neonatal mortality and morbidity from haemolytic disease of the newborn. Moreover, the neonatal morbidity associated with severe neonatal jaundice (kernicterus) led to life-long neurological disability. The clinical problems were associated with placental transfer of RhD positive red cells from the fetus to the RhD negative pregnant mother, who could then develop antibodies to the D antigen which, being immunoglobulin G (IgG), could cross the placenta and interact with the red cells of the fetus causing their premature destruction, anaemia and, in extreme cases, fetal oedema (hydrops fetalis).

In the mid-1960s, due to pioneering research in Liverpool, it was shown that an injection of anti-D IgG could prevent the RhD negative mother from mounting an immune response to RhD positive fetal red cells. Perhaps paradoxically, such an injection protected the fetus from the detrimental effects of endogenous anti-D.

In 1968, an intramuscular injection of anti-D IgG was introduced as a therapeutic. The specific IgG was obtained from sensitised donors and fractionated in the usual manner to produce a suitable intramuscular product. The mortality and morbidity fell dramatically over the ensuing few years as the treatment was established. An MRC study, published in 1974, set the scene for the optimal dose of anti-D to be given at delivery, namely 500iu. This has continued to be the most usual dose given in the UK.

In 1976, 1981 and 1991, successive guidelines were published for the use of anti-D. The most recent in this series was published in October 1999 as a 'green top' guideline (No. 22) by the Royal College of Obstetricians

and Gynaecologists (RCOG). This was the end-result of a multidisciplinary and international Consensus Conference sponsored jointly by the RCOG and Royal College of Physicians of Edinburgh in April 1997. This new guideline reinforces the statement from the Consensus Conference as well as subsequent interim guidelines from the British Blood Transfusion Society (BBTS) and RCOG published in March 1999. All three are in agreement.

The major change from the 1991 guidelines is the recommendation that antenatal anti-D prophylaxis should be offered to all RhD negative pregnant women at 28 and 34 weeks of gestation. The dose should be at least 500 iu on each occasion and is described as a Grade A recommendation, based upon the available published literature. The benefit of routine antenatal prophylaxis is to reduce the sensitisation rate by 1.0 to 1.5 percentage points over postnatal prophylaxis alone.

The economics of the procedure have been assessed, most recently by the Trent Institute for Health Services Research and published in April 1999. This group is a collaborative venture between the Universities of Leicester, Nottingham and Sheffield with support from the NHS Executive Trent. Antenatal anti-D prophylaxis, as recommended in the RCOG guidelines, was found to be robust to sensitivity testing: (95% Confidence Intervals) £5,148 to £8,212 per case of RhD disease prevented; £9,299 to £10,070 per lifeyear gained. These results indicate a similar level of cost effectiveness when compared with many other accepted health care interventions, for example haemodialysis for end-stage renal failure has a cost per life year gained of more than £20,000.

A notable difference in the new recommendation from the one in 1991, is that unless instrumentation is performed for abortions before 12 weeks (e.g. for retained products or for therapeutic abortion) anti-D is not needed.

The real benefits of all the regimens are only fully realised when compliance is complete. At the Consensus Conference, emphasis was placed on ensuring that anti-D is administered in compliance with the 1991 guidelines for postnatal administration, as well as for potentially sensitising events during pregnancy where some audits have shown that there is room for improvement.

Finally, the new guidelines now recommend anti-D, if platelets from an RhD positive donor have been given to a RhD negative woman of childbearing age. The dose recommended to prevent alloimmunisation by the contaminating red cells in the platelet preparation is 250iu of anti-D for every 3 adult doses of platelets. In patients with a bleeding diathesis, anti-D should be given subcutaneously, although this recommendation does not represent a change.

In conclusion, the new national guidelines confirm the practice of antenatal prophylaxis which has been implemented in some geographical locations over the last few years.

**Dr Clive Dash, Medical Director, BPL**  
November 1999

## Weighing the Issues Around Clinical FFP

Over the last few years there has been much discussion at all levels within and outside the NBS on the subject of the microbiological safety of fresh frozen plasma (FFP). The scientific information has been scrutinised and debated by various learned groups including, amongst others, MSBT (Advisory Committee on the Microbiological Safety of Blood and Tissues), SACTTI (Standing Advisory Committee on Transfusion Transmitted Infections) and BCSH (British Committee for Standards in Haematology). No single product has emerged as being universally preferable. This explains the lack of a definitive recommendation from any group or groups. This brief report attempts to summarise the background information available over the last few years to help the readers understand the conundrum.

Currently, FFP available in the UK is associated with a low risk of being contaminated with a pathogenic virus. The results of the continual monitoring of viral serology among blood donors gives credence to this conclusion. The theoretical risk of human immunodeficiency virus (HIV-1 or -2) being present in a blood transfusion is close to 1 in 3 million. For hepatitis C virus (HCV), the risk is less than 1 in over 200,000 donations and for hepatitis B virus (HBV) about 1 in 50,000 to 200,000 donations. Clinical FFP is only produced from repeat donors rather than first-time donors, so this reduces the risk further. There is no good epidemiology to quantify the risk of hepatitis A virus (HAV) or parvovirus B 19 infection from single unit FFP.

One possible method of reducing the risk of transmission of virus infection is to quarantine plasma until the donor returns to give their next donation. Although this method is being used elsewhere, it has been deemed as inappropriate for the UK largely for logistical reasons. The advantages of quarantine are that the plasma is only used once a subsequent donation has been shown to be negative on serological screening and after the donor has reported being in acceptable health throughout the interval between donations. This really is only feasible for apheresed plasma. A whole blood donor returns on average about once a year, which is too infrequent to operate the system particularly as this is close to the shelf life of the product. A large amount of cold storage would be needed to administer the scheme as well as a complex system to store, retrieve and, if a donor does not return within a reasonable time, to dispose of the donation. Clearly, a single unit donation is used, hence, without the risk of transmitting infection from pooling donations, but the security is only assured for those viruses for which tests are performed. Protection against chronic low level HBV carriers and antibody-negative HCV carriers is not provided.

It is against the chance of a transfusion transmitted infection that risks associated with other products which include a viral inactivation step, so called virally inactivated plasma (VIP) must be compared. Two technologies are currently available: solvent/detergent treatment and methylene blue plus white light. The inactivation of viruses by methylene blue and white light has been in use in Germany for a number of years. Single unit donations are mixed with a specified amount of methylene blue and then subjected to a fixed amount of illumination. The light energy activates the methylene

blue which interacts with extracellular nucleic acid causing its disruption. Methylene blue cannot penetrate cells so the FFP has to be filtered to remove cells before processing. The process is effective against lipid-enveloped viruses (such as HIV, HBV and HCV) but has little effect on nonenveloped viruses (such as HAV and B19). The process has been adopted by Grifols in Spain and Baxter has been developing a process for use by Blood Centres. The Baxter procedure has been fully investigated by the NBS over a number of years, during its development. Initially, the Baxter process used red light in a custom-built light box, which processed one unit of FFP every 30 minutes. This prototype was found to be technically unsatisfactory and a white light source was evaluated. The first production models of this device, which has been awarded the CE mark, are in use in Scotland. Unfortunately, the light box still only processes one unit every 30 minutes. The NBS, in conjunction with SNBTS, has carried out a significant amount of research on this system. However, the slow throughput and hence the space required to accommodate a suitable number of light boxes makes this option less practical for the NBS. The hoped for larger light box from Baxter seems unlikely to materialise. This would reduce the amount of bench space needed.

The advantage of the methylene blue system is that it uses single units of plasma. This does, of course, lead to a product with a variable content of coagulation factors, but clinicians are used to this variability. The disadvantages are that there is a reduction in the concentrations of labile proteins, most notably factor VIII and fibrinogen, and the rather precise volume of plasma to be added to the bag containing methylene blue to ensure the final concentration of methylene blue is within the specified range. A more theoretical concern is the *in vitro* mutagenicity of methylene blue - it must be remembered that methylene blue has been used intravenously to treat methaemoglobinemia in a dose at least one hundred times greater. While clinical use has been significant, especially in Germany, there is a paucity of documented data on neonates and in liver transplantation.

During the period that the Baxter process was being evaluated by the NBS and SNBTS, there was a report from Germany of a putative transmission of HCV from a unit of methylene blue illuminated plasma made by the German process.

Solvent/detergent treated FFP (SD-FFP) is made by pooling several hundred of ABO identical donations of FFP, incubating with an appropriate solvent and detergent, which destroy lipid-enveloped viruses. These chemicals are then removed and the plasma is filled into 200ml containers. The advantages are that the process is robust and well recognised to destroy lipid-enveloped viruses, but has no effect on those without a lipid envelope, such as HAV and B 19. It is probable that, because the plasma is pooled, there are sufficient neutralising antibodies to these viruses to render the product non-infectious. Recently, there has been a report of transmission of B 19 infection to a group of healthy volunteers involved in a clinical study in the USA.

There is consistency in the final concentrations of desirable proteins, at least within the same batch. The main anxiety about this type of product derives from the pooling process. If there is any (new) infectious agent which escapes the chemical onslaught and there are no neutralising antibodies present from other donations in the pool, potentially, all recipients of that batch will be infected.

The clinical data on SD-FFP are appreciable with the exception of neonates and children. The cost-effectiveness of SD-FFP has been assessed recently and, as could be expected, quality-adjusted survival was estimated to increase on average 1 hour and 11 minutes at a cost of over \$2M per QALY. Clearly, the major health benefit is for the rare individual who might otherwise receive an infected unit of FFP.

In conclusion, the quantified risk of transmission of virus infection from FFP which has not been subjected to virus inactivation, has to be weighed against the uncertain risk of transmission of a virus from a pooled plasma product with substantial, but limited, potential for virus inactivation. The risk & from FFP has been reduced recently by the introduction by the NBS of NAT testing for HCV and probably by the implementation of universal leucodepletion, to minimise the theoretical risk from vCJD, which is now complete.

Whether methylene blue illuminated single donations of FFP offer any better or worse risk compared with pooled SD-FFP remains uncertain. The process presents logistical difficulties for implementation, although these are not insurmountable. The final product, like standard FFP, is inconsistent in its components, but with a lower concentration of, particularly, factor VIII due to losses on illumination. Scientific views on pooling plasma when a non-pooled alternative is available are polarised. Antibodies against non-enveloped viruses may not be sufficiently neutralising in a pooled product and any new infectious agent which is not susceptible to the solvent/detergent process can be readily disseminated. It is difficult to really assess the relative strengths of these arguments with available information. The main differences reside in the relative risks for known and unknown viruses between the various options and these differences are changing as new tests are introduced to donations. The clinical tolerance of the products seems similar.

Detailed information from which this brief article was largely derived will be published shortly by Dr Derwood Pamphilon, Bristol Institute for Transfusion Sciences and NBS. In addition, information has been taken from the draft BCSH Addendum to Guideline on FFP, due to be published in 2000 and being prepared by Dr Lorna Williamson, Cambridge. I am grateful to both these colleagues for their help in the preparation of this brief overview.

**Dr Clive Dash, Medical Director , BPL**  
December 1999

## **NATIONAL CALL CENTRE**

### **Donor Helpline : 0345 711711**

For the first time National Blood Service donors and potential blood donors in England now have a single

point of telephone contact. Since 4 December 1998; all enquiries are directed to an external Call Centre managed by a private company, MM Group Ltd., in Bristol.

Meeting the increasing demand for blood and blood products relies on the effective recruitment and retention of new and regular donors. An important aspect of this is the ability to respond promptly and efficiently to all types of donor contacts. Professional and sensitive handling of donor queries or concerns is vital in maintaining public confidence in the Blood Service.

Until the advent of the National Call Centre all donor telephone contacts have been handled locally at each Blood Centre. These have traditionally provided a reliable service during the working day but were not staffed to provide cover for out-of hours routine calls. Nor were they equipped to deal efficiently with the huge increase in contacts which inevitably follows high profile major accidents or planned national or local advertising campaigns. As a result, many potential donors were lost through the Service's inability to always respond fully to fluctuations in call volume.

The National Call Centre offers a 24 hour, 365 days a year helpline with more than 200 telephone operators trained to deal with enquiries from blood donors and the public.

The staff follow agreed scripts which prompt them to collect all the relevant details from the caller. These details are transferred electronically to the relevant local Blood Centre for NBS staff to update the donor database. There are six menu driven routes which cover the main categories of enquiry as follows:

- Donor registration
- Session details
- Alternative sessions
- Change of details
- Clinical call
- General query/complaint

For complex calls operators switch between routes, eg: a regular donor rings with a change of address, needs details of the next local session and has a medical query about eligibility to donate.

New donors are automatically sent a registration pack containing information about the National Blood Service and a letter confirming details of the next local blood collection session.

An average of 100 blood collection sessions take place throughout the country on each weekday, fewer at weekends. Details of session venues and times are updated and sent electronically to the Call Centre from the Blood Service on a daily basis. Donors calling for session details are therefore provided with up-to-date information about local sessions and this is also confirmed in writing if the date offered is more than 3 days ahead.

In the first year of operation the National Call Centre has answered 775,000 calls, with 93% efficiency. 104,000 new donors have been enrolled and 325,000 callers were given details of convenient local blood collection sessions with the expectation of attending to donate. 25% of all calls dealt with changes in donor details.

35% of calls included an enquiry about eligibility to donate. Approximately half these are capable of being answered by Call Centre staff using carefully controlled scripts. These have been agreed by NBS Consultant staff with responsibility for donor selection and donor care who have supervised the training and monitor performance. Donors with queries which cannot be dealt with in this way are transferred directly to local Blood Centres where medical staff have dealt with more than 100,000 calls in the first year. This included important after care for the small number of donors who may have suffered adverse reactions or have concerns after giving blood.

Nominated senior managers and medical staff from the NBS have responsibility for the operational and clinical aspects of the service to donors. They liaise regularly with managers to ensure appropriateness of response and maintenance of standards.

The first year's experience of the NCC confirms that blood donors now have a greater opportunity to obtain local information and relevant advice about all aspects of the NBS in a prompt, efficient and consistent manner.

Building on the NCC's initial success, on-going developments include full electronic data transfer to maximise efficiency and communication with donors. Future plans will explore the opportunities provided by new media and Internet developments to further improve access to the Blood Service using 21st Century technology.

**Dr Liz Caffrey**

on behalf of the National Call Centre Implementation Group

## **A New Direction**

The last 12 months have been a challenging time for the National Blood Service. Chief Executive Martin Gorham presented his strategic plan to the NBA Board in March last year. Martin's subsequent paper 'A National Blood Service' set out the NBA's plans for a new strategic direction and organisation structure. The main aim was to move the Blood Service from its current zonal basis to an integrated national structure.

These plans focused clearly on the provision of high quality local services within a well-defined national framework. They also reflected a desire to clearly identify the key components of the Blood Service and put them together in a way which was most likely to enable the NBS to meet its current and foreseeable future demands.

Martin's paper was based on an understanding that the purpose of the NHS is to provide blood, blood components, blood products and tissues that are safe for patients and to provide related expert services.

### **A National Blood Service**

A new national Executive Management Team was appointed during the late summer and autumn of 1999 and this was built around the concept of clearly identified core activities, expert services and support functions. National Directorates were

identified as: Services to Donors and Processing, Testing and Issue (core), Medical and Diagnostics Development and Research (expert) and Public and Customer Services, Finance and Business Planning, Human Resources and Information Technology and Facilities (support).

To ensure that the leaders of these areas could focus clearly on their key tasks the NBA Board additionally took the innovative step of appointing a Director of Transition to coordinate and manage the change programme.

The work of this new team has been focused in three main areas. Firstly there was a prime requirement to put interim arrangements in place to ensure the maintenance of service quality and standards up to and over the millennium holiday period. These interim measures were designed to facilitate a smooth transfer to new national structures while, at the same time, addressing some shortfalls in the existing arrangements.

Finally, and perhaps most importantly, it was essential to consider the impact of new structures on staff working in Blood Centres, particularly in terms of day to day delivery of services to hospitals.

### **Local Service**

A great deal of work has been done to identify the factors leading to effective cross-functional team working at local level. The new structure acknowledges that Blood centres are the natural focal point for local services but it aims to put these within a clear national framework. A Blood centre is a community of several parts sharing a common purpose. For this community to work well there needs to be good understanding and practical working arrangements between the new directorates and the individuals who work within them. There also needs to be clear and effective links to the customer hospitals served by that centre. This is the main thrust of current work which has already identified new developments in how the NBS will manage certain aspects of 'Hospital Liaison'. *More details of how we intend this to work will appear in the next issue of Blood Matters, but it will be based on work successfully piloted in the Midlands and South West Zone.*

The new management team has recently outlined the next phase of the planned move towards a truly national structure and this work will largely be completed by the end of the financial year. While the team are confident that these new national arrangements provide an excellent starting point they are, of course, only part of the picture. A national management structure will not, in itself, deliver the kind of changes outlined by Martin Gorham last year. The new management team is very aware that the true test of these national structures will be determined by their effect on the services and products we provide to local hospitals.

Further information on the new management arrangements or the NBS development programme can be obtained from Terry Male, NBS Director of Transition, Leeds Blood Centre, Bridle Path, Leeds LS 15 7TW. Tel: 0113 214 4893.

**Terry Male**

Director of Transition

## **Red Cell Stock Levels During 2000 - 2001**

We have now completed our plans to ensure that the NBS holds appropriate stock levels to meet hospital needs during the coming year.

### **Planning Stock Levels**

The challenge when planning stockholding levels is to achieve the optimum balance between the requirement to hold sufficient stocks to meet hospital demand and the need to ensure that stock levels do not significantly reduce the shelf life of units issued to hospitals. We must also meet targets for the proportion of units that become time-expired.

To assist in this we have analysed hospital demand patterns for blood on both a yearly and weekly basis over the past four years. Coupling this with the hospitals' own anticipated blood requirements has enabled us to construct a "predicted weekly demand profile" for the year 2000 - 2001.

By examining historic blood donation patterns we are able to produce the same weekly profile for blood collection and by comparing this to the demand predictions we can identify weeks when collection levels need adjustment.

We are planning to maintain blood stocks at levels that vary between 3 and 6 days stock throughout the year and so allow us to collect blood when it is most convenient for the donors, for example, our donor sessions tend to be less busy during the summer months.

### **What This Means To The hospitals**

Currently, stocks are running at just over 5 days (53,000 units) and we are planning to increase this to 6 days as we approach the Easter holidays.

As a consequence, hospitals may notice a slight increase in the age of the units they receive during May.

As stock levels fall, in accordance with our plan, during the summer months, (to 3.5 - 4 days), hospitals should notice an increase in the shelf life of units.

There may again be a slight increase in the age of issued blood as we then build stocks during the Autumn months in preparation for Christmas and the New Year.

Should the trends in our stocks show that we are likely to fall outside the 3 - 6 day level, our stock monitoring systems will result in actions being taken to rectify the situation.

Although the average age of blood received by the hospitals may vary throughout the year, it will stay within a band of a few days.

We are confident that this will ensure adequate stock cover at all times without compromising the available shelf life of units issued to hospitals.

### **Platelet supply over Easter/Spring Bank Holiday**

The Easter/Spring Bank Holiday period will, like the millennium, present the Service with a new challenge. We will work to ensure that we can provide the hospitals with their platelet needs during a period that includes 3 bank holidays in the space of 11 days.

We have been preparing for this for some time and will

adopt the same approach that proved successful over the millennium. A programme has been developed for increased collection sessions and apheresis clinics over this period, supported by extra testing and processing activity right through the Easter and Bank Holiday weekends. We will monitor platelet stocks across the country very carefully over this time to ensure that platelets are held where they are needed.

Although we are confident these plans will ensure we can maintain our normal level of service, we would ask that hospitals work with us, as they did during the millennium, by examining their activity during this time and ordering appropriately to hold minimum stock levels.

If you have any issues which you would like to discuss regarding the Easter/Spring Bank Holiday period please contact your local NBS liaison consultant, Hospital Liaison Officer or Hospital Services manager

### **ISBT Code 128 Project**

From 1 December this year the NBS will begin to use the ISBT Code 128 donation number format only on all units of blood and blood components. This change is expected to be completed well before 31st January 2001 which is the last possible date on which any blood donations will be collected bearing the current "dual - label" donation number.

Recently, a diary planner was issued to hospitals to help plan this change (see box). This also outlined a number of associated barcoding and pack format changes.

The NBS has formed a small project team, led by a Project Director, Richard Bedford, which will oversee the transition to the new format. The project will provide support to hospitals and NBS departments and seek to ensure that all users of the donation number on units of blood and components are prepared for the change. This will include the provision of materials to assist in training and "dummy" packs to allow users to test their IT systems.


Following a questionnaire issued by SACIT in the summer of 1999, most (85%) of hospitals indicated that they expected their IT systems would be ready by 1 April 2000. Over the next few months the NBS will follow the progress of hospitals, blood bank computer suppliers and internal departments towards full readiness for the change to the new format. To help in this process we have devised a simple test using "dummy" packs. In April 2000 we will issue these packs to hospitals and ask each hospital to follow a test script designed to check if the hospital computer system is able to record information from ISBT code 128 barcodes, including the use of the "\*" check character symbol instead of the "+" symbol. Hospitals will be asked to complete a form detailing the outcome of these tests and return this to the NBS.

In future editions of Blood Matters we will report on the number of hospitals which are "ready" using a red, amber and green traffic lights system. Those hospitals which indicate that they expect to be ready but have not completed the test will be designated an "amber" status. Those which complete the test successfully and confirm their preparedness will be designated "green" status and will, additionally, be issued a "Code ISBT 128 readiness" certificate.

if you have any queries regarding the change to ISBT code 128 please contact the following members of the project group:

M&SW zone:	Teresa Turvey	01865 447931
Northern zone:	Ian Millar	0161 251 4212
L&SE zone:	Stuart Penny	0181 258 2805

## **ISBT 128 Diary Planner for Hospital Blood Users**

<p><b>Current status</b></p>	<p><i>The NBS will use the current label format throughout, displaying the donation number in both the Codabar and the ISBT 128 format and the blood group in the Codabar format.</i></p> <p><i>Hospitals can record the blood group in codabar and the donation number in either Codabar or ISBT 128 but should be preparing to make the transition to recording in ISBT 128 if this has not already been achieved.</i></p>
<p><b>System supplier meeting</b> April 11th 2000</p> <p><b>User tests &amp; communications</b> April 2000</p>	<p><i>The NBS/SACIT will facilitate a meeting with Hospital IT system suppliers to discuss their current implementation plans. The NBS will start to issue all hospitals with "dummy test packs" displaying the new label formats for the validation of any software changes which April 11th 2000 they have made to prepare for the ISBT 128 changes.</i></p> <p>Hospitals will need to undertake the tests and return the completed test script documentation to the NBS. <i>The NBS will then issue a compliance certificate.</i></p> <p><i>The NBS/SACIT will start to monitor and report the progress of suppliers, hospitals and other UK services in terms of readiness to receive ISBT 128 only components.</i></p> <p>(Posters and further information will be sent out from the NBS at this time)</p>
<p><b>Label Purchase</b> September 1st 2000</p>	<p>The NBS will place an order for "ISBT 128 only" donation number labels for the year 2001. <i>This will be the point at which the NHS is fully committed to the change.</i></p>
<p><b>New Labels "go live"</b> 1st December 2000</p>  <p><b>Year end label change</b> 1st December 2000 to 31st January 2001</p>	<p>The NBS will start to issue blood components which display <b>only</b> the ISBT 128 labelling format. There will also be minor changes to some of the eye readable information on the label.</p> <ul style="list-style-type: none"> <li>• The text size of the first 7 digits of the donation number will increase and will be consistent across all 14 characters which will be grouped to assist recording.</li> <li>• Letters will be dropped from the date bled and the expiry date. example:- 9th May 2000 will become 09 May 2000</li> <li>• The ISBT 128 donation and blood group barcodes will carry equal weight and will appear above the eye readable blood group text which now moves down the label to accommodate this change</li> <li>• The centre identification barcode will be removed and the Centre a text will change to the format "NBS, Centre" e.g. NBS, Bristol</li> <li>• On products displaying the year code "01", the "+" symbol will be replaced by an asterisk " * "</li> </ul> <p>Hospital user systems will need to be able to output the "+" when reading a year "00" (or earlier) donation number and output the " * " when reading a year "01" (or later) donation (a poster displaying a sample label will be made available nearer the time)</p> <p>To comply with the International Standard, the NBS will apply the year end change from year "00" to year "01". Blood components carrying the "00" labels may theoretically be supplied up to 1st February 2002.</p> <p>Hospital users will continue to see components with dual labels while stock and labels are working their way through the system and will need to ensure that their computer systems can handle <b>both</b> types of donation number simultaneously. The first products which hospitals will see with the single ISBT label format are generally expected to be granulocytes (buffy coats) &amp; platelets, followed by red cells and finally frozen components. Users will not be able to request dual labelled products. The NBS will stop manufacturing any components with the dual label format.</p>

**Note:- The NBS will not be recalling any products as a result of these labelling changes**

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