

Blood and Transplant

Information for hospitals served
by NHS Blood and Transplant

Matters

Inside

Editorial	2	Current Events in ISBT	17
Shot: A New Reporting System	3	The European Blood Alliance and its Tissue and Cells Working Party	19
NHSBT Divestment of Antenatal Testing	5	EUROCET: The European Network of the Competent Authorities for Tissue and Cells	22
The Transfusion Evidence Library – An Important New Resource Supporting The Work of Clinicians and Researchers in Transfusion Medicine	7	Targeted Cellular Immunotherapy for Cytomegalovirus Infection in Stem Cell Transplantation	27
National Comparative Audit of Blood Collection from the Hospital's Main Blood Fridge	9	Quality and Safety in Tissue Banks	29
Immunology for Dummies	10	Sir Magdi Yacoub – A Pioneer in Tissue Banking	31
Part 1: Innate Immunity and the Acquired Immune Response		CPD Questions for Blood and Transplant Matters 30	33
ICCBBA and ISBT 128 – Value for Money?	13	Diary Dates	35
ISBT 128 Labeling for Cellular Therapy Products	14		



Welcome to the second edition of *Blood and Transplant Matters*. In the last week or so I have sensed the appearance of a general sense of optimism: the days are lengthening, the worst of the bad weather is over, the incidence of swine 'flu is decreasing and the stretch of motorway heading north from the M5/6 junction is being widened at last! The team at *Blood and Transplant Matters* has been hard at it during the months of darkness and adverse weather to ensure that the pages of this issue are once again filled with articles that, on behalf of the Editorial Board, I hope you will find interesting. We are, as always, indebted to our contributors who write such scholarly articles - sometimes at short notice.

This issue includes articles describing the important new reporting system for SHOT written by its Medical Director Clare Taylor and a short description of how NHSBT is divesting its routine antenatal immunohaematology screening services by Vanessa Hook. In the first of two articles entitled 'Immunology for Dummies', Belinda Kumpel has tried to explain to us, in simple terms, how the immune system works. This is not an easy task but I feel that her article will help to make the functioning of the immune system more accessible to myself and other 'dummies'! If your appetites are whetted, be sure to read part two in the next issue.

Proper labelling of blood components, cells and tissues is a crucial and perhaps under-emphasised aspect of our work. With that in mind, this issue contains two articles, one on ICCBBA (the organisation that provides ISBT 128 labels) and the other on the use of ISBT 128 labelling for cell therapy products that aim to increase our understanding of this very specialised area of practice. As always we strive to maintain a balance between contributions on blood and blood component collection and use, cell and tissue therapies and organ procurement and transplantation and rely on you, our readers, to tell us if we have achieved our objectives.

It is not enough in the twenty-first century simply to believe that one's practice is sound – it must be evidence-based wherever possible and audited. It still surprises me how much of what we believe constitutes 'best transfusion practice' has very little evidence to substantiate it. The Transfusion Evidence Library described for us by Carolyn Doree is an essential resource as we conduct studies to better understand the optimal use of blood components. Our audit contribution from Megan Rowley and John Grant-Casey describes the outcome of the national comparative audit of blood collection.

Judith Chapman, Bob Parker and George Galea have contributed excellent reports on current events in ISBT, the career of Professor Sir Magdi Yacoub and tissue banking activities undertaken by the European Blood Alliance respectively. We will feature further contributions on the life and times of pioneers in transfusion and transplantation and welcome any suggestions that you may have. Also included in this issue is part two of Miranda Blanca's contribution on quality and safety in tissue banks and the EURO CET reporting system for stem cell transplantation.

The use of autologous immune cells or those from a healthy donor to treat cancer and viral infections occurring in immunocompromised patients e.g. after allogeneic transplants, is attracting much attention and Fred Chen explains for us how healthy donor T cells can be selected and used to treat patients with cytomegalovirus (CMV) infections in this setting. As usual we include CPD questions compiled by Rob Webster and a note of forthcoming meetings and articles to be featured in this publication.

Your feedback is always appreciated – we depend on it to ensure that we are producing the kind of publication that is of value both to colleagues in the hospitals that we serve as well as to those who work within NHSBT.

It must sometimes seem to us all, that the culture in which we work has become excessively risk averse and we spend hours in meetings discussing risk management strategies and so on. It seems, however, that Albert Einstein was, in absolute rather than relative terms, years ahead of us for he said "A clever person solves a problem; a wise person avoids it". He also said something that I think is relevant to this and other publications "Most of the fundamental ideas of science are essentially simple, and may, as a rule, be expressed in a language comprehensible to everyone." I hope that you feel this is the case – happy reading.

Derwood Pamphilon

Email: derwood.pamphilon@nhsbt.nhs.uk

3rd March 2010

Shot: A New Reporting System

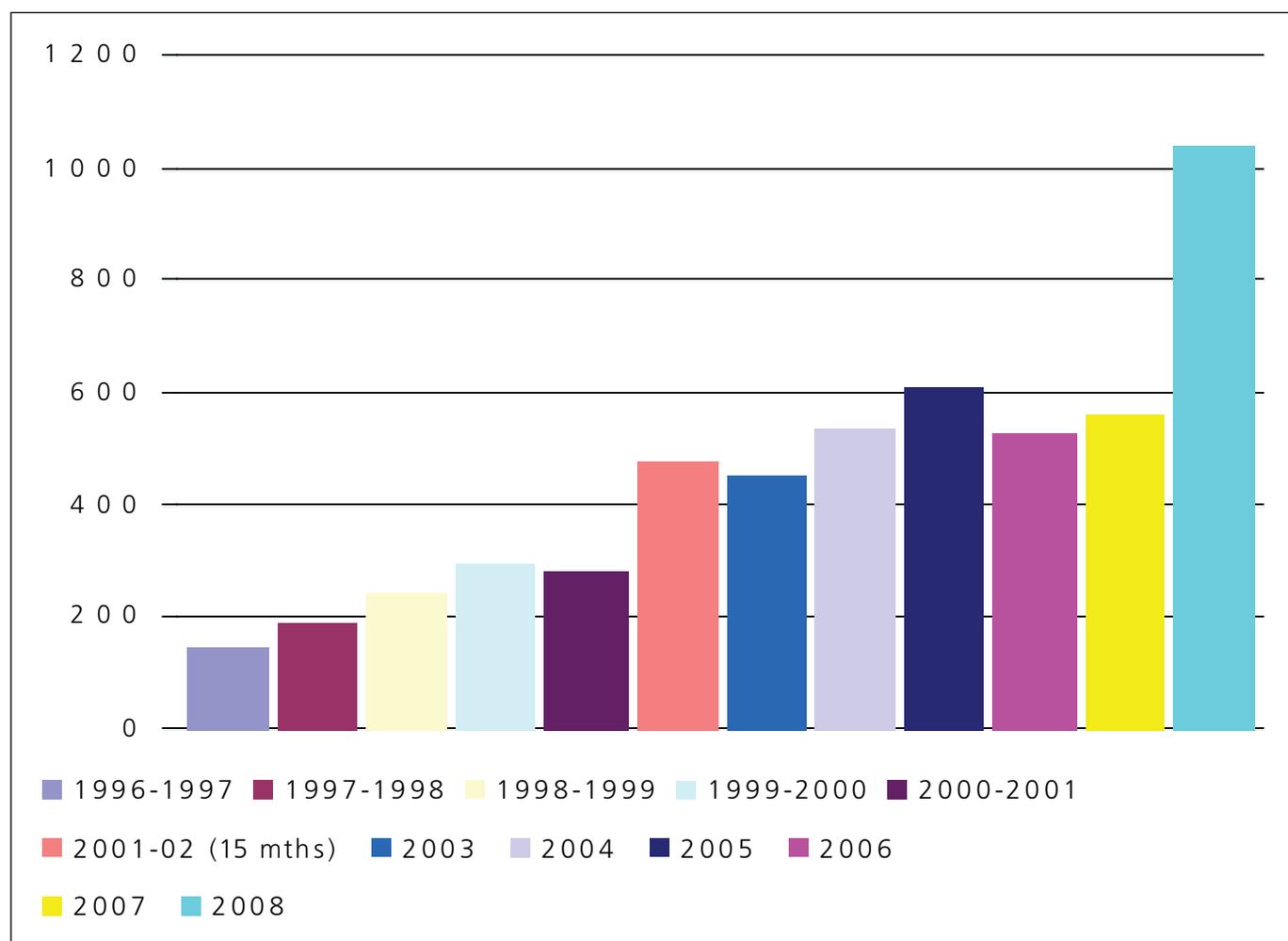
SHOT, the UK's professional haemovigilance organisation, started collecting adverse incidents reports in 1996 and in the first instance these were collected on paper questionnaires. The data were manually entered into various databases including Access and Excel. In 2003 SHOT tried the 'eyes and hands' system employed elsewhere in the NBS and this was used to read the questionnaires to feed them into a new database. However this venture was unsuccessful and SHOT kept a paper record that year and then reverted to the old system.

In 2005, with the advent of the Blood Safety and Quality Regulations, (BSQR), a collaboration with the Medicines and Healthcare products Regulatory Agency (MHRA) resulted in the setting up of the online SABRE (Serious Adverse Blood Reactions and Events) reporting system. In this system reporting to both MHRA and SHOT is commenced through a joint portal available to registered reporters through either of the websites. After an initial notification, the SHOT questionnaire was made accessible electronically to the reporter of the incident

and could be completed online. However this is still basically a paper questionnaire which is filled in online. The result is that it is quite time consuming for our reporters who have to scroll up and down many pages of the questionnaires in order to find the relevant sections in which to type their answers. A large amount of free text is required and this means that when it comes to analysis of the questionnaires they are again cumbersome. For the last three years these questionnaires have been downloaded from the Lotus Notes storage system where they are held within SABRE, into an Excel spreadsheet and these have been analysed individually by the group of authors for each section. The downloading of the data has been sub-contracted to an IT consultant who frequently works with MHRA and SABRE.

As the culture of quality in hospital transfusion laboratories and in clinical transfusion practice has become embedded, the number of adverse incidents reported to SHOT almost doubled in 2008, and is set to increase some more in 2009. This follows a steady year by year increase since 1996-97.

Total number of SHOT reports 1996-2008



During the same time period the questionnaires have evolved with further details being requested in various categories as new insights have been made into the events and reactions reported, and additional information and results have been required. There has also been a broadening of the categories and scope of SHOT, with inclusion of additional categories of adverse incident such as 'Inappropriate and Unnecessary transfusion', 'Handling and Storage errors', 'Transfusion Associated Circulatory Overload', and 'Near Miss'. A number of factors have combined to increase the number of reports submitted to SHOT annually, and it is not likely that this will plateau out just yet. These include continuing activities by the restructured and augmented SHOT team to raise awareness, the effect of the Chief Medical Officer's Better Blood Transfusion initiative and the BSQR, and the increasing remit of SHOT. With the best will in the world the questionnaire system was becoming much too difficult to handle given the large volume of data now coming into the system.

It was necessary during 2008 to develop a new way of reporting directly into the SHOT database which would make it quicker and easier for reporters. This would also mean that important data was not left out, perhaps inadvertently, as reporters had to scan whole questionnaires to find relevant parts to fill in. This has at times been a significant problem with only 50% of questionnaires having all the relevant sections completed, and important basic data such as whether an incident happened in a routine or an emergency setting was not entered. The SHOT Operations Manager, David Mold, was appointed with a particular remit to develop a new data collection system. Various possibilities were examined in detail and Dendrite Clinical Systems was chosen. Dendrite is a specialist supplier of clinical database and analysis software for the international healthcare sector. They have a unique and proven track record of such systems across the sector including single and multi speciality clinical information systems, national disease registries, specialist society databases and pharmaceutical observational registries. Current users include the European Association for Cardiothoracic Surgery, Vascular Society of Great Britain and Ireland and the British Society of Interventional Radiologists. Details of some of this can be found on the Dendrite website at www.e-dendrite.com.

The system is intuitive and logical and works very much to how the clinical or scientific mind works. In the new system reporters to SHOT will mostly be answering yes/no questions by clicking on a button or selecting from a dropdown list. The number of free text boxes has been much reduced throughout the questionnaires. However one of the valued and unique attributes of SHOT has been its use of the clinical vignettes. Case vignettes are

very important for teaching and learning as they relate directly to the day-to-day life and experiences of hospital and laboratory personnel. This material has been used extensively by educators in all sectors of the health service across the UK and beyond. Therefore at the beginning of each report there is a free text box in which the 'story' can be written in full.

Data which have been entered directly into the live database can then be analysed by SHOT office staff using the PATS (patient analysis and tracking system) which allows SHOT to query the data at will and to produce graphs and tables directly from the system. Data can be pulled out in any desired way and queries are simple to write after a small amount of training which will be given to the SHOT team members.

David Mold has been building the database working closely with Dendrite during 2009 ensuring that all of the SHOT dataset is included in a simple and intuitive way. The working expert group and chapter authors have had opportunities to check the questions and format for their area of SHOT reporting, and the Steering Group have been given overviews of the system periodically during the year.

Users will need to register for the new system as they will require a log-in and password in order to report. However overall reporting will not feel very different from the users point of view. The new database will be accessed through the SHOT or MHRA website as it is at the moment by notifying through the SABRE front pages. The reporters should then click the 'report to SHOT box' as before. This can be done in every case as SHOT is now collecting Near Miss cases (which often equate to serious adverse events in SABRE) as well as all the events relating to actual transfusion of components, including those occurring within the blood services or blood establishments. Once the SHOT box is ticked an email will be sent to the reporter within the next 24 hours containing a link to the correct part of the SHOT database for the new report to be entered. The MHRA generated report number and basic case details will be carried across automatically to the SHOT database. Once the email arrives in the inbox of the reporter all that they need to do is click on the link to the database, log-in, and get reporting. Anyone sending a SHOT report who has not registered with the new system will be telephoned by the SHOT office to arrange the user name and password.

The go-live date for the new look SHOT reporting system was January 4th 2010, so that the whole year's data will now be in the new database. User guides, and 'what to report' documents are available on the SHOT website at www.shotuk.org.

Dr Clare Taylor

Medical Director of SHOT

Secretary of International Haemovigilance Network

Consultant Haematologist

Email: clare.taylor@nhsbt.nhs.uk

References

Blood Safety and Quality Regulations 2005, ISBN 0110990412.

www.opsi.gov.uk/si/si2005/20050050.htm

Health Service Circular, 'Better Blood Transfusion – Safe and Appropriate Use of Blood'. HSC 2007/001. 19 November 2007.

http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Healthservicecirculars/DH_080613

NHSBT Divestment of Antenatal Testing

Background

In late 2007, a review of blood processing, testing and specialist services provided by the National Blood Service (NBS) was carried out. The challenges which the review sought to address were:

- Meeting the clinical need and demand for red cell and platelets;
- Addressing declining numbers of blood donors;
- Meeting current and future clinical, safety and accreditation standards;
- Providing a range of specialist (diagnostic) services which were financially sustainable;
- Stabilising the price of red cells, avoiding price increases above the level of inflation.

A number of changes were proposed as a result, and these were approved by the Board of NHS Blood and Transplant (NHSBT) in January 2008.

Prior to the review, it had been identified that the cost of providing specialist services to hospitals was not being recovered, and as a result these services were being heavily subsidised by the price of blood. As part of the review process, consultation with hospitals revealed the importance of retaining services such as Red Cell Immunohaematology (RCI) reference laboratories locally wherever possible. This feedback was taken into account, with a recommendation that a national network of eight RCI laboratories should provide such services in future. However, as part of delivering a more efficient and cost effective service it was also recommended that NHSBT withdraw from routine antenatal screening, managed over a three year period.

NHSBT currently provides approximately a third of routine antenatal screening in England and North Wales, with the remainder supplied by non-NHSBT pathology services such as laboratories within hospitals. NHSBT

wrote to hospital trusts in February 2008 signalling the intention to withdraw this service and since then we have been working closely with trusts to help make alternative arrangements, such as taking the work in-house or sourcing alternative providers. As part of this we have provided details of alternative providers of antenatal screening, and also organised a number of workshops to provide information and facilitate contact between hospital transfusion and microbiology laboratory managers, business managers and antenatal screening co-ordinators.

NHSBT will cease providing routine antenatal screening services on 31st March 2011. Alongside the practical support which is being provided to source alternative suppliers, our Commissioning team have contacted their purchasing contacts in all Trusts and PCTs which are current customers to ensure that they are aware of the date the service will cease. Formal notice of termination of contracts for antenatal screening was issued in October 2009, 18 months ahead of the date the service will cease. After 31st March 2011 NHSBT will no longer be able to provide routine antenatal screening services, so any samples received will be returned without being tested.

Advantages of Local Antenatal Screening Services

There are a number of advantages in routine antenatal screening being provided locally. These include the facility to transfer results from the hospital transfusion laboratory and microbiology laboratory to records electronically, removing the potential for human error in manual transcription from hard copy reports. The results are also likely to be available more readily which can be significant, for example if a woman's RhD type is required to determine whether or not she needs prophylactic anti-D. It is also critically important that any woman found positive for an infectious disease during pregnancy is

included into her local treatment network without delay. This speedy referral is best facilitated by local screening and confirmation of markers for infectious diseases.

Blood Grouping, Red Cell Antibody Screening and Follow-Up Testing

Many hospital transfusion contacts have expressed the view that taking blood grouping and red cell antibody screening services in-house presents no new problems, since it is essentially the same process as pre-transfusion testing on patient samples. However, follow-up testing, which might include titration of antibodies or quantification of anti-D and anti-c, might present a challenge for some hospital transfusion laboratories. Acknowledging this, NHSBT will continue to offer a red cell immunohaematology reference service and follow up service including the investigation of antenatal samples which have proved positive on antibody screening. This follow up service is already provided to many hospital transfusion laboratories which currently perform their own antenatal screening.

Microbiology Screening

Trusts which have taken their work in-house in the early stages of divestment have incorporated routine antenatal microbiology screening into the work of their hospital microbiology laboratories. Many hospitals are already undertaking some of this screening on antenatal samples, notably screening for rubella immunity. However, microbiology screening presents different challenges from those posed by blood grouping and antibody screening. The pregnant woman's right to decline any or all of the tests offered requires the careful checking of completed request forms for declined tests. The reporting of positive tests and the follow-up of requests for repeat samples also requires close collaboration with midwifery services. New standards for microbiological screening in pregnancy are anticipated within the next few months, and are likely to include recommendations for the responsibilities of the various parties involved in the follow-up of a microbiology positive pregnant woman.

Assistance

NHSBT is keen to continue providing Trusts with as much support as possible as they move towards finding alternative providers of antenatal screening services. For those Trusts which are working towards testing routine antenatal samples in-house, we can offer practical help including:

- Educational courses, such as the intermediate transfusion course offered by NHSBT Scientific and Technical Training. This includes a module on antenatal screening
- Invitation to visit RCI laboratories to observe antenatal screening
- Advice from NHSBT staff with considerable experience in screening
- Assistance from NHSBT Commissioning in identifying the source of funding within the Trust or PCT
- A 'toolkit' which is available on the NHSBT Hospitals website: http://hospital.blood.co.uk/diagnostic_services/antenatal_toolkit/, which contains
 - All relevant guidelines
 - Details of alternative providers
 - The following materials, which could be used as models:
 - A request form
 - Standard Operating Procedures (SOPs) used by hospital transfusion laboratories for antenatal screening
 - A Service Level Agreement (SLA).

Tess Hook and Gordon Burgess

*on behalf of the Antenatal Project Divestment Board
Leeds*

*Email: vanessa.hook@nhsbt.nhs.uk &
gordon.burgess@nhsbt.nhs.uk*

The Transfusion Evidence Library - An Important New Resource Supporting The Work of Clinicians and Researchers in Transfusion Medicine

Launched in September 2009, the Transfusion Evidence Library (<http://www.transfusinguidelines.org.uk>) is a freely available and up-to-date database of all systematic reviews and economic evaluations relevant to transfusion medicine. This article will provide the reader with information about the background to and remit of the Transfusion Evidence Library.

The Systematic Review Initiative

This new online library has been developed by the Oxford-based NHSBT research group, the Systematic Review Initiative (SRI), in association with the UK Blood Transfusion Services (UKBTS), and marks a major step towards the SRI's goal of mapping all the high-level evidence currently available in transfusion medicine. The Transfusion Evidence Library currently holds more than 430 systematic reviews and economic evaluations.

The Transfusion Evidence Library also houses references to the SRI's own completed systematic reviews in transfusion medicine (18 to date) and its overviews of clinically relevant topics (for example, the effectiveness of fresh frozen plasma).

Why Systematic Reviews?

It is generally agreed that the clinical decision for blood component transfusion should always be informed by the best available research evidence. However, in practice this evidence (where it exists) is frequently either difficult to find or is spread across a number of studies of varying size and quality, and which may report conflicting results. Systematic reviews aim to make this evidence more accessible to decision-makers by identifying, evaluating and summarising the data from all relevant clinical trials according to strict methodological criteria. As a result they have become increasingly important both to the development of clinical guidelines and to the establishment of evidence-based practice.

Key steps of the systematic review process include comprehensive searching of all relevant medical databases and the use of explicit criteria to assess the eligibility and methodological quality of the identified studies. Where included studies (usually randomised controlled trials) are sufficiently similar, data are combined in a meta-analysis in order to give an overall treatment effect. Where data cannot be combined, a narrative review plus summary of the results is usually presented.

As systematic reviews are the optimal method for summarising evidence of effectiveness, it is clearly important that they be readily accessible to health care professionals. Until recently, the retrieval of all systematic reviews relevant to a clinical question in transfusion medicine was only possible by searching a combination of

databases (for example, NHS Evidence, *The Cochrane Library*, MEDLINE and EMBASE). To ensure no important studies were missed, this time-consuming process involved identifying and applying appropriate index terms and search terms, in combination with a systematic review search filter. This inevitably can result in a large number of duplicate search results.

The Transfusion Evidence Library

Now, however, there is a quick and simple solution: the new Transfusion Evidence Library houses in a single



database all high-quality systematic reviews relevant to transfusion medicine, thereby providing a "one-stop shop" for evidence in transfusion. Like the systematic reviews it contains, the Transfusion Evidence Library has been compiled according to strict methodological criteria, with tried-and-tested strategies and filters used for systematically searching all the major medical databases. The proceedings of transfusion-related conferences (for example, from the annual meetings of the British Blood Transfusion Service (BBTS), the American Society of Hematology (ASH), the American Association of Blood Banks (AABB), the European Haematology Association (EHA), and the Network for Advancement of Transfusion Alternatives (NATA)) are also handsearched, both retrospectively and prospectively, for unpublished systematic reviews.

On retrieval by the SRI Information Specialist, each review is obtained in hard copy and individually appraised. Those of sufficient quality are then indexed for ease of searching, and included in the Transfusion Evidence Library. Full citation details are given for each review, plus a link to its entry in PubMed and another link to enable readers to view the full text (where available – for recent papers, journal subscriptions are usually required).



Examples

Topics covered by the systematic reviews in the Transfusion Evidence Library include:

- the use of red cells in cardiac surgery
- critical care and obstetrics
- autologous transfusion (including cell salvage, pre-operative donation and acute normovolaemic donation) in surgery
- stem cells in the treatment of haematological malignancies
- volume replacement in critical care
- the use of immunoglobulins, epoetin and factor VIIa in a variety of clinical settings.

Important topics covered by systematic reviews recently added to the Transfusion Evidence Library include stem cell donation, the use of colloids in intensive care and quality of life and the use of red cell transfusion in myelodysplastic syndromes.



Use of the Transfusion Evidence Library and Next Steps

The Transfusion Evidence Library offers simple and advanced searching options, including the ability to combine, edit and delete searches using the Search History, and to email, save and print search results. The Transfusion Evidence Library will be updated monthly. It is intended that, in the future, it will also contain randomised controlled trials relevant to transfusion medicine.

Please visit the Transfusion Evidence Library at: <http://www.transfusinguidelines.org.uk>. For more information contact Carolyn Dorée, SRI Information Specialist, at: carolyn.doree@nhsbt.nhs.uk

Carolyn Dorée (on behalf of the SRI)

Information Specialist

Systematic Review Initiative/UKBTS

NHSBT Oxford Centre

John Radcliffe Hospital

Oxford

Email: carolyn.doree@nhsbt.nhs.uk

References

Pamphilon, D., Siddiq, S., Brunskill, I S., Doree, C., Hyde, C., Horowitz, M., Stanworth, S. (2009) Stem cell donation – what advice can be given to the donor? *British Journal of Haematology*, **147**, 71-6.

Ertmer, C., Rehberg, S., Van Aken, H., Westphal, M. (2009) Relevance of non-albumin colloids in intensive care medicine. *Best Practice & Research. Clinical Anaesthesiology*, **23**, 193-212.

Pinchon, D.J, Stanworth, S.J., Doree, C., Brunskill, S., Norfolk, D.R. (2009) Quality of life and use of red cell transfusion in patients with myelodysplastic syndromes. A systematic review. *American Journal of Hematology*, **84**, 671-77.

National Comparative Audit of Blood Collection from the Hospital's Main Blood Fridge

The National Comparative Audit of Blood Transfusion has recently reported the findings from an audit of the blood collection process which gives us a snapshot of who is collecting blood, what systems are in place to support blood collection and the success of the implementation of training and competency assessments for this critical step. Hospitals should look at this report to see if the standards are met within their own organisation by accessing the newly launched homepage for audit users at www.nhsbtaudits.co.uk/.

Audit of Blood Collection

In June 2009, a National Comparative Audit was undertaken of the process of collection of blood from the main blood issue fridge against standards derived from the BCSH guidelines and NPSA Safer Practice Notice; 'Right Patient, Right Blood'.

The audit aimed to ascertain if, at the time a unit of red cells was collected from a hospital's main blood fridge, the person collecting the unit had been trained and assessed as competent to undertake the role, was in possession of a document containing adequate patient details and completed the procedure for collection safely and accurately.

Who is Collecting Blood?

During this audit, porters and health care assistants undertook the majority of the 5,059 collections (34% and 22% respectively) with nurses collecting blood only 38% (1,927) of the time. The remaining 6% of collections were made by a wide variety of staff groups including non-Hospital Trust staff including hospital volunteers and drivers.

What Systems are in Place?

Nineteen percent (986 collections) of blood were collected exclusively using automated electronic fridge tracking systems, which have inbuilt alerts and barriers to prevent incorrect blood collection. A further 12% used partly electronic tracking and partly paper systems to collect blood but the majority of collections continue to use paper-based fridge registers where manual checking and recording is required.

How Robust is the Check?

The risk of collecting the wrong unit of blood is comparable with the risk of giving blood to the wrong patient although there is at least one subsequent checking stage prior to blood administration.

Despite guidelines which are clear on the procedure for collecting blood for transfusion and the training and competency framework from the NPSA, 4% (199) of staff collecting blood did not bring documentation with them containing the patient's identity (ID), to enable the correct unit of red cells to be identified and collected.

The patient ID documentation brought by the collector should contain all four core patient identifiers (forename, surname, date of birth and patient ID number) but one or more of these was missing for 7.1% (347 of 4,860 with documentation). The patient ID number, as the only truly unique identifier, was reported to be missing from the documentation in 2.6% (125 cases).

The audit found that, when the patient documentation was available, it was not used to check against the patient details on the blood bag label in 3.7% (182) of collections.

Thus in 14% (714) cases overall there was a risk of the wrong unit of blood being collected as a consequence of the patient ID being unavailable (199), incomplete (347) or otherwise not used (168), and if the bedside check is not robust, that risk could translate into wrong blood being given.

What Problems Were Encountered?

Auditors' comments on 408 problems identified with the collection process were classified using the NPSA '7 steps – Root Cause Analysis' material, (which describes how and why things might go wrong), into 'Care Delivery Problems' (CDP) or 'Service Delivery Problems' (SDP). CDPs (290) related to the individual collector and reflected the training, education and development of the member of staff. SDPs (118) arose from the system in place. The observational nature of this audit enabled the auditor to intervene, where appropriate, to prevent or correct unsafe practice.

Documentation of Collection

In order to maintain a complete audit trail and to verify the cold-chain (that is, to ensure that the blood remains within the agreed temperature when taken out of storage prior to transfusion), the date and time of collection and the identity of the collector needed to be recorded. Generally this was done very well during the audit.

Training and Competency Testing

Auditors asked staff members collecting blood whether they had been trained and 96.5% (4,884) had, with 80% (3,919) of these having being trained in the

last year. Porters, nurses and healthcare assistants collected most of the blood during this audit (94%) and the proportions *not* trained in these staff groups were 1.6%, 3.8% and 4.4% respectively. Training should be targeted to staff groups based on their role within the transfusion pathway and knowledge based training should be followed by observational competency testing.

Recommendations

- Only staff authorised, trained and assessed as competent should collect blood components and *systems should be in place to restrict access to issue fridges if these criteria are not met.*
- The person collecting blood must bring a documented patient ID to check against the label attached to the blood bag and *systems should be in place to prevent blood collection if there are any discrepancies.*
- When blood is collected, there should be a *robust and auditable mechanism* for recording the details.

Next Steps

The BCSH will shortly be updating their guidance and hospitals should use this with their audit results to review the blood collection policy. The audit report explains the use of the Hazard Analysis and Critical Control Points (HACCP) audit tool that can be used to identify critical failure points and re-engineer blood collection processes. A regional slideshow of the key audit messages is available and the National Comparative Audit of Blood Transfusion team will work with Regional Transfusion Committees offering workshops and supporting sharing good practice events over the next few months.

Megan Rowley

Consultant Haematologist

Colindale

Email: megan.rowley@nhsbt.nhs.uk

John Grant-Casey

Manager NCABT

Oxford

Email: john.grant-casey@nhsbt.nhs.uk

on behalf of the Blood Collection Audit Project Group,
National Comparative Audit of Blood Transfusion

References

National Comparative Audit of Blood Transfusion :
Blood Collection Audit Report October 2009
[http://hospital.blood.co.uk/safe_use/clinical_audit/
National_Comparative/NationalComparativeAuditReports/
index.asp](http://hospital.blood.co.uk/safe_use/clinical_audit/National_Comparative/NationalComparativeAuditReports/index.asp)

BCSH guidelines for the administration of blood and blood components and the management of transfused patients. *Transfusion Medicine* 1999; 9(3): 227-39 and <http://www.bcshguidelines.com/>

National Patient Safety Agency. Right patient, right blood: advice for safer blood transfusions. November 2006 at <http://www.nrls.npsa.nhs.uk/home/>

National Patient Safety Agency. Seven Steps to Patient Safety: The full reference guide. July 2004
[http://www.nrls.npsa.nhs.uk/resources/collections/
seven-steps-to-patient-safety/](http://www.nrls.npsa.nhs.uk/resources/collections/seven-steps-to-patient-safety/)

Immunology for Dummies

Part 1: Innate Immunity and the Acquired Immune Response

Successful transfusion and transplantation of cells or tissues into another individual is largely based on understanding and alleviating the immune responses that can occur. Here, an outline of how the human immune system works is given. In the next issue, immunological complications arising from the above procedures are addressed.

Immune systems of animals evolved to combat infection, primarily bacterial, that can rapidly kill the host. Invertebrates utilise phagocytic cells and anti-microbial proteins. Vertebrates employ similar mechanisms but in addition, complement-like components enhance microbial destruction. This is called innate or unlearned immunity. This system then further diversified and adaptive (acquired) immunity developed in warm-blooded

birds and mammals to increase the efficiency of pathogen elimination. In humans, individual components of the immune system work together to achieve a complex but effective defence.

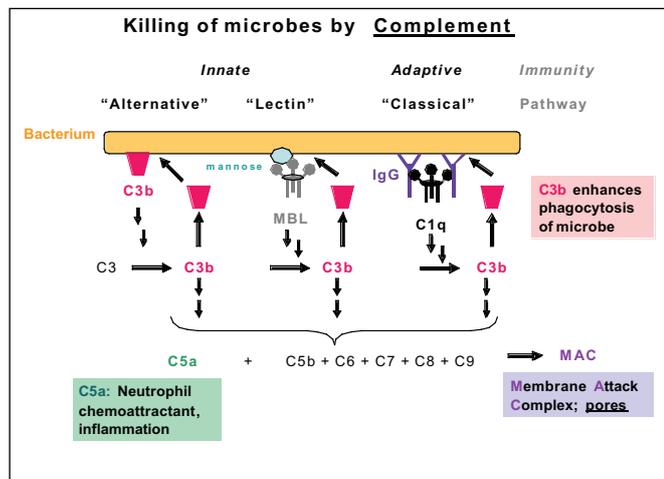
Innate Immunity

Several types of granulocytes in the blood and tissues destroy different pathogens. Macrophages ("big eaters") phagocytose bacteria, yeast, old cells and tissue debris. Neutrophils specialise in phagocytosis of bacteria, killing them with oxygen radicals and digestive enzymes. Eosinophils attack large parasites such as worms by secreting extracellular granules containing toxic enzymes and proteins, often resulting in collateral tissue damage. Basophils and mast cells respond to anaphylatoxins and

chemicals with release of histamine and inflammatory mediators, enhancing neutrophil migration to the site of infection. Natural killer (NK) cells lyse cells infected with intracellular pathogens (viruses, protozoa). All these pathogens can be recognised directly on first encounter by these cells.

Other components of innate immunity are antimicrobial proteins, including the complement (C) system. This comprises multiple serum proteins and membrane receptors that react, when triggered, in a highly regulated enzyme cascade. It has three main effector functions – recognition and opsonisation of antigenic cells or particles (“labelling” them for destruction), production of inflammatory mediators and lysis of target cells (Figure 1).

Figure 1



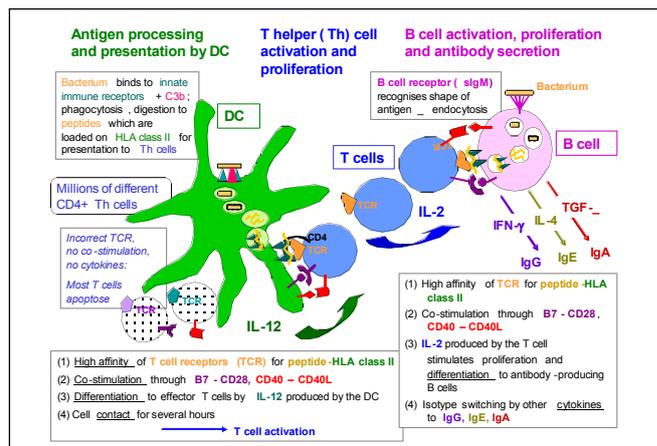
Activation in innate immunity is triggered either via the alternative pathway with binding of C3b (one of the components of the complement system) to microbial membrane chemical groups or via the lectin pathway after adherence of serum carbohydrate-binding proteins (e.g. mannose binding lectin) and deposition of C3b on the microbe. (C1q fixed to antibody on opsonised cells or in immune complexes also results in C3b deposition (classical pathway) but is an effector mechanism of adaptive immunity). Three components of the ensuing complement cascade enhance killing of microbes. C3b bound to the pathogen increases phagocytosis. C5a is inflammatory and attracts neutrophils to the site of infection. Deposition of the Membrane Attack Complex (polymerised C9) on the organism, punches holes in the microbe’s cell wall. Together, granulocyte and complement activation in the absence of antibodies comprises innate immunity that is very fast acting and efficient but relatively non-specific.

Adaptive (Acquired) Immunity

Adaptive immune responses are slow, requiring “information” from the pathogen to be processed and passed between several cells. However, they are very specific and retain memory of the pathogen. This enables

rapid secondary responses targeted to the immunising antigen. The adaptive immune response to bacteria is acquired in stages (Figure 2).

Figure 2



First, the microbe is recognised by the innate immune system by multiple Pattern Recognition Receptors on macrophages. These include lectin receptors for foreign carbohydrates, receptors for endotoxins and the recently discovered Toll Like Receptors specific for a variety of soluble and membrane microbial molecules. These microbial adjuvants deliver inflammatory stimuli that are essential for driving the subsequent adaptive immune response. The microbe is phagocytosed and digested by lysosomal enzymes into peptides (the antigenic microbial “information” from its proteins). These peptides are loaded onto human leucocyte antigen (HLA)-class II molecules and these complexes transported to the macrophage cell surface. This is known as antigen presentation. Meanwhile, the inflammatory signals mature the macrophages into dendritic cells (DC), enhancing surface expression of HLA class II and co-stimulatory molecules (CD80/86, CD40) (see footnote) and inducing secretion of cytokines such as interleukin (IL)-12 and interferon (IFN)- γ by DCs. Soluble antigens in peripheral tissues are acquired by fluid phase endocytosis by DCs, processed and peptide-HLA class II complexes are expressed on the DC membrane.

Second, these antigen-loaded DCs must now migrate to organs where T lymphocytes congregate – the lymph nodes or white pulp of the spleen – because they must activate naïve antigen-specific CD4+ T helper (Th) cells. Billions of different T cells each have unique antigen-specific T cell receptors (TCR). T cells constantly move amongst the DCs to enable selection of those “one in a million” T cells whose TCR binds the peptide-HLA class II complex on the DC with high affinity. The adherent Th cells are then activated by the DC if there is also sufficient co-stimulation through CD80/86 and CD40 on the DC with their respective ligands (L) on T cells, CD28 and CD40L. Adequate cytokines from the DC are also required. If all these three signals (cytokines,

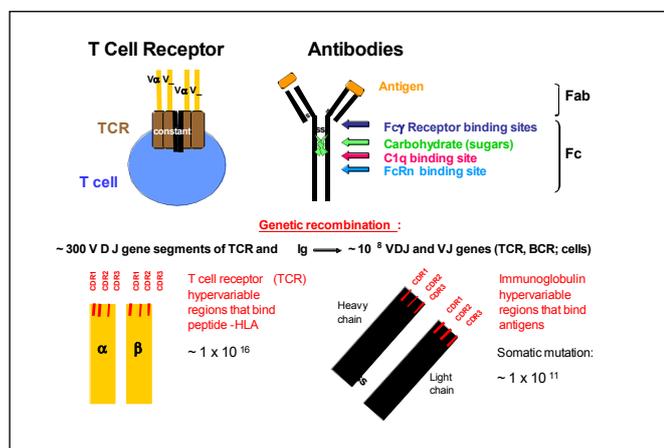
costimulation and high affinity TCR interaction with the peptide-HLA class II complex) continue for a period of about 8-24 hours contact time, the activated Th cells then produce IL-2 and proliferate about 1,000-fold. This increases their chances of contacting rare antigen-specific naïve B lymphocytes when they have migrated to the B cell areas of lymphoid organs.

The third stage in the immune response requires contact between these Th cells and naïve B cells which occurs if a B cell expresses the antigenic peptide "information" on its surface HLA class II. Although B cells, like DCs, are antigen presenting cells, they recognise antigens very differently. B cells acquire antigen after specific recognition of its conformational shape by the B cell receptor (BCR, surface IgM), followed by binding, endocytosis, antigen processing and presentation. Then there is a "mirror image" stimulation of this B cell by the T helper cell through its TCR binding the peptide-HLA class II complex, with also CD28 and CD40L costimulation through CD80/86 and CD40 ligation on the B cell and secretion of cytokines. The activated B cell then proliferates and produces antibody, about 10,000 molecules/second. The specificity of the secreted antibody is the same as the BCR and is normally IgM initially.

Lymphocyte Diversity

The huge diversity of TCRs and antibodies (BCRs and immunoglobulin (Ig)) is caused by genetic recombination (Figure 3). Both have three hypervariable (CDR) regions on each paired chain; α and β chains and heavy and light chains, respectively. About 300 variable (V), diversity (D) and joining (J) gene segments of TCR and Ig genes recombine randomly in a "pick and mix process" to form 10^8 VDJ and VJ genes, then with somatic recombination and junctional diversity this forms about 10^{16} TCR and 10^{11} Ig genes encoding the hypervariable antigen binding regions. Each TCR or BCR is unique to one lymphocyte. Billions of T and B cells are produced daily in the bone

Figure 3



marrow, travel in the blood to lymphoid organs (T cells via the thymus for deletion of autoreactive cells) where a few will proliferate and differentiate if contact is made with antigen, as described above. The vast majority of naïve T and B cells die by apoptosis because they do not recognise antigen or receive the three signals from the appropriate cell. Those that survive mature into memory T and B cells or plasma (B) cells that secrete antibodies.

Antibodies

Antibodies have two light and two heavy chains. Binding to antigen occurs at the variable ends of these symmetrically paired chains (Figure 3). Antibody isotype (class) is determined by the heavy chain constant regions (Fc). IgM, a pentamer, kills opsonised pathogens by binding complement, initiating lysis, and by agglutination, preventing invasion. Antibodies increase in affinity after secondary immunisation by somatic mutation. Localised cytokines drive class switching (IFN- γ , IL-4, TGF- β to IgG, IgE and IgA, respectively) (Figure 2). IgG stimulates phagocytosis through IgG Fc receptors (Fc γ R) on macrophages and neutrophils. Another receptor for IgG, FcRn, prolongs its half life and also enables placental transfer of passive immunity to the fetus. Most IgA is secreted as a dimer into the mucosa where it agglutinates bacteria; neutrophils also phagocytose through Fc α R. IgE bound to Fc ϵ R on eosinophils and basophils mediates extracellular lysis of parasites and on mast cells triggers release of histamine by allergens. Thus antibodies enhance and accelerate the innate immune cellular and molecular responses.

Footnote

Knowledge of the phenotype and functions of leucocytes (immune cells) and other cells has advanced enormously by studies using monoclonal antibodies, which can be clustered into groups according to the cell surface molecules they bind. The nomenclature is known as the "cluster of differentiation" (CD), with currently more than 350 CD markers identified.

Lecture slides on this topic may be viewed by googling my name, accessing www.bbts.org.uk/PDFs/events/Immunology%20for%20Dummies.pdf

Dr Belinda Kumpel, PhD

Senior Research Scientist,
 Bristol Institute for Transfusion Sciences
 Email: belinda.kumpel@nhsbt.nhs.uk

Part 2 of Immunology for Dummies will appear in the next issue of Blood and Transplant Matters.

ICCBBA and ISBT 128 - Value for Money?

With the increasing movement of substances of human origin (blood, cells, tissues and organs) across national borders there is a growing need for international standardisation in their identification, coding and labelling. The World Health Organisation have recognised the importance of such an initiative in their Guiding Principles on Human Cell, Tissue and Organ Transplantation and the need for a common coding system at the European level is identified within the European Directive on Tissues and Cells.

The only existing international standard that is able to meet these needs is ISBT 128. This standard is widely used in blood transfusion with 3,400 blood centres in 49 countries producing more than 40 million ISBT 128 labelled blood components each year. It has also been approved by an international consensus as the standard for coding and labelling of cellular therapy products. NHS Blood and Transplant were the pioneers for the use of ISBT 128 for tissues, and other European countries are in the process of implementing it; however there has been resistance from some quarters on the basis of the license fee costs charged by ICCBBA.

In order to assess the 'value for money' that the ICCBBA fees represent, it is necessary to identify the user community needs that an international standard must deliver. Of particular importance are the following:

- 1) Stability – users must be confident in the stability of a standard, as it is required over for a long term application (EC requirements for data to be stored and traceable for 30 years);
- 2) User focus – the user community are the experts in their field and the information standard needs to meet, rather than dictate, their needs;
- 3) Flexibility – as clinical and scientific knowledge grows, there is rapid development with changing information needs. The standard must be flexible enough to accommodate these needs;
- 4) Responsiveness – with a rapidly developing field, the standard needs to be able to respond to user needs in a timely manner;
- 5) Globalisation – the need for a truly international standard with endorsement worldwide;
- 6) Implementation – a standard is only of value if it is widely used;
- 7) Compatibility – standards do not work in isolation but need to interface with equipment, software and other standards.

Meeting these needs will clearly have a cost. Stability and flexibility requires a robust organisation that can manage the development and maintenance of the standard, and one that is not overly dependent on key personnel. User focus requires developing forums for discussion, either by conferencing or face-to-face meetings and the globalisation requirement means this will require long distance travel and international calls. Achieving implementation requires a substantial educational and technical support effort. Responsiveness can only be ensured with sufficient staffing. Compatibility involves time working with related organisations, but can deliver real cost saving to users as suppliers begin to deliver products where compatibility with the international standard is a standard feature.

A review of the ICCBBA Annual Report shows how ICCBBA delivers the ISBT 128 Standard to meet these user needs. With a small permanent staff they support a large group of expert volunteers who form technical advisory groups with global input. Their help desk provides rapid response to requests and staff provide an educational programme through participation in international congresses. They ensure that development of the ISBT 128 Standard meets user needs through comprehensive expert review and a robust change control process. They work closely with the suppliers of equipment, software and labels and have over 90 such suppliers providing products that use the ISBT 128 standard.

To support its activities ICCBBA charges a license fee for the use of the ISBT 128 Standard. In 2008 the total income for the ICCBBA was just under \$990,000 (approx £620,000 or €712,000). As a tax-exempt, non-profit organisation all of this income is directed to achieving the ICCBBA mission: "to enhance safety for patients by managing the ISBT 128 international information standard for use in transfusion and transplantation."

Value-for-money is a subjective assessment but it is one that needs to be made on an informed basis. Cost must be balanced against value delivered, taking into account the user community needs. As a user of the ISBT 128 Standard, a volunteer expert on a technical advisory group, and a volunteer member of the ICCBBA Board of Directors I believe ICCBBA offers exceptionally good value for money.

Ineke C M Slaper-Cortenbach

*Director of the Gene and Cell Therapy Facility and the Stem Cell Transplantation Laboratory
University Medical Center Utrecht, Netherlands
Email: I.Slaper@umcutrecht.nl*

References

Guiding Principles on Human Cell, Tissue and Organ Transplantation. World Health Organization 2009. http://apps.who.int/gb/ebwha/pdf_files/A62/A62_15-en.pdf. Accessed 1 Feb 2010.

Directive 2004/23/EC of the European Parliament and Council on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. Official Journal of the European Union 2004.

Ashford P, Fearon M, Bedford R. Report on the joint IBEPAG/ICCBBA survey on import/export and blood component labelling. *Vox Sang* (2010) 98:85-86.

Annual Report 2008. ICCBBA. http://iccbba.org/info_annualreport.pdf Accessed 1 Feb 2010.

ISBT 128 Labeling for Cellular Therapy Products

International Society for Cellular Therapy
ISCT 

Cellular therapy applications are continually evolving and developing. This reality is a source of great joy and accomplishment as well as an ever present challenge. Product nomenclature, labeling and applicable standards are part of the challenges we face. So it is important to stay informed and up-to-date with ISBT 128 information.

Recently at the ISBT 128 for Cellular Therapy workshop during the 2009 International Society for Cellular Therapy, (ISCT) Annual Meeting in San Diego, we reviewed some of the changes and additions for cellular therapy applications. For those of you who were unable to attend the annual meeting, the International Cellular Therapy Coding and Labeling Advisory Group, (CTCLAG), published a year end review of activities. The group plans to publish future annual reports to inform the cellular therapy community of accomplishments and ongoing developments.

As of December 31, 2008, 169 Cellular Therapy facilities in 31 countries have registered with ICCBBA. The number of registered facilities continues to grow in 2009. The advisory group is very excited about this news as an ongoing goal is to continue to promote the adoption of the ISBT 128 standard in cellular therapy facilities around the world. The entire annual report, which includes the results from a practice survey and answers to frequently asked questions, is available for review on the ICCBBA Cellular Therapy website at <http://iccbba.org/ctannualreport.pdf>.

The intent of this article is to provide some up-to-date information as well as review the applicability of the existing standards. Hopefully this will help to increase understanding of the ISBT 128 Standard for Cellular Therapy and its application.

Since the ISCT Annual Meeting, the *United States Consensus Standard for the Uniform Labeling of Cellular Therapy Products using ISBT 128 Version 1.1.0* has been published. It is the result of the collaborative efforts of AABB, ASBMT, ASFA, FACT, ICCBBA, ISCT, and NMDP.

The document is posted on the ICCBBA Cellular Therapy website at http://www.iccbba.org/usconsensusstandard_cellulartherapy.pdf.

You might be thinking, "This is great news; but, don't we already have an ISBT 128 Standard for Terminology and Labeling of Cellular Therapy Products?" Actually the US Consensus Standard is a complementary addition to two key existing standards.

ISBT 128 Standard Technical Specification, Version 3.6.0, May 2009.

Originally defined as a labeling standard, ISBT 128 is currently defined as:

"An international standard for the transfer of information associated with human tissue transplantation, cellular therapy, and blood transfusion. It provides for a globally unique donation numbering system, internationally standardized product definitions, and standard data structures for bar coding and electronic data interchange".

Figure 1

ACRONYMS	
AABB	American Association of Blood Banks
ASBMT	American Society for Blood and Marrow Transplantation
ASFA	American Society for Apheresis
CTCLAG	Cell Therapy Coding and Labelling Advisory Group
FACT	Foundation for the Accreditation of Cell Therapy
ICCBBA	International Council for Commonality in Blood Banking Automation
ISCT	International Society for Cellular Therapy
JACIE	Joint Accreditation of ISCT and EBMT
NMDP	National Marrow Donor Program

Essentially, the definition of data structures and the placement of bar codes, and their corresponding eye readable text (the text version of the data content of the bar code) that appears immediately beneath a bar code, are strictly standardised. These label elements must appear exactly as specified in the ISBT 128 Standard Technical Specification.

Due to the dynamic nature of the application, updated versions are issued to incorporate the changes and or additions. In the current version, Section 1.1 New In This Version, identifies additions to the standard. Section 1.3 ISBT 128 Standard Technical Specification Version Control contains a table which identifies the section, defines the change and provides the rationale for the change. These key sections allow the user to quickly review additions and or changes within the standard to assess the level of impact, if any, to their applications.

Standard Terminology for Blood, Cellular Therapy, and Tissue Product Description, Version 3.27, June 2009

This document provides a standard terminology for describing transfusion and transplantation products. It is designed to allow distinction between products where such is required on safety, clinical practice, or inventory management grounds. The underlying structure of the terminology is based on the concepts of Class, Modifiers, and Attributes.

Although primarily developed to ensure standard labeling of products, the terminology has a wider application in ensuring a common international understanding of specialised terms. Other professional and accreditation bodies have adapted their terminology to be consistent with this document.

Figure 2
ISBT 128 Label for Haemopoietic Progenitor Cells (HPC), Apheresis



As the field of cellular therapy is constantly evolving so too is the terminology. So with the joy of a new application or development comes the responsibility of a terminology addition, revision or update. In addition to adding and modifying terminology, 148 new Cellular Therapy product codes were added in 2008 at the request of facilities in Austria, Canada, the Netherlands, Sweden and the USA.

United States Consensus Standard for the Uniform Labeling of Cellular Therapy Products using ISBT 128, Version 1.1.0, June 2009

If you are in the United States, the US Consensus Standard is the third document which will provide standards for labeling applications. Within the information standard, certain elements, bar code text (the interpretation of the information in the bar code) and other text are generally left to national authorities to define in order to accommodate different languages and regulatory requirements. Additionally, the use of some data structures (e.g. collection date) are nationally defined.

Figure 3
ISBT 128 Label for Therapeutic Cells (TC) – T Cells



After the publication of the international standard, the US Consensus Cellular Therapy Advisory Group, with representatives from AABB, ASBMT, ASFA, FACT, ICCBBA, ISCT, NMDP and a liaison from the FDA, was formed to define elements specific to labeling of cellular therapy products for the United States. The resulting document, The United States Consensus Standard for the Uniform Labeling of Cellular Therapy Products Using ISBT 128 defines for the United States the areas that are the prerogative of national authorities. This standard must be used in conjunction with the ISBT 128 Standard Technical Specification to design labels for cellular therapy products.

Every effort has been made to ensure label designs suggested in this document are in compliance with AABB, FACT, NMDP, and FDA requirements. However, cellular therapy is very much an evolving field and requirements are still being developed. This document will be updated regularly to ensure compliance with new requirements. It is important to note that applicable FDA regulations take precedence over any requirements in this document. For newer products, it would be advisable to confirm labeling requirements with the FDA during the product development process.

While many accrediting organisations support ISBT 128 terminology for Cellular Therapy, it is not feasible to require complete implementation at this time. For example, until recently, with the publication of the US Consensus Standard, the label and software vendors in the United States could not provide the appropriate warning statements for the product label. Consensus documents for other countries which address specific national authority regulations may be necessary to facilitate complete implementation. For the United States, with the completion of the US Consensus Standard, more pieces are coming together and facilities should move toward implementation in order to make the transition as seamless as possible.

Current and future editions of the accrediting body cellular therapy standards include language specific to ISBT 128 nomenclature. However, this too has presented some areas of confusion and concern. At present, there is no “cross walk” document to help you merge the requirements of the accrediting bodies, the ISBT 128 Standards and the FDA or national authority regulations. There is however, support for and a commitment to improving clarity and finding solutions. Remember at the beginning of this article, I mentioned the ever present challenges. As you move forward with this process, please contact the accrediting bodies, ICCBBA or national authority for guidance.

Frequently Asked Questions

Q. What if I am not in the United States and my products are not regulated by the FDA?

A. ISBT 128 Standard Technical Specification and Standard Terminology for Blood, Cellular Therapy, and Tissue Product Description are two key documents to use for the ISBT 128 labeling of cellular therapy products. In addition, you have the responsibility to meet any requirements defined by your national authority.

Q. Is ISBT 128 labeling for cellular therapy products required?

A. No, currently there is no requirement for the use of ISBT 128 bar codes, or that the ISBT 128 label design, be on cellular therapy products. However, FACT, JACIE, and AABB require that ISBT 128 terminology be used when labeling cellular therapy products.

Q. If it is not required, why should anyone care about the ISBT 128 terminology and standards documents?

A. As a member of the International Cellular Therapy Coding and Labeling Advisory Group, I would have to say, “To support the need for global standardization of product nomenclature, quality assurance and safety”.

Leigh Sims Poston, BS MT(ASCP)

*On behalf of the International Cellular Therapy Coding and Labeling Advisory Group (CTCLAG), International Society for Cellular Therapy, (ISCT) representative
Email: leigh.poston@yahoo.com*

Article originally published in ISCT Telegraft Vol 16 #2, June 2009.

References

ISBT 128 Standard Technical Specification, Version 3.6.0 May 2009.

Standard Terminology for Blood, Cellular Therapy, and Tissue Product Description, Version 3.27 June 2009.

United States Consensus Standard for the Uniform Labeling of Cellular Therapy Products using ISBT 128, Version 1.1.0 May 2009.

ISBT 128 Cellular Therapy Coding and Labeling Advisory Group 2008 – A Year End Review.

Current Events in ISBT

Tibor Greenwalt writes in the "History of the International Society of Blood Transfusion" that according to the Central Archives of the Society, the first international blood transfusion meeting was held in Rome in 1935. Twenty nations were represented and eight Red Cross Societies.

At the close of the congress in 1937 Professor Leopold Mayer, Brussels proposed that the Societe Internationale de Transfusion Sanguine (SITS) (International Society of Blood Transfusion) should be formed. The proposal was accepted and it was decided to have a permanent office in Paris. The office remained in Paris until 2003 when the Central Office was established in Amsterdam and ISBT was legalised under Dutch law. This year ISBT will celebrate 75 years of congresses with its XXXIst congress in Berlin.

The aims of ISBT include:

- To connect with blood transfusion professionals;
- To provide opportunities for the exchange of information on science, clinical practice and research and development related to blood transfusion medicine and associated disciplines;
- To promote and to maintain a high level of ethical, medical and scientific standards in blood transfusion medicine;
- To promote safe and sufficient transfusion therapy globally.

ISBT carries out these aims in a number of ways through:

- It's regional and international congresses;
- It's support for educational activities;
- The activities of its working parties;
- It's communications;
- It's support for World Blood Donor Day.

For many years there was only one ISBT international congress every two years. This changed in 1989 when the first ISBT regional congress was held in Lugano, Switzerland. In 1991 the second regional congress was held in Hong Kong. Since 1995 ISBT has held two regional congresses in every odd year; one in Europe or the Eastern Mediterranean region, one in Asia and one international congress. Attendance at congresses has grown, over 2,000 individual delegates attended the 2008 International congress in Macao and 3,000 delegates are expected in Berlin. ISBT also has input into educational events run independently of the Society. ISBT supported the establishment of the Arab Transfusion Medicine Course (ATMC) which was set up as an

educational activity for the Arabic speaking countries. One of the founder members of this course is Dr Gamal Gabra well known to many in the UK. The ATMC held its 7th course in Algeria in December 2009.

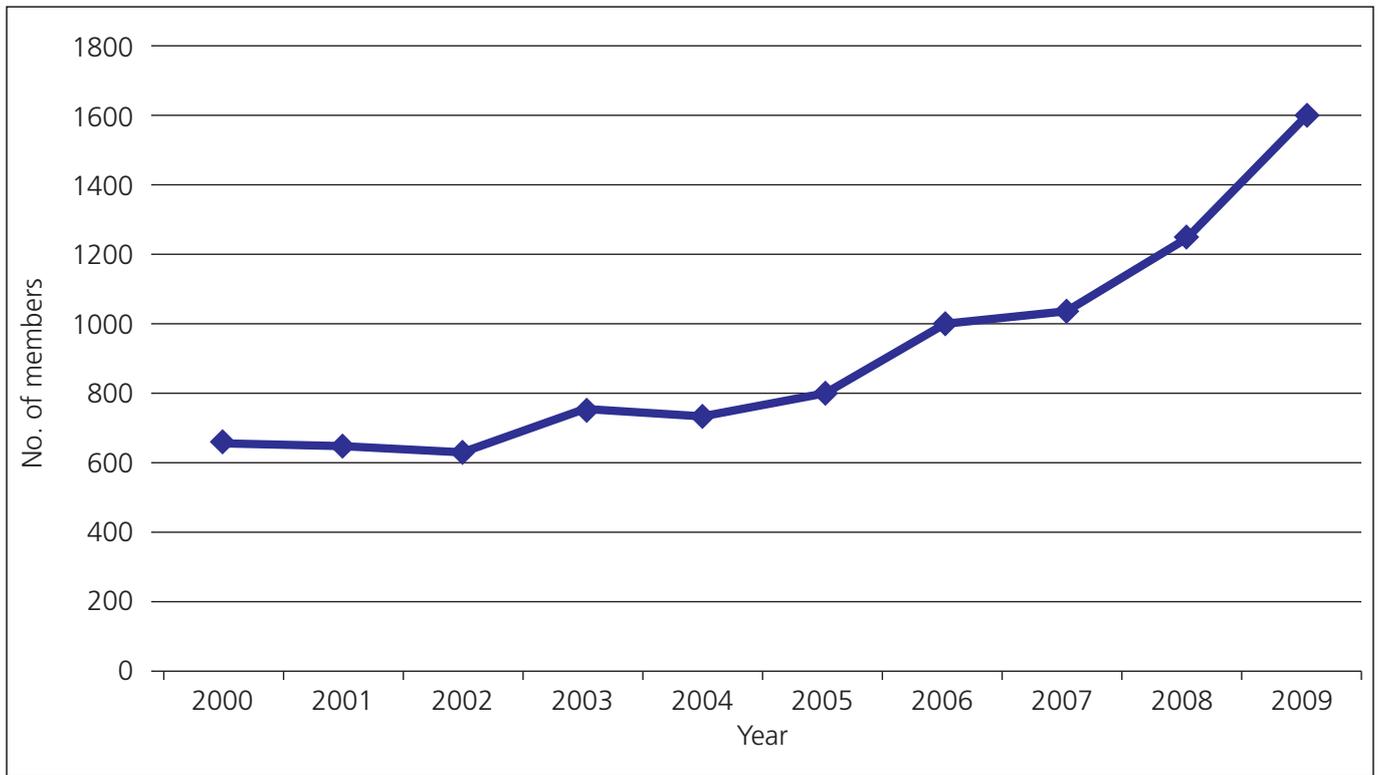
ISBT has 14 working parties covering many topics in Transfusion Medicine from donors through to haemovigilance. The working parties perform an important role in the global development of transfusion practice, eg the red cell immunogenetics and blood group terminology working party chaired by Geoff Daniels is responsible for providing a genetic classification of blood groups in addition to a set of unique names. The Information Technology Working Party has recently published guidelines for Validation of Automated Systems in Blood Establishments (Vox Sanguinis Vol 98 Issue s1 (February 2010). They will soon publish RFID (Radio Frequency Identification) guidelines, again in Vox Sanguinis. The Haemovigilance Working Party have published a Standard for Collecting and Presentation of Data on Complications Related to Blood Donation. The Rare Donor Working Party's objectives are:

- To develop guidelines for standardisation of listing, labelling, shipping, testing and reimbursement for rare donors blood;
- To provide a resource for providing ongoing information on matters related to rare blood;
- To develop and extend the liaison with the International Blood Group Reference Laboratory (Bristol, England).

This will assist blood services internationally to be aware of, and contribute to, the WHO International Donor Panel ISBT's communications include its website www.isbt-web.org, a quarterly bulletin, Transfusion Today and an electronic newsletter which is distributed to the members monthly.

ISBT is one of the four founding partners of World Blood Donor Day (WBDD) held on 14 June every year as a worldwide celebration to honour and thank those people who donate their blood on a voluntary, unpaid basis. WBDD provides a special opportunity to create public awareness and build a culture of voluntary blood donation and the need for availability, safety and appropriate use of blood and blood products.

Over the last few years the activities of ISBT have increased and this is reflected in a substantial increase in membership. At the end of 2009 there were over 1600 members and members are present in 97 countries worldwide.



The ISBT vision is “to be a global leader in transfusion medicine, promoting science and education relating to blood and cellular therapies.”

The ISBT 2009-2011 strategic plan includes the goals of:

- Expanding the Scientific Profile of ISBT;
- Developing a portfolio of high quality effective communication channels;
- Positioning ISBT as a global leader in Transfusion Medicine Education;
- Developing a High Standard of Corporate Governance;
- Strengthening the ISBT Congresses.

The elements of this strategy are taking place and some of the actions required to ensure that the goals of the strategy are achieved will be easier to undertake with the appointment of the ISBT’s first Executive Director. The scientific profile is expanding and ISBT now embraces the developing field of cellular therapies. It has established, jointly with AABB, a cellular therapies working party and there are dedicated cellular therapy sessions at the ISBT congresses.

During 2010, ISBT members will see some significant changes particularly around its image and communications. Transfusion Today will have a new look and the website will be redesigned and developed. These changes will ensure that the identity of ISBT is more 21st century. The citation of Vox Sanguinis, the ISBT journal, continues to rise and the outputs of the working parties will ensure that ISBT is positioned as a global leader in Transfusion Medicine. The appointment of the Executive

Director means that the Society is in a good position to develop high standards of corporate governance and ensure that they are maintained. ISBT is committed to growing its congresses and ensuring that they continue to take place in all parts of the world, taking ISBT to its global membership.

Judith Chapman

*Executive Director
ISBT Central Office
J. van Goyenkade 11
1075 HP Amsterdam
The Netherlands
E-mail: chapman@isbt-web.org*

The European Blood Alliance and its Tissue and Cells Working Party

The European Blood Alliance (EBA) was established in 1999. Its purpose is to contribute to the safety, security and cost effectiveness of the blood and tissue and cell supply for the citizens of Europe by developing and maintaining an efficient and strong collaboration amongst European blood and tissue services.

A blood service may qualify as a Member of the Alliance where:

- It is the national service of the state concerned or is an alliance of blood services that represents the majority of blood establishments in the state;

- The state in which its main activities are based is a member of the European Union or European Free Trade Area;
- Its activities are based on the principle of the voluntary and non-remunerated donation of blood.

Current membership of the EBA Board is listed in Table 1

Table 1

MEMBERS AND THEIR REPRESENTATIVES AT THE BOARD	
Austria	Austrian Red Cross Blood Transfusion Services
Belgium	Belgian Red Cross-French: Blood Service, Red Cross-Flanders: Blood Service
Denmark	Organisation of Transfusion Centres in Denmark
Estonia	North Estonia Regional Hospital, Tartu University Clinic
Finland	Finnish Red Cross Blood Service
France	French National Blood Service
Germany	German Red Cross Blood Transfusion Services, German Association of Blood Transfusion Services
Greece	Blood Transfusion Committee-National Blood Centre
Hungary	Hungarian National Blood Service
Iceland	The Blood Bank
Ireland	Irish Blood Transfusion Service
Italy	Italian Institute of Health
Latvia	Latvian State Blood Centre
Lithuania	National Blood Centre
Luxembourg	Blood Transfusion Service of the Luxembourg Red Cross
Malta	Maltese National Blood Transfusion Service
The Netherlands	Sanquin Blood Supply Foundation
Norway	National Transfusion Council
Portugal	Portuguese Blood Institute
Spain	Scientific Committee on Transfusion Safety
Slovenia	Blood Transfusion Centre of Slovenia
Sweden	Swedish Blood Alliance
Switzerland	Blood Transfusion Service of the Swiss Red Cross
United Kingdom	National Health Service: Blood & Transplant (England), N. Ireland Blood Transfusion Service, Scottish National Blood Transfusion Service, Welsh Blood Service

Other countries (e.g. Cyprus) and associations (ABC [American Blood Centres] and IPFA [International Plasma Fractionation Association]) sit as observers and the Board has expanded significantly over the past 10 years as it embraced new members as the European community of nations enlarged.

In 2009 a strategic review was undertaken by EBA, ten years after its inception to ensure that its activities remained relevant. A number of themes emerged as key core objectives:

- Improve performance through collaboration;
- Support legislation and engage in regulatory affairs to promote best practice;
- Facilitate information collection and knowledge exchange;
- Use global leverage to be more effective on behalf of the membership;
- Promote the safe transfusion of the optimal quantity of blood;
- Provide an adequate supply of safe tissues and cells.

In support of the last objective, the EBA Board decided to establish a working party on tissue and stem cell banking. It was felt by many members that such an activity was being increasingly undertaken by members of the Alliance but had never been quantified. Moreover the regulatory environment for the provision of tissue and stem cell services had recently changed with the adoption of the European Directive 2004/23/EC (EUTCD).

I have been asked and accepted to co-chair this working party with Dr Kari Aranko (from the Finnish Red Cross) and with support of the secretariat (Dr Thomas Bart- Switzerland) the first task was to produce a simple questionnaire to assess two areas:

1. How many EBA members are involved in tissue/stem cell banking.
2. For those performing tissue/stem cell banking, what is their level of involvement in meeting the country's need for tissues and cells.

The questionnaire was sent to all members and two reminders were also sent with the deadline being extended to maximise returns. It is therefore assumed that members that have not responded are not involved in this activity.

The percentage response rate was 62%.

Bone

Of those members that responded 53% (ten out of 17) indicated that they are involved in bone banking. The majority are involved in the banking bone from live donors. Some are also involved in procuring bone from deceased donors, but they appear to be in a minority.

EBA members' assessment of the proportion of bone supplied by them in comparison to other organisations, indicates that there is quite a variation in the proportion of bone supplied. However nearly 50% of responses indicated that EBA members, support more than half their country's needs.

Table 2: Activity of Tissue and Cell Banking Amongst EBA Members

EBA Members	Bone	Other Tissues	Stem Cell	Cord Blood
Austria (1) Linz		✓	✓	
Austria (2) Wien	NIL	NIL	NIL	
Belgium (1) Flanders				
Belgium (2) Wallonia				
Denmark (1) Funen	✓		✓	
Denmark (2) Zealand	✓			
England (NHSBT)	✓	✓	✓	✓
Estonia (1) Tallinn	✓		✓	
Estonia (2) Tartu				
Finland	✓			✓
France	✓	✓	✓	✓
Germany (1) GRC	✓		✓	✓
Germany (2) GABTS				
Hungary				
Iceland				

Table 2: Activity of Tissue and Cell Banking Amongst EBA Members. Continued

EBA Members	Bone	Other Tissues	Stem Cell	Cord Blood
Ireland				
Latvia	NIL	NIL	NIL	NIL
Lithuania	NIL	NIL	NIL	NIL
Luxembourg				
Malta				
Netherlands	✓	✓	✓	✓
Norway				
Northern Ireland				✓
Portugal				
Scotland	✓	✓	✓	✓
Slovenia		✓	✓	✓
Sweden	✓	✓	✓	✓
Switzerland			✓	✓
Wales				✓

Other Tissues

Seven of the 17 members (42%) indicated that they are involved in banking other tissues. Some members' tissue establishments appear to be tissue specific (e.g. amniotic membranes) whilst others are involved in banking a range of tissues, ranging from two to five tissue types.

Interestingly members involved in banking these other tissues claim that they provide at least 60% of them in the country and 50% believe that they are practically a monopoly supplier for the tissues they bank.

Thus, EBA members play a significant role in tissue banking as well as bone. The range of tissues banked varies amongst members. No attempt has been made at this stage to assess the level and type of processing of the tissues concerned.

Cells

Fourteen out of the 17 respondents (72%) indicated they are involved in some form of stem cell banking. Three countries are only involved in cord blood (16%). Two countries are only involved in autologous stem cell work (11%). The rest (44% – eight out of 17 respondents) are involved in a broad range of stem cell activity including allogeneic and autologous stem cell transplants.

Imports/Exports

The significant proportion of respondents indicated that import and export activity takes place within the country. This is, not surprisingly, most obvious in allogeneic stem cells/ cord blood. However the reasons for such level of exchange in other tissues need to be

better understood.

Tissue & Cells Working Party

The activity of tissue banking is significantly smaller quantitatively than blood. Units are measured in low thousands of units, not millions. However the complexities of tissue procurement and processing are very significant and are very often tissue specific. Performing these activities whilst maintaining quality standards and compliance with legislation is costly and complex.

Having established baseline information it was decided that there was much merit in meeting on a regular twice yearly basis, thus creating a structured forum for members to discuss relevant issues.

The Tissues and Cells group has met on four occasions. The format of the meeting is that the group meets the night before for a dinner sponsored by the host organisation followed by a full day meeting. This format is important since the group only meets twice a year and dinner provides the only opportunity to get to know each other better. In fact after four meetings it is clear that the group is beginning to gel.

Meetings are very well attended with delegates representing Finland, France, Switzerland, Scotland, Denmark, The Netherlands, Wales, Germany, Sweden, Belgium, Austria, England and Slovenia attending.

The terms of reference for the group has been agreed and approved by the EBA board.

Visit from DG Sanco

Thomas Bregeon from the DG Sanco attended the meeting in September in Frankfurt. He gave a detailed background on the work programmes funded to date and the priorities for the forthcoming years. He also gave a comprehensive review of the regulatory framework for tissues and cells and touched on the new directive being discussed for organs. This was an extremely useful interaction. Most importantly there was recognition for the first time of the involvement of blood services within the tissues and cells area.

Request from EBA Benchmarking Group

There has been a request from the EBA's benchmarking working group to get involved in some of our work. This has been seen as an important collaborative area and two members of our group have been nominated to join the benchmarking group. Moreover there is significant interest in this area from an economic research group in Finland. This is a core activity of our group and will produce some key data in the future.

Web Site

Improving and maintaining communication is key for our group. It is intended that web base communication methods are used extensively and a web site has been developed by the Swiss Blood Stem Cell Foundation for our members. It is beginning to be used increasingly as the main forum for discussion.

Conclusion

In conclusion I believe that a lot has been achieved in the past two years. The programme is varied, but we are confident that more cooperative work will be done in the future. The Blood Services have much to offer in this sphere of activity. The case was strongly made at the 10th Anniversary Symposium of EBA earlier this year. Although tissue and cell banking will never be solely under the auspices of the Blood Services, co-operation amongst us will provide a strong professional voice in this field. Maybe even more...

George Galea

Tissues and Cells Medical Director

SNBTS

Co-chair EBA Tissues and Cells Group

Email: george.galea@nhs.net

The author is very grateful for the input provided by members of the EBA Tissues and cells group for providing all the information for this manuscript.

EUROCET: The European Network of the Competent Authorities for Tissue and Cells

Background

Competent Authorities (CAs) in each European Member state are organisations with the authority and capacity to perform a specific function, delegated or appointed by law. In the tissues and cells framework, they are organisations, designated by Member States (MS), in charge of the implementation of quality and safety standards related to donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells, as defined by the *Directive 23/2004/ EC (ECD)*. Each MS can appoint more than one CA with specific roles, competence, and expertise. For example in the UK there are two CAs, one the Human Tissue Authority licences facilities concerned with tissues and cells including haemopoietic cells, relating to the ECD and the Human Fertilisation Authority oversees the assisted reproduction sector. Other countries have other models.

EUROCET (European Registry for Organs, Tissues and Cells) was a project, started in September 2005 and finished in February 2007, funded under the e-TEN programme of the European Commission (DG INFSO). During the meeting of May 30th, 2008 held in Brussels, the CAs for Tissues and Cells endorsed Eurocet as:

- The official European (EU) Registry of CAs for tissues and cells. Among cells, there are Hematopoietic Progenitor Cells (HPC);
- The registry of Tissue Establishments (TEs) from all CAs. Eurocet responds to the requirements set out in article 10 of the Directive 2004/23/CE, since it publishes an updated official registry of all TEs;
- A tool aiming to collect data on donation and transplantation activities of tissues, Hematopoietic Progenitor Cells (HPC) and reproductive cells, provided by all national CAs;

- The official information website for all EU and extra-EU citizens, patients, professional operators and institutions, with interactive and user friendly tools.

Now Eurocet is the network of CAs as foreseen by article 10 of the ECD, thanks also to the technical and financial support of the Italian National Transplant Centre (Italian CA for Tissues and HPC).

Methods

In order to achieve these goals, Eurocet has created a network among CAs and has developed a website (www.eurocet.org), where the list of TEs authorised by the CAs and official data of activity on donation, procurement, banking, distribution and transplantation are published. This website is multilingual and public. There is also a restricted area devoted only to the CAs. The Italian National Transplant Centre supports Eurocet efforts to foster the network among CAs and to respond to the obligations of the tissues and cells Directives. In the last meeting of the CAs, Eurocet has been invited to show the annual data, collected asking to all CAs to fill in an *ad hoc* form. Concerning HPC data, almost two years ago Eurocet initiated a collaboration with the European Group for Blood & Marrow Transplantation (EBMT) for the mutual exchange of data on transplantation activity.

Results

All data collected from the CAs are available on the website and published in an annual report. Complete HPC data resulting from the TEs registry and from the 2008 Activity Report are listed below.

The 33 participating countries (all MS, 3 Candidates, 3 other EU countries) are shown in Fig. 1. There are 44 CAs for HPC:-

- 22 countries have only 1 CA;
- 8 countries have 2 CAs;
- 2 countries have 3 CAs;
- 1 country does not have a CA.

TEs registered for HPC are 1,313 (58.5% of the total number of TEs for tissues and cells): 494 centres for HPC transplant, 274 for retrieval, 174 for donation, 310 are cord blood donation centres, 61 are cord blood banks.

The 2008 activity data for HPC recorded by the CAs in Eurocet Registry are in Fig. 2. The data collected are related to the national activity on: potential donation, searching in the national registries, donation, banking of cord blood, transplantation per origin and per pathology, transplantation activities per centre. For every type of pathology, there is the number of countries that have sent data. The activity report per every transplant centre can be found on Eurocet website.

Discussion

At the present, almost 50% of the participating countries have sent 2008 activity data to Eurocet. The results could seem low in qualitative terms, but they are quantitatively relevant for the following reasons:

- This is the first time that official data on HPC are published in Europe;
- The number of countries that have recorded data is more than doubled since 2007;
- The collection of activity data represents a new function for many CAs compared to the past and it underlines the transposition of the obligations of the Directives by the MS. In order to increase the information, the collaboration with EBMT allows Eurocet to complete the data collection on HPC transplantation activity for each EU country.

Conclusion

The EC encouraged the use of the Eurocet portal as a way to fulfil the obligation of the Tissues and Cells Directives. In the draft of the first report to the Council, the EU Parliament, the EU Economic and Social Committee and the Committee of the Regions on the application of Directive 2004/23/EC, distributed at the last meeting of the CAs, the EC states: "According to Article 10(3), MS and the Commission should establish a network linking the national tissue establishment registers. Currently this network linking is made by EURO CET, which is a registry of national tissue establishments and activity reports managed by the Italian Competent Authority". However the Eurocet website is not only dedicated to the CAs for tissue and cells, it also helps medical professionals to improve patient care and promotes common standards within different regulatory and cultural environments. Moreover it offers real-time information to all European and extra-European institutions, patients, and citizens with interactive and user friendly tools. This information can increase public awareness regarding the social value of organ and tissue donation.

Acknowledgements

The Eurocet team owes a special debt of gratitude to all the CAs for their efforts dedicated to the data collection, to EBMT for the precious collaboration in the mutual data exchange and to the personnel at the Italian National Transplant Centre.

Lead Author: Angelo Ghirardini

Eurocet Team Manager:
Italian National Transplant Centre
Via Giano della Bella, 34
00162 Rome
Italy*

*Phone +390649904104
Fax. +390649904101
Email: info@eurocet.org*

Eurocet team: Angelo Ghirardini, Maura Mareri, Paola Di Ciaccio, Francesca Vespasiano, Alessandro Nanni Costa.*

References

Directive 2004/23/EC - "Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells".

Directive 2006/17/EC - "Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells".

Directive 2006/86/EC - "Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells."

Fig.1 The 33 countries participating to Eurocet

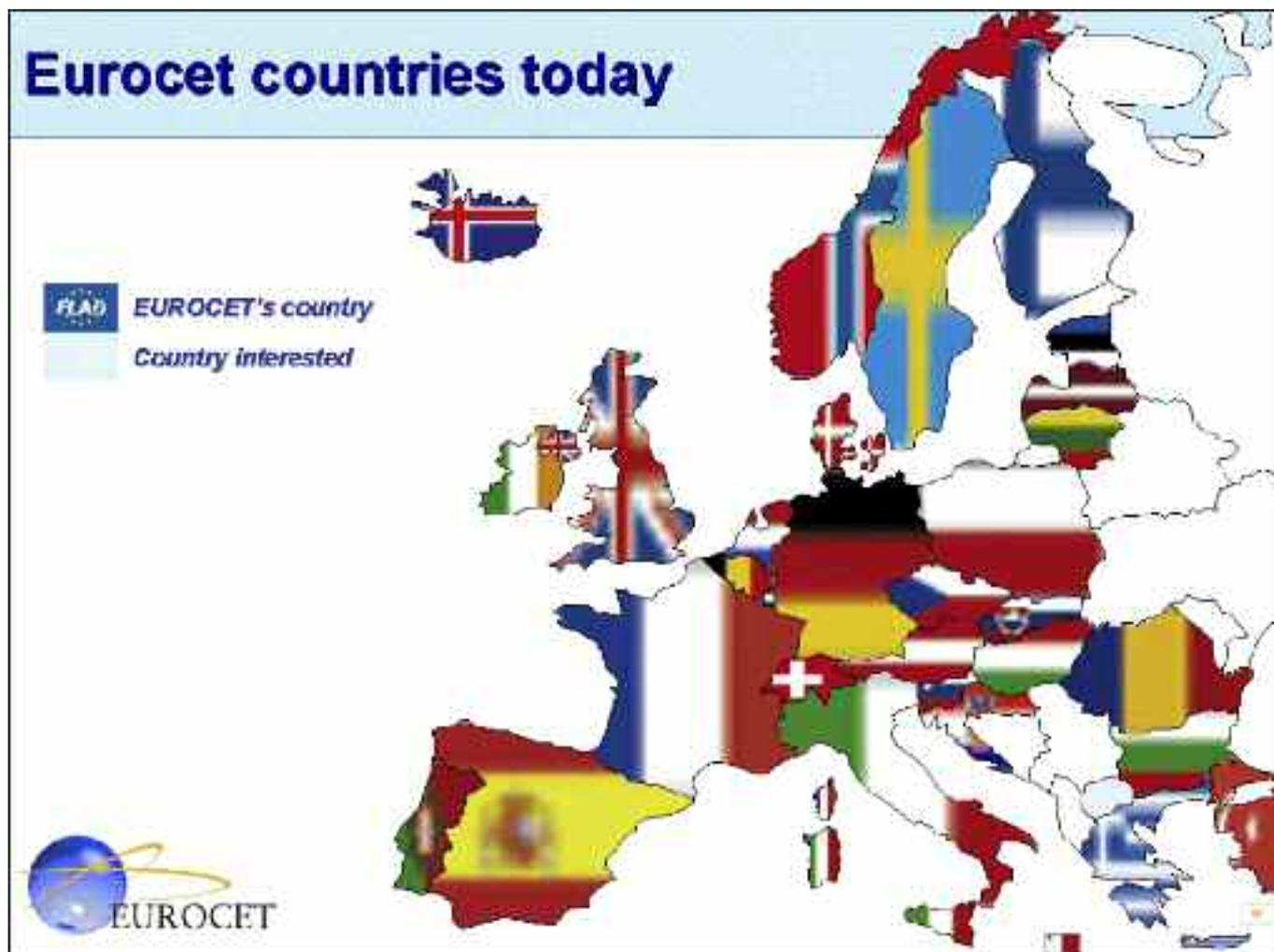


Fig.2 The 2008 activity data for HPC recorded by the CAs in Eurocet Registry

No. of countries recorded data in EURO CET registry				12	
Potential Donation	Registered at 01/01 00:00	Enter in the year	Exit in the year	Unspecified data	Registered in 31/12 24:00
No. of HPC - M potential donors	891.897	81.429	25.107	5.454	953.673
No. of HPC - Cord Blood units	30.412	9.166	423	30.501	59.656

Searching in the National Registries	Origin of request			Total
	Country	EU	EXTRA EU	
No. of Searches requested	5.177	13.403	12.300	30.880
No. of Searches performed in the national registry	2.999	12.106	12.124	27.229
No. of Searches performed in the abroad registry	4.972			4.972
No. of Unrelated donation	1.520	236	102	1.858
- from the own COUNTRY	354	236	102	692
- from the EU countries	862			862
- from the EXTRA EU countries	304			304

No. of countries recorded data in EURO CET registry				15	
Donation	Autologous	Allogenic		Total	
		Related	Unrelated		
No. of Donation	42.449	15.411	11.110	69.020	
- from Bone Marrow (M)	456	346	483	1.285	
- from Peripheral Blood (A)	12.327	1.535	1.502	15.364	
- from Cord Blood (C)	17.388	140	4.898	22.426	
- unspecified	12.328	13.390	4.227	29.945	

No. of countries recorded data in EURO CET registry				11	
Banking of Cord Blood	Collected at 01/01 00:00	Collected	Discarded	Distributed	Collected at 31/12 24:00
No. of Unrelated cord blood units	36.169	28.798	11.404	526	78.174
- in the own COUNTRY	29.884	23.673	10.774	274	71.107
- in the EU countries	0	0	0	125	0
- in the EXTRA EU countries	0	0	0	77	0
- unspecified	6.285	5.125	630	50	7.067
No. of Related cord blood units	7.351	3.723	184	115	10.700
- in the own COUNTRY	7.346	2.541	32	115	9.758
- in the EU countries	5	34	3	0	36
- in the EXTRA EU countries	0	0	0	0	0
- unspecified	0	1.148	149	0	906

No. of countries recorded data in EURO CET registry			15
Transplantation per HPC's origin	Autologous	Related	Unrelated
No. of Transplants	15.352	3.185	6.028
- from Bone Marrow (M)	349	877	1.489
- from Peripheral Blood (A)	13.610	224	3.654
- from Cord Blood (C)	1	34	657
- from combination	29	15	3
- other	1	1	1
- unspecified	1.362	2.034	222

No. of countries recorded data in EURO CET registry			10
Transplantation per Pathology	Autologous	Related	Unrelated
No. of Transplants	6.119	1.491	1.313
1. Acute myeloid leukaemia	428	461	347
2. Acute lymphoblastic leukaemia	177	269	298
3. Chronic myeloid leukaemia	10	42	61
4. Myeloproliferative syndromes	3	27	21
5. Myelodysplastic syndromes	13	116	118
6. Chronic lymphocytic leukaemia	100	47	37
7. Hodgkin's lymphoma	763	73	47
8. Non-Hodgkin's lymphoma	1.482	137	105
9. Myeloma/Plasma cell disorders	2.213	80	56
10. Aplastic Anaemia	66	66	57
11. Solid tumors	469	10	5
12. Auto immune disorders	41	1	2
13. Immune deficiencies	1	8	14
14. Inherited disorders of metabolism	2	15	39
15. Haemoglobinopathies	0	63	12
99. Others	351	76	94

Targeted Cellular Immunotherapy for Cytomegalovirus Infection in Stem Cell Transplantation

Introduction

Allogeneic haemopoietic stem cell transplantation (HSCT) offers the possibility of cure for many patients with haematological malignancies. The procedure involves intensive chemo-radiotherapy followed by infusion of allogeneic haemopoietic stem cells harvested from Human Leucocyte Antigen (HLA)-matched donors.

Although HSCT has had a tremendous success in treating previously incurable haematological malignancies in the past 30 years, considerable mortality remains associated with the procedure. The main causes of death following HSCT are related to the deficiency or dysfunction of the adopted immune system, namely disease relapse from inadequate graft versus leukaemia effect (GVL), infections from deficiency in pathogen-specific immunity and graft versus host disease (GvHD).

A common infective complication of HSCT is the reactivation of latent cytomegalovirus (CMV) in previously CMV-infected transplant patients. Although current antivirals have dramatically improved the prognosis of the infection, a significant number of patients have disease that is refractory to these drugs. The challenge in these patients is to restore their CMV-specific immunity to eliminate the virus.

CMV and Disease

Around 50% of the population in the UK is infected with CMV. The virus is usually transmitted asymptotically by salivary contact and by blood product transfusion. In the healthy immunocompetent person, after primary infection, the virus establishes lifelong latency in the host where viral replication is controlled by a competent immunity. When this immunity is suppressed by drugs or by disease, CMV reactivation occurs. In the transplant setting, CMV can cause life-threatening pneumonitis, gastritis, hepatitis, colitis, retinitis and bone marrow suppression. The incidence of CMV reactivation amongst CMV seropositive patients is over 50%, depending on the conditioning chemotherapy and immunosuppression used for the transplant. Transplants from unrelated donors and those that use reduced intensity conditioning with removal of alloreactive T cells have higher rates of CMV reactivation.

Immune Response to CMV Infection

The protective immunity against CMV is mediated primarily by CMV-specific T lymphocytes. They recognise infected cells through the specific binding between the T cell receptor (TCR) and HLA molecules complexed to CMV-derived peptides. HLA molecules can be synthesised

in the laboratory and assembled into HLA tetrameric complexes (HLA tetramers) conjugated to fluorochromes e.g. phycoerythrin (PE) for use as diagnostic reagents. They can be used to stain and quantify CMV-specific CD8 T cells in patients' blood by flow cytometry. When CMV-specific HLA tetramers are used in conjunction with viral monitoring, the relationship between CMV reactivation and the magnitude of the CMV-specific CTL responses can be analysed. Studies of CMV+ HSCT patients have demonstrated the critical role of CMV-specific CTL in controlling CMV reactivation after allogeneic BMT. Delayed or absent CMV-specific T cell reconstitution after HSCT can lead to persistent viraemia and refractory disease.

Current Therapeutic Strategies

There are several ways to prevent and reduce CMV infection, such as matching CMV seropositive patients with CMV-seropositive donors to allow transfer of donor CMV-specific immunity to the recipient, use of prophylactic antiviral drugs e.g. ganciclovir, and the use of CMV negative blood products for transfusion. The use of pre-emptive ganciclovir for CMV reactivation has reduced the morbidity and mortality of CMV. However, these agents are highly toxic causing renal impairment, and their use has been associated with increased late CMV reactivation, possibly due to the immunosuppressive effect of the antiviral. Such late reactivation is associated with a significant mortality.

Adoptive Cellular Immunotherapy for CMV

Recognising the role of CMV-specific CD8 T cells in the control of viraemia, a phase I clinical trial was conducted where healthy donor CMV-specific T cells were infused into the patient to replace deficient cellular CMV-specific immunity. CMV-specific CD8 T lymphocytes were selected immunomagnetically from donor whole blood using HLA tetramers and magnetic beads. This approach led to a dramatic 250 fold in vivo expansion of CMV-specific T cells in the patient and to the resolution of CMV viraemia (figure 1). Eight out of nine patients (89%) treated had a complete resolution of the viraemia without any adverse events or GvHD attributable to the transferred cells. Only half a million CMV-specific CD8 T cells were required to achieve this, obtainable from a single blood donation. Non-specific potentially alloreactive cells which might cause Graft versus host Disease (GvHD) accounted for less than a total of 10^4 cells, which is below the generally accepted risk threshold for GvHD of 10^4 /kg.

The HLA tetramer technology used for selection is the same as used for detection of antigen-specific T cells in the blood. The CMV-specific HLA tetramers specific were

linked to PE fluorochromes. A second reagent consisting of anti-PE monoclonal antibodies linked to paramagnetic beads were used to select out the relevant cells that are bound to the HLA-tetramers (figure 2). The immunomagnetic selection was conducted using a GMP grade magnetic column (CliniMACS®). Phase II clinical trials are now underway using a new generation of HLA-tetramers. The phase II randomised trial for adoptive CMV immunotherapy for HSCT transplant patients at high risk of CMV reactivation will commence soon. This uses a single GMP grade reagent (Streptamers®) where the HLA molecules are directly linked to the magnetic beads and which dissociate from the cells following selection so that they are not co-infused with the cells into the patient. In order to minimise the risk to donors, CMV-specific CD8 T lymphocytes are selected from the original stem cell harvest which are lymphocyte-rich. The selected cells are cryopreserved for off-the shelf use when the patient develops CMV reactivation (figure 3).

Adoptive Cell Therapy: Future Challenges

Adoptive cell therapy has come a long way in the last 20 years, first with the recognition of the graft-versus-leukaemia (GVL) effect transferred with the donor graft to the recipient, the use of non-specific Donor Lymphocyte Infusions (DLI) for treating post-transplant leukaemia relapse, and then the development of targeted virus-specific immunotherapy. Several trials have used time-consuming laboratory expansion protocols to increase the number of antigen-specific T cells, but it is becoming increasingly clear that only small number of cells are necessary. The early post-HSCT phase offers an unique immunological environment for introducing adoptive T cells. In the profoundly lymphopenic environment which exists after HSCT, the 'vacated space' allows rapid homeostatic expansion of lymphocytes driven by cytokines.

In contrast to labour-intensive and prolonged in vitro culture of cells, the use of a small number of directly ex vivo selected antigen-specific T cells for transfer to recipient is currently the most promising strategy for adoptive cell therapy. Patients can have almost immediate access to cell therapy selection procedures which can be undertaken by routine cell therapy laboratories with experience in immunomagnetic selection. In addition to its efficacy, costs are comparable to prolonged pharmacological antiviral therapy.

Adoptive immunotherapy for CMV has served well as a model for future adoptive immunotherapy. Programmes are in progress for Epstein Barr Virus and Adenovirus infections. The future challenge will be to develop targeted cellular immunotherapy against leukaemia and other malignancies.

Figures

C MV-specific T cells expand in vivo following transfer

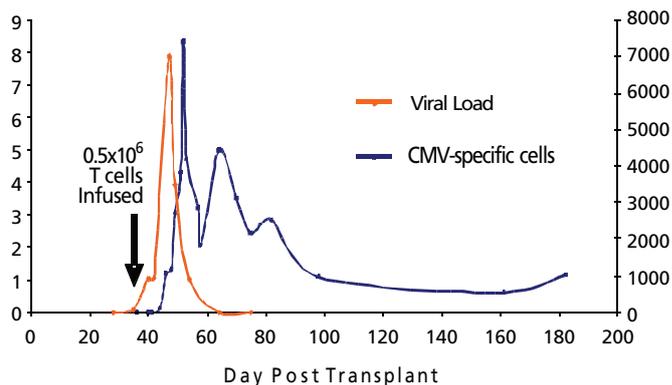


Figure 1. CTL control of CMV reactivation. The graph illustrates the post HSCT longitudinal monitoring of CMV viral load by PCR and CMV-specific CD8 T cell levels by HLA tetramers. Donor CMV-specific T cells were infused on reactivation of CMV. After a short lag phase of a week, the expansion of CMV-specific T cells takes place which leads to the resolution of the viraemia.

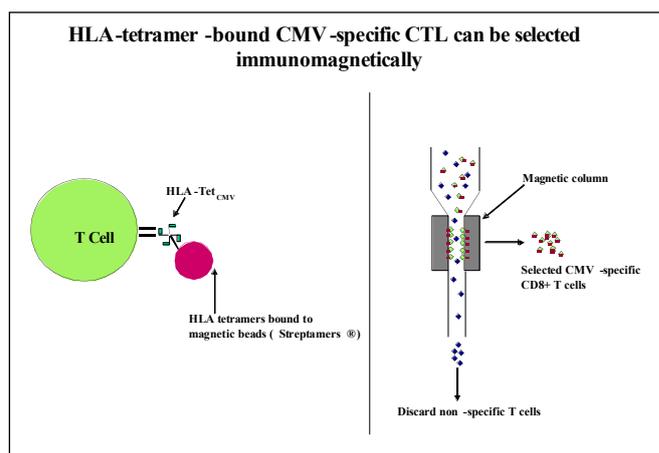


Figure 2. Immunomagnetic selection of CMV-specific CD8 T lymphocytes. Left: A streptamer, consisting of HLA tetramers directly linked to a magnetic bead, is bound to a CMV-specific CD8 T lymphocyte. Right: Following incubation with streptamers, cells are transferred to an immunomagnetic column which selects out the bound CMV-specific T cells.

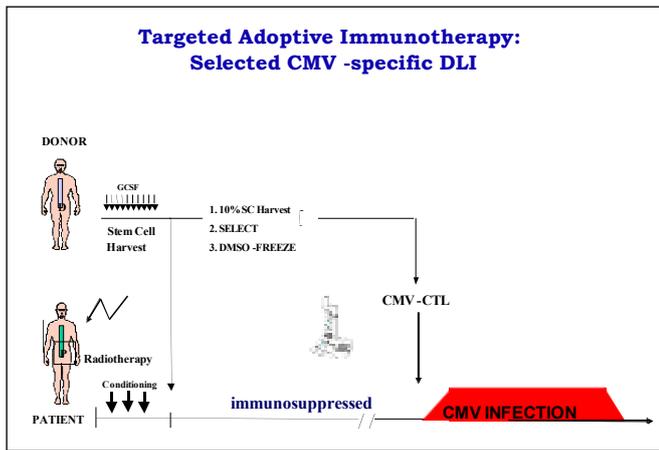


Figure 3. Adoptive CMV Immunotherapy for HSCT patients. Donor CMV-specific CD8 T cells are immunomagnetically selected using a clinical grade magnetic column (CliniMACS®) from 10% of the original donor stem cell harvest and cryopreserved. Post-HSCT, the patient is monitored weekly for CMV viraemia by quantitative PCR. When the CMV reactivates, the cryopreserved CMV-specific T cells are taken 'off the shelf', thawed and infused into the patient.

Frederick Chen

Consultant Haematologist

NHSBT Stem Cells and Immunotherapy & University Hospital Birmingham

Email: Frederick.Chen@nhsbt.nhs.uk

References

Altman, J. D. et al. Phenotypic analysis of antigen-specific T lymphocytes. *Science* 274, 94–96 (1996)

Aubert, G. et al. Cytomegalovirus-specific cellular immune responses and viremia in recipients of allogeneic stem cell transplants. *J. Infect. Dis.* 184, 955–963 (2001).

Riddell, S. R. et al. Restoration of viral immunity in immunodeficient humans by the adoptive transfer of T cell clones. *Science* 257, 238–241 (1992).

Cobbold, M., N. Khan, et al. Adoptive transfer of cytomegalovirus-specific CTL to stem cell transplant patients after selection by HLA-peptide tetramers. *J Exp Med* 202(3): 379-86 (2005).

Paul Moss and Alan Rickinson, Cellular Immunotherapy for viral infection after HSC transplantation. *Nature Reviews Immunology* 5, 9-20 (2005)

Quality and Safety in Tissue Banks

Although a rare occurrence, diseases have been transmitted to patients through the transplantation of human tissue allograft. Not only can infections be due to unrecognised problems in the donor, but it may arise from contamination acquired during recovery and processing. These risks remain, even when there are formal surveillance protocols, for a number of reasons including, the limits of testing sensitivity, some tissues cannot receive strong disinfection or sterilisation without damage to structure and/or biological properties and also because human errors cannot be entirely avoided.

There are basic preventative rules which are the key to minimise risk which are listed below:

- Strict donor evaluation and screening;
- Absolute avoidance of monetary incentives to donation;
- Consistent donor physical examination and laboratory testing;
- Standard operating processes specifically designed to prevent contamination both during removal and processing;
- Tissue disinfection, decontamination and sterilisations procedures used whenever possible.

Many countries and international bodies have produced guidelines or rules for tissue processing and/or banking operators in order to ensure the quality and safety of the products. Some are statutory rules like an EU Directive and some are recommendations such as the WHO Aide-Mémoire.

Many countries particularly in the European Community have begun to organise surveillance programs to detect and communicate unexpected adverse reactions and events. These kinds of vigilance systems are key to detecting potential complications in allograft recipients as soon as they arise in order to prevent other recipients of tissues or cells from the same donor or same processing batch being affected. This can be prevented by quarantining or recalls of issued tissues and to develop other or additional preventative measures if needed.

There are no specific binding rules in the Latin American countries regarding basic preventative measures to ensure the quality and safety of tissues and similarly, no biovigilance systems have been set up in the region yet.

The Donation and Transplantation Council/Network of Latin-American Countries recently produced and approved an essential recommendation containing guidelines to ensure quality and safety of tissues and cells.

The guidelines were produced after a careful review of existing standards and/or requirements in various countries (Canada, USA, Australia), the EU Directive, the Council of Europe's Guide for Safety and Quality for the Transplantation of Tissues and Organs World Health Organisations Aide Mémoire.

Guidelines applying to tissues and cells contain basic statements in relation to the following points:

- 1 Altruistic donation;
- 2 Confidentiality of donors;
- 3 The need to control promotion and publicity relating to donation;
- 4 Requirements for deceased donation;
- 5 Requirements for living donation;
- 6 Requirements for autologous donation;
- 7 Minimum donor screening requirements;
- 8 Need for official authorisation/certification by the Competent Authority or other regulator to carry out tissue retrieval, processing and banking;
- 9 Minimum requirements and conditions for tissue labelling, coding, storage and distribution;
- 10 The need for systems to ensure traceability and to facilitate biovigilance.

The principles included in guidelines need to be implemented in the near future.

We shall see how step-by-step legal and organisational frameworks are being modified or amended in order to include adopted standards for safety and quality of tissues and cells.

Training Programs

Training is of utmost importance to ensure that quality standards and requirements, guidelines or binding statements are adequately applied to actual practice and that there is proper implementation.

The first international organisation that took the initiative to begin training programs specifically dedicated to tissue banking was the International Atomic Energy Agency.

The program originated in the 1970's when it was resolved that there were advantages in the use of ionizing radiation to sterilise human and animal tissue. The IAEA programme for the promotion and development of tissue banking began in the mid-1980's and includes both tissue facility infrastructure development and also training programs. In the Latin-American region IAEA has supported the formation of seven tissue banks and trained 66 tissue bank operators including in Argentina, Brazil, Chile, Cuba, México, Peru

and Uruguay which all benefited from such programmes.

One of the priorities and objectives of the Latin-American Transplant Network is the development of training programmes. The network set up the so called "Alliance Programme" in 2005. For two months each year the Spanish organ and tissue procurement units open to receive Latin-American professionals. Between 40 and 50 medical doctors or senior nurses come every year. Besides their stay in the unit they have specific face-to-face training courses focussing on the process of organ donation, evaluation and retrieval as well as the family approach for donation.

Up to now 134 health professionals have been trained. For the first time in 2007 we hosted two attendees who were appointed to a tissue unit which was a new pilot experience in the programme offered to professionals from South America. In 2008, seven of the 41 attendees were tissue banking professionals employed by tissue banks. They attended the general courses, were taught in tissue establishments and received specific face-to-face courses in Quality management as applied to tissue procurement, processing and banking. The 2009 edition is also open to receive people specifically interested in the tissue activities training programme.

The course that we offered on Quality Management became a European Project called European Quality System for Tissue Banking.

Besides the Spanish and European editions of the training where we already had some Latin-American attendees, we have also established three Latin-American face-to-face courses, two in Brazil and one in Argentina which were developed specifically for Latin-American professionals

The topics addressed in these training courses are summarised as follows:

- Donor screening;
- Tissue transmissible diseases;
- Quality management and control;
- Risk assessment;
- Adverse events and reactions;
- Good tissue and manufacturing practices: Operational conditions design, planning and maintenance of tissue facilities;
- Biovigilance and recalls;
- Validation and qualification.

The courses also include practical exercises in tissue retrieval and processing using pig tissues in an animal laboratory facility.

Conclusions

- Training programmes need to be continued in South America;
- Problems such as absence of an adverse event reporting system, large numbers of small and uncontrolled banks, inadequate tracking process, and uncontrolled tissue import need to be addressed;
- Organisational efforts should be promoted in to improve tissue procurement and registries of both accredited tissue establishments and their activities.

Author: Blanca Miranda

Director of Transplant Services Foundation and Transplant Co-ordination

This follows on from the author's article in the previous edition.

Email: BMIRANDA@clinic.ub.es

References

- Newsletter Transplant. Council of Europe. International Figures on Donation and Transplantation. Vol 14 n°1 Sept. 2009
- Eastlund T, Smoug DM: Infectious Disease transmission through tissue Transplantantion Advances in Tissue Banking vol. 7 Singapore scientific publishing Co. 2003-51-131
- Aide-mémoire or key safety requirements for essential minimally processed human cells and tissues for transplantation. WHO: www.who.int/programmes
- Recomendacion REC-RCIDT-2007 (7) sobre guías de calidad y seguridad de células y tejidos humanos para trasplante Red/Consejo Iberoamericano de donación y trasplante- Newsletter II n° 1 oct. 2008 ONT website
- IAEA web site: www.iaea.org
- Kaminsky A, Uhrynowska I, Miranda. B. Navarro A, Manyalich M: Design and validation of a training model for tissue bank personel as the result of the European Quality System for Tissue Banking. Transpl.Poc. 2007:39.2698-2700.

Sir Magdi Yacoub – A Pioneer in Tissue Banking



Magdi Yacoub is world renowned for his work in heart transplantation, but is less well known, except in cardiac circles, for his innovations in heart valve banking, where he has been a pioneer for over 40 years.

Magdi Yacoub was born in Egypt and studied at Cairo University where he qualified as a doctor in 1957. His father, two of his uncles and his elder brother were also doctors: the latter died from a subdural haematoma and became a multi-organ donor giving Magdi a close insight as well into the donor relative's perspective on organ donation. Carrying on the family tradition, his younger daughter is also a doctor specialising in tropical medicine, whilst his elder daughter runs Chain of Hope, a charity Magdi set up to offer paediatric cardiac surgery to patients from the less developed countries, performed either in their own country or in the United Kingdom. As Magdi married a nurse the odd man out in the family is his 747 pilot son. His aunt's death from mitral stenosis gave Magdi the idea of becoming a cardiac surgeon. He moved to the United Kingdom in 1962 and was the Senior Surgical Registrar at the National Heart and Chest Hospitals from 1964-1968. He worked with Donald Ross, who was the first person to implant a cardiac valve

allograft in 1962, who went on to develop the use of pulmonary and mitral homografts and after whom the pulmonary autograft operation is now named. At this time cardiac allografts were sterilised with ethylene oxide and stored freeze dried or with radiation and freezing at -70°C , but both of these methods caused harmful effects on the tensile strength and geometry of the valves, while rendering them non-viable, so surgeons were on the look out for improved methods. When Magdi became Instructor and Assistant Professor of Cardiac Surgery at the University of Chicago in 1969 he worked with Frederick Kittle and they developed an antibiotic formulation consisting of cephaloridine, neomycin and amphotericin B which disinfected 97% of the valves whilst retaining the physical properties of the valve.

On Magdi's return to Britain he became Consultant Cardiothoracic Surgeon at both the National Heart Hospital and Harefield Hospital and at the latter he set up a Heart Valve Bank which was to function until Magdi's retirement from the National Health Service and the merger of Harefield with Royal Brompton Hospital to found a combined Trust. Magdi's belief is that heart valves for transplantation should have the minimum amount of treatment as possible and he was always a proponent of low level antibiotics and no additional storage methods such as addition of DMSO and cryopreservation. From the early 1980's he pioneered the use of "homovital" valves which were harvested under

sterile conditions from cardiac transplant recipients or brain dead multiorgan donors (where the heart itself was unsuitable for transplantation). The valves on removal were immediately placed in tissue culture medium containing extremely small doses of penicillin and streptomycin and kept at 4°C and used at the first opportunity which varied from two hours to 60 days with 95% implanted within three days. Magdi was able to access these valves effectively as he is reputed to have performed more heart transplant operations worldwide than any other surgeon. He advocated the use of domino transplants, in which the heart from the patient who receives a heart and lung transplant is used as a cardiac transplant, while the heart removed from the latter patient has the valves dissected for use as allografts. Prof Yacoub has shown in several papers that these "homovital" valves have outperformed valves that have had normal level antibiotic disinfection and either stored at 4°C or cryopreserved.

During his operating career, Magdi performed over 20,000 open heart operations of which over 1,500 were heart transplants. He cannot remember how many valve allografts he has used but the number is likely to be similar to the number of transplants performed, encompassing recipients from a few hours to the mid eighties. The Heart Valve Bank at Harefield processed over 5,000 valves and these valves were not only used at that hospital but by numerous other surgeons in hospitals both in United Kingdom and in all the continents (except Antarctica) of the world.

For the last twenty years, Magdi's research interests in heart valves (rather than transplants) have centred on the immunogenicity of valves and the use of decellularised valves and the use of constructs as substitutes for valves. Magdi and his co-workers showed in 1995 that all allografts stimulate a strong donor HLA specific antibody response and there was a higher level with the homovital valves than with the cryopreserved valves. The immunogenicity is mediated mainly by the endothelial cells and it is known that these are the cells most prone to be lost during processing and the donor's endothelial cells are rarely found if an allograft has to be removed from three weeks after surgery onwards. His co-workers at the Magdi Yacoub Institute, a Research foundation that he has set up at Harefield Hospital are looking at making valve cusps from biological matrices and then overlaying these with the recipient's own cells. They are also considering the use of decellularised xenografts as another possible substrate for overlaying recipient cells.

Even though Magdi at 74 is no longer regularly operating, he spends a tremendous amount of time at conferences worldwide both on transplantation and valvular cardiac surgery as well as taking an active role in the Royal Society where he is one of the few surgeons nowadays who are Fellows of that institution. Hopefully he also has time for his other passion in life – orchids, on which he is one of the most knowledgeable amateurs in the country and plants from his collection have adorned many a conference at Harefield Hospital.

Robert Parker

Heart Valve Bank Manager

Royal Brompton & Harefield NHS Foundation Trust

Email: R.Parker@rbht.nhs.uk

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 31 will feature articles on:

- Rudolph Klem (Czech Pioneer in Tissue Banking)
- Part 2 of Immunology for Dummies – Immune Responses to Transfusion and Transplantation
 - Antibody Production for Diagnosis and Therapy
 - Pathogen Inactivation/Reduction
 - Nurse Prescribing of Blood
 - Online Blood Ordering System (OBOS)
- The Transfusion Support of Stem Cell Transplant Patients
 - Where is the Red Book Going in the Future?

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

SHOT

1. In 2008, the number of adverse incidents reported to SHOT:

- A. Almost halved.
- B. Almost doubled.
- C. Almost trebled.
- D. Was almost static.

2. In 2008 only:

- A. 40%.
- B. 80%.
- C. 60%.
- D. 50%.

Of questionnaires had all relevant sections completed.

The Transfusion Evidence Library

3. The Transfusion Evidence Library holds:

- A. 430.
- B. 300.
- C. 240.
- D. 130.

Systematic reviews and economic evaluations.

4. Systematic Reviews:

- A. Present the most popular result or conclusion.
- B. Calculate the mean, median and mode of all trials.
- C. Identify, evaluate and summarise data from all relevant clinical trials according to strict methodological criteria.
- D. Identify the largest trials available.

5. To obtain all high-quality systematic reviews relevant to transfusion medicine, it is necessary to search:

- A. The Cochrane Library only.
- B. NHS Evidence only.
- C. EMBASE only.
- D. Transfusion Evidence Library only.

6. The Transfusion Evidence Library can be found:

- A. In the High Street.
- B. At <http://www.transfusionguidelines.org.uk>.
- C. Only after applying to DoH for a subscription.
- D. Only at NHS Direct.

National Comparative Audit

7. When patient documentation was available, it was not used to check against patient details in:

- A. 7.1%.
 - B. 0%.
 - C. 3.7%.
 - D. 2.6%.
- Of collections.

8. In what percentage of cases was there a risk of the wrong unit of blood collected?

- A. 10%.
- B. 12%.
- C. 14%.
- D. 16%.

Immunology for Dummies

9. Invertebrates:

- A. Utilise phagocytic cells in the immune system.
- B. Utilise complement-like components in the immune system.
- C. Have no immune system.
- D. Utilise adaptive immunity.

10. Innate immunity is:

- A. Very fast acting.
- B. Specific.
- C. Reliant upon antibodies.
- D. Not found in mammals.

11. The adaptive immune response to bacteria is acquired in the following stages:

- A. Recognition and opsonisation of antigenic cells, production of inflammatory mediators and lysis of target cells.
- B. Antigen processing and presentation by dendritic cell, T helper cell activation and proliferation, B cell activation, proliferation and antibody secretion.
- C. Activation of alternative pathway, activation of lectin pathway, release of histamine.
- D. Sensitisation of extra cellular granules, release histamine in response to anaphylatoxins, phagocytosis.

12. About 300 variable (V), diversity (D) of joining (J) gene segments of T cell receptor (TCR) and immunoglobulin (Ig) genes recombine randomly:

- A. To form 10^{16} TCR and 10^{11} Ig genes.
- B. Enabling survival of all naive T and B cells.
- C. Enabling each lymphocyte to carry a TCR or BCR.
- D. To form 10^8 VDJ and VJ genes.

13. Cluster of Differentiation (CD):

- A. Arises from maturation of Dendritic Cells (DC).
- B. Classifies cytogenes.
- C. Cause lymphocytes to apoptose.
- D. There are more than 350 CD markers identified.

Cytomegalovirus (CMV) infection in Stem Cell Transplantation

14. Current therapeutic strategies to prevent and reduce cytomegalovirus:

- A. Matching CMV seronegative patients with CMV seropositive donors.
- B. Use CMV untested blood products, as most donors are CMV negative.
- C. Matching CMV seronegative patients with CMV seronegative donors.
- D. Use reduced intensity conditioning with removal of alloreactive T cells.

15. Sir Magdi Yacoub:

- A. Has performed over 20,000 open heart operations.
- B. Was the first person to implant a cardiac valve allograft.
- C. Has performed 1,000 heart transplants.
- D. Has an orchid named after him.

Diary Dates

2010

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
Anemia Effects and Management

Fluid Therapy/Oxygen Carriers

Haemostasis and Thrombosis

Abstract Submission Deadline: 1st December 2009

12 April/6 May/7 May/18 May/26 May 2010

Managing the Nation's Blood Supply.

Location: Various Venues around the UK

The Blood Stocks Management Scheme have organised five regional road shows at various venues in England. Registration for these events is now open.

For more information contact: bsms@nhsbt.nhs.uk or

<http://www.bloodstocks.co.uk>

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

BBTS Hot SiG Meeting.

Location: Austin Court, Kingston Theatre, Birmingham City Centre, UK

Details:

Transfusion issues in haemoglobinopathies – the clinical and laboratory challenges.

For more information contact:

<http://www.eventsforce.net/hot10>.

14-15 May 2010

ASH.

Rio de Janeiro, Brazil

Highlights of ASH in Latin America

For more information contact:

<http://www.hematology.org>

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>

16-17 June 2010

WMDA – 8th International Donor Registry Conference.

Trinity College, Dublin

For more information contact:

<http://www.wmdadublin2010.com>

26 June - 1 July 2010

31st Annual Congress, International Society of Blood Transfusion.

International Congress Centre, Berlin, Germany

For more information contact:

<http://www.isbt-web.org/berlin>

.....

10 July 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.

Location: Bournemouth International Centre, UK

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

or <http://www.eventsforce.net/asm10>

.....

29 September - 1 October 2010

21st Annual Conference: British Society for Histocompatibility and Immunogenetics.

The Royal College of Physicians of Edinburgh

For more information contact:

<http://www.bshi2010.org.uk>

.....

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.

.....

9-12 October 2010

AABB – Annual Meeting & CTTXPO.

Location: 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 register online

go to: <http://www.kenes.com/ISH2010>

.....

4-7 December 2010

ASH – 52nd Annual Meeting and Exposition.

Orange Country Convention Center, Orlando, FL, USA

For more information contact:

<http://www.hematology.org>

.....

6-10 December 2010

BSI Congress 2010.

Arena & Convention Centre, Liverpool

For more information contact:

<http://www.immunology.org/congress2010>

.....

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

ANNUAL SHOT SYMPOSIUM

TUESDAY 6TH JULY 2010

THE LOWRY, MANCHESTER

Guest Speaker :

Professor Mark Popovsky

Clinical Professor of Laboratory Medicine Boston University Medical School
Associate Clinical Professor of Pathology Harvard Medical School and Beth Israel deaconess Medical Center Boston

"Pulmonary complications of Transfusion"

The Symposium will be introduced by:

Professor René de Vries

President of the International Haemovigilance Network

CALL FOR POSTER ABSTRACTS

Please submit abstracts on Haemovigilance of no more than 500 words by 23rd April 2009 to shot@nhsbt.nhs.uk

2009 SHOT data

State of the art talks

Poster competition

Commercial exhibition

Registration fee £25

Please contact the SHOT

office and book now

Tel No: 0161 4234208

Blood and Transplant Matters is prepared and issued by NHS Blood and Transplant, Oak House, Reeds Crescent, Watford, Herts WD24 4QN (Telephone 0117 921 7414)

Editorial Board:

Derwood Pamphilon, *Consultant Haematologist, (Editor)*,
NHS Blood and Transplant, Filton Centre, Bristol.
Email: derwood.pamphilon@nhsbt.nhs.uk

Carol Griffin, *Senior PA, (Editorial Assistant)*,
NHS Blood and Transplant, Filton Centre, Bristol.
Email: carol.griffin@nhsbt.nhs.uk

Catherine Howell, *Chief Nurse Patient Services*,
NHS Blood and Transplant, Oxford.
Email: catherine.howell@nhsbt.nhs.uk

Derek Norfolk, *Consultant Haematologist*,
NHS Blood and Transplant, Leeds.
Email: derek.norfolk@nhsbt.nhs.uk

Penny Richardson, *Media and PR Manager (North)*,
NHS Blood and Transplant, Liverpool.
Email: penny.richardson@nhsbt.nhs.uk

Clare Taylor, *Consultant Haematologist and Medical Director of SHOT*,
NHS Blood and Transplant, Colindale, London.
Email: clare.taylor@nhsbt.nhs.uk

Ruth Warwick, *Consultant Specialist for Tissue Services*,
NHS Blood and Transplant, Colindale, London.
Email: ruth.warwick@nhsbt.nhs.uk

Rob Webster, *Consultant Haematologist*,
NHS Blood and Transplant, Sheffield.
Email: rob.webster@nhsbt.nhs.uk