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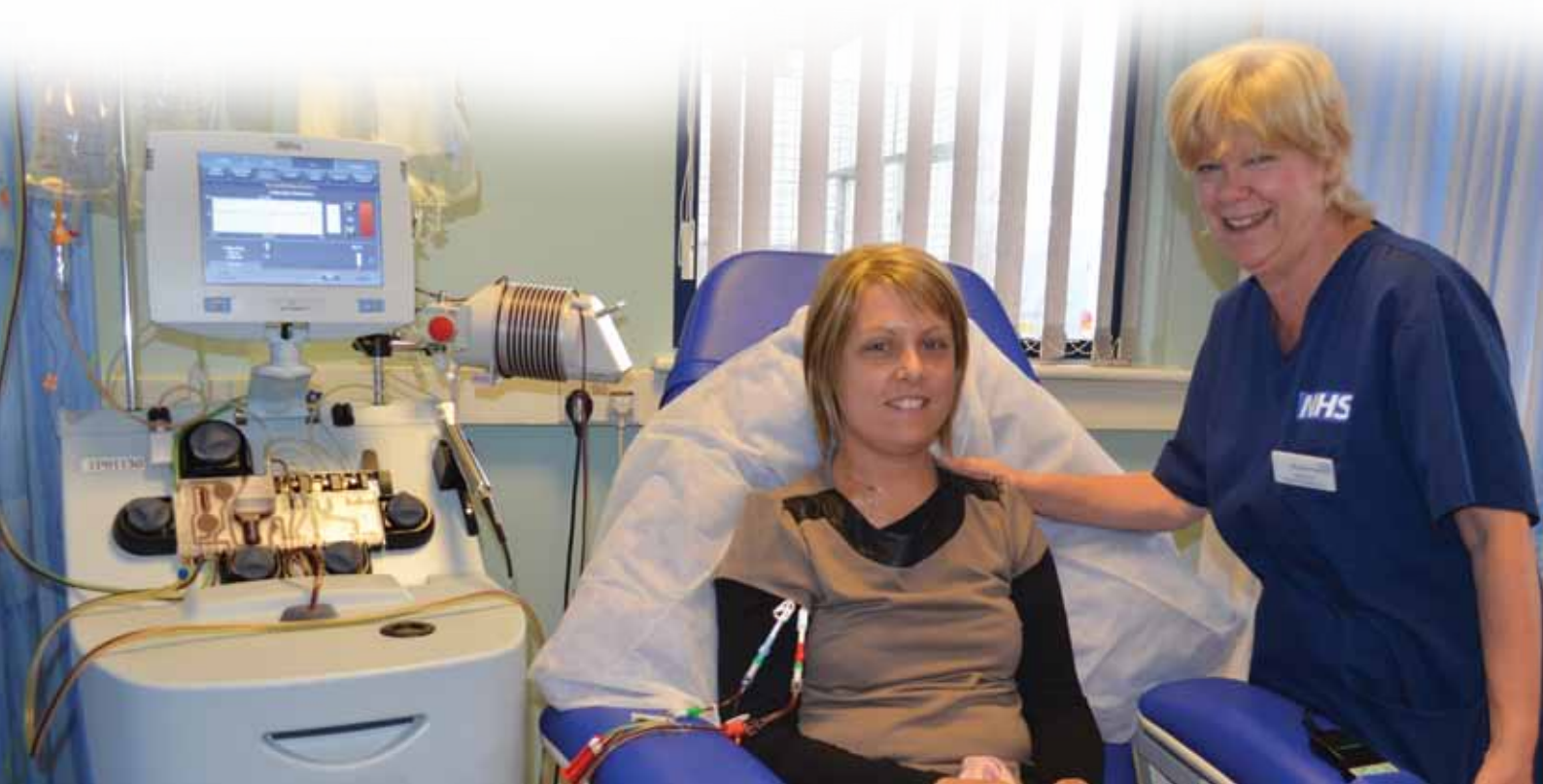
NHS Blood and Transplant

# Blood and Transplant Matters

Information for hospitals served by NHS Blood and Transplant

## Inside





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# Next Edition

**Issue 40 will feature articles on:**

- Photopheresis ECP
- Clinical Studies Unit
- Living Donor Kidney Transplantation: Building the Future
- Tissue Engineering Products for Airways Regeneration: Production, Safety and Ethical Issues

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

# EDITORIAL

Welcome to the latest edition of *Blood and Transplant Matters*, the eagle eyed among the readership may have noticed a change in the Editorial Board; Carol Griffin has passed on the mantle of Editorial Assistant to Lynne Hodkin. Carol has worked hard over the last four years and survived a change in Editor only last year. However, due to her work commitments she has reluctantly had to hand over this particular job. The entire Editorial Board, and myself in particular, thank her for her hard work and welcome Lynne Hodkin as the new Editorial Assistant. As always, the excellent parts are due to the authors and the rest of the Editorial Board, but any mistakes are entirely mine.

In this edition, Dr Gail Miflin and Dr Lizanne Page report on a new initiative that not only will help improve the blood supply but will also help a certain group of patients in a novel way. Denise Watson looks at some of the issues surrounding Implementing Nurse Authorisation of Blood Components. Next, we take a look at use of red cells and in particular, Dr Shubba Allard discusses the challenges and advances for Haemoglobinopathy patients and Jennifer Heyes reports on red cell alloimmunisation in patients transfused for trauma. Communications in the 21st Century is the next topic covered by Léonie Austin – even I use a 'smart' phone although according to my children not in a very smart way! Following on 21st Century Communication is the story of how Wendy McSporran and Dr Lise Estcourt developed an app to aide the better use of platelets. The use of which may encourage more novel ways of providing transfusion education, as there is large variation in that provision as reported by Kairen Coffey.

All now perform some audit, so it was interesting to read of Samantha Knight's day as a Senior Clinical Audit Facilitator. It is no doubt that Stem Cells are a therapeutic agent. Davina Potok, Dr I Jun-Lau, Dr Sylvia Benjamin and Sophie Clarke despite the introduction of a new machine that collects Stem Cells from peripheral blood.

Chronic lower limb ulceration is a major problem in the NHS and Dr Richard Lomas and Dr Akila Chandrasekar report on work that has produced a promising novel treatment and demonstrate an improvement in the quality of life for such patients.

Daniel Hollyman outlines the role NHS Blood and Transplant has in cellular and molecular therapies and looks to future possible roles.

Finally, I hope the regular CPD and Clinical Cases sections provide some amusement and possible education. Even if the red cell panel results are not routine practice. Please have a go at interpretation – one or two are very straightforward.

Any comments can be sent to blood&transplantmatters@nhsbt.nhs.uk.

We have had queries regarding both distribution of hard copies and use of the postal system. Those willing to accept electronic versions only can inform us by emailing blood&transplantmatters@nhsbt.nhs.uk, your name will then be removed from the 'mailing list'.

However, as to using internal mail or other means of delivery of a hard copy the cost of actually separating those that can only be sent by the postal system would offset any potential savings – but thank you again for the suggestion.

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# New NHSBT Initiative for Blood Donors with Genetic Haemochromatosis

Genetic haemochromatosis (GH) is a disorder of iron metabolism characterised by a high body iron content. Over time, iron may be deposited in tissues such as the liver, heart, endocrine organs and joints. If GH is left untreated, these organs may become damaged leading to potentially serious complications such as cirrhosis and cardiac failure. The most common treatment for GH is therapeutic venesection, which is very similar to blood donation.

Until recently donors with GH, who are well and on the maintenance phase of their treatment have been able to donate blood as regular blood donors at the maximum donation frequency of twelve weekly. Some patients, however, require therapeutic venesection more often, occasionally as frequently as every four to six weeks. Thus blood which could be used for patients has been discarded. NHSBT has acted to offer eligible GH patients an option to attend a blood donation session and thus to donate their blood which is withdrawn as part of their maintenance venesection for patient use rather than have it 'wasted'. Since 1 October 2012 NHSBT has enabled eligible donors with GH to give as frequently as six weekly and their extra donations enter the blood supply chain. This provides NHSBT with a valuable additional source of safe blood with a cost-benefit to the NHS while giving GH donors a heightened sense of contribution and satisfaction.

### *Genetic haemochromatosis*

GH is a hereditary condition with an estimated prevalence of 1:200 people of European ancestry, with lower incidence in other ethnic groups. The most common form of GH is caused by mutations in the HFE gene. It is the commonest autosomal recessive condition in the UK in Caucasians. The protein of the HFE gene regulates the interaction of the transferrin receptor and transferrin in the gastro-intestinal tract and consequently regulates iron absorption. A mutated gene results in dysregulation of this process and inappropriate iron absorption.

The clinical picture for GH is variable, however in the more moderate to severe phenotypes it results in an iron overload condition in which there is increased absorption of iron from a normal diet, resulting in entry of iron into the blood stream in excess of that required for erythropoeisis. This excess iron may be deposited in many tissues particularly the liver, heart, endocrine organs and joints. Untreated, the accumulation of tissue iron can cause pathological changes of tissue structure and function such as cirrhosis, cardiomyopathy, endocrine dysfunction such as diabetes and, in later stages, hepatocellular carcinoma.

### *Therapeutic venesection*

The standard treatment for GH is regular therapeutic venesection which involves the removal of blood in a similar way to how a donor gives a unit of blood. The frequency of venesection is determined by a variety of factors, including the total iron burden and the ability of the patient to tolerate venesection. Typically, the venesections may initially be as often as weekly, resulting in iron depletion. Once targeted iron levels are reached, the frequency changes to a 'maintenance regimen' aiming to keep the iron levels below this target. Maintenance venesection frequency is variable, but is usually around every twelve weeks, however in some patients this may be required as often as every four to six weeks. Historically patients requiring maintenance venesection more often than twelve weekly have found it difficult to donate blood and have tended to continue to have venesections done in hospitals. Blood collected through therapeutic venesection in a hospital setting is discarded as it has not been collected according to the regulatory, quality and safety standards required for patient use.

### *Is blood from HC patients safe for patient use?*

There is no evidence that the blood of asymptomatic individuals with GH poses a risk for the health of recipients. Surveys show that a large percentage of the people diagnosed with GH already served as blood donors before they were informed of their condition. The use of blood collected from GH patients has been controversial because of the non-voluntary character of the donation. Altruism is implicit in every blood donation and there have been concerns that GH donors would benefit from their donation. However Pennings (2005) proposes that the health benefits are connected to the phlebotomy and not to the donation and concludes that, although GH patients have a need for phlebotomy, they are free to decide what should be done with the blood.

With respect to blood safety, there is no evidence to suggest that blood from uncomplicated GH donor-patients carry more risks for transfusion recipients than blood from other donors. It has been speculated that since incidence of infections caused by *Yersinia enterociltica* and *Vibrio vulnificus* is higher in patients with iron overload there might be a higher incidence of bacteraemia in these donors. However, studies by Jolivet-Gougeon *et al* (2007) show no evidence to support this view. Leon de Gonzalez (2007) reported that there is also no evidence of adverse quantitative or qualitative changes in the erythrocytes or plasma of patients with uncomplicated GH.

### *Blood donation*

The majority of patients with GH do not require a formal venesection programme, however those who are well, have no tissue damage and who require no treatment other than maintenance venesection, may now donate at up to six weekly intervals as advised by their consultant if this would be beneficial to them. Donors with GH who wish to remain donating at twelve weekly intervals will continue to donate as regular blood donors irrespective of whether they require venesection for therapeutic purposes. GH Donors who wish to donate more frequently will need to make special arrangements for their appointments, this is because the NHSBT computer system is set to ensure that we do not collect donations more than every twelve weeks from regular donors. Donors are advised to discuss how frequently they should donate with their hospital Consultant. NHSBT works with hospital Consultants to ensure that such donors will be advised how often they should donate, and to ensure that their Consultant continues to monitor and advise on their condition including donation frequency. Donors are advised that NHSBT collects blood from donors for the benefit of patients and not as a form of treatment. The health of every blood donor is assessed every time they attend; if a donor with GH is unable to donate, for another reason, then they are advised to inform their Consultant in case venesection in hospital is required.

NHSBT is delighted that we are now able to collect more blood from patients with GH and would like to thank the Haemochromatosis Society for helping us achieve this.

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## Implementing Nurse Authorisation of Blood Components

The Medicines and Human Use (Prescribing) (Miscellaneous Amendments) Order of May 2006 and associated medicines regulations enabled nurses who have successfully completed a nurse independent prescribing course to prescribe any licensed medicine, for any medical condition within their clinical competence.

In 2008, a collaborative project was undertaken by NHS Blood and Transplant (NHSBT) and the Scottish National Blood Transfusion Service (SNBTS) to investigate if it would be feasible for nurses and midwives to 'prescribe' blood components. The project found that Section 130 of the 1968 Medicines Act had been amended by Section 25 of the Blood Safety and Quality Regulations 2005 (Statutory Instruments 2005). In effect, this meant that blood components are excluded from the legal definition of medicinal products and therefore, can not be 'prescribed' by any practitioner. The term 'authorisation' was adopted as an alternative and it was established that there is no legal barrier to nurses authorising a blood transfusion.

Following wide consultation, 'A Framework to Support Nurses and Midwives Making the Clinical Decision and Providing the Written Instruction for Blood Component Transfusion' was produced to support development of this role. This document provides clear guidance for suitably experienced qualified nurses and midwives who wish to extend their role to include making the clinical decision for blood component transfusion and providing the written instruction in a safe and appropriate manner (Green and Pirie, 2009).

It is the responsibility of individual Trusts or hospitals to implement non-medical authorisation of blood components as part of their service improvement plans. However the NHSBT Customer Services Patient Blood Management (PBM) Team are able to offer support to hospitals in England and North Wales with this initiative. A variety of tools and templates are available from the PBM team to assist Trusts in developing local policies, education packages and assessment tools to enable nurses and midwives to authorise blood components competently.

In March 2011, the North East (NE) of England Regional Transfusion Committee (RTC) approved regional guidelines to allow specific Haematology/Oncology nurses to authorise red cells and/or platelets. Trusts then decided if they wanted to incorporate these guidelines into their own local Trust policies. It is important that Trusts have a policy for nurse authorisation of blood components which states which practitioners can authorise a blood component, the patient criteria that needs to be met, which blood components are covered eg red cells, platelets, Fresh Frozen Plasma and the training/level of experience required by the practitioner.

To support Trusts implement nurse authorisation in the NE of England region a small sub-group of the RTC was formed to facilitate a number of one day educational events in May, September and November 2011. Due to the success of these events the NE RTC supported an additional two day event specifically for Intensive Therapy Unit Advanced Nurse Practitioners in 2012. For further information on courses available see: http://www.transfusionguidelines.org.uk/Index.aspx?Publication=RTC&Section=28&pageid=1169

In March 2012, NHSBT piloted a four day training course aimed at senior nurses and midwives who are working towards making the clinical decision and providing the written instruction for blood component transfusion. The pilot course was run at the NHSBT Blood Centre in Manchester and delivered the core theoretical knowledge required for this role to staff attending. Candidates then returned to their practice in the clinical area under the guidance of a clinical mentor, completing a portfolio of evidence to support their application for endorsement by their Trust. Due to its success the course was repeated in November 2012 and made available to all staff within England and North Wales. A further course is already planned for March 2013 and the intention is to run it regularly each year. The NHSBT course was shortlisted as one of the finalists in the Training Journal Awards 2012, which promotes excellence, best practice and innovation in Training and Learning & Development. For further information on the course available see: http://hospital.blood.co.uk/training/programmes/programme_diary/

Although the NE and the NHSBT events are different in the content/length of course they do have the following in common:

- Delegate numbers kept to a maximum of 16
- Delegates are up-to-date with transfusion training and competencies within their Trust
- Delegates are in a role/area of clinical practice where making the clinical decision to transfuse and authorise a blood component is relevant
- Delegates have identified a clinical mentor to support the learning in practice
- Delegates have support from the Trust to undertake the course.

A short survey was carried out in February 2012 to assess nurse authorisation in practice in the NE of England. Of the 28 delegates surveyed 16 responses were received and found that six of the seven practitioners who were either fully competent or authorising with supervision attended the first event in May. The survey found that in order for nurse authorisation to be embedded into healthcare practice a period of time is required to allow the practitioners an opportunity to authorise blood components under supervision and to complete their competency assessments within their Trust.

The reasons why nurse authorisation had not been implemented in some hospitals was due to local policy still to be amended or agreed, priority of other practitioners needing to authorise, workload and staff shortages, meaning practitioners were unable to spend time with their clinical supervisor/mentor. In only one case had the practitioner changed job role/employer.

The survey also found that nurse authorisation of blood components has reduced the unnecessary waiting time for patients and provided an opportunity for practitioners to better manage their patients and provide a more holistic approach.

Authorisation of blood components by practitioners should be reviewed by individual Trust Transfusion Committees through audit of compliance; any non-compliance by the practitioner should be dealt with as per local Trust policy.

It is the responsibility of the authorising practitioner to ensure that their skills and competence are maintained in order for them to correctly authorise blood components. It is recommended that their skills and competence should be reviewed during their Personal Development Review.

This extended role may seem quite daunting to some, but the educational events, support from the clinical mentor and guidance from the Trust provides an environment whereby practitioners can embed nurse authorisation into their every day clinical practice and be a great benefit to patient care.

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## The Provision of Blood for Patients with Haemoglobinopathy – Challenges and Advances

### *Introduction*

Regular blood transfusions are a mainstay of therapy for many patients with haemoglobinopathy. Patients with 'thalassaemia major' syndromes are dependent on monthly red cell transfusion whereas patients with 'thalassaemia intermedia' may need transfusion support on an intermittent basis. Red cell transfusion may be required in sickle cell disease (SCD) either as an emergency measure eg for acute chest crisis or on a long-term basis for the prevention or management of complications such as stroke.

There is a lack of accurate data currently in the UK on the numbers of patients with haemoglobinopathy needing regular transfusions though increasing participation in the National Haemoglobinopathy registry may help address this. It is estimated that there are approximately 800 transfusion dependent thalassaemia patients in the UK (personal communication UK Haemoglobinopathy Forum). It is also estimated that there are approximately 12,000 patients with sickle cell disease in the UK and around 10% of these require regular transfusion. There may however, be higher proportions of patients with SCD needing regular transfusions with the introduction of Doppler screening followed by transfusion regimes as stroke prophylaxis for at risk children.

### *Red cell alloimmunisation in patients with haemoglobinopathy and consequences*

There are significant differences in antigen frequencies between donors and patients based on ethnic background, which are relevant to increased rates of alloimmunisation seen particularly in SCD patients. A common Rh genotype for sickle cell patients is $R_o$ which is thought to occur in approximately 50-60%. This genotype is positive for the D antigen, but lacks C and E. In order to provide the closest match to prevent development of antibodies, whilst $R_o$ blood is preferred, Rh negative blood (rr) is often transfused.

The overall risk of alloimmunisation in patients with sickle cell disease (SCD) has been reported as high as 20-35% but with considerable variation, with some series quoting very high rates of around 50% with also development of multiple alloantibodies. In around 50-66% the specificity of alloantibodies is against Rh antigens with approx 20% against K, $Jk^a$ and $Jk^b$.

While the overall risk of alloimmunisation in patients with thalassaemia is perceived to be lower than that seen in sickle cell disease, there is considerable variation in the reported rate of antibody formation. The lowest rates (around 4%) are seen in patients starting a regular transfusion programme at a very young age but higher rates have been reported if later onset of transfusion, in the absence of policies for RBC phenotype matching and if there are differences between the donor and recipient population. Matching donor units with the patients' extended Rh (D, Cc, Ee) and K types significantly reduces the risk of alloimmunisation against these particularly antigenic blood groups.

Patients with alloantibodies are at risk of acute or delayed (5-14 days after transfusion) haemolytic reactions.

The presence of multiple and complex antibodies can result in significant delays in sourcing appropriate red cell units in patients with SCD in whom the transfusion need may be urgent. Patients may also develop concurrent antibodies against their own red cell antigens with autoimmune haemolysis or less commonly may develop hyperhaemolysis.

The UK Serious Hazards of Transfusion (SHOT) haemovigilance scheme has particularly highlighted the problem of alloimmunised patients with SCD developing acute and delayed transfusion reactions.

### *Selection of blood for patients with Haemoglobinopathy*

**Compatibility testing:** Recently updated BCSH guidelines on compatibility testing emphasise the need for using fully automated systems for ABO typing where possible to mitigate the risks of interpretation and transcription error. Antibody screening should always be performed as part of pre-transfusion testing to detect the presence of clinically significant antibodies. If an alloantibody is detected in the screening procedure, its specificity should be determined. If the patient is known to have formed a red cell alloantibody, each new sample should be fully tested to exclude the presence of further alloantibodies.

**Extended red cell genotype – serological, molecular:** The patient's red cells should be phenotyped as fully as possible prior to transfusion. If the patient has not been transfused within the preceding three months, then phenotypic testing can be undertaken serologically. Where patients have already been transfused, the genotype needs to be determined by molecular techniques. An extended phenotype (or genotype) should include C, c, E, e, K, k, $Jk^a$, $Jk^b$, $Fy^a$, $Fy^b$, MNSs. Undertaking further extended red cell typing of patients aids further serological testing in the event of antibody formation and appropriate selection of antigen negative blood.

**Blood group selection**: As a minimum, red cells should be matched for Rh (D, C, c, E, e) and K antigens. If the patient has any current or historical red cell antibodies that are clinically significant then the red cells selected should also account for those antigens. Red cells used for top up transfusion should ideally be less than 14 days old with the aim of maximizing red cell survival post transfusion. For sickle cell patients, units should be HbS negative and also the red cells used for exchange transfusion should be <seven days old. However this should be balanced against the need to provide antigen negative blood where needed in particular in patients with antibodies.

Frozen (or cryopreserved) red cells are derived by processing of whole blood within five days of collection and stored using a cryopreservant at -60°C to -80°C or below. These are important to maintain a supply of rare donor units for patients who have unusual red cell antibodies or who are missing common red cell antigens.

### *New advances*

### *National Haemoglobinopathies Project*

This project commissioned by the Department of Health aims to improve the quality of care provision for patients with sickle cell and thalassaemia with emphasis on integrated, equitable services with networking across acute trusts and the community care setting. The first national peer review programme to quality review all providers of services for haemoglobinopathies is now underway.

### *Guidelines and Audit*

There are BCSH guidelines now in preparation for transfusion in haemoglobinopathy. A National Comparative Audit of transfusion in Sickle Cell Disease is currently being planned.

NHSBT has recently completed a six month retrospective review of data on phenotype and red cell antibody formation in patients transfused for haemoglobinopathy as part of a potential prion filter post marketing surveillance exercise and the results should be available soon.

### *SP-ICE*

A recent development allows hospitals to look on the NHSBT's SP-ICE national database, for previous antibody testing results on any patient currently under their care, so that hospitals have timely information on antibodies, including historical ones which should be taken into account when providing blood.

### *Red cell genotyping*

The lack of phenotypic compatibility in particular between patients with SCD and the donor pool is an important contributory factor to alloimmunisation. Currently extended phenotyping is largely undertaken on targeted donors only but large scale red cell antigen typing of donors could allow more extended matching, provided that sufficient donors of required phenotypes or genotypes are available. The use of molecular techniques and the feasibility of wider application (including high throughput testing) to improve the provision of antigen matched blood for patients with haemoglobinopathy is an important area for current and future research.

### *Red cells from stem cells – towards the 'Holy Grail' of Transfusion?*

Obtaining red blood cells from stem cells *in vitro* represents a truly exciting potential method of ensuring an adequate and safe supply of blood cell components. This is an area of active research aimed at overcoming the many challenges in

translating this potential development into clinical practice.

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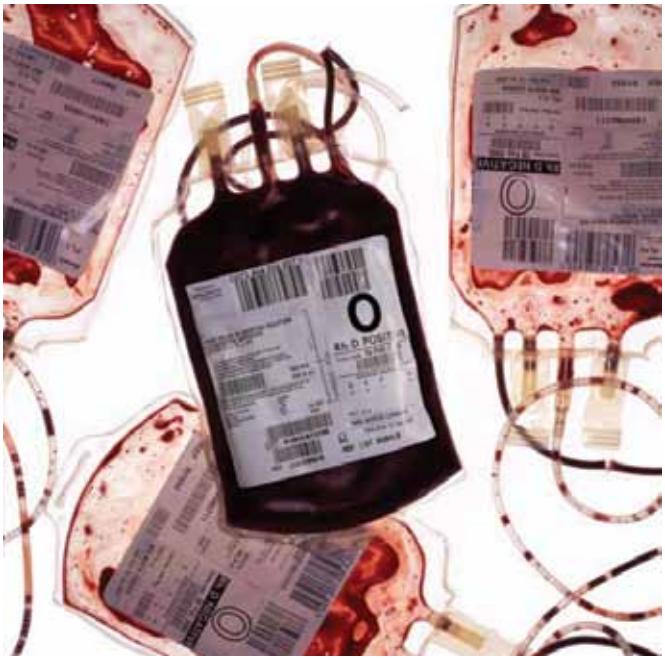
## Red Cell Alloimmunisation in Patients Transfused for Trauma

### *Aims of study*

The aim of the study was to calculate the alloimmunisation rate in patients that had received an emergency transfusion of group O red cells as treatment for trauma. All transfusion records for patients admitted into A&E as a trauma between January 2005 and December 2009 were reviewed. Trauma patients that received uncrossmatched emergency red cells were included. In addition to the overall immunisation rate, the study also aimed to determine the alloimmunisation rate in RhD negative patients who were transfused O RhD positive blood.

### *Background*

The production of red cell antibodies post transfusion is a risk associated with the transfusion of all red cells. The rate of immunisation can vary depending on diagnosis with an average reported of 2-3%. This rate increases with



the number of transfusion events the patient is subject to. There is, however, very little published data in the trauma setting. The rate of anti-D production in healthy RhD negative volunteers injected with RhD positive blood has been reported as high as 80% although in small subsequent studies in patient groups the rate has been reported as low as 20%. The development of red cell antibodies can lead to haemolytic transfusion reactions in subsequent transfusions or haemolytic disease of the foetus and newborn in women of childbearing age.

Massive haemorrhage accounts for approximately 40% of deaths from trauma and is an important cause of preventable mortality. The immediate administration of red cells is recommended for the treatment of massive haemorrhage caused by trauma and due to the severity of the injuries, trauma patients presenting with massive haemorrhage often require emergency blood transfusion with Group O (HT-, K-) red cells before the blood group of the patient is established. At the Royal London, male trauma patients whose blood group is unknown are transfused RhD positive red cells in order to preserve O RhD negative red cells for women of childbearing age in whom the development of anti-D may cause haemolytic disease of the foetus and newborn during pregnancy. It is normal practice in transfusion medicine to issue RhD matched red cells to prevent sensitisation and for this reason the majority (82% in one study) of RhD positive red cells issued to RhD negative patients occurred in Accident and Emergency departments.

## *Method*

The blood transfusion laboratory database was used to review the data of all trauma patients that received uncrossmatched group O red cells (UORBC) on admission from January 2005 to December 2009. The number of uncrossmatched red cells infused was recorded along with the patient's age, sex, blood group, pre and post transfusion antibody screen and patient outcome.

## *Results*

In this time period 487 patients received UORBC's, of these, 156 died before a follow-up sample could be obtained; 75 patients did not have follow-up samples taken and follow-up samples for 85 patients were received less than ten days post transfusion and were therefore not included in the final analysis. Therefore, the total number of patients studies was 171, of which 134 patients were male and 37 female with median age of 35 years. Of these patients, six developed atypical red cell antibodies classed as clinically significant giving an alloimmunisation rate of 3.5%. Nine RhD negative male patients received RhD positive red cells and one made anti-D. Anti-K, anti-C and anti-E were detected in female patients of childbearing age. All patients that developed red cell antibodies had received further transfusions over a period of 11-365 days after the initial transfusion of UORBC's.

From 2005 to 2009 a total of 1,863 UORBC's were given to trauma patients. From the data as can be seen that 80% of the trauma patients were male and received ≈1,200 units of O RhD positive red cells, thus reducing the demand for O RhD negative red cells. Over a period of five years one of these patients was found to have developed anti-D antibody.

## *Conclusions*

We found an alloimmunisation risk of 3.5% in our trauma patients but it is worth noting that all had received further red cells after the initial emergency transfusion. Care is needed to avoid inadvertent transfusion of K positive blood to women of childbearing age. The risk of anti-D formation in males requiring emergency transfusion must be balanced against the need to preserve essential

**Table 1:** Patients that developed blood group antibodies following transfusion of UORBC's between 2005 and 2009. Anti-Lea and Leb are not classed as clinically significant but are included in the table as they required investigation by the laboratory.

| Patient | Sex | Age | Number of UORBC's | Further Transfusions | Antibody detected |
|---|---|---|---|---|---|
| 1 | M | 16 | 6 | Yes | D |
| 2 | M | 25 | 6 | Yes | E+M |
| 3 | M | 42 | 9 | Yes | $Jk^a$ |
| 4 | F | 47 | 16 | Yes | C |
| 5 | F | 33 | 3 | Yes | K |
| 6 | F | 34 | 16 | Yes | E |
| 7 | M | 27 | 7 | Yes | $Le^{a+b}$ |
| 8 | M | 37 | 9 | Yes | $Le^a$ |

O RhD negative red cell stock for use in females.

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## Communications in the 21st Century – Challenges and Opportunities


Communications in the 21st Century are instant, accessible and global. These characteristics create great opportunities as well as challenges for us all, both professionally and personally.

Communications are 24/7 and the default channel is digital. A post on a website or an email can reach thousands in minutes. A tweet can reach millions of people in seconds as the famous and not so famous share their most intimate thoughts and views with anyone who chooses to follow them. We can find answers on anything as we 'Google' how to cook tonight's dinner or self-diagnose what this pain in my stomach means and it is global. Through social and digital media people across the world can access and share information that was not possible even a few years ago. This has, literally, changed the course of history as people across the Middle East used social media to change Governments in what became known as the Arab Spring.

Digital, particularly social media, has changed the communications landscape for ever. Research by Ofcom[1] shows that in 2011 television, the internet and mobile phones would be the most-missed media activity by all age groups with the last two increasing in importance over the past five years. Radio, newspapers and magazines have decreased as channels that would be missed.

Interesting is the difference across the generations. For 16-24 years olds they would miss their mobile phone most followed by the internet and then television. They would not miss newspapers or magazines at all. At the other end of the age range, those over 65 would miss television the most, then radio followed by newspapers and magazines.

The internet is now an essential part of everyday life. The Ofcom report shows that there has been a substantial increase in the proportion of the population now using the internet, from 59% in 2005 to 79% in 2011. Internet users are also spending more time online, self-reported weekly hours have risen from 9.9 hours in 2005 to 15.1 in 2011.

This increasing access to information via the internet means we can now all be experts, albeit superficial, in matters once reserved for professionals who spent years training and acquiring knowledge. With a press of a button we can find out anything we want to know. This means patients and families are more demanding of the health service and can ask more searching questions about their care and treatment.

This is a challenge but also a great opportunity as patients can take more responsibility for their health and wellbeing. It provides an environment in which we can encourage patients to ask more intelligent questions. For transfusion, for example, NHSBT supports patients discussing with their

clinician the most appropriate treatment for them and possible alternatives through a range of information leaflets explaining the reasons for transfusion and what they need to know and ask, hospital.blood.co.uk/library/patient_information_leaflets.

Operationally NHSBT is exploring ways we can make better use of digital communications to help those working in hospitals. We have recently launched a mobile website to help promote the appropriate use of platelets. It provides easy access to national guidance taking into account individual patient details such as weight and enables clinicians to search quickly for up-to-date, national advice to ensure appropriate transfusion. Further details of the new platelet transfusion mobile site appear in the next article. We are also working with users on improvements to the Electronic Offering System (EOS) for organs to provide electronic notification of donor number and offer details. Recipient centres will be able to go directly on to a dedicated EOS website with one password via a web browser on a PC or mobile device and look at a summary of the core donor data. It will be rolled out to all centres next year and we expect it to become the only source for viewing offers for all organs.

Social networking has been an area of particular growth increasing from 22% of internet users in 2007 to 59% in 2011 (Ofcom). NHSBT has taken advantage of this massive growth in social media to reach out to donors and potential donors. We launched our blood Facebook page in June 2011 and within months it became the most liked Facebook site for any blood donation service in the world. We launched our first app for blood donation in June this year enabling users to search for sessions and appointments. It has had a very good response with positive 5* user ratings on the Apple and Google app stores.

In May we announced a partnership with Facebook to help boost the number of people on the Organ Donor Register by including the intention to become an organ donor on a person's timeline. This enables people to post key life events and milestones to their Facebook profile with the added benefit of sharing that information with friends and family. The facility provides a link to NHSBT's Facebook page where people can register officially their wish to be an organ donor.

There is no sign that the pace of change will let up. The iPad went on sale in the US on 3 April 2010, Apple sold three million in the first 80 days. In two years tablets are already becoming essential business and personal communications tools. The future is mobile as increasingly internet access is anywhere on any device.

The communications channels are growing and changing at a faster pace than ever before, but the connections they make have always taken place. Digital has made things more accessible and instant, social media has made them more visible. But what we want to say and know is largely the same. We want answers, we want to know what is going on, we want to understand what is happening, we want to share our experiences. So, although the 'how' we communicate has changed dramatically in a very short period of time, the 'what' we communicate is largely unchanged since the world began.

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## The New Platelet Transfusion Mobile Site – A Bedside Tool to Aid Decision Making

### *Background to Development*

The National Comparative Audit (NCA) of platelet transfusions in haematology patients 2010 demonstrated that 28% of all platelets transfused were outwith national guidelines. Previous national audits of platelet transfusions had been criticised for not taking all possible factors for transfusion into consideration before deeming the transfusion inappropriate. In response to this feedback, the 2010 NCA developed algorithms to assess whether transfusions were outside national guidelines and ensured that other reasonable reasons for transfusion were taken into consideration. Despite this 28% of the transfusions

could potentially have been avoided. The audit also showed that the majority of platelet transfusions were given prophylactically (69%) and that 10% of these prophylactic transfusions were double the standard adult dose. A recent large study that randomised 1,272 patients to receive low, medium or high dose prophylactic platelet transfusions concluded that the dose of platelets had no effect on the incidence of bleeding. This has led to the development of a poster by the Customer Services Better Blood Transfusion Team with the heading 'Don't use two when one will do.'

The demand for platelets is rising. In 2011/12 the demand for platelets grew by almost 9% compared to the previous year and NHS Blood and Transplant (NHSBT) have been examining the reasons for this sharp increase. It is likely to be due to a variety of reasons. Haematology patients are the biggest users of platelet transfusions. Some of this rise will therefore be due to the increase in the number of people with a haematological malignancy due to an aging population. Also, due to advances in treatment options many of these patients are being treated more intensively and surviving for longer. However, a proportion of this rise will be due to transfusions being given outside guidelines or at double the standard dose.

The predominant factor that drove the initiative of a platelet mobile site was the potential to influence patient care by decreasing the number of unnecessary platelet transfusions. The more platelet transfusions a patient receives the less likely they are to have a significant rise in their platelet count post transfusion, even if they haven't developed HLA-alloimmunisation. Reducing unnecessary use would therefore mean that when the patient requires a transfusion because they are bleeding or they need a procedure, the platelet transfusion is more likely to be effective. It would also minimise patients' exposure to the risks of transfusion.

What leads to platelet transfusions being 'prescribed' outwith guidelines or patients transfused and no post count taken prior to a procedure? Could one of the factors be as simple as not having direct access to guidelines and thresholds at the time of writing the instruction to transfuse? The majority of 'prescribers' are not experts in transfusion medicine and are unlikely to be familiar with the national guidelines. Hopefully having a tool that enables access to guidelines at the bedside will help to resolve that particular issue. The potential impact of a platelet mobile site will only be realised if enough 'prescribers' download and use it regularly. It has to be intuitive and meet the needs of the user.

Most doctors and health care professionals have a smartphone, any readers who have recently delivered a training/teaching session to FY1 or FY2's will probably already know this. If the audience are not entertained while the session is ongoing they will let you know by surreptitiously surfing the web as you talk! Ofcom's communications Market Report 2012 indicates that 40% of UK adults now own a smartphone, with the same proportion saying their phone is the most important device for accessing the internet. Tablet ownership has jumped from 2% to 11% in twelve months. It was clinicians that suggested and requested the development of mobile sites for transfusion so that they had access to the information at the right point in time.

### *Development*

A search of transfusion 'Apps' and mobile sites quickly established that there was a gap in the market for a tool that could facilitate the decision to transfuse platelets. As the demand for platelet transfusions has increased and audits have shown a proportion are inappropriate, it was decided that a platelet mobile site may have the potential to reduce unnecessary platelet transfusions. NHSBT had developed and launched the Blood Donor App so they had the relevant expertise and were committed to modernising the services and tools provided to hospitals. They therefore readily agreed to fund and build a HTML5 website.

A working group was established; a member of the Customer Service Better Blood Transfusion Team, two Transfusion Practitioners, a Haematologist and research fellow in transfusion and the New Media lead from NHSBT. It began life with a wall of paper diagrams and a few revisions and months later surfaced as a brand new mobile site.

**Table 1:** Main features of the mobile site

- Indications for the use of platelet transfusions
- Platelet thresholds prior to common procedures
- Reasons for prophylactic thresholds to be increased
- Paediatric dose calculator
- Contraindications to platelet transfusion
- Alternatives to platelet transfusion.

The site was then piloted via the Regional Transfusion Committee Chairs, the NHSBT Patient Consultant Team and other stakeholders involved in transfusion. Feedback was received from a variety of stakeholders including anaesthetists, surgeons and foundation doctors; it identified the need for improvement in the 'user journey' and wording clarification for non-haematology users.

Promotional postcards were then developed that incorporated the QR code, these can be ordered free of charge from https://ww3.access-24.co.uk/. Please contact the NHSBT Customer Service Administration Office on 01865 381042 to obtain log in details. The QR code can be found at http://goo.gl/sO7fh.

### *Implementation and monitoring Impact*

The mobile site is free to download and access. How often it is accessed will be monitored over the future months. It is hoped that clinicians will feedback and the site will evolve into a tool that can not only guide platelet usage but other areas of transfusion. There have already been requests to include the guidelines for red cells, fresh frozen plasma and how to manage a major haemorrhage. Essentially the people who manage the patient and the transfusion at the bedside day in and day out are not transfusion experts and this provides an opportunity to have expert advice when required.

We welcome as much constructive feedback on this mobile site as possible. This will ensure that this mobile site continues to develop and improve.

Email *NHSBT.CustomerService@nhsbt.nhs.uk* with your comments.

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## Variability in Transfusion Education for Doctors, Nurses, Midwives and Operating Department Practitioners – The Results So Far...

### *Introduction*

Blood transfusion is generally a safe process that saves lives and improves the quality of life in a large range of clinical conditions. However, there are a number of risks associated with transfusion; while deaths from blood transfusion complications and errors are rare, both errors and 'near miss' events still happen with alarming frequency, leading to hundreds of reports of adverse patient outcomes and as many, if not more, of potential harm (2011 Annual SHOT Report, 2012). Taking the time to conduct transfusion procedures correctly in the midst of staff shortages and rising time pressure is undoubtedly difficult. The Serious Hazards of Transfusion (SHOT, 2011) annual report concluded that the NHS must go 'back to basics' on blood transfusion. Standardised, structured education and training is required for all healthcare professionals involved in the transfusion process to aid improvements in this area. This is not a new recommendation and has been recognised for several years.

The National Blood Transfusion Committee (NBTC) established an Education Working Group in 2011 to review transfusion training at all levels. The core group, chaired by Dr Shubha Allard, Consultant Haematologist at Barts and NHSBT, included representatives from the NHSBT Better Blood Transfusion and Patient Clinical Teams, SHOT and a Transfusion Practitioner. Work was divided into two distinct phases as detailed below:

- The remit of Phase 1 was to understand and explore transfusion education and training amongst healthcare professionals. This included:
- Undertaking a comprehensive review of transfusion training and education in UK (England for Nurses, Midwives and Operating Department Practitioners)
- Providing a set of recommendations to inform development of a work plan for delivery for Phase 2
- In collaboration with the Royal College of Nursing (RCN), review and update their transfusion standards ('Right blood, right patient, right time').

### *Method*

For doctors, a survey of transfusion training compiled as a survey monkey tool was circulated to 31 UK medical schools and 25 foundation schools.

The questions included:

- How is transfusion training delivered?
- Who delivers the training and when?
- How is competency assessment undertaken in transfusion and when?
- Which topics are covered?

The latest versions of curricula for various postgraduate specialities available on the General Medicine Council website were searched for transfusion training content using key 'blood transfusion' terms.

For nurses, midwives and ODPs, initial meetings were undertaken with representatives from the Nursing and Midwifery Council (NMC), the Royal College of Nursing (RCN) and the President of the College of Operating Department Practitioners (COPD) to get a better understanding of what standards were set nationally in relation to transfusion.

A similar survey was then sent out (as used for the doctors but tailored to the specific staff group) to 100 institutions of higher education responsible for training undergraduate nurses, midwives and operating department practitioners.

## Results

A total of 24 medical schools and ten foundation schools responded and all stated that they covered transfusion medicine in their training. The method of training was variable with didactic lectures being the most popular, and e-learning (http://learnbloodtransfusion.org.uk) developed by UK Blood Services was also used. In addition to this, some education providers used clinical scenarios as a learning tool.

In the vast majority of cases, haematologists delivered the training, often assisted by Transfusion Practitioners. Topics covered included:

- Blood groups, antibodies and their clinical significance were covered by all
- Safe prescribing, administration, patient information and consent and transfusion reactions were covered in some but not all
- Massive haemorrhage was included in the majority of curricula
- Paediatric transfusion was covered only in four (16.6%).

It varied greatly as to whether students were formally assessed or not.

In postgraduate core medical and higher speciality training there was considerable variation in the level of content and assessment in relation to training in Transfusion Medicine between specialities. Some curricula have very good content, eg obstetrics and anaesthetics while others have very little.

For the other professional groups, core curriculum content and design is devolved locally to approved (NMC or COPD) institutions. Neither the NMC nor the COPD make any overt references or stipulation to include transfusion education in undergraduate/pre-registration training.

Of the 100 institutions of higher education responsible for training undergraduate nurses, midwives and ODPs, just seven completed survey monkey questionnaires were received. This included one midwifery, five nursing and one ODP institution. All stated that transfusion training was taught but it was delivered at different stages in different institutions.

In collaboration with the RCN, it was agreed that a review and update of their transfusion standards: *Right blood, right patient, right time RCN guidance for improving transfusion practice* (2005) would take place and the revised version was launched at the RCN Congress in April 2013.

## Conclusions

Substantial variation was found in the content, delivery and assessment with relation to training in Transfusion Medicine within medical schools and foundation schools.

Due to the poor response rate from Higher Education Institutes and Universities responsible for delivering Nurse, Midwifery and ODP education, it is difficult to build an accurate picture of what the core curriculum content is with regard to transfusion education but the design and delivery appears to be different in each Institute.

## Recommendations for Phase 2

There needs to be a clear mechanism for ensuring that transfusion education is consistent for both pre registration and post registration training of all Health Care Professionals.

- Certain key areas such as safe prescribing and transfusion reactions should be universal and mandatory
- Positive patient identification should be a core clinical skill
- Training should include patient information and consent for transfusion
- Learnbloodtransfusion e-learning should be included in all undergraduate curricula
- Mandatory formal assessments based on adequate underlying knowledge are required across all the disciplines to ensure that future healthcare professionals can deliver safe and appropriate transfusion and reduce.

The remit of Phase 2 is to develop a work plan based on the findings of Phase 1. In collaboration with key stakeholders, the remit is to produce recommendations for transfusion education in the core curriculum for HCPs pre and post registration and implement relevant educational recommendations from the SaBTO consent for transfusion

consultation. It is critical to actively engage Royal Colleges, Higher Education Institutes and other influential key stakeholders, to promote this recommended core curriculum content for transfusion education.

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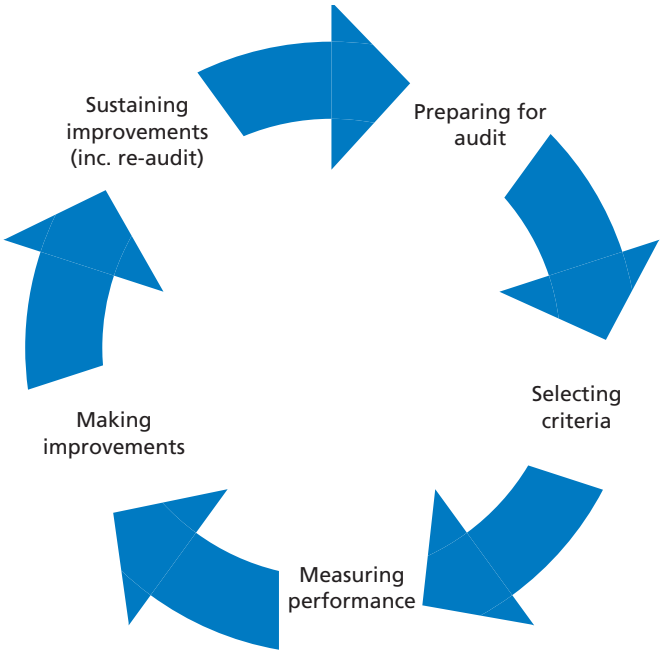
## A Day in the Life of a Senior Clinical Audit Facilitator

I am a Senior Clinical Audit Facilitator working for NHS Blood and Transplant in the Statistics and Clinical Audit department. The Clinical Audit side of the department consists of nine staff – a Clinical Audit Manager, two Senior Facilitators, five facilitators and an administrator. We are based in offices around the country, with my team and I based in NHSBT headquarters in Watford, Hertfordshire. We facilitate audit projects that cover the whole of England. Our job is to undertake quality improvement projects for the three clinical directorates within NHSBT.

Our work involves setting up clinical audits with Clinical, Nursing and Scientific staff who act as leads for the project, undertaking data collection and analysis and seeing a project right through to the end where agreed improvements to practice are put in place. The majority of our audits come from the Clinical Audit Programme. Each year, the different functions within NHSBT decide on audit topics to be carried out in the forthcoming year. We also carry out adhoc audits where any individual can approach us with an idea for a clinical audit and be taken through a proposal and approval process. The topics can come from the strategic plan, Quality Incidents that have occurred as well as the organisation's risk register. We also provide training for staff that require knowledge and skills for undertaking clinical audits in their workplace.

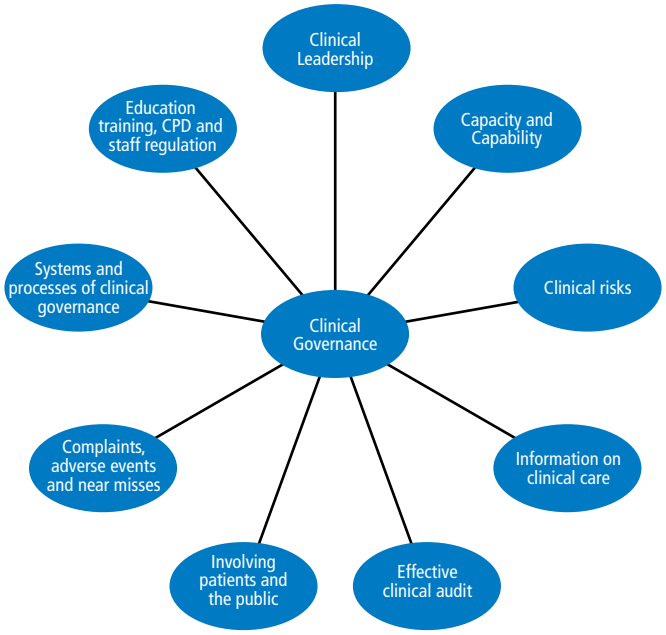
Clinical Audit is a quality improvement process that compares actual practice against agreed standards that describe best practice and then changes are made, based on the findings. The Care Quality Commission (CQC) views the five stages of clinical audit as shown in the diagram.




*Based on 'Engagement in Clinical Audits' Care Quality Commission.*

*http://archive.cqc.org.uk/periodicreview/nationalcommitmentsandpriorities2009/10/acuteandspecialisttrusts/nationalpriorities/engagementinclinicalaudits.cfm*

Clinical Audit is part of a quality improvement framework called Clinical Governance. Clinical Governance gives NHS organisations a statutory duty to improve and monitor the quality of service they provide. Other quality improvement initiatives are described in this diagram.




There isn't really a typical day working in Clinical Audit as our work is project based and I can be working on several different audits simultaneously.

My first task of the day is to check phone messages and emails. Being part time, my first day of the week is Tuesday which can mean lots of messages from the previous day. I used to be full time until I had my daughter and due to childcare restrictions, I came back part time. Today, my inbox is a little bit more full than normal due to my recent requests for information from the Stem Cell Laboratory Managers for an audit on red cell contamination in ABO incompatible allogeneic HPC-A. My email was forewarning them of data collection due to start in a couple of weeks and asking them to let me know if they thought they would need any help. So far, the laboratories are saying they can handle it, which is good news.

There are occasions when a phone call or email pops up and I have to act on it immediately. This time, I have had an email requesting that changes to a clinical audit report be done asap because it needs to go to the Red Cell Immunohaematology Senior Management Team for approval the following day, and therefore needs distributing beforehand. So, I find the report on my computer and make the requested changes which luckily are not too many. I then email the report back and ask for someone to contact me to let me know if the report gets approval for publishing. Once I receive confirmation of approval, the next stage will be to distribute the report to all the stakeholders and put a copy on our intranet page.

I have a team of just two staff that I am directly responsible for. They are both Clinical Audit Facilitators and undertake audit projects that I am requested to lead on. I review their work with them and together we decide on the best way forward. Today, I am reviewing the data analysis of an Infection Prevention and Control re-audit. A re-audit occurs after actions from the first audit have been implemented and the new practice has had time to embed. We discuss how best to display the data that we have collected from blood collection teams and what the key findings might be. We do this so that we can start putting together the audit report.

My 'phone rings and it's my manager asking me for an update on some outstanding actions from audits I have been involved with. We provide Key Performance Indicator (KPI) data for each clinical directorate. They use this information to assess how well the directorate is doing at implementing actions from Clinical Audits. They can also see whether any actions need escalating or extending if there is difficulty with implementation. I check the follow-up forms for the audits that he asks about and let him know what the status is on their actions. Some have been completed and there are some that I need to chase for a progress update as they are nearing their deadlines.

After lunch, I have to travel to our Colindale centre for a meeting with a clinical lead to set up a new national audit. It is with Tissue Services and they want to do some work around bacterial testing of heart valves. This is one aspect of the job that I really like. Getting out and about, meeting people and seeing how their departments work. We discuss the topic and the rationale for the project. During these types of meetings, it is my job to ask lots of questions so that I can get a clear picture of how a particular process works. This enables me to come up with a sound methodology for data collection that suits everyone. We discuss what standards to measure practice against, types of data needed, where the data will come from, who will obtain the data and the time frame for all the different stages of the project. This particular audit requires a deadline for the whole project to be in six months time as it is to be presented at a conference.

At the end of the meeting I realise that there is no time to go back to the office so the working day is over for me. Time to go home!

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# Introduction of Spectra Optia Cell Separators for the Collection of Peripheral Blood Stem Cells in NHS Blood and Transplant

The NHS Blood and Transplant (NHSBT) Specialist Therapeutic Services (STS) team has a long history of providing life-saving and life-enhancing therapeutic apheresis services within the NHS.

The service is delivered from six units that are based within NHS Trusts and which operate an outpatient model for non-acute patient procedures. Delivering services from within an acute setting enables STS to offer a peripatetic outreach model for paediatrics and acutely unwell patients. Units are located in the following NHS Trusts:

- The Christie NHS Foundation Trust
- North Bristol NHS Trust
- Oxford University Hospitals NHS Trust
- Sheffield Teaching Hospitals NHS Foundation Trust
- Leeds Teaching Hospitals NHS Trust
- Royal Liverpool and Broadgreen University Hospitals NHS Trust.

Treatments are delivered to patients referred from specialities such as haematology, oncology, renal and neurology with haematology being the largest referring speciality. Related and unrelated donors also attend the units to undergo peripheral blood stem cell collection.

For more than 20 years the Cobe Spectra machine has been the main technology used to deliver the majority of therapeutic apheresis procedures. The Cobe Spectra is a multifunctional cell separator machine, which can perform stem cell and other white cell collection procedures; bone marrow processing; plasma and red cell exchange procedures; and platelet and white cell depletions. It was also used for many years by the blood services for the collection of donor apheresis platelets.

During 2012, the new therapeutic machine Spectra Optia, was introduced into all STS units in NHSBT. This technology replaces the Cobe Spectra, which has come to the end of its lifespan following a decision by Terumo BCT to discontinue manufacture of this machine and its replacement parts from January 2013.

The Optia uses centrifugation to separate the blood removed from the donor/patient into component parts, each of which can be removed and/or replaced. During a stem cell procedure, mobilised stem cells are collected for transplant and all remaining components are returned.

Prior to introduction of this new technology in NHSBT, a working group was established to define the optimum machine settings for peripheral blood stem cell collection The group included representatives from TerumoBCT, Stem Cell Immunotherapy (SCI), Quality, STS clinical staff and a service user.


*The TerumoBCT Spectra Optia Apheresis Blood Cell Separator (The machine separates a patient's/donor's blood using centrifugation. This allows the removal of specific blood components as the blood circulates through the machine in a single use sterile closed circuit tubing set, before returning back to the patient/donor).*

The group produced a protocol outlining the agreed settings and the rationale for each, including references to available literature (which reported only 6-36 patients per publication). The settings chosen were aimed at ensuring patient and donor safety, while optimising the stem cell product collected within reasonable and acceptable timeframes.

The introduction of Optia into STS was phased to ensure that robust training and consolidation of practice was undertaken before transferring over entirely to the new equipment.

Some procedural differences in the way the Optia collects stem cells mean that both procedure times and product volumes can vary with respect to Spectra. This gave initial concerns about the potential for increased frozen volumes of stem cells for storage. Analysis of initial results confirmed that this is not an issue in practice.

Calculation of 'collection efficiency' for every stem cell collection has been introduced with Optia implementation. Early results show mostly excellent efficiency, optimising the collection of this important product and demonstrating which procedures should be examined to adjust machine settings to improve results and products in future.

Until the change over to Optia, STS units undertook collection procedures based on historically agreed local machine settings. The change to the Optia, and standardisation of the procedure settings throughout all STS units, provides an excellent large database on stem

cell collection, as the team undertakes over 1,000 stem cell collections per annum. Initial results were used to validate the new procedures and ensure quality of product was maintained or improved. Further data will be collected over a twelve month period, through the cooperation of NHSBT STS and SCI departments. This will be a much larger data set than any previously published and will inform Optia users on how to optimise its use for the benefit of donors/patients. This gives an opportunity for NHSBT to propose optimal collection settings for the future, through the publication of robust research with large numbers of patients and procedures.

The introduction and validation of Optia technology for patient treatments within NHSBT has contributed to a better patient/donor experience, improved working for STS nurses and optimised procedures and products, giving the opportunity for study to establish an 'ideal' stem cell collection procedure.

The benefits of using Optia over the Spectra machine are shown below.

**Table 1**

| Advantages of Optia over Spectra |
|---|
| User interactive touch screen display |
| Less operator input freeing up time for patient care |
| Easier installation of disposable harness sets |
| Less platelet depletion reducing need for platelet transfusions |
| Lower extracorporeal volume reducing the need for blood prime |
| Optical sensors for continuous real time monitoring |
| Real time display of procedure parameters including fluid balance |
| Machine settings can change during treatment to optimise outcome |
| Retrievable procedure data documentation |
| Easier and quicker to perform exchange procedures |
| Increased portability of smaller and lighter machine |

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**Further information on STS can be found at:**

http://hospital.blood.co.uk/specialist_therapeutic_services/index.asp

## Decellularised Dermis: A Promising Novel Treatment for Chronic Lower Limb Ulcers

Treatment of chronic ulcers of the lower leg and foot, caused by diabetes or venous insufficiency, are a significant drain on NHS resources, with the total expenditure on the treatment of diabetic ulcers alone estimated to be more than £400 million per annum in the UK. More importantly, these are painful and unpleasant wounds that restrict patient's mobility, reduce their quality of life and can in severe cases result in full or partial below knee amputation.

When treating these wounds, clinicians are faced with a situation where a small initial wound has progressed to a large, deep ulcer, with consequent destruction of dermal tissue. Due to the underlying aetiologies of these wounds, they often have poor self-regeneration capacity, because of restricted blood flow or persistent infections. Therefore, to progress from simply managing these wounds to actually healing them, innovative approaches are required. One such approach is to use a decellularised dermal matrix to provide a supportive scaffold into which the patient's cells can migrate and regenerate the lost skin.

Skin allograft is widely used in the treatment of serious burn injuries as a temporary graft to protect healing burn wounds. It is however not suitable for permanent replacement of lost skin as it contains donor cells which provoke an immune response, resulting in the graft being

rejected after a period of time. However, by removing the donor cells from the skin, it is possible to make a decellularised dermis (DCD) matrix that lacks immunogenic donor cells and can serve as a permanent graft, whilst retaining the normal architecture of human dermis. This material has been evaluated for the treatment of diabetic ulcers in the US, with promising results. However, these commercially available grafts are very expensive.

NHSBT Tissue Services has developed its own DCD graft, using technology originally developed in a collaborative study with the University of Leeds and subsequently developed and refined in our Tissue Development Laboratory. The DCD is prepared from split skin grafts donated by deceased tissue donors. The graft is first treated with a hypertonic salt solution, which dissociates the epidermis from the dermis. The dermis is then sequentially incubated in a hypotonic buffer, anionic detergent solution and nuclease solution, which serve to lyse the cells, solubilise and remove the cell remnants and digest and remove nucleic acids. This results in a decellularised dermal matrix which retains the structure and architecture of normal dermis, including vascular channels. Importantly, it also retains a functional basement membrane which is essential to support regeneration of the epidermis. The resulting matrix is then cut to the required size, before being terminally sterilised.

To evaluate our DCD graft for the treatment of chronic wounds, a collaborative study was set up with the University Hospital of South Manchester. This small scale pilot study, to treat 20 patients, commenced in January 2012. Recruitment was complete by June 2012, and all patients were followed up for six months. Follow-up was completed by the end of November 2012. The study was primarily a safety evaluation of this novel graft, but was also designed to evaluate the efficacy of DCD for treatment of these problematic chronic wounds. An ethically approved treatment protocol was used which involved debridement of the wound with a high-pressure water jet, application of the DCD graft, followed by application of a negative pressure therapy dressing to the wound. Key features of the treatment protocol are that it can be performed in clinic without the need for anaesthetic, and it is a single stage procedure. The negative pressure therapy was continued for seven days (the time of the first dressing change). The patients were then followed up at regular intervals up until six months post grafting, with the wound area being measured and blood flow in the wound bed assessed with laser perfusion imaging at each follow-up appointment. Biopsy samples from the wound periphery were taken at 0, three and six week follow-up.

The results of the study have been promising. From a safety perspective, no graft related adverse events were encountered. The DCD rapidly integrated into the wound bed, becoming indistinguishable from the patient's own tissue within two weeks of application. Twelve of the twenty treated ulcers healed completely within the follow-up period and a reduction in size was found in all ulcers; even in those that did not completely heal; an average 68% reduction in size was found. The results of histological assessment and measurement of blood flow in the wound bed, indicated that the graft was highly vasculogenic. Figures 1 & 2 show an example of wound healing following DCD graft application, and biopsy sections from the wound bed, showing how the epidermis regenerates over time.

**Figure 1**

*Application of graft, and progression of wound healing. In this case, the patient (a 92 year old great grandmother with an ulcer that had persisted for two years) healed completely within 72 days of graft application*

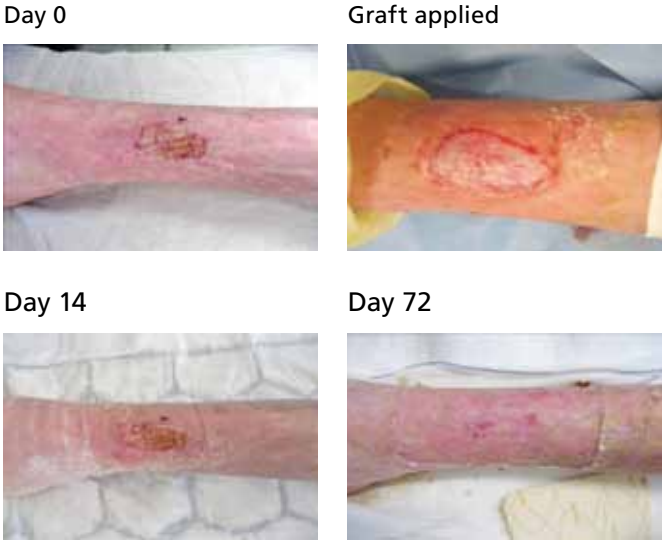
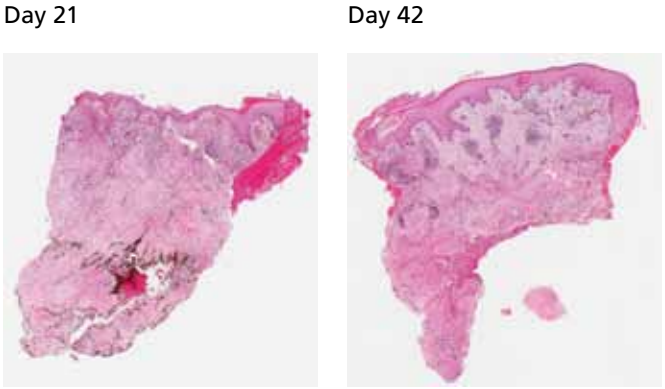



**Figure 2**

*Biopsy specimens taken at three and six weeks post-application. In the later sample, regeneration of a mature epidermis is evident.*




These results suggest an important role for DCD in the treatment of chronic wounds. Whilst it has been shown to be an effective treatment for diabetic ulcers in previous studies, this is the first report of its use for the treatment of

venous ulcers. Moreover, healing is achieved with a single treatment which can be performed without anaesthetic in clinic. Much of the cost of managing this type of wound is generated by the need for patients to continually be visited in the community, or attend specialist clinics to have their wounds assessed and dressings changed. A treatment which reliably results in complete healing obviates these wound management expenses. We intend to build on this data by performing further randomised controlled studies using this graft in wound healing. Moreover, DCD has potential to be used as a graft material in other anatomical areas, such as an adjunct to the repair of damaged tendons and scar revision. We have recently been granted Research Ethical Committee approval to perform an evaluation of the efficacy of DCD use in the repair of rotator cuff tears, which we hope to commence in early 2013.

This study is an example of how scientific advances in the field of tissue transplantation can be translated into clinical practice to provide more effective treatments for patients and improve their quality of life.

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## Cellular and Molecular Therapies in the UK: NHSBT's Current and Future Roles

The treatment of patients using bone marrow transplantation and cellular therapy is not a recent development, with pioneering work dating back to the 1950's, but the broadening application of stem cell and immunotherapies to treat an ever expanding range of haematological, malignant and genetic disorders is a more recent development and has led to a rapid expansion in both the manufacture of cellular therapies and the ability of NHS patients to access such novel treatments within the UK. NHS Blood and Transplant, through its Stem Cells & Immunotherapies (SCI) function, currently undertakes the testing, processing, storage and distribution of cells for human application via seven Human Tissue Authority (HTA) licensed and Joint Accreditation Committee – ISCT and EBMT (JACIE) accredited facilities, geographically located to cover 50% of the current UK bone marrow transplantation activity.

Regenerative medicine, which among other areas encompasses cellular therapies and tissue engineered products, is seen as a key future industry for the UK. In a 2011 position paper on regenerative medicine, The Department of Health noted 'that NHSBT's unique position in the UK and international recognition of its expertise in this area would make it a natural partner in any national regenerative medicine strategy'. NHSBT's Stem Cell Services Strategic plan (2013-18) aims to formalise NHSBT's commitment to continue to provide its current stem cell services to the NHS, while investing in supporting the next generation of therapies within the UK.

Central to NHSBT's future role in regenerative medicine is the expansion of SCI services and licensing by the MHRA, allowing SCI to develop and manufacture future cell therapies that go beyond the 'minimally manipulated' cell products that are the mainstay of current bone marrow transplantation practice. Liverpool SCI, based at Speke, is the first SCI site to open an Advanced Therapy Unit (ATU) and obtain an Investigational Medicinal Products (IMP) licence from the MHRA. The Liverpool SCI/ATU, currently manufacturing clinical trial products under full Good Manufacturing Practice (GMP) with commercial partners, has provided a blueprint for further sites to obtain licensing and an opportunity for staff from other SCI sites to train in the manufacture of GMP products. Several further SCI sites, including Oxford, Birmingham and Filton are in the process of final preparations to obtain MHRA manufacturing authorisation to produce IMPs within dedicated and well resourced ATUs.

SCI/ATU units will have close links with Tissue Services based at Liverpool who have considerable expertise in consent and tissue retrieval, Specialist Therapeutic Services (STS) providing apheresis services at multiple national sites and the Clinical Biotechnology Centre (CBC) in Bristol, whose expertise lies in the manufacture of clinical grade biologics. Recently the strategic plan brought SCI and CBC together to form the new Cellular and Molecular Therapies function, giving NHSBT the unique position of having multiple cell therapy facilities supported by a facility able to manufacture GMP grade molecular

**Table 1**

| Product | Established or Novel | Clinical Application | Process | Laboratory | Collaborator/ Client |
|---|---|---|---|---|---|
| Dendritic cells | Novel/Clinical trial | Liver and haematological cancers | Affinity selection, cell culture | Birmingham Leeds | Birmingham Liver Unit. St James' Hospital – CRUK |
| Purified stem cell subsets | Novel/Clinical trial | Liver disease | Affinity selection | Birmingham Oxford | Birmingham Liver Unit. Imperial College London |
| T cells (several) | Novel/Clinical trial | CMV infection | Affinity selection, gene transfer/ chimaeric T cells | Birmingham Manchester UCL | University of Birmingham Cell Medica Manchester – CRUK |
| Purified stem cell subsets | Novel/Clinical trial | Myocardial infarction | Affinity selection | Bristol | Bristol Heart Institute |
| Cell subsets | Novel/Clinical trial | Multiple sclerosis | Selection | Bristol | Frenchay Hospital |
| Saphenous vein cells (funded and planned) | Novel/Clinical trial | Myocardial infarction | Affinity selection | Bristol | Bristol Heart Institute |
| Cartilage progenitor cells (pre-clinical) | Novel/pre-clinical | Cartilage injury | Extended culture | Liverpool | Progenteq |
| Neural cell line (pre-clinical) | Novel/pre-clinical | Stroke | Extended culture | Liverpool | Reneuron |
| Mesenchymal cell bandage | Novel/Clinical trial | Cartilage injury | Extended culture | Liverpool | Azellon |
| Mesenchymal stem cells (planned, pre-clinical) | Novel/pre-clinical | Liver disease Inflammation Auto-immune disease | Extended culture | Birmingham | Birmingham Liver Unit |

therapies. The national network of SCI/ATU facilities is supported by integrated infectious disease, bacteriology, red cell immunohaematology and tissue typing testing departments, national logistics support and cold chain supply, all covered under the umbrella of an overarching Quality Management System (QMS). NHSBT is currently supporting exciting developments in molecular therapies both in house at the CBC in Bristol and with external partners by providing Quality Assurance (QA) and Qualified Persons (QP) support to external organisations including the Wolfson Gene Therapy Facility at University College London.

Along with the development of facilities and staff, future bioprocessing and clinical technologies will also play a key role. SCI has already invested significant effort in the development of closed system bioprocessing technologies for routine patient use. New grant funded projects are aimed at the development of cell therapy manufacturing platforms, underpinned by investment in scale up technologies such as cell factories and closed system disposable bioreactors. Through its Research and Development (R&D) function and National Institute for Health Research (NIHR) funded programs, NHSBT is also developing the next generation of cellular and molecular therapies, for example the production of human red cells

from stem cells. There is also an increasing understanding within the cell therapy field that using research materials that are 'GMP-like' is desirable at an early stage. Data gathered on efficacy, stability and safety during early stages of development of a new cell therapy is therefore more likely to translate to the clinic and provide a greater degree of reassurance that cell therapies are both safe and fit for purpose once translated to human application. SCI is supporting several clinical trial programs in pre-clinical development, supplying collaborators with high quality cell products that are able to be scaled up at a later date, for example 'GMP-like' mesenchymal stem cells for evaluation in models of liver disease and inflammation.

The majority of cell therapy clinical trials are currently in early phases i.e. I or I/II and often involve a limited number of clinical study sites. As trials progress there will be an increasing need not only for the manufacturing scale up but also for organisations able to manufacture at multiple sites supported by a single overarching QMS, QP support and integrated national cold chain supply. NHSBT, via its SCI, QA and Transport functions is able to provide this infrastructure to support late phase cell therapy clinical trials, having already been running a fully integrated stem cell service program and early phase clinical trial manufacturing program.

Through its different functions, NHSBT is supporting the UK regenerative landscape during all life cycle stages of novel cell therapies, including research, development, procurement, testing, GMP manufacturing and distribution (Table 1). Future success in the development of novel cellular and molecular therapies for human application is dependent on multi-disciplinary teams, including but not limited to clinical, regulatory, legal, manufacturing and scientific staff working towards a common goal of delivering novel therapies to populations for whom existing therapies have not provided a solution.

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**References:**

Taking Stock of Regenerative Medicine in the United Kingdom. Office for Life Sciences, Department for Business Innovation and Skills & the Department of Health, July 2011.

Development of a UK national network of GMP facilities for the manufacture of advanced therapy medicinal products (ATMPs). Hollyman *et al*, Oral Abstract, O1456, 39th Annual meeting of EBMT, London, April 2013.

The Development and Validation of the CryoDoc system; a Novel Method for the Cryopreservation of Cell Therapy Products without the Use of a Clean Room. Hollyman *et al*, *Transfusion*, Vol 52, Issue Supplement s3, Sept 2012.

## CPD Questions

**Genetic Haemochromatosis (GH)**

1. **Donors with GH can donate blood for patient use:**
   a) Never
   b) Maximum of twelve weekly
   c) Maximum of eight weekly
   d) Maximum of six weekly.

2. **Genetic Haemochromatosis (GH) has an estimated prevalence of:**
   a) 1:50
   b) 1:100
   c) 1:150
   d) 1:200.

3. **Genetic Haemochromatosis (GH) Blood Donors:**
   a) Have a higher incidence of bacteraemia
   b) Are assessed just as any other donor, prior to donation
   c) Once enrolled, must always donate
   d) Benefit from donation more than phlebotomy alone.

4. **Nurse Authorisation of Blood Components:**
   a) Blood has to be prescribed by law
   b) Section 130 of the 1968 Medicines Act has not been amended
   c) Blood components are excluded from legal definition of medicinal products
   d) Section 25 of the Blood Safety and Quality Regulations 2005 covers prescribing of blood components.

5. **Nurse Authorisation of Blood Components:**
   a) The NHSBT BBT Team are able to offer support to hospitals in England & North Wales
   b) Only one training course is available at present
   c) Has led to an increase in unnecessary waiting time for patients
   d) Has interfered with practitioners managing their patients.

6. **Decellularised Dermis:**
   a) Treatment of chronic ulcers of the lower leg and foot are effective and cheap
   b) Skin allograft is suitable for permanent replacement of lost skin
   c) Decellularised Dermis matrix lacks immunogenic donor cells
   d) Commercially available DCD grafts are available and cheap.

7. **Decellularised Dermis Matrix:**
   a) Retains the structure and architecture of normal dermis
   b) Looses a functional basement membrane
   c) Fails to support regeneration of the epidermis
   d) Has been shown to be ineffective in the treatment of chronic wounds.

8. **Transfusion Education**

   **Medical Training – Undergraduate and Post Graduate:**
   a) All medical students are taught about paediatric transfusion
   b) Anaesthetic higher speciality training curricula has a very good transfusion content
   c) All medical students are formally assessed in transfusion medicine
   d) Almost all higher speciality training has curricula with very good tranfusion content.

9. **Red Cell alloimmunisation in Patients for Trauma**

   **In the reported study, alloimmunisation rate was:**
   a) 2%
   b) 2.5%
   c) 3%
   d) 3.5%.

**10. Cellular and Molecular Therapies:**

a) Liverpool SCI have obtained an Investigational Medicinal Products Licence from the MHRA

b) NHSBT is not involved in regenerative medicine

c) Only one NHSBT site has Human Tissue Authority

d) NHSBT covers only 5% of the current UK Bone Marrow Transplant activity.

**11. Cellular and Molecular Therapies:**

a) NHSBT is not involved in molecular therapies

b) Liverpool NHSBT site is currently Manufacturing trial products under full GMP

c) NHSBT work only involves blood cells

d) NHSBT is not involved with cell therapy manufacturing platforms.

**12. Haemoglobinopathy:**

a) Red Cell Transfusions are only given on a long-term basis

b) Approximately there are 500 transfusions dependent thalassaemic patients in the UK

c) Around 10% of sickle cell patients require regular transfusions

d) Introduction of Doppler screening of SCD patients will reduce proportion of those patients needing regular transfusion.

**13. What is $R_o$:**

a) Negative for D antigen, but lack C and E

b) Positive for D antigen, but lack c and E

c) Negative for D antigen, but lack c and E

d) Positive for D antigen, but lack C and E.

**14. In SCD the specificity of alloantibodies are approximately:**

a) 20% against Rh antigens

b) Around 50-66% against $Jk^a$

c) 20% against anti-D

d) 20% against K.

*The CPD Section is a self-assessment exercise which allows readers to evaluate their understanding of each article. The answers are to be found within the articles themselves. Most CPD schemes allow this type of exercise to be eligible for credits as self-directed learning.*

## Clinical Case Studies

### *Case 1*

A 69 year old female with CLL who has had three uneventful pregnancies and two previous blood transfusions presents with an Hb of 6.0 and is very breathless. Urgent transfusion is required.

### *Laboratory Results*

| Blood grouping | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Anti-A | Anti-B | Anti-A,B | Anti-D (1) | Anti-D (2) | Reagent Control | Reverse Group (cells) | | | | Antibody Screen (IAT) | | |
| | | | | | | $A_1$ rr | $A_2$ rr | B rr | O $R_1$r | Cell 1 | Cell 2 | Cell 3 |
| 0 | 0 | 0 | 5 | 5 | 0 | 0 | 0 | 0 | 0 | 4 | 3 | 4 |

| Rh Phenotyping | | | | | |
|---|---|---|---|---|---|
| Anti-C | Anti-c | Anti-E | Anti-e | Anti-K | Reagent Control |
| 5 | 0 | 0 | 5 | 0 | 0 |

| DAT | | | | | |
|---|---|---|---|---|---|
| Anti-IgG | Anti-IgA | Anti-IgM | Anti-C3c | Anti-C3d | Reagent Control |
| 4 | 4 | 0 | 0 | 0 | 0 |

| Antibody identification panel | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Rh | M | N | S | s | P1 | $Lu^a$ | K | k | $Kp^A$ | $Le^a$ | $Le^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | SAL R/T | Enz | IAT |
| 1 | **$R_1{}^wR_1$** | 0 | + | 0 | + | 0 | 0 | 0 | + | 0 | + | 0 | + | + | 0 | + | 0 | 5 | 4 |
| 2 | **$R_1R_1$** | + | 0 | + | 0 | 4 | 0 | + | + | 0 | 0 | + | + | 0 | + | 0 | 0 | 5 | 4 |
| 3 | **$R_2R_2$** | 0 | + | 0 | + | 3 | 0 | 0 | + | 0 | 0 | + | 0 | + | + | 0 | 0 | 2 | 0 |
| 4 | **r'r** | 0 | + | 0 | + | 0 | 0 | 0 | + | 0 | 0 | + | 0 | + | 0 | + | 0 | 5 | 4 |
| 5 | **r''r** | + | 0 | + | + | 3 | 0 | 0 | + | 0 | 0 | + | + | 0 | 0 | + | 0 | 2 | 1 |
| 6 | **rr** | 0 | + | + | 0 | 5 | 0 | 0 | + | 0 | 0 | + | 0 | + | + | 0 | 0 | 3 | 2 |
| 7 | **rr** | + | + | 0 | + | 3 | 0 | + | + | 0 | + | 0 | 0 | + | 0 | + | 0 | 3 | 2 |
| 8 | **rr** | + | 0 | + | 0 | 3 | + | 0 | + | 0 | + | 0 | + | 0 | + | + | 0 | 3 | 2 |
| 9 | **rr** | + | + | 0 | + | 4 | 0 | 0 | + | + | 0 | + | 0 | + | 0 | + | 0 | 3 | 2 |
| 10 | **rr** | 0 | + | 0 | + | 5 | 0 | + | 0 | 0 | 0 | + | + | 0 | + | 0 | 0 | 3 | 2 |
| Auto | | | | | | | | | | | | | | | | | 0 | 4 | 4 |

### *Questions:*

1. Explain the blood grouping results?

2. Explain the antibody investigations results?

3. What other investigations are required before blood can be selected for transfusion?

4. If there is no time for further investigations what blood type would you select for transfusion? Justify your selection.

### *Case 2*

A 32 year old male patient with CRF received an ABO compatible kidney transplant five days ago. The kidney is functioning well but the patient is showing signs of anaemia and haemolysis is suspected. Two units of blood have been requested.

### *Laboratory Results*

| Blood grouping | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Anti-A | Anti-B | Anti-A,B | Anti-D (1) | Anti-D (2) | Reagent Control | Reverse Group (cells) | | | | Antibody Screen (IAT) | | |
| | | | | | | $A_1$ rr | $A_2$ rr | B rr | O $R_1r$ | Cell 1 | Cell 2 | Cell 3 |
| 0 | 5 | 5 | 5 | 5 | 0 | 5 | 5 | 1 | 0 | 0 | 0 | 0 |

| DAT | | | | | |
|---|---|---|---|---|---|
| Anti-IgG | Anti-IgA | Anti-IgM | Anti-C3c | Anti-C3d | Reagent Control |
| 4 | 0 | 0 | 0 | 0 | 0 |

| Antibody identification panel | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Rh | M | N | S | s | P1 | $Lu^a$ | K | k | $Kp^a$ | $Le^a$ | $Le^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | | | IAT |
| 1 | $R_1^WR_1$ | 0 | + | 0 | + | 0 | 0 | 0 | + | 0 | + | 0 | + | + | 0 | + | | | 0 |
| 2 | $R_1R_1$ | + | 0 | + | 0 | 4 | 0 | + | + | 0 | 0 | + | + | 0 | + | 0 | | | 0 |
| 3 | $R_2R_2$ | 0 | + | 0 | + | 3 | 0 | 0 | + | 0 | 0 | + | 0 | + | + | 0 | | | 0 |
| 4 | r'r | 0 | + | 0 | + | 0 | 0 | 0 | + | 0 | 0 | + | 0 | + | 0 | + | | | 0 |
| 5 | r''r | + | 0 | + | + | 3 | 0 | 0 | + | 0 | 0 | + | + | 0 | 0 | + | | | 0 |
| 6 | rr | 0 | + | + | 0 | 5 | 0 | 0 | + | 0 | 0 | + | 0 | + | + | 0 | | | 0 |
| 7 | rr | + | + | 0 | + | 3 | 0 | + | + | 0 | + | 0 | 0 | + | 0 | + | | | 0 |
| 8 | rr | + | 0 | + | 0 | 3 | + | 0 | + | 0 | + | 0 | + | 0 | + | + | | | 0 |
| 9 | rr | + | + | 0 | + | 4 | 0 | 0 | + | + | 0 | + | 0 | + | 0 | + | | | 0 |
| 10 | rr | 0 | + | 0 | + | 5 | 0 | + | 0 | 0 | 0 | + | + | 0 | + | 0 | | | 0 |
| Auto | | | | | | | | | | | | | | | | | | | |

### *Questions:*

1. What is the most likely explanation for these findings?

2. What further tests are required to confirm your suspicions?

3. What blood type would you select for transfusion?

### *Case 3*

A six year old child was admitted with Hb 9 g/dl, with antecedent viral infection. Two days later Hb dropped to 6.2 g/dl. The bilirubin level was 40 µmol/l(normal range 2-17 µmol/l) with raised LDH. You are provided with DAT and ABO grouping results. No free antibody detectable by IAT/papain-treated erythrocytes at 37°C. The child was transfused with two RBC units. Post transfusion Hb level was 9.4 g/dl. Two days later Hb dropped to 4.3 g/ldl. Again, no free antibody detected by IAT /papain-treated erythrocytes at 37°C on this admission.

### *ABO Blood Group Results (room Temperature 20°C)*

| | Patient's red cell reaction with: | | | | Patient's plasma reaction with: | | | |
|---|---|---|---|---|---|---|---|---|
| Case No. | Anti-A | Anti-B | Anti-A,B | Anti-A1 | $A_1$ RBCs | $A_1$ RBCs | B RBCs | O RBCs |
| | 0 | 5 | 5 | 0 | 5 | 5 | 2 | 2 |

| Polyspecific AHG | IgG | C3d | Control |
|---|---|---|---|
| ++ | - | ++ | - |

### *Questions:*

1) You are provided with DAT and ABO Grouping results:

   a) Comment on the DAT and ABO grouping findings

   b) What is the likely blood group?

   c) How would you confirm the patient's ABO group?

2) a) What is the most likely diagnosis?

   b) What further laboratory investigations would you carry out to confirm the diagnosis? Outline the principle of this test.

3) The child needs further transfusion.

   a) What blood would you select?

   b) What further measures would you take?

### *Case 4*

A baby born to a mother who has had two previous uneventful pregnancies has developed severe jaundice two days post delivery. The bilirubin has reached 260 µmol/l and may require exchange transfusion.

### *Laboratory Results*

| Blood grouping | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Anti-A | Anti-B | Anti-A,B | Anti-D (1) | Anti-D (2) | Reagent Control | Reverse Group (cells) | | | | Antibody Screen (IAT) | | |
| | | | | | | | $A_1$ rr | $A_2$ rr | B rr | O $R_1$r | Cell 1 | Cell 2 | Cell 3 |
| Mother | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 5 | 5 | 0 | 0 | 0 | 0 |
| Baby | 0 | 4 | 4 | 4 | 4 | 0 | N/A | | | | | | |

| DAT – Baby | | | | | |
|---|---|---|---|---|---|
| Anti-IgG | Anti-IgA | Anti-IgM | Anti-C3c | Anti-C3d | Reagent Control |
| 4 | 0 | 0 | 0 | 0 | 0 |

### *Questions:*

1. What is the most likely explanation for the positive DAT?
2. How would you confirm your diagnosis?
3. If further investigations proves the most likely diagnosis to be incorrect what else may explain the findings?
4. What blood type would you select for exchange transfusion? Is there any special requirements for the selected blood?

## *Answers to Clinical Case Studies*

(Based upon what action was taken. This was a fictitious case made up using elements of true cases).

### *Case No.1*

1. No detectable anti-A,B due to hypogammaglobulinaemia
2. Auto anti-C+e
3. Exclude alloantibodies using either $R_2R_2$ panel or adsorption studies
4. $R_1R_1$ K- rather than $R_2R_2$

### *Case No.2*

1. Passenger lymphocyte syndrome – transplanted with group O kidney
2. Include group B cell when testing eluate
3. Group O RhD Pos (HT-)

### *Case No.3*

1. a. DAT by complement only. Reverse grouping reacting with all cell tested at RT (?cold antibody)

   b. Blood group B with cold antibody

   c. Sample warm washed at 37°C with saline and repeat ABO typing

2. a. PCH

   b. Donath-Landsteiner test
   Detection of biphasic antibody
   Antibody binds at lower temperature and causes complement activation at 37°C
   IgG antibody with anti-P specificity

3. a. Select blood group B/Rh matched compatible units

   b. Keep ambient temperature > 24°C, to consider using blood warmer. NB Only very rarely need pp blood.

### *Case No.4*

1. Immune anti-B coating infant red cells
2. DTT treatment/titration tests on maternal anti-B-eluate from baby red cells and test for anti-B
3. Antibody to low incidence paternal antigen
4. If immune anti-B group O HT-red cells. Paediatric exchange unit – CMV-, CPD, <five days old, adjust haematocrit, irradiated

# Diary Dates

## 2013

**14-15 May**
**BBTS Joint Meeting Hospital Transfusion and Transfusion Practitioners**
Location: Crowne Plaza Hotel, Birmingham
For more information contact:
www.bbts.org.uk/events

**2-5 June**
**ISBT**
Location: Amsterdam, RAI Convention Centre, Amsterdam
For more information contact:
www.bbts.org.uk/events

**6-7 June**
**Scotblood**
Location: Stirling University, Scotland
For more information contact:
www.bbts.org.uk/events

**13-16 June**
**18th EHA Annual Congress**
Location: Stockholm, Sweden
For more information contact: www.b-s-h.org.uk

**10 July**
**SHOT 2013**
Location: Royal Society of Medicine, London, UK
For more information contact:
www.bbts.org.uk/events

**22-25 August**
**ISEH Society for Hematology and Stem Cells 42nd Annual Meeting**
Location: The Imperial Riding School Renaissance Hotel, Vienna, Austria
For more information contact: www.iseh.org

**23-25 September**
**Institute of Biomedical Science (IBMS)**
Location: International Convention Centre, Birmingham, UK
For more information contact:
www.bbts.org.uk/events

**23-25 September**
**International Conference on Haematology and Blood Disorders**
Location: Raleigh, North Carolina, USA
For more information contact
www.b-s-h.org.uk/events

**3-5 October**
**7th Annual Sickle Cell and Thalassaemia Conference**
Location: Evelina Children's Hospital & St Thomas Hospital, London
For more information contact:
www.b-s-h.org.uk/events

**12-15 October**
**AABB Annual Meeting and CTTXPO 2013**
Location: Denver, Colorado, USA
For more information contact:
www.aabb.org/events

**16-18 October**
**BBTS Annual Conference 2013**
Location: International Convention Centre, Birmingham, UK
For more information contact:
www.bbts.org.uk/events

**6-7 November**
**ESH International Conference on Haematological Disorders in the Elderly**
Location: Barcelona, Spain
For more information contact:
www.esh.org/conferences

**20 November**
**NEQAS 2013**
Location: National Motorcycle Museum, Birmingham, UK
For more information contact:
www.bbts.org.uk/events

**25 November**

**The Royal Marsden Haematology-Oncology Study Day**

**Location:** The Royal Marsden Hospital, London

For more information contact:

www.b-s-h.org.uk/events

**7-10 December**

**ASH 55th Annual Meeting and Exposition**

**Location:** New Orleans, USA

For more information contact:

www.hematology.org/meetings

## 2014

**17-18 January**

**Highlights of ASH 55th Annual Meeting and Exposition**

**Location:** New York & Dallas

For more information contact:

www.hematology.org/meetings

## Notes

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*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)*