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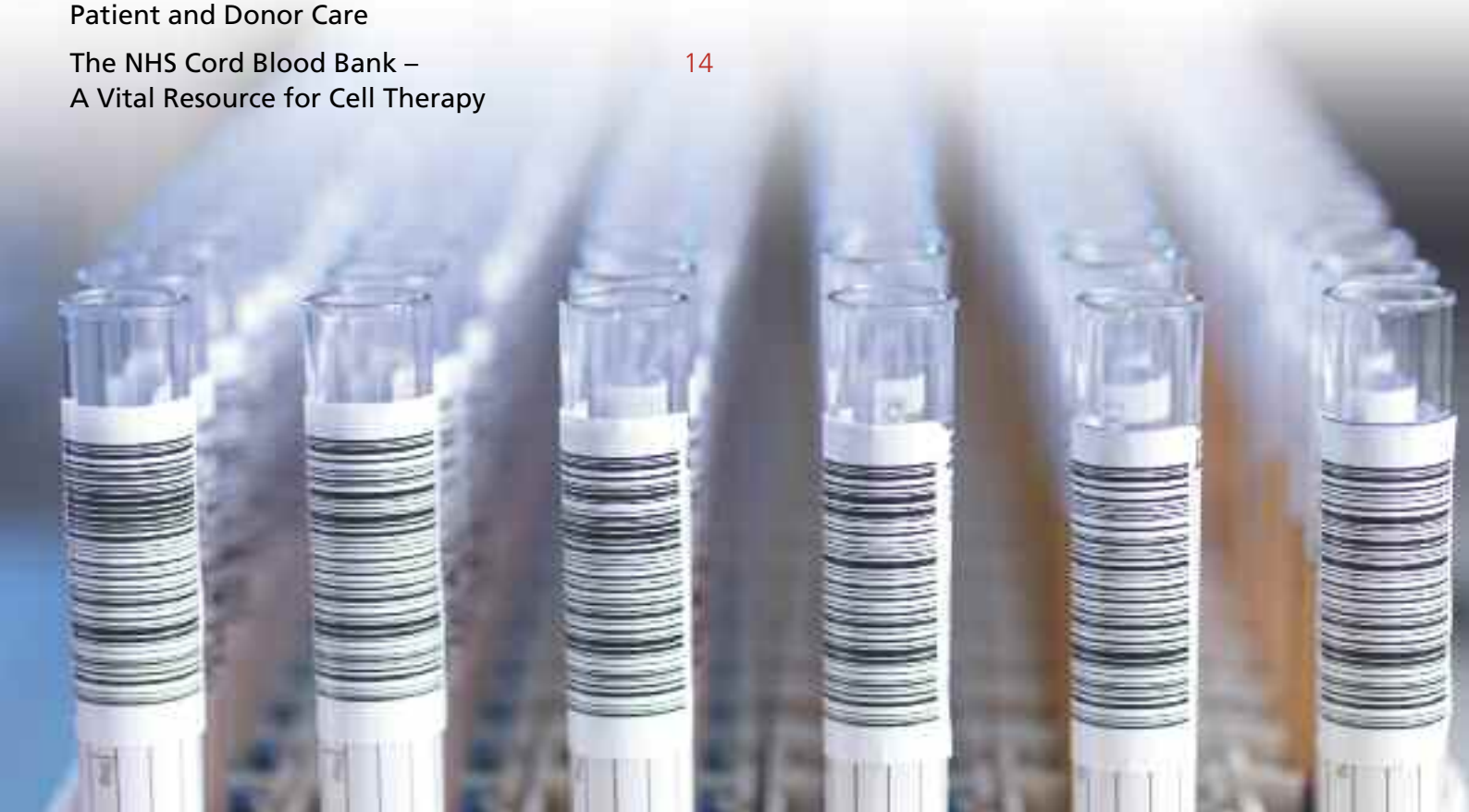
NHS
Blood and Transplant

Blood and Transplant Matters

Information for hospitals served by NHS Blood and Transplant

Inside



EDITORIAL

It is a great pleasure to be penning an editorial for the first edition of *Blood and Transplant Matters.* The Editorial Board agreed recently that we should change the name of Blood Matters to reflect the fact that NHS Blood and Transplant is concerned with the collection, processing and transfusion/transplantation of blood, tissues, stem cells and organs. I would like to draw your attention to the *Bulletin* edited by Henny Fordham which deals specifically with transplant issues and which is circulated mainly to those in organ donation and transplantation. We recently met and agreed that the two publications were complementary, each presenting information in different formats. However, in future we will publicise each others forthcoming attractions and contents pages and some articles of clear interest to a broad readership (or brief synopses of them) will appear in both publications.

We are starting to introduce some regular features to *Blood and Transplant Matters* such as the 'Day in the Life' series which starts with a personal view of the world of a Clinical Transfusion Microbiology Specialist written by Pat Hewitt. Another initiative kicks off with an article by Robin Knight describing transfusion in Malawi; we hope to publish accounts of blood transfusion in other developing countries in forthcoming issues. In the next issue you will find an account of one of the household names in transplantation, Professor Sir Magdi Yacoub to initiate our series of articles on pioneers in transfusion and transplantation.

As always we strive to maintain balance between the different types of articles that appear in *Blood and Transplant Matters* and hope that its broadly accessible content will appeal to all our readers. At the same time we are committed to maintaining the high scientific standard that our contributors have provided up to now and rely on your feedback to inform us whether or not we have done a good job. With this in mind, we have excellent contributions on the Blood Stocks Management Scheme and the Demand Planning Process, an online survey of hospital compliance with Better Blood Transfusion 3, preventing transfusion transmitted infections and the NHSBT preparations to ensure continuity of its services as the number of cases of swine flu rises this winter.

Articles on clinical audit have been well received in previous issues and we are pleased that Dave Collett who is head of NHSBT's Statistics and Clinical Audit describes for us how his department works. There is also another contribution from Buddika Samarasinghe, this time on the importance of SEA (read on if you don't know what SEA is!) and how it can improve patient and donor care.

The growth of human umbilical cord blood banking and transplantation worldwide prompted the editorial board to commission four articles which describe the NHS Cord Blood Bank, The Anthony Nolan initiative to bank cord blood stem cells, the FACT-NetCord Standards that all banks must adhere to and how cord blood is used clinically. The future use of cord blood in immunotherapies and tissue regeneration as well as 'straightforward' stem cell transplants is an area of huge interest at present. Finally Blanca Miranda from Barcelona describes for us how tissue banking is organised in South America and Hazel Tinegate gives a short summary of the ISBT Regional Congress in Cairo earlier this year.

I am prompted to remind you that we do not publish the answers to the CPD questions, rather the relevant information is easily found in the text of the articles themselves. That said, I am reminded of a commercial for a well known beer that ran on our television screens many years ago where a dehydrated traveller seeking a glass of his favourite brew was blandly informed by a barman that 'you are the twentieth person I've told this morning that there's no demand for it'! We will keep the situation under review. As always we welcome your feedback and suggestions for future articles and hope that you will agree with the advice that the present selection contains, unlike GK Chesterton who said 'I owe my success to having listened respectfully to the very best advice, and then going away and doing the exact opposite'. Happy reading.

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December 2009

How NHSBT Manages Stocks of Blood Components

Forecasting the Demand for Blood by Hospitals

Demand planning in NHSBT is the responsibility of the Demand Planning Group (DPG). This is an expert group made up of senior representatives from across the blood supply chain areas in NHSBT and includes hospital representation. This group is responsible for forecasting the annual issue levels for red cells, platelets and frozen products. Initially the group will agree totals for each financial year, they then meet each quarter to monitor past issues and revise the forecasts if necessary. The forecasts calculated by the group form the basis for supply planning and stock management within NHSBT.

Supply Planning

Once the DPG have agreed the overall annual issue figure for red cells, this is then broken down into estimates for each day, week and month of the year. From this, the required number of whole blood donations each week can be calculated and this forms the basis of the blood collection plan for the year ahead. These collection plans are then allocated to over 109 collection teams.

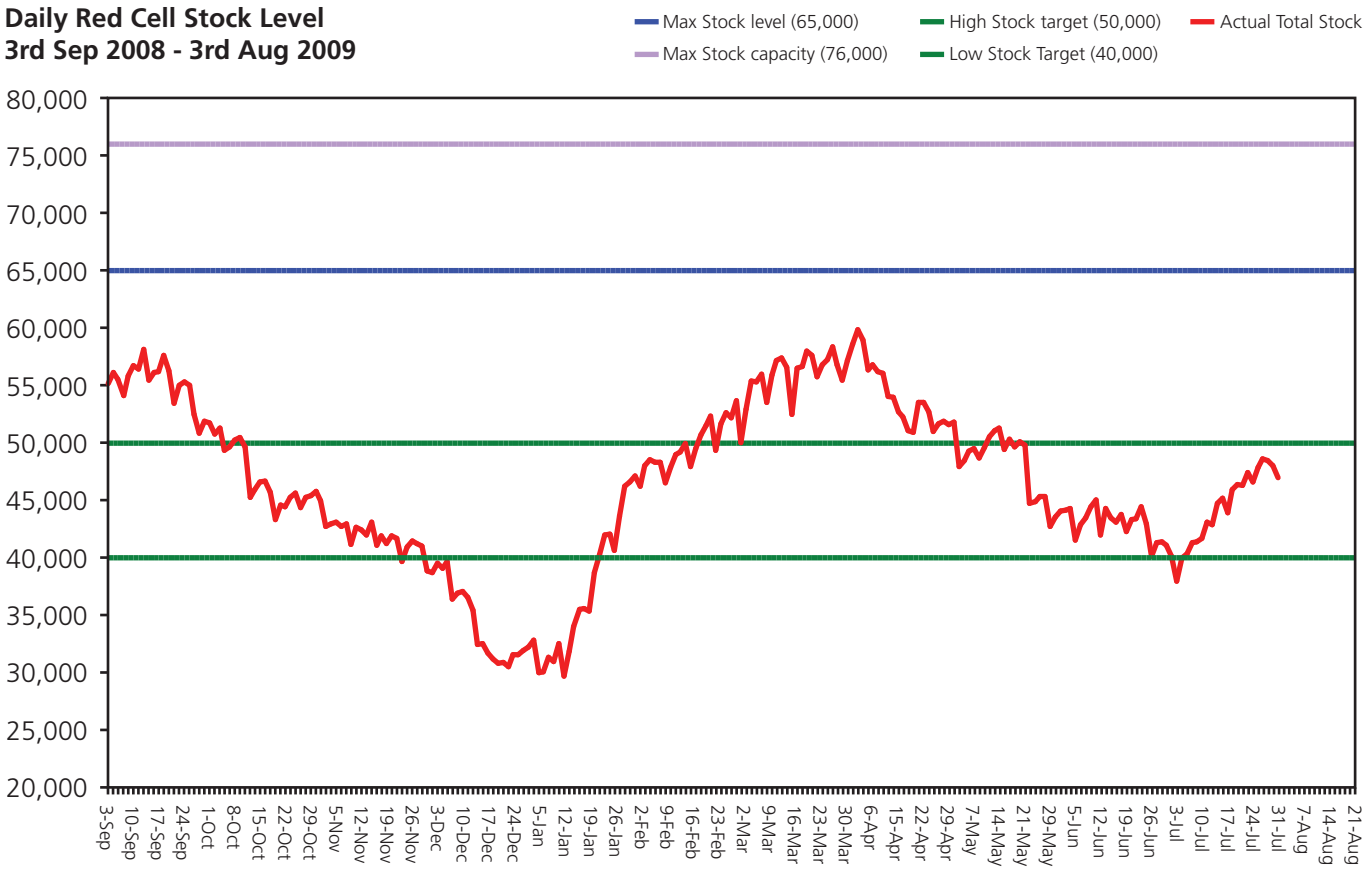
The collection plans for component donation (apheresis) platelets are created in a similar way: we estimate the weekly volume of platelets that we expect to issue and create a detailed collection programme for each component donation clinic to deliver the required amount.

Stock Target Setting

NHSBT stock targets for red cells, platelet and frozen products are reviewed every year based on the most recent years issue data. The overall target within NHSBT is to hold 40,000 to 50,000 red cells and maintain all groups above four days stock. Four days worth of stock of all groups is between 23,000 & 24,000 units. The overall target is set higher than this because of the variation in supply and demand on an individual group level and to provide a buffer, as any marketing activities to attract extra donors have a lag time before the effects are realised on sessions. NHSBT is conscious of the need to hold the optimal level of stock as this leads to newer stock at the point of issue and reduces wastage within hospitals.

Platelet stock targets vary throughout the week. The minimum acceptable level is 1.25 times the average demand on each day; however the targets are increased towards the end of the week to compensate for lower collections at the weekend. The target for stock of frozen products is between 14 and 30 days for UK sourced and 12 weeks for non-UK sourced.

Figure A: Chart used within NHSBT to monitor overall red cell stock levels



The actual stock held is monitored closely by the Stock Planning and Action Group. This group is responsible for the maintaining overall stocks at the specified target levels and developing and implementing action plans to prevent stock dropping below these levels.

Manufacturing Plans

Pooled platelet and plasma component manufacture is controlled on a daily (platelets) or weekly (plasma) basis. Platelet manufacture is adjusted each day based on the number of units in stock, the amount we expect to issue that day and the number collected the previous day which is in the process of being tested.

Plasma product manufacture is controlled on a weekly basis and is based on the amount in stock and the amount that we expect to issue over the coming week. Blood collection teams are issued with detailed session plans outlining which blood pack configurations are to be used on sessions to ensure that the required numbers of buffy coats and plasma can be manufactured when they are returned to the processing centres.

Challenges

Certain events cause challenges in the supply of blood components. These could be regular events such as Bank Holidays or sporadic such as pandemic flu.

Planning for bank holidays requires detailed preparation within NHSBT. Stock planning begins around two years ahead of a Bank Holiday with donation venue booking to ensure availability. This is to ensure that the locations are within a geographical location close enough to the processing centre to ensure the swift return to a processing site to maximise platelet production. Over 12 months in advance of a Bank Holiday, we estimate how many units we expect to issue each day over this period, using previous issue levels. Based on this, the collection requirement is developed and then sent to the Blood Donation directorate. Blood Donation then spend time allocating this collection requirement on a regional basis (eight months before the Bank Holiday) and on an individual collection team basis (five months before the Bank Holiday). Six weeks before a Bank Holiday, the collection and manufacturing teams are required to formally sign up to the final plan to give assurance that they will deliver their part of the requirements.

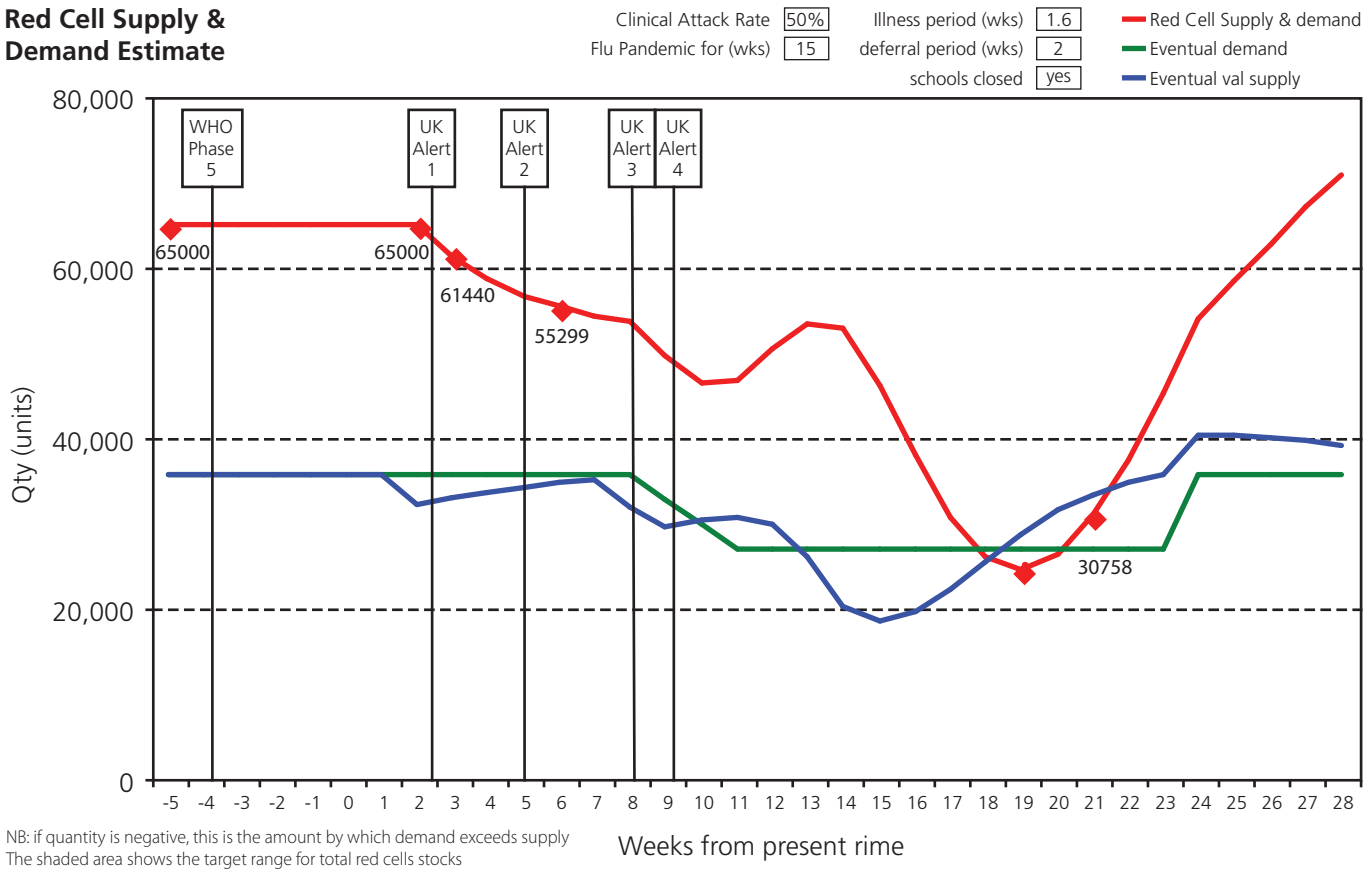
Planning for pandemic flu is critical to ensure sufficient stock is available during a pandemic and NHSBT has been developing and refining its plans for several years. Current planning guidance from the Department of Health suggests that pandemic flu has the potential to infect around 30% of the population over the course of the pandemic. This in turn means 30% of blood donors and translates to a reduction of donations collected. In order to mitigate this, we have recently undertaken a controlled stock build whereby we increased stock to around 65,000 red cells by mid September of this year*. Our modelling has shown that in order to maintain supply throughout a pandemic wave, the starting stock position needs to be at this higher level, rather than the normal 40,000 to 50,000 stock level. Even with this higher level of stock it is possible that NHSBT will have to activate the red cell and platelet shortage plans. The stock situation is as always, being carefully monitored and if predictions and models show a severe shortfall in the number of donations compared to the predicted demand then these plans will be activated. This activation may be in advance of an actual shortage in numerical terms to ensure that blood continues to be available throughout the entire pandemic period for those who most need it.

Please refer to the article on page 10 where the latest information regarding pandemic influenza is detailed.

Figure B: Pooled Platelet Manufacture Instructions

01-Aug-09 7am Monday	Centre A						
	O Pos	O Neg	A Pos	A Neg	B Pos	B Neg	Total
current validated stock (by ABO & Rh) at 7am	22	13	19	14	1	0	69
current target stock (by ABO & Rh)	22	7	26	7	3	1	66
apheresis units awaiting validation	28	7	21	14	3	6	79
no, of buffy coats in processing (W.I.P.)	65	15	59	22	0	0	161
Pools required	0	0	7	4	0	0	11
National Instruction			ALL	ALL			ALL

Figure C: An example of red cell stock forecasting using the pandemic flu model



NB: if quantity is negative, this is the amount by which demand exceeds supply
The shaded area shows the target range for total red cells stocks

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Results of Online Survey on the Implementation of the Health Service Circular 2007/001 *'Better Blood Transfusion – Safe and Appropriate Use of Blood'*

Background

The Health Service Circular *'Better Blood Transfusion – Safe and Appropriate Use of Blood'* (HSC 2007/001) was issued in November 2007, detailing the actions required of NHS Trusts, NHS Blood & Transplant (NHSBT) and clinicians to improve transfusion practice. It included an action plan and an ongoing programme for *Better Blood Transfusion* to be implemented in each NHS Trust by November 2008, when the first national audit of compliance would be undertaken.

Methods

The survey was carried out in December 2008 and January 2009, and for the first time conducted online. One collated response was requested from the Hospital Transfusion Team (HTT) in each NHS Trust or Independent hospital.

Results

153/166 (92%) NHS Trusts and 33/59 (56%) of Independent hospitals responded to the survey. This was comparable to the 2004 and 2006 surveys.

The key results for NHS Trusts included:

- 148/153 (97%) reported they had a Hospital Transfusion Committee which met at least three times/year.
- 146/152 (96%) have a Transfusion Practitioner, and this percentage is unchanged from the last survey in 2006.

- 85/152 (56%) have a lead consultant for transfusion with dedicated sessions for blood transfusion in their job plan, compared to 48% in the previous survey, indicating that 44% of HTTs do not have a lead consultant with sufficient time for involvement in transfusion activities.
- 149/153 (97%) reported they have a clear reporting line to senior Trust management, but 26% have not developed an action plan for transfusion safety and quality and 36% do not make an annual report to senior management as recommended in the *Better Blood Transfusion* action plan.
- 135/153 (88%) reported that their medical staff receive training in transfusion at their induction and at regular intervals thereafter. The equivalent figures for nurses were 96%, phlebotomists 93%, and porters 79%. These figures for regular training are improved in comparison to the survey in 2006, which asked separate questions about induction and regular training.
- Participation in local, and national audit have all increased. For example, 145/153 (95%) of NHS Trusts had carried out at least one local audit of transfusion in the last 12 months. 135/153 (88%) had participated in the national audit of bedside practice carried out by the Royal College of Physicians/NHSBT national comparative audit of blood transfusion programme in 2008. This audit found evidence of improved bedside practice, but there were still too many patients (3%) with inadequate identification i.e. without wristbands, and too many (10%) not being adequately monitored during transfusions.
- NHS Trusts were asked about progress with compliance with the National Patient Safety Agency (NPSA) Safer Practice Notice 14 '*Right Patient, Right Blood*'. 97% reported they had started to implement an action plan for training and competency assessment, but only 12% have assessed 50% or more of their staff, which was a requirement by May 2009. Only 83% of NHS Trusts indicated that they were not using a compatibility report or the patient's notes as part of the pre-transfusion bedside check. Only 59% had appraised the use of bar code patient identification and blood tracking. Only 13 Trusts administer >10% of transfusions using bedside IT, and only five Trusts take >10% of blood samples for transfusion using electronic patient identification.
- 141/152 (93%) have a certificate of compliance from the Medicines and Healthcare and products Regulatory Agency (MHRA) compared to 83% in 2006, and 86/153 (56%) have been inspected by MHRA compared to 21% in 2006.
- 96/152 (63%) of NHS Trusts have a blood conservation strategy but only 44 NHS Trusts have implemented a blood conservation strategy.
- The number with policies for blood usage was little changed from 2006 e.g. the use of red cell transfusions in surgery (58% in 2006 and 61% in 2008) and critical care (70% in 2006 and 67% in 2008), and the use of platelet transfusions in haematology (78% in 2006 and 74% in 2008).
- 98/152 (64%) have established local protocols to empower blood transfusion laboratory staff to query clinicians about the appropriateness of requests for transfusion against local guidelines for blood use.
- 147/150 (98%) provide patients with written information, usually in the form of NHSBT information leaflets, but only 16% Trusts estimated that more than 50% of transfused patients actually receive written patient information.
- 48% estimated they anticipated an increase in blood usage and 51% anticipated a decrease. Reasons for an increase included increased workload, increased complexity of care, and an ageing population. Reasons for a decrease included greater use of cell salvage, an increase in the use of electronic issue of blood, and implementation of lower blood count thresholds for transfusion.

There was evidence of regional variation in the responses to most of the questions. The national and regional results are available on the National Blood Transfusion Committee section of www.transfusionguidelines.org.uk.

Conclusions

- There has been good progress in the implementation of some but not all of the recommendations in the action plan of the HSC 2007/001 *Better Blood Transfusion – Safe and Appropriate Use of Blood.*
- NHS Trusts indicated that key factors preventing implementation were inadequate staff for the HTT, that transfusion is not a high priority for NHS Trusts and Strategic Health Authorities, and that compliance with the UK Blood Safety and Quality Regulations and the NPSA SPN 14 are significant competing demands for the HTT and blood transfusion laboratory staff.
- Key factors which would assist implementation included additional staff for the HTT, strengthening of

the role of the HTT within NHS Trusts, and funding for electronic blood tracking.

- The detailed results have been provided to Regional Transfusion Committees for wider dissemination in a format to allow comparison with other Regions. This information should be used to plan further local and regional initiatives to implement the Better Blood Transfusion action plan and improve transfusion practice.

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on behalf of the National Blood Transfusion Committee

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Preventing Transfusion Transmitted Infections: An Asymptotic Endeavour

How do you assess the risk from transfusion-transmitted infections?

In the USA in the early 1970s prospective studies in recipients of blood transfusion showed that approximately 10% of patients developed post-transfusion hepatitis. Currently in the developed world transfusion-transmitted infections (TTIs) are so infrequent that such prospective studies would have to be so large to obtain significant results that they are not a practical proposition. Nor can one rely on anecdotal data or the sporadic published reports of 'interesting' TTIs as these provide an incomplete picture.

In practice, two approaches are currently available. The first is to collate, on a national basis, all reports of adverse events following blood transfusion. This 'haemovigilance' has been in place in the UK since 1996 in the form of the Serious Hazards of Transfusion (SHOT) and an analysis of the 2007 Report appeared in a previous edition of *Blood Matters* (Autumn 2008, No 26). All reports of potential TTIs are followed up in both patients and donors and an invaluable national picture of the clinical impact of TTI is obtained. The shortcomings of this approach are that it is dependent on full reporting from hospitals, transmission of 'unexpected' agents may not be recognised as linked to the transfusion and asymptomatic and chronic sequelae are less likely to be ascertained. Detection of acute, severe reactions such as bacterial complications are therefore favoured.

The second approach is to mathematically calculate 'residual risk' per donation for a given infectious agent to estimate the chance that a particular blood donation had been made by an individual during the period when infectious organisms were present in the blood but at levels undetectable by the screening tests in use (see figure 1).

Figure 1: Calculating residual microbial risk

$$\text{risk} = \frac{\text{infectious 'window period' defined via 'seroconversion panels'}}{\text{Seroconversion rate defined as the rate of new infections (incidence) in repeat donors}}$$

'Seroconversion panels' are sequential plasma samples from individuals undergoing an acute infection during a course of plasmapheresis and are a valuable by-product of the commercial plasma fractionation industry.

In the UK the components of risk due to errors in testing (very rare now because of automated testing systems) and to any deficiencies in the sensitivity of routine tests are also built into estimates of risk.

What are the risks?

For the period 2006 to 2008 in the UK the overall residual risks per χ million donations from transfusion for HBV, HCV, HIV 1 and 2 and HTLV I are show in table 1.

The laboratory tests in place over this period were:

- HBV: HBsAg assays.
- HCV: anti-HCV antibodies or combined antigen/antibody tests (combi), plus HCV RNA amplification (using pools of samples); also called nucleic acid testing or NAT.
- HIV: Ag/Ab combi, plus HIV RNA amplification (using pools of samples).
- HTLV-I: (ELISA) on pools of samples.

The number of confirmed blood transfusion-transmitted infections in the UK between October 1996 and December 2008 are shown in table 2: data from Scotland was included from October 1998.

Bacterial transmissions account for more than half the total and they remain the major microbial risk of transfusion, not least because 25% of transmissions prove fatal.

In addition to the well recognised microbial risks, many of which involve persistent infection, around the world acute infections (especially if at high incidence) are becoming increasingly important. Apart from HAV and HEV, agents such as WNV in North America have had a major impact on transfusion services and two instances of transfusion-transmitted dengue virus infections were reported in 2008. The additional risks from 'emerging infections' have been reviewed by Dodd in a previous edition of *Blood Matters* No 26, Autumn 2008.

How do you reduce the risks?

Paradoxically the transfusion risks for HIV, HBV, HCV and HTLV (each at 1 in a million or less) on an actuarial basis would be considered 'negligible'. However, EU product liability requirements and blood safety directives treat blood as a product rather than considering provision of blood as a service. This renders the producers liable for any adverse event, regardless of the measures taken to ensure blood safety. The risks are obviously increased if patients receive several units of blood or components or have a long term requirement for blood thereby increasing their individual risk. As discussed, bacterial transmission risks are significantly higher than for viruses and emerging agents remain a continuing threat (as demonstrated by WNV). Apart from all this, the risk from vCJD with its associated high 'dread factor' requires quite novel methods for mitigation because there are as yet no suitable tests or inactivation methods for prions. Fortunately the number of vCJD cases in the population is low and the threat *may* eventually prove to be self limiting.

The recruitment of voluntary non-remunerated blood donors and their careful education and selection remain the foundation of microbial safety of blood. In addition to this, laboratory testing of blood for an ever increasing range of agents with tests of ever increasing sensitivity has been a standard approach for many years. New technologies such as NAT have reduced the 'window period' of non-detection dramatically. But the testing approach is complex and expensive and, even more importantly, is 'reactive'. Tests can only be developed after an agent has been shown to be an actual or potential transmission threat. The development of such tests takes time.

In the perfect world a mechanism for complete inactivation of all TTIs, in all blood components, without reduction of product efficacy and with no risk to the recipient would seem to offer the ideal solution. With such a perfect microbial inactivation system one could stop testing blood for a whole range of microbial agents such as CMV, malaria, Chagas' disease and WNV. HAV, HEV and 'emerging' agents would not be a threat and even bacterial risks would be eliminated. Bacterial risks have indeed been reduced by enhanced arm cleansing and 'diversion' of the first 20ml of blood collected. In some, but not all, countries bacterial testing of platelet preparations is also in place, but even then some bacterial transmission can still occur. Reduction in microbial tests would offset the cost of 'pathogen inactivation/reduction' (PI/R) technologies but it would be prudent to continue testing for HIV, HBV, HCV and probably syphilis, to avoid the return of infected donors with subsequent re-challenge to the routine microbial risk-reduction systems in place. Infected donors would also need to be notified to avoid the risk of secondary transmission.

Table 1: Estimated frequency of infectious blood donations issued, after testing, in UK: 2006-08

	HBV	HCV	HIV 1&2	HTLV 1
Overall risk: 1 in:	0.9*	71.9*	5.4*	23.9*

*Data courtesy of Lisa Brant (HPA/NHSBT). *million donations.*

Table 2: Confirmed TTIs in UK, 1996 to 2008

Bacteria	HAV	HBV	HCV	HEV*	HIV	HTLV	Malaria	vCJD prion	TOTAL
38	3	10	2	1	2	2	2	4	64

Data from 2008 Annual SHOT Report (2009)

**Hepatitis E Virus*

Unfortunately, 'perfect' inactivation systems are not yet available and although some degree of PI/R is in place in various blood services, none can inactivate prion and as yet there are no simple cost-effective technologies capable of treating whole blood so that the subsequent components would not require individual inactivation. PI/R technologies has advanced considerably but blood services are wary of investing in them until they can be confident that they can cost-effectively replace testing. Manufacturers therefore do not have the revenue to continue development to enhance the methodology and so far this has proven to be an intractable problem. This conundrum does not apply to implementation of initially imperfect testing systems, with subsequent improvement of methodology because testing infrastructure has predated PI/R technology. A concise but comprehensive summary of the state of nucleic acid testing and PI/R in Europe up to 2008 has been presented by Professor JP Allain [see references].

Notwithstanding these dilemmas, blood transfusion is safer today than it has ever been, but the search for effective blood substitutes and the encouragement of blood salvage during operations continues. Strict adherence to the principles of 'appropriate use of blood' might also help avoid the tragedy of a rare microbial transmission event occurring in a recipient who did not really need a blood transfusion.

Similar considerations to those discussed above for blood and component transfusion also apply to the use of cells and tissues. Indeed, considerable progress has been made in surveillance and risk assessment in this field.

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ABBREVIATIONS	
Ag/Abcombi	Assay to detect both antigen and antibody
Anti	Antibody to
CMV	Cytomegalovirus
ELISA	Enzyme linked immunosorbent assay
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HBsAg	Hepatitis B Surface Antigen
HCV	Hepatitis C Virus
HEV	Hepatitis E Virus
HIV	Human Immunodeficiency Virus
HTLV	Human T Cell Leukaemia/Lymphotrophic Virus
PI/R	Pathogen Inactivation/Reduction
RNA Amplification	Method to increase the number of copies of RNA to enhance sensitivity
vCJD	Variant Creutzfeldt-Jacob Disease
WNV	West Nile Virus

How NHS Blood and Transplant is preparing for Pandemic Influenza

NHSBT has updated its pandemic influenza plan bringing it in line with other NHS organisations by basing response on a three level structure:

- Strategic (Gold)
- Tactical (Silver)
- Operational (Bronze)

These command and control arrangements were activated in May and, although the plan is still based on Department of Health guidance, the specific assumptions are being reviewed and revised with the current epidemiological information. NHSBT has appointed Richard Rackham as the Executive Lead for Flu Response and the Gold team has met under his chairmanship to lead and manage the review of assumptions and NHSBT's response. This team represents the Executive and holds delegated power to act on behalf of the Executive for 'flu response'.

The second wave of swine flu is likely to have started in late September and, with other winter pressures, will affect the number of donors attending to donate blood and platelets. Having modelled and tested a number of scenarios, NHSBT took the decision to increase red cell stocks to 65,000 units, a challenging target that was achieved in early September.

Several groups of activities are underway, including:

- Ensuring that stock remains healthy by the recruitment of new donors through marketing activity;
- Providing systems and mechanisms for understanding and managing the consequences of staff absence;
- Providing appropriate HR policy guidance to managers and staff;
- Working with stakeholders including the UK forum, MHRA, hospital representatives and the DH to ensure that stock is robust;
- Ensuring the availability of critical consumables.

A recovery task group has been established which will allow recovery to be prepared effectively. Having a separate recovery team will enable NHSBT to concentrate on both the peak response and the recovery process simultaneously. The recovery task group will report in to the same overall management structure and will gather intelligence to begin detailed recovery planning whilst the other teams are still finalising response actions and managing the response.

Like all NHS organisations, NHSBT is working on undertaking the objectives set by Ian Dalton, National Director of NHS Flu Resilience, in his letter to Chief Executives on 2nd July. This includes testing pandemic preparedness and vaccinating front-line staff as well as some of those issues addressed above. The exercise undertaken by NHSBT raised a number of learning points that are currently being taken forward to enhance the response provided by NHSBT. With these preparations and planning NHSBT is confident that, should planning assumptions be borne out in reality, blood stock will outlast the pandemic.

Those donors who responded so swiftly to our appeal, to build blood stocks to ensure sufficiency during the predicted second wave of swine flu, demonstrated their commitment to helping save and improve the lives of those patients who rely on donated blood and blood products. It has been especially pleasing to see so many of our donors had heard our appeal to 'bring a mate to donate' and many donations were given by new donors coming for the first time. But increasing stocks to this higher level is only half of the story. 65,000 is a 50% increase in our normal stock levels and it will be a constant challenge to make sure we can continue to meet hospital demand during the coming weeks and months.

Collecting blood during the pandemic will present an even greater challenge. This is why we are asking donors to keep on responding to our invitations to donate. For those of you who have always meant to donate, but never got around to it, now would be a great time to start. It is really easy to enrol, just call 0300 123 23 23 or visit www.blood.co.uk and please make the effort to come when we invite you.

At the end of October, new planning guidance for pandemic influenza as issued by the Department of Health. They used data from the first wave in the UK and from Australia and other countries with a developed health service and health surveillance systems. This planning guidance significantly reduces the impact of pandemic flu with a headline figure of the attack rate being reduced from 30% to 12% of the population. Whilst this is good news, there is still cause for concern and NHSBT is planning, throughout November and December, to maintain stocks between 45,000 and 50,000.

We would like to take this opportunity to thank all our hospitals for their ongoing support with the appropriate use of blood.

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New Developments in Statistics and Clinical Audit

The development of an evidence base for the furtherance of organ donation and transplantation, blood and tissue services, haematology and transfusion medicine relies heavily on sound statistical underpinning and clinical audit. To meet the demand for the design and analysis of quantitative studies in all these areas and to strengthen clinical audit activity, a new Statistics and Clinical Audit service has been established by NHSBT. Readers of *Blood and Transplant Matters* will be quite familiar with examples of how service evaluation and clinical audit can lead to improvements in blood and tissue services. Because of this, and the fact that much statistical work is focussed on organ donation and transplantation, some examples from this area are given to illustrate the breadth of activity. Opportunities in other areas are then highlighted.

Studies in organ donation and transplantation

The identification of factors that affect waiting time to transplantation, and graft and patient survival time following transplantation, is important for a number of applications. In particular, this information indicates the factors that need to be accounted for in an organ allocation scheme, enables estimates of survival rates to be obtained for patients with particular characteristics, and facilitates the monitoring of centre specific outcomes. For example, an analysis of factors associated with death on the liver transplant list has led to the development of an index of the severity of liver disease in patients registered for a transplant. The index is now being used to ensure that the condition of patients being registered is comparable between the liver transplant centres, so that there is equity of access to transplantation.

Data associated with the introduction of novel transplant procedures enables their advantage to be quantified. To this end, a national registry of antibody incompatible kidney transplants has been established to enable outcomes following ABO and HLA incompatible transplantation to be defined, as well as establishing permissive levels of antibody. Initial results have shown that unadjusted three year graft survival rates are similar for both ABO and HLA incompatible transplantation, and are close to the 88% survival rate for deceased donor kidney transplantation. As the size of this patient group increases, more detailed analyses that incorporate risk adjustment will become possible.

In organ allocation, a national allocation scheme for both pancreas and islets has been developed. Following the identification of key factors associated with outcome, namely waiting time, level of sensitisation, cold ischaemic time and donor body mass index, over 40 different allocation algorithms were compared using a simulation process. A particular scheme has now been agreed with the pancreas transplant community and the IT infrastructure needed for its implementation is under development. The merits of a universal liver allocation scheme based on either clinical need or transplant benefit are now being investigated.

Much information about the potential for donation in the UK, and statistics such as the proportion of potential donors who actually donate, known as the conversion rate, has been obtained from the Potential Donor Audit (PDA). This study of whether patients who die in intensive care units across the UK become organ donors has shown that there are three obstacles to the supply of deceased donor organs for transplantation. These are the identification of potential donors, referral of potential donors to donor transplant coordinators and obtaining the consent of relatives; for example, the audit has shown that when approached, only 60% of relatives give consent for solid organ donation to proceed. Procedures that are designed to improve these aspects of the donation pathway are now being introduced.

Studies in transfusion medicine, stem cell and tissue transplantation

One of the main drivers for the establishment of NHSBT's Statistics and Clinical Audit service was to provide increased support for observational studies designed for service evaluation in all areas. This has led to our involvement in a number of major projects. These include a multi centre observational study on the use of blood components in paediatric cardiac surgery, a study funded by the National Institute of Health Research on traumatic coagulopathy and massive transfusion, and a study of bleeding tendency in children in Intensive Care Units. An important issue in many of these studies is how the need for blood products, or the incidence of coagulopathy, depends on demographic characteristics, the clinical management of a patient, and other factors, and this in turn requires the development and validation of statistical models.

In her editorial in the Spring 2009 issue of *Blood Matters*, Ruth Warwick commented on the long history of following up recipients of solid organ and corneal transplants, and indeed the quality and completeness of data in the UK Transplant Registry is of a standard comparable to that of many clinical trials. The need for outcome data following stem cell transplantation, and the transplantation of tissues is now recognised, and we are looking forward to contributing to the development of a process that will enable clinical practice in these areas to be informed by an evidence base built on outcome analyses.

Clinical Audit

Clinical audit is essential for quality improvement in all areas of NHSBT activity, and real improvements in service result from aligning clinical audit to the clinical risks associated with the donation and transplantation of blood, tissues and organs. Plans for future audits are likely to be stimulated by the specification of appropriate triggers for an audit, and the audit cycle used to promote quality and clinical effectiveness. New partnerships between clinical audit staff and statisticians will mean that audits are based on sound sampling strategies, with sufficient numbers of individuals to ensure that the results are meaningful. The audit results will then provide a sound basis for subsequent action.

The Care Quality Commission now requires all NHS organisations to comply with standards for clinical audit. For NHSBT, these include the formulation of an audit programme to facilitate improvements in the service that we provide to both donors and patients. In addition, the establishment of the National Clinical Audit Advisory Group demonstrates an increasing emphasis on the importance of clinical audit within the NHS.

The Future

We all welcome the opportunity to collaborate with scientists and clinicians in services related to blood, tissues and organs, who are developing observational studies designed to evaluate service provision, as studies in their own right or as a prelude to a clinical trial. We also encourage early discussion of proposals for clinical audit. More substantive engagement on project work will generally be through funded projects, and we are particularly keen to be involved at an early stage in the development of grant proposals where statistical input is anticipated.

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The importance of SEA and how it can benefit Patient and Donor Care

Learning from incidents or events is a very important component for organisational learning. To learn from incidents they must first be reported to the organisation. This article highlights the importance of incident reporting and explores the reasons why under reporting is common in healthcare. It has demonstrated the role Significant Event Audit (SEA) could play in overcoming the barriers to incident reporting and explores the vital role it could play in organisational learning and as a clinical governance tool.

Incident Reporting and Healthcare

Incident reporting has been used as an error intervention tool in many high risk industries such as aviation, petrochemical, nuclear and the military. In healthcare there are many diverse activities that require human judgement and interventions where a small mistake by a healthcare professional could lead to a detrimental outcome for the patient. Studies in the UK have shown that errors in healthcare are unacceptably high and it has been suggested that learning from critical incidents and adverse events plays an important role in improving the safety record.

Barriers and Limitations

Under reporting is a widespread issue in healthcare. Many studies have revealed under reporting as a salient limitation of hospital incident reporting systems. Staff can be reluctant to report certain types of incident compared to others. A key factor, highlighted by many authors, is the fear of reporting that prevents organisational learning and improvement. Research in healthcare and other industries indicate that professionals are reluctant to report safety incidents if they perceive that doing so exposes them to blame or other unjustified negative consequences. A non punitive approach taken by the aviation industry has proved to be a significant contributing factor to impressive safety records. The National Patient Safety Agency in 2004 also highlighted the importance of creating a strong safety culture. There is a key belief that nothing will be done in response to reporting incidents. Timely feedback and recommendations to improve practice are important factors in preventing under reporting of incidents.

Overcoming the Barriers

The main factors that affect under reporting can be overcome by active involvement from all levels of staff within the organisation in the incident analysis process. This provides the opportunity for staff to reflect on practice in a multidisciplinary environment and understand the importance of incident reporting. By doing so staff can voice their concerns relating to the incident and management can gain a clear idea of the reasons why the incident occurred. This collaborative approach ensures different levels of staff in the organisation work together to find effective solutions. Staff become less fearful with this democratic approach and it helps them understand the educational and service

Figure 1: The SEA Process

improvement value of incident reporting. More importantly, the analysis should be done with the staff who were involved in the incident supported by a facilitator.

Significant Event Audit (SEA) is an incident analysis methodology that provides opportunity for the staff to analyse the incident with the aim of improving practice. SEA is a modern name for an important old concept. SEA is defined as "a process of analysing individual cases, in which there has been a significant occurrence (not necessarily involving an undesirable outcome for the patient), in a systematic and detailed way to ascertain what can be learnt about the overall quality of care and to indicate changes that might lead to future improvements". In the NHS, SEA started in general practice. A randomised controlled trial of SEAs was completed in 20 British general practices and its effectiveness was demonstrated as a quality improvement tool.

SEA appears to be a simple process but it requires skill and a non threatening environment to enable an in depth analysis of an event between team members. This in depth analysis can be assisted by documents such as case notes and guidelines where necessary. The SEA meeting needs a facilitator who has the skills to help the team to undertake this. The analysis requires time in order to improve patient and donor care. The group discussion should take place with representation from all staff involved in the incident and a senior member of the group should write a brief report including the agreed actions and learning points. It is important that everyone in the group agrees with the content of the report. Where possible, corrective actions can be implemented locally but further issues may need to be taken to relevant senior management or clinical groups. In other words this creates the opportunity to work together with relevant senior management and clinical groups to learn from incidents and improve practice. A number of research studies have shown the benefits of SEA at personal, professional and corporate levels. Overall, if done well, it is likely that SEA will result in: Improved patient and donor care and experience, improved team working, a more open and trusting culture among staff and identification of staff training needs. SEA takes significantly less time to complete, compared to clinical audit or service evaluation. SEA addresses all five cornerstones of clinical governance (system awareness, team working, communication, ownership and leadership) in a very practical way.

Summary

Due to regulatory and policy requirements NHS organisations have developed various incident reporting systems. It is questionable how well these reporting systems have been utilised for organisational learning and to improve practice. SEA provides an important link between learning from incidents and improving practice in a multi-professional setting. Most importantly, SEA can overcome under reporting by removing the barriers which are common in healthcare. As a clinical governance tool, SEA has a powerful role to play in improving patient and donor care.

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The NHS Cord Blood Bank – A Vital Resource for Cell Therapy

The NHS Cord Blood Bank (NHS CBB) was the brainchild of Professor Dame Marcela Contreras and started banking cord blood donations in February 1996. Recently, an initiative from the Anthony Nolan Trust has seen the establishment of their cord blood bank; reviewed in this edition by Sergio Querol. The first transplant using cord blood stem cells was performed at the Hôpital Saint Louis, Paris by Professor Eliane Gluckman and colleagues more than 20 years ago in a child with Fanconi Anaemia. Since then cord blood banks have been established all over the world and there are now over 400,000 units available with more than 20,000 transplants carried out using unrelated cord blood stem cells. Whilst more cord blood transplants (CBT) have been carried out in children (3,046 versus 2,157 between 1994 – 2009; data from Eurocord); its use in adults continues to increase, so that in each year since 2006 more transplants have been reported in adults. The advantages of CBT include ease of collection, ready availability, low rates of transmission of CMV and other latent viruses, lack of donor attrition and naivety of T cells leading to greater tolerance of 1-2 mismatches at the HLA-A, B or –DR loci (a full match by these criteria being 6/6). Rare haplotypes are also represented at higher frequencies in CBB, since targeting of ethnic minorities is easier. There are also some disadvantages, for example a second donation of stem cells or donor leucocytes is not possible and the dose of stem cells is low and this may be associated with delayed engraftment.

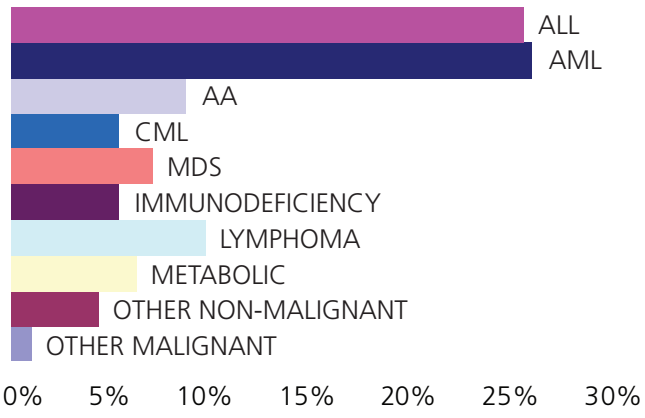
Since its inception the NHS CBB has collected 13,800 donations, 40% from minority ethnic donors. The main aim of the bank is to provide a minimum of 20,000 cord blood donations as a source of stem cells and other critical cell populations for cell therapy, so as to improve the lives of patients with a range of malignant and non-malignant disorders. By aiming to bank a high proportion of donations derived from ethnic majority donors, the NHS CBB aims to help redress the current imbalance in ethnic majority representation found in adult stem cell donor registries. It is the fourth largest CBB in the world and contains the second highest percentage of rare HLA phenotypes.

The NHS CBB is currently located on two sites within NHS Blood and Transplant. Collection is now based at the Colindale Centre and undertaken by dedicated, locality-based staff at five hospitals: Barnet District, Luton and Dunstable, Northwick Park, St Georges Tooting and Watford General. Potential donors are selected using rigorous criteria and a medical check that includes lifestyle, ethnicity and travel histories. The counselling and consent procedures are detailed, as required by recent legislation, and all donations are collected by trained NHS CBB staff ex utero. A follow up check on the mother and baby is conducted by telephone 12 weeks after delivery and this is added to the results of haemoglobinopathy testing. Prior to issue the UK Congenital Malformations Registry is also searched.

Processing, storage and issue of cord blood units for transplantation is from October this year, located at NHSBT's centre in Filton, Bristol. Seventy five percent of all donations collected are suitable for banking and all undergo rigorous testing for markers of infectious disease, cell counts, ABO and RhD typing, CD34 analysis and colony-forming unit (CFU) growth. They are also typed for HLA-A, B, C and DRB1 loci by molecular techniques and then available for search in Bone Marrow Donors Worldwide via the British Bone Marrow Registry (also run by NHSBT on behalf of the English, Scottish and Northern Irish Blood Services) and NETCORD.

Cord blood donations issued by the NHS CBB have been used for transplantation in both malignant and non-malignant conditions as shown in figure 1.

Figure 1: Distribution by disease type of the first 215 CB donations issued from the NHS CBB



To date the NHS CBB has issued 277 donations to transplant centres in 22 countries worldwide, roughly 30% of which were from donors from ethnic minority groups and 30% have been for double CBT, which is currently the object of much clinical investigation. A recent analysis of 209 transplants performed with cells provided by the bank between 1998 and 2008 showed an overall actuarial survival of 48.4% at 5 years and engraftment [n=178] of 87.3%.

We now work in a closely regulated environment and the NHS CBB has recently been reinspected by Netcord-FACT and accredited. In addition it is licensed by the Human Tissue Authority following a detailed inspection in May 2009.

The optimum size for a UK CBB is frequently debated and recently Querol and colleagues have determined that

with a bank size of 50,000 donations, 80% of patients would have at least one donor unit available at the 5/6 match level and 98% at the 4/6 match level. It is estimated that one out of four patients requesting an unrelated allogeneic transplantation would benefit from a national cord blood bank initiative aiming to establish a bank of this size – around 200-300 patients per year in the UK alone. Currently the future size of the cord blood banking programme in the UK is under active discussion with the Department of Health (DH). In addition the structure and organisation of cord blood banking in the UK has been the recent subject of a detailed enquiry carried out by Technopolis for the DH. This report suggests that there should be a national policy for cord blood, a high level advisory committee and further commissioned research to obtain information on public-private banking models. The NHS CBB will continue in collaboration with clinical transplant teams and others to provide grafts for cell therapy and research.

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Towards a UK National Cord Blood Programme

Why Cord Blood?

Cord blood is peripheral blood of foetal origin retained in the placenta following birth, and can be considered as a natural waste biological product. Basic biological studies have demonstrated that this blood has unique properties. Specifically, it contains high levels of circulating stem cells as well as cells with potent immunomodulatory properties. Following delivery, placental blood can be easily collected without risks for the newborn and mother instead of being discarded. Once established, cord blood collection programmes provide an ethical and feasible source of naturally produced stem cells for clinical transplantation and for use in regenerative medicine.

Establishing a Cord Blood Bank

The therapeutic properties of cord blood were first demonstrated in 1988 when a patient affected by Fanconi Anaemia, was successfully treated. Since then more than 20,000 cord blood transplants have been performed worldwide mostly to treat acute leukaemia in children and adults lacking a suitable sibling or adult volunteer donor.

A cord blood bank (CBB) can be seen as an integrated team responsible for the collection, processing, testing, banking, selection and release of cord blood and for the analysis of outcomes of the resultant allogeneic transplants or regenerative medical uses (according to Netcord-FACT international standards for cord blood banking). The objectives of a qualified CBB are:

1. Meeting all applicable licences, certifications, registrations, and other authorisations required to operate;
2. Donor screening and cord blood collection best practice;
3. Processing methods intended to protect the health and safety of donors and stem cell recipients as well as improving stem cell usage and outcomes, particularly

with regard to controlling the transmission of harmful infections;

4. Accreditation by recognised organisations;
5. Establishing a system of strict confidentiality to protect the identity and privacy of patients and donors in accordance with existing laws;
6. Systems to encourage donation by a genetically diverse group of donors;
7. The development of a system to confidentially maintain a linkage between product and donor.

The use of Cord Blood

a. Haematopoietic Transplantation (CordBank)

The early observation that transplantation of HLA-matched umbilical cord blood from related donors causes less GVHD led to the hypothesis that this graft source might be used as an unrelated source for haematopoietic transplantation. Cord blood banks were therefore established. Safety and efficacy has now been demonstrated in both children and adults as alternative source of stem cell for allotherapies. Main conclusions of different retrospective analyses published show a delayed engraftment with respect to bone marrow grafts, a lower incidence and severity of acute GVHD, and overall comparable survival rates. Recently, Eapen and colleagues reported better outcomes for children receiving matched cord blood compared with adult sources. This data has driven the CBB to increase number of units available since results improve with better HLA matches. Virtual inventories of hundreds of thousand of cord blood units would be necessary worldwide.

b. Cell Therapy (CordPharm)

Once established, a cord blood bank receives large amounts of products. Cord blood buffy-coats are used today in bone marrow transplantation as an alternative to unrelated adult stem cell donation. But other applications are also envisaged. One possibility is the ability to generate a universal, off-the-shelf, minimally manipulated source of cellular components for cell therapy or transfusion medicine.

c. Cord Blood Bio-Bank (CordResearch)

More than a half of the harvested cord blood units are discarded in the cord-blood processing centre. These discarded units are defined by cell content and not by intrinsic quality criteria making them suitable for clinical research. This surplus allows the possibility of generating a bio-repository of samples ethically approved for research use. This biological resource could be made available for any researcher in the UK and worldwide through mechanisms controlling both project quality and ethics. Making the cord blood donated available for clinical use or research will help to develop new biomedical strategies in multiple fields.

National/Global Benefits

Establishing a national cord blood programme will reduce the proportion of patients for whom no donor is found. As the bone marrow programme demonstrates, a joint initiative with NHSBT will be efficient and effective. There is a need to develop a national collection programme of cord blood, which would allow for rapid access and rapid treatment of patients in need. There has been significant debate regarding the optimal number of cord blood units required in the UK but a recent publication based on UK data, calculates that we would be able to meet the needs of 95% of suitable patients, irrespective of their ethnic background, with a cord bank containing 50,000 high quality cords. This is an opportunity to create a self sufficient cord blood programme for the UK which will save many more lives. Whilst cord blood offers many patients the only chance of a match, it also offers a faster treatment option over using adult donors. This shorter time may improve patient outcomes.

Reasons for Developing the Anthony Nolan Cord Blood Bank

Anthony Nolan was set up on a simple and powerful premise, *to save lives*. This work has continued since 1974 with over 7,000 people being given the chance of life. Last year, the Anthony Nolan Register were able to find matching donors to provide the chance of life for 736 people, the highest ever. But still that only helped 50% of the people in need of a stem cell transplant in the UK. Last year alone Anthony Nolan imported and used 89 cord units that constituted the 80% of all cord blood transplantation activity in the country. It was evident that the numbers of units required for an efficient national programme to support the steady increase in the UK clinical usage decreasing the big dependency on imported units justified the need for further public cord blood programmes in UK. Having two big adult registers complemented with two adequately sized cord blood banks will add benefit facilitating achievement of proposed targets on time. In 2008, the Anthony Nolan Trust opened the Anthony Nolan Cell Therapy Centre for the storage and processing of cord blood units to complement the adult register but more important to broaden the donation programme in UK, to fasten the growth to obtain 50,000 units required, and to lead translational research for new application in cellular immunotherapy and regenerative medicine. We anticipate that this valuable resource if collected widely would enable us to save an extra 200-300 people per annum in the UK. Our recent study at Kings College Hospital, shows that when using a combined adult donor

and cord blood search, fewer than 5% of patients would fail to find a suitable match.

Conclusion

In conclusion, it is feasible to bank cord blood for future use with the potential for use in three main areas:

a. Haematopoietic transplantation, where large inventories of different cord blood units with genetic diversity are a benefit in finding a suitable match for patients from ethnic minorities.

b. Regenerative medicine, where different lineage-specific or multi-potent stem cells could be used for tissue regeneration using a universal, ready-to-use, therapeutic product.

c. Cellular immunotherapy, taking advantage of the presence of unique naïve T cells with immunomodulatory properties.

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The International FACT-NetCord Accreditation Scheme and Standards for Cord Blood Banks

The successful outcome of the first umbilical cord blood transplant performed by Elianne Gluckman in 1988 led to the realisation that in order to facilitate these transplants in the future, large numbers of well characterised and high quality cord blood units (CBUs) would be required worldwide. Also, as unrelated cord blood transplantation increased throughout the world, it became clear that this activity would require the import and export of cellular products across different countries making it necessary for CBBs to operate within a regulated environment in order to ensure that the donations provided for transplantation were safe and met the highest quality standards.

As a result a number of investigators began to develop procedures for the safe collection and storage of these CBUs and these efforts culminated with the establishment of the first cord blood bank (CBB) in New York in 1991. This was soon followed by the establishment of other CBBs in the USA and Europe including the NHS-CBB which was set up in 1996.

With the formation of these CBBs it was soon realised that networks at both national and international level would be required to share the information kept in each CBB and this led to the foundation of NETCORD in 1998. The main remit of NETCORD was to establish an international registry of CBUs and to develop procedures and standards for the safe exchange and clinical use of the banked units. Consequently, NETCORD, in collaboration with the Foundation for the Accreditation of Cellular Therapy (FACT), published the first edition of the *NetCord-FACT International Standards for Accreditation of Cord Blood Collection, Processing, Testing, Banking, Selection and Release* (2000). These standards which cover all aspects of cord blood banking, form the basis of the FACT-NetCord accreditation scheme. At present, the accreditation scheme operates in

compliance with the 3rd edition of the NetCord-FACT Standards but these are now under revision and it is expected that the new (4th) version will be in place in 2010.

The main objective of the NetCord-FACT standards is to promote best practice throughout all aspects of cord blood banking including donor selection, methods of collection, processing, testing and storage of the units, and in those areas covering the release and transportation of the CBUs to the transplant centres. These standards state that all laboratories supporting CBB activities need to have the relevant additional accreditations in place, e.g. EFI or ASHI for the HLA aspects and that those aspects of the CBB programmes related to the registration, searches, selection and HLA matching of the CBUs need to operate under the guidelines of the World Marrow Donor Association (WMDA). The registry should then be WMDA accredited or in the process of accreditation.

To be compliant with the standards, CBBs must use validated methods; qualified supplies, reagents, and equipment; maintain a comprehensive, properly documented Quality Management (QM) programme and perform a clinical follow-up of the patients who receive CBUs from that bank. This clinical follow-up is performed in collaboration with Eurocord.

The inspection and accreditation process is carried out by trained inspectors and involves the submission of written documents and an on-site inspection of the CBB facilities, including the CBB office, collection sites, processing and storage facilities. Depending on the number of collection sites associated with the CBB programme, all or a subset of the collection sites are inspected.

Under the FACT-NetCord accreditation scheme, CBBs are not required to have a specific structure and they may contract services for their operations. However, to be eligible for accreditation, each bank must have processes in place to meet all NetCord-FACT standards.

It should be noted that the standards for the transplantation of allogeneic or autologous cord blood units are covered by FACT-JACIE *International Standards for Cellular Product Collection, Processing and Administration* and not by NetCord-FACT standards.

The NetCord-FACT standards apply to CBBs storing allogeneic cord blood units from unrelated altruistic donations and from related donations for directed use by a specific individual recipient or family member of the donor. They also apply to CBBs storing CBUs for autologous use.

At present there are 128 unrelated CBBs in different parts of the world with over 450,000 frozen units immediately available for transplantation. There are 19 CBBs accredited with FACT-NetCord, and more than 40 are in the process of applying for accreditation.

The American Association of Blood Banks (AABB) has now also developed standards and an accreditation scheme but these operate primarily in the USA.

The European Union Tissues and Cells Directive (EUTCD), implemented in 2006, requires all member states to have inspection and accreditation systems in place to ensure that all banks providing these services comply with an agreed set of standards. In the UK this is regulated by the Human Tissue Authority (HTA) set up in 2004 and which was implemented in April 2006. All CBBs within the UK are required to be HTA licensed.

The Food & Drug Administration (FDA) is the regulatory authority in the USA.

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Clinical Umbilical Cord Blood Transplantation

Introduction

Allogeneic haemopoietic stem cell transplantation has been used for over four decades to cure children and adults with life-threatening malignant and non-malignant disorders of the bone marrow and immune system. Only 30% of patients who might benefit from an allograft have a Human Leucocyte Antigen (HLA) identical sibling available. Despite the expansion of unrelated donor registry panels, the likelihood of finding a volunteer donor for those without a matched sibling is dependant on the individual's ethnic background, being around 90% in Caucasians, but less than 20% for some races. Even when a suitable volunteer donor is identified, it may take three to four months to acquire the haemopoietic stem cells required for transplantation. This can be too long for patients in an unstable remission who may relapse or even die of their disease without ever reaching transplant. These difficulties have led to exploration of the use of alternative donor stem cells, including unrelated umbilical cord blood.

Outcomes of Umbilical Cord Blood Transplantation

The first related donor umbilical cord blood transplant was performed in 1988 for bone marrow failure associated with Fanconi Anaemia. This patient remains well and in haematological remission 20 years later and for the first time demonstrated that full haematological and immunological reconstitution could be achieved using umbilical cord blood which had been harvested, cryopreserved, thawed and infused. Since, then over 10,000 allogeneic cord blood transplants have been performed worldwide and a number of key features of this stem cell source have emerged.

The likelihood of achieving haematological engraftment following cord blood transplantation is lower when compared to unrelated donor haemopoietic stem cell transplantation, with a longer duration of neutropenia. However, the incidence and severity of acute and chronic graft versus host disease, an important cause of post transplant morbidity and mortality, is lower when umbilical cord blood is used. Despite this, there is no increased risk of relapse following cord blood transplantation. In children, the overall and disease free survival achieved with HLA – mismatched unrelated cord blood is equivalent to that observed following HLA – matched unrelated donor bone marrow transplantation. Thus, cord blood transplantation has become widely accepted as an alternative stem cell source in paediatric practice. Early experience of cord blood transplantation in adults was associated with poor engraftment of donor haemopoietic cells and subsequent survival. However, a better understanding of cord unit selection and optimisation of conditioning regimens, has led to a substantial improvement in overall and disease free survival, such that HLA – mismatched cord blood transplantation in adults is now at least equivalent to HLA – mismatched bone marrow transplantation. As a result, umbilical cord blood is being increasingly used in older patients for whom a conventional HLA – matched volunteer donor cannot be identified within an acceptable time frame for their disease.

Advantages of Umbilical Cord Blood Transplantation

Table 1 summarises the advantages and limitations of cord blood transplantation compared to other haemopoietic stem cell sources. Cord blood is generally harvested after delivery of the placenta with no risk of harm to the donor, unlike the potential risks associated with bone marrow harvest or peripheral blood stem cell collection and exposure to granulocyte colony-stimulating factor (GCSF). Since cord blood units are pre-tested, cryopreserved and stored in specific repositories, there is no risk of donor attrition. Units are also rapidly available, within a median of two weeks, facilitating urgent transplantation when clinically indicated and re-scheduling of transplantation date if necessary. In addition, the reduced risk of graft versus host disease associated with cord blood transplantation permits less stringent donor-recipient HLA matching than is necessary with adult donors, thus increasing the probability of identifying an 'acceptable' donor for a specific patient. Access to transplantation is further increased by efforts of cord blood banks, such as the NBS Cord Blood Bank, to concentrate their collections in centres with a high proportion of ethnic groups which are poorly represented on adult donor panels.

Current Limitations of Umbilical Cord Blood Transplantation

Despite the many advantages of umbilical cord blood, a number of important limitations have also been identified (Table 1). Once the transplant has been performed, there is no possibility of obtaining further cells from the cord blood donor in the event of graft failure, falling levels of donor-derived cells (donor chimerism) or relapse. There is also the potential for transmission of unanticipated congenital disorders.

However, the principle obstacle to the wider use of cord blood transplantation, particularly in adolescents and adults, is inferior engraftment with the duration of neutropenia continuing for an average of one or two weeks longer than unrelated donor bone marrow or

Table 1: Advantages and Disadvantages of Alternative Donor HSCT (from Hough, *et al* 2009)

	Unrelated BMT	Unrelated UCBT	Related Haplo-identical PBSC
Available pool	>11 million	>250,000	-
Likelihood of suitable donor	10/10=40% ≥9/10=70% Ethnic minority=20%	≥5/6=40% ≥4/6=70%	>90%
Speed of access	3-4 months	2-3 weeks	Immediate
Cost of obtaining graft	High	High	Low
Risk to donor	Low	None	Low
Ability to re-arrange infusion date	May be difficult	Easy	Easy
Re-access	Possible	No	Yes
Quality of product	Assured	Variable	Assured
Speed of engraftment	Moderate	Slow	Fast
Graft rejection	Low	Moderate	Moderate
GVHD risk	High	Moderate	Low
Speed of immune reconstitution	Moderate	Moderate	Very slow
Speed to GVL effect	Moderate	Moderate	Very slow
Risk of viral transmission	Yes	No	Yes
Risk of transmission of congenital disease	No	Yes	No

peripheral blood stem cell transplants respectively, which increases the risk of transplant related mortality. A number of strategies designed to address this limitation are under investigation and include 1) augmenting the infused cell dose by co-infusion of haploidentical family CD34+ selected peripheral blood stem cells or ex vivo expanded cord blood units, 2) improved homing by direct intraosseous (intrabone) injection of cord blood cells, 3) minimising the duration of neutropenia by allowing transient autologous myeloid recovery until cord-derived haemopoiesis is established and 4) perhaps most successfully to date, the co-infusion of two umbilical cord blood units. If the aspirations of these approaches are realised, cord blood transplantation will become an increasingly attractive therapeutic option in larger children and adults.

Conclusion

Umbilical cord blood is now internationally established as an acceptable alternative haemopoietic stem cell source for transplantation in children, with increasingly encouraging results in adults. The use of cord blood now facilitates urgent transplantation for those with unstable disease and provides a suitable donor for many patients with life-threatening disorders who would historically have been precluded.

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Tissue donation activities in Latin America

Introduction

Progress in medical science has made it possible to obtain and transplant human organs and tissues, facilitating the recovery of health, improving survival rates and quality of life. For more than 60 years the scientific community and society as a whole has recognised the medical and the humanitarian value of donating and grafting organs and tissues.

One single donor can be the source of more than 400 tissue fragments, pieces or units. The availability of these human tissues depends on both the willingness of citizens to donate and the donation structures and systems that are also responsible for safety and quality requirements. In particular to prevent the transmission of diseases.

Guidelines and legal statements have been published and adopted in Europe and beyond to state basic requirements for authorisation and certification of activities related to obtaining, processing and distributing human tissues. However in many countries legal requirements are retained under the umbrella of the organ transplant laws.

There are no official data on tissue donation activities or on the amount of tissues that are being used and distributed all around the world. No complete registers or statistics are available except for some specific geographic areas. However it can be estimated that every year more than 4 million people receive some form of processed human tissue (medical devices including human tissues are excluded). Several years ago it was reported that in the US the number of bone graft procedures exceeded 500,000 per year and were probably over 2.2 million world wide. Recently, the American Association of Tissue Banks (AATB) published data that stated that nearly 1,300,000 patients were treated with musculoskeletal tissue, 170,000 more were treated with soft tissue and more than 420,000 receiving some kind of medical device containing human bone in the US alone. This gives an approximate potential of musculoskeletal users of around 4,000 patients per million population per year, a figure that may increase. As there is a need for tissues for medical treatment, the coordination and promotion of tissue donation needs to be enhanced in all countries.

In our experience at least 10% of all hospital deaths can be considered for multi-tissue donation (and cornea donors would double these figures). However, except in a few cases, only organ donors (1% of hospital deaths) also become tissue donors so that most of the potential for tissue donation from multi-organ donors is being lost. In addition to this loss of donor identification and family refusal rates specifically to tissue donation also contribute significantly to loss of tissue donors.

In the US there is an annual average of 26,000 multi-tissue donors (excluding eye-only donors) and among them 85% are musculoskeletal donors. However donor family refusal rates rise up to 70% so that promotion of tissue donation is an essential aim. Tissue donation promotion does not get the same support and recognition as organ donation. Every effort should be made to inform families about the need for and the results of tissue transplantation.

Latin American Countries – An Overview

Latin American countries, with a population close to 550 million people commenced transplantation programs several years ago. As in the rest of the world kidney transplants led the way. General figures can be summarized as follows:

- With the current donation rates only 8,000 patients receive a kidney transplant every year (40% of them from living donors).
- It has been calculated that 70,000 new patients will need renal replacement therapy every year; nevertheless only 50,000 will gain access to transplants.

The need for a significant improvement in the situation promoted the creation of the Latin America Transplant Network.

Transplant Networks in Latin America

Four years ago, 19 American countries, Spain and Portugal became members of the Iberoamerican Network/Council of Donation and Transplantation. This Forum was supported by the Health Ministries and Government Presidents of all the countries during the annual 2005 summit.

The model of organisation that was developed was based on the one that was operative for the transplant group of the Council of Europe. The latter is a permanent forum formed by one country representative, that meets twice a year, with a clear objective of promoting donation and transplantation:

- Development of social promotion and related activities;
- Courses, meetings, conferences and other training programmes;
- Preparation of reports including analysis of the situation of the Region;
- Preparation of, recommendations and agreements.

The WHO (World Health Organisation) is represented in that forum by a PAHO *(Pan American Health Organisation)* delegate. This connection, together with

official support and funding, make it possible for the transmission and practical implementation of the initiatives adopted by the delegates.

From the very beginning the priority was placed on solid organ donation and many activities in that field have been developed. However, step by step, tissue donation and transplantation is becoming a part of the current work. The basic and most important agreements adopted in this Forum are:

1. Development and approval of consensus documents in different transplant topics:
   - Autologous cord blood banking;
   - Minimum standards of training for donation professionals;
   - Requirements and function of a National Organisation of Transplants.
2. Publication from 2007 of an annual Newsletter including all available data on donation and transplantation as well as the contents of the agreement documents;
3. Opening of the network to other Scientific Societies as consultants;
4. Centralised negotiation for the distribution of immunosuppressive drugs for transplantation through WHO/PAHO;
5. Slow but continuous improvements with development of legislative and organisational frameworks in Latin America;
6. Development of training programs and bilateral cooperation projects for the promotion of organ and tissue donation and transplantation.

Tissue Donation and Transplantation in Latin America

While solid organ donation and transplantation is increasing and obtaining more professional and official support, tissue activities have had a different and less dynamic development.

Human tissues raise different concerns, but as with solid organs, there is a global problem of demand with need exceeding available supply. It has been estimated that between 3 and 5 million tissue transplants take place every year globally, with the highest demand in the US (>50%). All these figures are estimations since there are only incomplete data on the actual levels of activity. By comparison with the USA similar usage figures could be expected in the Latin American Region but much less activity is reported.

Despite the potential for the transmission of infections via allografts, no specific rules have been adopted in South American countries, whereas requirements have been published for the US and the European Union. Although there is a need for standardisation of the current definitions of practices in quality and safety, there is no harmonisation of National laws for tissue banking nor is there a general registry of activities and general definitions.

General data can be obtained from the National Transplant Organisations websites and the Latin America Forum for Transplantation see Table 1.

Websites for the data shown in Table 1

Argentina: Instituto Nacional Central Único Coordinador de Ablación e Implante: http://www.incucai.gov.ar

Bolivia: Comisión Coordinadora Nacional de Trasplantes de Órganos y Tejidos de Bolivia: http://www.trasplantesorganos-bo.org

Brasil: Coordenaçao-Geral do Sistema Nacional de Transplantes: http://www.abto.com.br

Canada: The Canadian Association of Transplantation: http://www.transplant.ca

Chile: Corporación Nacional de Trasplantes de Child: http://www.trasplante.cl

Colombia: Red de Donación y Trasplante: Instituto Nacional de Salud: http://www.ins.gov.co

Cuba: Grupo de Coordinación Nacional de Trasplantes: http://www.sld.cu/sitios/trasplante

Mexico: Centro Nacional de Trasplantes (CENATRA): http://www.rnt.gob.mx

United States of America: United Network for Organ Sharing: http://www.unos.org

Uruguay: Instituto Nacional de Donación y Trasplante de Células, Tejidos y Órganos (INDT): http://www.indt.hc.edu.uy

Venezuela: Sistema de Procura d Órgaos y Tejidos: http://www.ontv-venezuela.org

Apart from a few countries, legal statements for tissue are included within general transplant laws, but these only refer to very basic aspects such as consent. We cannot find specific developments for tissues, with reference to any requirement for retrieval, processing or distribution and the same can be said for coordination and organisational aspects. From our review we find that general requirements for tissue donation and processing exist in some countries' frameworks, such as Argentina, Uruguay and Brazil, covering some of the points related to tissue donation and allocation (basically corneas), but basic items that should be included are not found. There are no statements on traceability, control of the import/export or requisites for good tissue practices. All establishments involved in cell or

Table 1: General Data

	Population (million inhabitants)	GDP $USS /Cap.) Ppp	HDI	Life Expectancy Year	Transplant law/Tissues incl.	Transplant organ organisational system/ Tissues incl.	Tissue data available
Argentina	39,9	14,280	0,869	74,8	Yes/Yes	Yes/Yes	O-CV-S-MSK
Brazil	194,3	8,4	0,8	71,7	Yes/Yes	Yes/Yes	O-CV-S-MSK
Chile	16,8	12,02	0,867	78,3	Yes/ -	Yes/ -	O-CV-S-MSK
Cuba	11,265	6	0,838	77,7	Yes/ -	Yes/ -	O
Dominican Republic	9,5	8,2	0,779	71,5	Yes/ -	Yes/ -	O
Mexico	107,8	10,7	0,829	75,6	Yes/ -	Yes/ -	O
Paraguay	6,23	4,6	0,755	71,3	Yes/ -	Yes/ -	O
Uruguay	3,35	9,96	0,852	75,9	Yes/Yes	Yes/Yes	O-CV-S-MSK
Venezuala	28,12	6,63	0,792	73,2	Yes/ -	Yes/ -	O

0 = Ocular CV = Cardiovascular S = Skin MSK = Musculoskeletal

tissue therapies should be placed on a registry showing that they adhere to strict criteria for quality control, professional training and record keeping, but unfortunately this is not currently the case.

It can be seen that Brazilian activity is quite high for corneal transplantation, registering more than 70 transplants per million people (pmp). Globally speaking, US figures are the highest with 150 transplants pmp, which is the same as in some Spanish regions like Catalonia. However, European countries remain below 80 transplants pmp and most of them below 50 transplants pmp, and the same can be said for other Latin American countries. Reported activity for other tissues is far from published data for other countries. Probably not all data are reported and the need for musculoskeletal, skin or cardiovascular tissues is much higher than is registered.

Conclusion

Tissue donation and transplantation is rising rapidly. Both the diversity of tissues and ways to process them are under continuous development. One single donor can be the source of tissues for hundreds of recipients. In addition, tissues are subject to exchange between tissue establishments internationally and there needs to be a general consensus on the need for good practice guidelines to ensure quality, safety and traceability.

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A Day in Clinical Transfusion Microbiology

I work in a small team based at Colindale, but located in Borehamwood, Hertfordshire. We have three medical staff, each spending two – four sessions per week in Clinical Transfusion Microbiology, and working closely with clinical scientists, Infection Surveillance, and office staff. We cover the blood centres in south-east England plus Southampton and parts of the Bristol area.

Our work is divided as follows:

- Deal with reports issued by the National Transfusion Microbiology Reference Laboratory (NTMRL) where a donor has confirmed infection, or may have an infection and requires further investigation;
- Make clinical decisions about quality incidents; for instance, post-donation information which calls into question the suitability of a donation;
- Receive reports from hospitals/clinics/GPs when a blood transfusion recipient, or an ex-blood donor, has been diagnosed with a blood-borne virus infection. Make decisions on the need for investigations, further actions, etc.

Rule number 1: there is no typical day. Usually, all three of us are in the office on Fridays. The task is to review and prioritise the work. We update each other, particularly if we have dealt with a case which another of us has handled previously. There are several different tasks.

"New" results

We review results on donors who have tested positive: usually first time donors, born outside the UK, and with English as a second language. Many blood-borne infections have a geographical distribution, reflected in the donors: hepatitis B (South East Asia, China, Africa, Eastern Europe), hepatitis C (Eastern Europe), HTLV (the Caribbean) and HIV (Sub-Saharan Africa). The only exception is syphilis infection.

For each donor, we review test results and information recorded on the Donor Health Check. We decide on the appropriate letter for office staff to prepare. For hepatitis B, hepatitis C and HTLV, we give donors information in a letter and leaflet and invite them to telephone for a discussion. HIV positive donors are sent an appointment and donors with evidence of syphilis infection are asked to telephone us. Apart from HIV, we do not see donors face-to-face.

Review the files of donors who have not responded to letters

Files return to us when repeated attempts at contact with the donor have failed. We discuss strategies depending upon the infection and the donor's circumstances. Has the donor probably received the initial letter? Some do not have a permanent address, so letters may fail. Mobile phones are our second line of communication, but often unsuccessful. Such donors may not be registered with a GP, removing another possible avenue of communication. Today's list includes:

- A male from Democratic Republic of Congo with syphilis infection. His address is a Church in London. We "google" it: the church runs a refugee centre. We speak to an advice worker. Most of the refugees are not based in London and are frequently moved around by the Home Office. The advice worker gives us the latest address, which tallies with the GP address we already have. Apparently, Data Protection is less of an issue here!
- A Chinese man with hepatitis B infection has not responded to letters, nor answered his mobile phone. Last week, we sent a standard letter informing him that we will send the results to the GP unless we hear within 14 days. This letter often elicits a response! The donor has now written: he was staying with friends, but did receive the first letter. Now, four months on, he has moved, changed GP and wants further advice. In view of the time lapse we agreed to write to the new GP and encourage the donor to attend.

Communicating with donors who have responded to letters

- An Ukrainian who has lived in this country for some years, but has not registered with a GP, does not believe that he has hepatitis B. He eventually agrees to register with a GP and have another blood sample taken. A satisfactory outcome. I complete the forms and surveillance information and note in the file that he does not believe the results. If someone else deals with him next, they have the background and will be alert to the issues.
- An HIV positive donor from Cameroon (West Africa) who did not respond to the initial appointment offer. He donated at his workplace and the local organiser knew that he went away on a course. No contact on his return, but the local organiser located him. By this time, despite our best efforts, he telephoned on a Friday. He could not come to see us, but agreed to go to his local Genito-Urinary medicine clinic after the weekend. He did not attend. The GUM clinic has chased him but he has telephoned us. Although he speaks English, talking is difficult over the telephone. After patient persuasion, he agrees to attend the clinic but we detect reluctance because of fear about his occupation. Next, I follow-up with a telephone call to the GUM clinic to put them in the picture.

Samples for further investigation

- A hospital has reported a patient with hepatitis B infection, transfused five years previously and negative before the transfusion. I ask clerical staff to start a file and print off relevant documents from the PULSE IT system. I complete infection surveillance forms, decide on further action with respect to the donors and retained archive samples, and notify NTMRL to expect samples for further investigation.
- Finally, I review an HIV post-transfusion infection file. A patient with more than 100 donor exposures is now HIV positive and it has not been possible to define the time of infection. Clerical staff have prepared the documentation relating to all the donations/donors. I have examined the records to see which donors can be excluded by further HIV negative blood donations: 19 have not re-attended. We have sent letters explaining that we want to test another blood sample. One of the donors was exceedingly anxious. I had a long discussion with him. We now have his test results, so I telephone him and ask the staff to send a letter of confirmation. I review how many donors have not responded, and decide on a second letter. This is slow progress but for everyone's benefit we want to resolve the case as quickly as possible. I complete more paperwork.

So ends another day in Clinical Transfusion Microbiology. Varied, challenging and (usually) very satisfying work.

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Blood Transfusion in Malawi

The categories of patients receiving blood transfusions in a particular country reflects the prevalent diseases and level of health care attained there. In the UK more elderly patients with haematological malignancies are being transfused than a decade ago whereas in Botswana, in southern Africa, about 30% of transfusions are for the anaemia associated with antiretroviral therapy used for HIV/AIDS patients. In many tropical African countries half of all red cell transfusion are given to children with malaria.

Malawi, known as the *warm heart of Africa*, is an economically poor country of some 13.8 million people situated to the west of Africa's third largest lake, Lake Malawi. Until recently all blood used for transfusion was collected as and when needed from the family or friends of the patient needing transfusion – so called 'family replacement donations'. If a transfusion was needed in an emergency there was usually no stock of blood available and donors had to be found. Once bled the donations were tested for HIV and hepatitis by using rapid, often insensitive methods, and the only compatibility testing in most cases was to check the ABO and RhD groups of both patient and donor(s) on a tile.

The Malawi Blood Transfusion Service [MBTS] was set up with funding from the EU and within five years was supplying up to 80% of the country's needs from volunteer non-remunerated donors. All donations are fully tested, with reliable test kits, for HIV [antibody and p24], hepatitis B and C, syphilis and grouped by tube techniques for ABO and RhD. As malaria is endemic in Malawi a thick blood film is made from all donations, stained and examined microscopically for malaria parasites. Any donation found 'positive' is labelled as such but still used if needed, with the patient receiving anti-malarial drugs. All donations are tested at the Blantyre National Centre in the populous south of Malawi. There are now two other Regional Centres that collect blood and make components but they send the samples south, by road or air, for testing.

Component therapy is new to the country and MBTS produce red cells in SAGM, platelet concentrates, FFP, cryoprecipitate and some whole blood donations. The change for the hospital blood banks has been huge, moving from finding, bleeding and testing replacement donors to storing and handling blood and components from the new Blood Centres and performing serological compatibility testing. To facilitate this change resources had to be found from external funders for training hospital laboratory staff in handling components and compatibility testing, and for training doctors and nurses in using components. As part of this on-going training MBTS has set up an external quality assessment scheme for hospital blood banks to help them improve their grouping and crossmatching – or in many of the smaller District hospitals to introduce an indirect antiglobulin test as part of a crossmatch.

There is a lack of good up-to-date data on many aspects of transfusion in most African countries and too many decisions are based on supposition or anecdotal data. Therefore, in Malawi a study was made of 1,000 adult patients from hospitals across the country. This showed, for example, that 10% of these patients had previously been transfused, whereas the commonly held view was that very few patients received more than one

transfusion. Red cell antibodies were found in 11 patients; the specificities were anti-D [2], anti-S [2], anti-M [6, but 4 in non-transfused males were probably naturally acquired] and one anti-Le^{a+b}. Only 3.7% of the population are D negative; 0.8% S-s- [a similar figure to other published data] but 98.2% of donors are Fy(a-b-), higher than for most African populations (M'baya *et al 2008).*

The protein carrying the Duffy [Fy] antigens on red cells acts as the receptor for the malaria parasite *Plasmodium vivax* to enter red cells. As the red cells of individuals who are Fy(a-b-) lack this protein they are resistant to invasion by this species of malaria and consequently *P vivax* is rarely found. However *P. falciparium* is all too common and is one of the major causes of fatality in children. During the rainy season in Malawi, from November to March, a large number of children contract malaria. Their haemoglobin levels drop dramatically and many are admitted to hospital, often after an arduous journey from a remote village, with Hb levels of 2 or 3g/dL. Some don't make it alive. Those with a Hb <4 g/dL are transfused but if the Hb is between 4-6 g/dL then transfusion is only recommended if there are clinical signs of complicated anaemia or severe malnutrition. Approximately half of the children admitted with malaria to the Queen Elizabeth Central Hospital in Blantyre are transfused; with some 200-300 transfusions a month during the malarial season even with this low Hb transfusion threshold.

A study of transfusion in children undertaken in Kenya some years ago concluded that in severe anaemia transfusion was associated with decreased mortality if given during the first two days of admission and that reliance on family donors did not enable blood to be given at the time they could benefit from it. (Lackritz *et al* 1992). The availability of a stock of fully tested blood in a hospital's blood bank is a major factor in improving the survival rate for children admitted with malaria.

As the rate of HIV in the general population in Malawi is about 14%, students are targeted because as donors, these young people have a lower incidence of HIV. With the increasing number of repeat donors, the rate of positive tests for transfusion transmissible infections, TTIs, has fallen over the past five years (see table). During the rainy [malaria] season, which includes Christmas, colleges are closed and many students return home and are not available for blood donation. Travelling to donor sessions during tropical rains can be hazardous as roads and bridges often get washed away. Therefore, at the time of greatest need the conditions for collecting blood in Malawi are at their worst. To make the most efficient use of every donation many are 'split' into four bags each containing approximately 100-140 mL of whole blood or red cells in SAGM; sufficient volume for most of the small children with malaria.

Although the principles of transfusion are standard, practice has to be tailored to suit local circumstances. The new Malawi Blood Transfusion Service has demonstrated that, given well directed external funding, a sustainable service based on non-remunerated volunteer donors can provide the nation with a safe supply of blood and blood components.

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Statistics supplied by MBTS.

Blood Collections		% Positive TTI				
Year	Number of units	HIV	HBV	HCV	Syphilis	MPs*
2004	5,520	5.2%	7.7%	0.3%	1.2%	0.2%
2005	18,939	4.8%	7.0%	2.8%	1.8%	1.6%
2006	24,196	3.1%	5.9%	2.1%	1.5%	1.4%
2007	31,234	2.9%	5.4%	1.7%	1.0%	1.4%
2008	37,276	2.4%	5.7%	1.0%	1.8%	1.1%

**MPs – malaria parasites*

Report from the XIXth Regional Congress of the ISBT, Eastern Mediterranean and Europe, 21-25 March 2009, Cairo, Egypt

The population of metropolitan Cairo is estimated at 18 million, about the same as the combined population of Sweden, Finland and Norway and this bustling city played host to the 19th Regional Congress of the International Society for Blood Transfusion (ISBT), for the Eastern Mediterranean and Europe, from 21 to 25 March 2009. This meeting included presentations of material of importance to delegates, particularly those involved in transfusion in Egypt and the Middle East and the president of the Congress, Dr Faten Moftah, and the local organising committee of which she was the chairperson, worked hard to ensure that this meeting was successful.

As a patient-facing consultant, I have highlighted the aspects of the meeting that particularly appealed to me, but many donor-facing issues, and other aspects of transfusion medicine, were covered by simultaneous sessions, and ISBT members can access the presentations on http://www.isbt-web.org/default.asp

Human Development Index and Blood Safety

One part of the educational programme followed blood and components "from vein to vein". The session began by reviewing donation practices in different countries. Practice may be more determined by geography than by cultural values. It is interesting to note that donor programmes involving volunteers are gaining ground in sub-Saharan Africa. However, family, replacement or paid donors continue to provide more than 50% of the blood collected in developing countries. The role of processing, testing and inventory management were covered, as were haemovigilance and look back and recalls, the latter talk being given by Dr Pat Hewitt. It was salutary to be reminded, however, of the tragedy that those parts of the world with a low index of human development usually have the highest risk of transmissible disease. In Botswana, the HIV prevalence in regular donors has fallen from 7.7% but is still high at 1.8%. A presentation from Mombasa highlighted the difficulties of blood storage and the fact that one unit of blood may be transfused, over a period of days, to several children.

Safety has no price?

The marked inequalities in blood safety around the world were addressed by Professor Marcela Contreras in the plenary session on controversies. The title of her talk was "Safety has no price?" She stressed that in the third world the focus should be on "patient safety" rather than "product safety". The majority of the audience were in favour of blood users, rather than blood centres, deciding on the level of blood product safety that was required.

The titles of the other controversial presentations in this excellent session were "Donors have no rights?" and "Blood is a global commodity?" Commodities are items whose quality is the same regardless of supplier, with closely specified standards. Cost is determined by the market as a whole. The audience felt more sympathetic to the concept of blood as a commodity if the word "exchange" was substituted for "trade". The audience were in agreement that donors had the right to be treated well, but did not have the "right" to donate.

Influential papers: good or bad?

Dr Holland from Sacramento delivered a summary of publications that have most influenced transfusion practice in the last 10 years. Previous lists have always been headed by the 1999 study by Hebert *et al* that demonstrated that a restrictive strategy of red cell transfusion is at least as effective, and possibly superior to a liberal transfusion strategy in critically ill patients, but it should be remembered that that paper is now ten years old. Topics of the papers included the potential risk of microchimerism in transfusion of trauma victims, excess mortality of patients treated with Aprotinin as an antifibrinolytic agent, and a study from the German trauma registry showing that early, aggressive use of FFP is associated with improved survival in massive haemorrhage. Two randomised controlled trials have demonstrated the benefit of red cell transfusion in children in sickle cell disease.

The SPRINT trial, which demonstrated the therapeutic efficacy and efficiency of pathogen reduced platelets was discussed.

The speaker also pointed out that, occasionally, papers with flawed methodology have become influential, thus highlighting the need for careful critical appraisal.

Haemovigilance

Dr Rene de Vries pointed out that Europe now has a safer blood supply than ever before, potentially safer than most medicinal products. Most preventable side effects result from human errors within the hospital. Dr Georges Andreu compared two serious side-effects of Transfusion: Related Acute Lung Injury (TRALI) and the increasingly-recognised complication of Transfusion-Associated Circulatory Overload (TACO).

Celebrations

The conference dinner was held in a large Bedouin tent, in sight of the floodlit pyramids. This provided an unforgettable end to a very successful conference.

Hazel N Tinegate
Consultant, Patients' Clinical Team, NHSBT
Email: hazel.tinegate@nhsbt.nhs.uk

References

Maegele M, Lefering R, Paffrath T, *et al* (2008) Red blood cell to plasma ratios transfused during massive transfusion are associated with mortality in severe multiple injury. *Vox Sanguinis,* **95:** 112-119.

Mangano DT, Miao Y, Vuylsteke A, *et al* (2007) Mortality associated with aprotinin during 5 years following coronary artery bypass graft surgery. *JAMA,* **297:** 471-9.

Utter G, Lee T-H, Rivers R *et al* (2008) Microchimerism decades after transfusion among combat injured veterans. *Transfusion,* **48:** 1609-1615.

Please let us know if the mailing address for your copy of Blood and Transplant Matters is not correct
carol.griffin@nhsbt.nhs.uk

Next Edition

Issue 30 will feature articles on:

- SHOT Update from the new database.
- Antenatal Serology.
- Is the ICCBBA a commercial organisation – Fact or Myth?
- Antibody Production for Diagnosis and Therapy.
- The European Blood Alliance: Report on its Tissue Banking Activities.
- The Life and Work of Professor Sir Magdi Yacoub.
- EUROCET – Reporting of Stem Cell Data.
- Current Events in ISBT
- The Transfusion Evidence Library – An important new resource supporting the work of clinicians and researchers in transfusion medicine.

If you would like to comment on any of the articles in this edition of ***Blood and Transplant Matters*** please email the Editor: derwood.pamphilon@nhsbt.nhs.uk

CPD Questions for Blood and Transplant Matters 29

How NHSBT Manages Stocks of Blood Components

1. Required number of weekly whole blood donations are:

A. Fixed year on year.

B. Estimated from agreed overall annual issue figure for red cells.

C. Left to individual collection teams to determine.

D. Number of red donations actually collected.

2. Bank Holiday Planning

A. Starts a week before.

B. Starts eight months before.

C. Starts two years before.

D. Starts six weeks before.

Implementation of HSC 2007-08

3. On-line Survey on the Implementation of HSC 2007/001, showed

A. Adequate staff for the HTT.

B. Excellent compliance with NPSA SPN 14.

C. Improved compliance with MHRA as compared with 2006.

D. No regional variation.

Preventing TTI's

4. Data for the period 2006 to 2008 in the UK suggest that

A. HBV

B. HIV

C. HCV

D. HTLV1

Has the greatest overall residual risk.

5. For confirmed TTI's in UK, 1996 – 2008

A. HBV

B. HCV

C. HIV

D. Bacteria

Carry the major risk.

6. How do you reduce the risks?

A. EU product liability requirement and blood safety directive consider provision of blood as a service.

B. New testing technologies have reduced the complexity and expense.

C. On an actuarial basis the risk for HIV is negligible.

D. Adequate pathogen inactivation/reduction methods exist, sufficient to stop testing.

How NHSBT is preparing for Pandemic Influenza

7. A Target stock of

A. 65,000

B. 45,000-50,000

C. 35,000-40,000

D. 24,000

Units of red cells has been set.

New developments in Statistics and Clinical Audit

8. Initial results for incompatible kidney transplantation have shown that unadjusted three year Graft survival rates are:

A. Higher for ABO as compared with HLA incompatible.

B. Higher for HLA as compared with ABO incompatible.

C. Much lower for incompatible as compared with deceased donor kidney.

D. Similar for both ABO and HLA incompatible.

9. Significant Event Audit

A. Is another form of incident reporting only.

B. Provides timely feedback and recommendations to improve practice.

C. Ensures only senior management can make recommendations.

D. Is only another form with boxes to be ticked.

NHS Cord Blood Bank

10. Disadvantages of Cord Blood Transplant include:

A. Second donation of stem cells or donor leucocytes is not possible.

B. Can be used with children only.

C. High rates of CMV transmission.

D. Poor tolerance of 1-2 mismatches at the HLA-A, B or -DR loci.

11. The NHS Cord Blood Bank

A. Has collected over 20,000 cord blood donations.

B. Is the tenth largest Cord Blood Bank.

C. Contains second highest percentage of rare HLA phenotypes.

D. Has only 25% donations from black and ethnic minority donors.

12. The percentage of donations suitable for banking is:

A. 45%

B. 50%

C. 65%

D. 75%

Towards a UK National Cord Blood Programme

13. It has been recently suggested that the UK would be able to meet the needs of 95% of suitable patients with a cord bank containing:

A. 10,000 high quality cords.

B. 20,000 high quality cords.

C. 50,000 high quality cords.

D. 100,000 high quality cords.

Clinical Umbilical Blood Transplantation

14. Advantages of unrelated UCBT include

A. No risk to donor.

B. Fast engraftment.

C. No risk of transmission of congenital disease.

D. Low cost of obtaining a graft.

Tissue Donation Activities in Latin America

15. Which Latin American Country has the highest tissue donation?

A. Argentina.

B. Cuba.

C. Chile.

D. Mexico.

Diary Dates

2009

5-8 December 2009

51st ASH Annual Meeting.

Ernest N Morial Convention Center,
New Orleans, LA
For more information contact ASH on
ash@hematology.org
The programme can be viewed and to register online go to: **http://www.hematology.org/meetings/2009/index.cfm**

10 December 2009

Bleeding, Clotting & Haemorrhage – An Update.

Portland Place, London
For more information contact:
Gemma Williams on tel: 020 7631 8808 or
via email: gemmawilliams@aagbi.org
The programme can be viewed and to register online go to: **http://www.aagbi.org/events/seminars.htm**

2010

28-30 January 2010

T-cell Lymphoma Forum.

Hyatt Regency Maui, HI
For more information contact:
Damaris Cruz on tel: 001 201 594 or 0400 or
via email: dcruz@jwoodassoc.com
The programme can be viewed and to register online go to: **http://www.tclf2010.com**

Details:

The T-cell Lymphoma Forum will feature talks, case and slide presentations followed by interactive question and answer sessions. This forum will provide a platform for discussion about the classification, epidemiology, prognosis and pathogenesis of several T-cell lymphoma subtypes. In addition, the latest information on novel agents and treatment approaches will be presented by T-cell lymphoma experts from all over the world. This meeting is intended for hematologists, oncologists and other clinicians and scientists with an interest in T-cell lymphoma.

2 February 2010

Haematology for Paediatricians.

Institute of Child Health, London
For more information contact: Charlotte Mendoza on tel: 020 7829 8692 or via email: info@ichevents.com
The programme can be viewed and to register online go to: **http://www.ich.ucl.ac.uk/education/short_courses/courses/2S-94**

Details:

The 2010 Haematology for Paediatricians course will cover the approach, investigation and management of all the main haematological dilemmas and conditions faced by general paediatricians. There will be ample opportunity for discussion and participation during case studies. It is aimed at General Paediatricians, Shared Care Consultants and Haematologists with an interest in paediatrics.

3-4 March 2010

Late Effects in Cancer Survivors.

Cutlers' Hall, Sheffield, UK
For more information contact: Information on tel: +44 (0) 114 2265208, Registration needs to be completed by 12th February 2010.

4 March 2010

Apheresis SiG.

Austin Court, Kingston Theatre,
Birmingham City Centre, UK
More details to be available soon.

5 March 2010

Regulatory T Cells in Inflammatory and Infectious Diseases.

UCL, Institute of Child Health, London, UK
For more information contact:
http://www.regonline.co.uk/regT2010

Details:

This meeting will provide an update on phenotypic and functional aspects of regulatory T cells, aiming to inform, educate and entertain. Presentations will be delivered by world-class leaders in their respective fields and a lively discussion will follow each series of talks. This meeting has CPD accreditation.

10 March 2010

Haematology Trainees Research Day.

Royal College of Pathologists, London, UK

For more information contact:

Conference Department on tel: 020 7451 6715

or via email: meetings@rcpath.org

Details:

This meeting offers haematology trainees in medicine and clinical science guidance and advice on how to pursue and integrate research in their training. It is aimed at trainees who are considering applying to undertake a period of research in the near future. The objective of the meeting is to provide practical guidance on how to go about obtaining funding, seeking the right post and obtaining ethical approval.

22-23 March 2010

Introduction to Immunology.

Warwick University, Coventry

For more information please contact:

Steve Hicks via email: s.j.hicks@warwick.ac.uk

The programme can be viewed and to register online go to: **http://www2.warwick.ac.uk/fac/sci/bio/shortcourses/calendar**

Details:

This course is aimed primarily at personnel from the pharmaceutical industry, the medical community and academic scientists, although it would be suitable for anyone seeking a grounding in immunology. It stands on a highly successful base of custom-built courses and will draw on the resources of a department with extensive expertise to provide a thorough grounding in this important field.

8-9 April 2010

Network for the Advancement of Transfusion Alternatives: 11th Annual Symposium.

Barcelona

For more information contact:

NATA Secretary on tel: +33 (0) 1 42 53 03 03

Details:

Blood Transfusion Services/Risks of Transfusion

Transfusion Practice

Blood Conservation Strategies/Autologous Transfusion

Anaemia Effects and Management

Fluid Therapy/Oxygen Carriers

Haemostatsis and Thrombosis

Abstract Submission Deadline: 1 December 2009.

19-21 April 2010

British Society for Haematology 50th Annual Scientific Meeting.

EICC, Edinburgh, Scotland

For more information telephone: 020 7837 5813.

30 April 2010

Improving Immunohistochemistry 2010.

UCL, Institute of Child Health, London

For more information contact:

enquiries@euroscicon.com

The programme can be viewed and to register online go to: **http://www.regonline.co.uk/IHC2010**

Details:

This annual event, now in its seventh year, is dedicated to the technique of Immunohistochemistry and in-situ hybridisation. The meeting has been created to merge the need for technical-based updates in the areas of immunohistochemistry, clinical histopathology and in-situ hybridisation. With a mixed array of academic speakers, this meeting should appeal to the clinical, academic and pharmaceutical organisations. Technical presentations of 30 minutes' duration will be interspersed with 15 minute scientific contributions from commercial speakers. The event has CPD accreditation and will have a trouble-shooting panel. On registration, questions can be submitted to the panel that will be asked by the chair on the day of the event.

11 May 2010

Hot SiG Meeting.

Austin Court, Kingston Theatre,

Birmingham City Centre, UK

Details:

Transfusion issues in haemoglobinopathies – the clinical and laboratory challenges.

14-18 May 2010

Platelets International Symposium.

Ma'ale Hachamisha, Israel

For more information contact:

Jonathan Wood & Associates tel: 201 594 0400

or via email: info@jwoodassoc.com

The programme can be viewed and to register online go to: **http:/www.platelets2010.org**

6 July 2010

2010 SHOT Annual Meeting.

Lowry Centre, Manchester

More details to be available soon.

10 July and 7 October 2010

Induced Pluripotent Stem Cells: Production and Utility in Regenerative Medicine.

BioPark Hertfordshire, Broadwater Road, Welwyn Garden City, Hertfordshire AL7 3AX, UK

For more information contact:
Astrid Englezou tel: 08714 890 134
or via email enquiries@euroscicon.com

The programme can be viewed and to register online go to: http://www.regonline.co.uk/IPS09

Details:

The production of iPS cells from dermal fibroblasts has generated intense interest in the utility of such cells for research purposes and clinical applications. iPS cell production currently requires the use of transcription factor gene delivery to reprogramme cells into iPS cells. Hence, both gene delivery technology and iPS cell characterisation and subsequent cell differentiation are critical aspects of iPS cell biology. The meeting will address both issues. The meeting has CPD approval.

9-11 September 2010

BBTS – 28th Annual Conference/Scientific Meeting.

Bournemouth International Centre, UK

For more information contact:
http://www.bbts.org

9-12 October 2010

AABB – Annual Meeting & TXPO.

Baltimore, Maryland, USA

For more information contact:
http://www.aabb.org

10-13 October 2010

XXXII World Congress of the International Society of Haematology.

Jerusalem, Israel

For more information contact: ISH 2010 via email ish2010@kenes.com

The programme can be viewed and to registers online go to: http://www.kenes.com/ISH2010

4-7 December 2010

ASH – 52nd Annual Meeting and Exposition.

Orange County Convention Center, Orlando, FL, USA

For more information contact:
http://www.hematology.org

2011

10 March 2011

Identifying T Cell Subset Phenotype and Function in Infections.

BioPark Hertfordshire, Broadwater Road, Welwyn Garden City, Hertfordshire AL7 3AX, UK

For more information contact:
Astrid Englezou tel: 08714 890 134
or via email enquiries@euroscicon.com

The programme can be viewed and to register online go to: http://www.regonline.co.uk/tparasite09

Details:

A revolution in the basic understanding of immunology occurred in the late 1980s with the discovery that CD4+ helper T cells were not a homogeneous population but could be divided into Th1 and Th2 subsets based on their cytokine profiles. 20 years later the field of T cell subset phenotype and function remains fast-moving with the recently demonstrated existence of T regulatory and Th17 cells adding extra layers of complexity. The meeting will explore current ideas about the roles played by these varied T cells subsets in a variety of infections with presentations from leaders in the field. The meeting has CPD approval.

A full diary of events and training courses can be viewed on the following websites:

www.transfusionguidelines.org.uk
www.blood.co.uk/hospitals
www.bbts.org.uk

Notes

Notes

Blood and Transplant Matters is prepared
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