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Next Edition

Issue 50 will feature articles on:

- First Steps in Process for the Manufacture of Stem Cell Derived Platelets for Transfusion.
- New Research Centre to Underpin the Safety and Efficiency of Blood Donation.
- Organ Donation Memorials – A Goal for every UK Hospital.

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
Welcome to Editorial 49 of Blood and Transplant Matters, I hope you found the last edition useful and will enjoy reading this edition.

The arrival of Hepatitis E virus (HEV) screened components for specific groups of patients, caused a stir in the hospital transfusion community. In this edition, Pat Hewitt outlines some of the rationale and describes the process behind supplying appropriate components. She also reminds us that HEV is not just a transfusion risk. Alan Kitchen describes how all four UK Blood Services monitor and assess future infection threats to the Blood Supply. As a result of an external review of the Infections Disease Horizon Scanning Process, the approach has been simplified and increased effectiveness of the process.

The result of a large Anonymous Online Survey of UK Blood Donors to Assess Disease Risk Behaviours and Compliance with Attitudes to Donor Selection is outlined by Katy Davison and Su Brailsford. This has given NHSBT confidence that compliance with the Donor Selection Guidelines concerning infectious disease risk behaviours was very high and further analysis may contribute to the consent Safety of Blood, Tissues and Organs (SaBTO) review of donor selection policy.

Management of Pre-Operative Anaemia should reduce delayed operations, secondary case referrals, length of stay and post-operative mortality. However, the process seems to be full of barriers.

In the next article, Jaya Ganvir-Roche, Kate Pendry and Sharran Grey discuss those barriers and suggest potential solutions along with a full description of a successful ‘Management of Anaemia in Primary Care Pathway’. An excellent example of full collaborative work by the North West Regional Transfusion Committee.

Wing Roberts, Kathryn Musgrave and Hazel Tinegate describe a patient with IgA deficiency, with IgA antibodies and known reaction to blood components who was successfully supported through treatment of Acute Myeloid Leukaemia and a Stem Cell Transplant.

Wrong Blood in Tube (WBiT) still occurs, as demonstrated by the audit conducted by the West Midlands Regional Transfusion Committee and the results are reported for Blood and Transplant Matters by Brian Hockley, if the recommendations are followed there may be a reduction of WBiT incidents.

Dale Gardiner provides the rational for the provision of excellent intensive care Donor Optimisation and outlines the duty of care the intensive care owes to the potential donor for the quality of the organs donated.

Next is a case report of a successful ABO Incompatible Kidney Transplant, following Use of Glycorex Immunoadsorption Column by Moji Gesinde and Abby Wilson. Fiona Carley outlines some of the uses of donated Tissue in Ocular Surgery and its life enhancing capabilities. Staying with eyes, Akila Chandrasekar and Richard Lomas describes the Role of NHSBT in Serum Eye Drops Service Provision for patients with dry eyes.

As always, there are both CPD questions based upon these articles with answers appearing in the next edition and some interesting cases with suggested answers, which I hope are both interesting and informative. In the CPD question section, there are a couple of different styles of question on this occasion and at least one answer, which needs more knowledge than in the relevant article.

Have a happy read. Any comments should be sent to myself or my hard working Editorial Assistant Lynne Hodkin at blood&transplantmatters@nhsbt.nhs.uk.

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Hepatitis E virus (HEV) is a common virus in animals, especially pigs. It can also infect humans and the number of confirmed hepatitis E infections has increased significantly in the UK since 2003 (Public Health England, 2016). A study in 2012/2013 (Hewitt et al., 2014) showed that more than 1 in 3,000 blood donors in the south of England were infected with the virus, and the majority of these people never felt unwell.

We think that HEV in the developed world is passed directly from animals to humans, and that many cases are due to eating undercooked or raw pig meat. There may be other ways that it is passed on in the UK, to both animals and humans. For example, we know that HEV can be passed on through blood transfusion in the short period of time when the virus is present in the blood stream of a donor. An infected person will not necessarily feel unwell, and therefore may give blood at this time.

HEV usually causes a mild, or no, illness, with some inflammation of the liver (hepatitis) and rapid recovery. In a person with a healthy immune system the infection is cleared from the body within weeks. Patients such as very young babies, people having organ transplants, and those being treated for leukaemia, have immune systems which do not work normally. Such people are at risk of persistent HEV infection leading to chronic liver disease.

In 2015, the Specialist Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) convened a working group to consider HEV and blood safety and recommended that certain patient groups should receive HEV screened blood components, to reduce the risk of infection through blood transfusions. The two patient groups identified were those undergoing solid organ transplantation, and those who have allogeneic stem cell transplants.

In response, NHS Blood and Transplant (NHSBT) convened an HEV Project Board and Implementation Team. In addition to the patient groups identified by SaBTO, the Project Board added a third group to receive HEV screened blood components: neonates and children less than one year of age. NHSBT was therefore tasked with testing a proportion of blood donations to provide HEV screened blood components for three patient groups.

The HEV Project Implementation Team was drawn from all involved areas of NHSBT. There must be close liaison between the critical areas of Testing, Manufacturing, and Hospital Services, to make sure that the right level of testing is carried out, and of blood components manufactured, to maintain satisfactory stock levels of all blood groups at all issue sites. Any new initiative requires oversight by the Quality Department, to make sure that Change Controls are logged and signed off, and all necessary controlled documents are written. All staff need training in the new processes. Communications, both within NHSBT and with external stakeholders, most importantly blood transfusion laboratories in hospitals, Hospital Transfusion Teams, and key clinicians, are of paramount importance and representatives of the Hospital Liaison Team and the Communications Team played a pivotal part in trying to ensure that key messages were being communicated at the right time to the right people.

Screening test results must be confirmed in the NHSBT Reference Laboratory. Donors whose blood is confirmed HEV positive must be notified and given further advice from the Clinical Transfusion Microbiology Team, as they should not donate again for six months. Donor Clinic and Clinical Support Team staff within NHSBT need to be familiar with the processes so that they can answer questions from donors. Thus, introduction of HEV screening of donations involved most areas of NHSBT.

A further important issue at both NHSBT and hospitals was the inability of existing IT systems to cope with the new initiative within the short term. Hospitals needed a system to flag up to the laboratory that certain patients required HEV screened blood components, and would not necessarily have this information from request forms. Hospitals which could not make the necessary changes to their laboratory systems to flag patients requiring HEV screened components investigated surrogate methods, such as using the irradiated component flag for the dual purpose of irradiated and HEV screened. What seemed a reasonable fix for the hospital would have completely overwhelmed NHSBT resources for production of irradiated components and would have significantly increased costs of the implementation. Much dialogue was needed to try and reach solutions for the short term for the benefit of all concerned.

Planning the implementation of HEV screening was very complicated. In many ways, it would be easier to implement universal screening of all blood components than to try and estimate how much screening would be needed to meet hospital demand, but this option was not pursued in the interests of limiting increased costs for NHSBT and hospitals. Hospitals themselves were initially unable to estimate how much they would require because there was no clear definition of the period of time over which at risk patients would require HEV screened
components. Both hospitals and NHSBT were therefore operating with some degree of guesswork at the time of “go live” and hoping that estimates were not wildly wrong! Daily teleconferences within NHSBT were needed to fine-tune each day’s testing and manufacturing, as well as frequent conversations between Patient Services staff and hospital transfusion teams. Numbers tested rose each month, and a steady state has not yet been reached, but the numbers tested over April and May, if extrapolated over the whole year, indicate that over 25% of all donations will be screened in order to ensure sufficient stocks of HEV screened components to meet hospital demands. Not a small undertaking, and a significantly greater number than that envisaged when the SaBTO decision was first made.

The next steps? SaBTO has reconvened the HEV Working Group to look at further issues. And the donation screening results indicate that HEV infection is now even more common in England, with more than 1 in 1,400 donors coming to give blood while unknowingly infected with HEV. These results mean, of course, that patients are still at risk of HEV infection through the food they eat, even when the risk through blood transfusion is addressed, and reinforce the need for vulnerable patients to receive dietary advice as well as screened blood components.

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References:

Horizon Scanning for Infectious Threats

Microbiological safety is an important issue in the provision of products of human origin for clinical use. Minimising risk of transmission of infection is achieved primarily through the laboratory screening of donors/donations for evidence of the presence of a number of infectious agents, which are considered to be of highest risk to recipient groups, and which are considered to be of ‘universal’ risk in the donor population. Infected donors cannot be identified on the basis of specific risk behaviour alone and therefore all donations need to be screened for these infectious agents. However, prior to donation and subsequent laboratory screening, is the donor selection process which screens, through questioning, the donors prior to donation. In respect of infection risk donor selection seeks to identify donors who may have been exposed to a range of infectious agents through such elements as behaviour, specific activities, employment, healthcare interventions or travel, and on the basis of the information obtained either defer donors permanently or temporarily, or require additional testing to be performed on the donation collected. For example, donors with malaria or West Nile Virus (WNV) risk through travel need to be shown, through additional laboratory screening, not to have any evidence of current infection.

To be able to identify infection risk in donors, the donor selection process must be fully informed in respect of the range of infectious agents that would be of concern and the normal routes of exposure to these agents; donors can then be assessed for any risk of exposure and either deferred or set for additional laboratory screening. Key to developing and maintaining the ability to assess such risk in donors is a good understanding of the infectious threats that may be present in the donor population, and especially the changing nature of these threats. Infectious threats may arise in a number of different ways: newly identified infectious agents such as Severe Acute Respiratory Syndrome (SARS) or Middle East Respiratory Syndrome (MERS-CoV), re-emerging infectious agents such as malaria, existing infectious agents increasing significantly in incidence such hepatitis E virus (HEV); all of these may impact on the UK blood services in many ways and it is critical that the UK Blood Services are well informed and in advance of any potential threats.

For many years the UK Blood Services have monitored changing disease patterns and the rise and fall of infectious agents that may be transmitted through donated products, the information being used to inform policy making in relation to laboratory screening and the development of comprehensive and appropriate donor selection guidelines, for blood, tissue and cell donors. However this was performed by a number of different groups within and
across the individual UK Blood Services with the potential for duplication. An external review of NHS Blood and Transplant’s (NHSBT) infectious disease horizon scanning process determined that although horizon scanning was indeed being performed, it was not fully co-ordinated and consequently not performed in an efficient manner as it could be. To address this NHSBT initiated work to develop a horizon scanning system that ensured that the relevant infectious disease data were captured, collated, analysed and, where necessary, acted upon, but importantly through a single focussed system. Although this work was initiated by NHSBT the information is used to inform the common policy and guidelines for all four UK Blood Services and during the development of this system it became clear that responsibility for the system should be UK-wide rather than just NHSBT. Responsibility for the horizon scanning system was therefore passed to the UK Joint Professional Advisory Committee (JPAC) to action through its Standing Advisory Committee on Transfusion Transmitted Infections (SACTTI). JPAC is accountable to the UK Forum, the Medical Directors and Chief Executives of the four UK Services (http://www.transfusionguidelines.org.uk/about).

Key to horizon scanning is the capture of relevant information and the analysis of that information to determine any significance to the UK Blood Services. On a monthly basis the joint NHSBT/Public Health England Epidemiology Team collates notifications of disease outbreaks, incidents and other data related to emerging infectious disease activity. This monthly report is sent to the Chair and Secretary of SACTTI who then review in detail and determine any possible risk to the safety of donated products; any risks identified are graded to determine if action is required and the urgency of any action. Risks are graded from ‘Low risk’ with no action required to ‘Risk present’ with the possibility of immediate action being required. Any specific risk identified by the initial assessment is then identified and recorded using a risk assessment tool which looks in detail at each risk identified to define more specifically the level of risk and potential actions available. Any action required, whether changes to country associated travel risk, inclusion of an additional ‘risk activity’ in the donor selection guidelines or response to the identification of a new infectious threat, are reported by the Chair of SACTTI to the Chair of the relevant Standing Advisory Committee, the Chair of JPAC and the JPAC Manager, the urgency of action being defined within the risk assessment and any subsequent discussions. If necessary ad hoc Standing Advisory Committee and/ or JPAC meetings could be called to discuss the risk and determine broader actions needed, including escalation to Department of Health advisory bodies.

This approach has simplified and increased not only the effectiveness of the on-going horizon scanning process, but has also put in place an effective mechanism for acting upon the outcomes of this process, including the ability to more objectively and consistently assess threats and act immediately if required. Although only in place from late 2015 the new horizon scanning process has ensured that the emergence of Zika and the potential threats from Zika to donated products collected in the UK have been monitored, assessed and responded to in an appropriate manner. The Geographical Disease Risk Index is being regularly updated as Zika appears in countries previously unaffected, and the emerging risk of Zika transmission through sexual contact and the implication to blood donation has been assessed.

Although it is hoped that Blood Services generally are not constantly having to assess new infection threats, the UK Blood Service’s horizon scanning system will ensure that such threats to the safety of donated products in the UK are identified and assessed in good time, allowing the appropriate measures to be identified and implemented.

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In Search of the Bigger Picture: An Anonymous Online Survey of UK Blood Donors to Assess Disease Risk Behaviours, and Compliance with and Attitudes to Donor Selection

The Rationale

The joint NHS Blood and Transplant/Public Health England (PHE) Epidemiology Unit have been monitoring the numbers and rates of infections detected on blood donation screening among UK donors since 1995. Our surveillance programme is relatively unique in collecting such a comprehensive, large data set at a national level. Routinely we collate, analyse and report microbiological, clinical and epidemiological data for surveillance purposes, but the information is also used to inform transfusion
policy in relation to donor selection and donation testing. One such policy is the donor selection guideline relating to the deferral of men who have sex with men (MSM) from blood donation.

In 2010, the UK Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) recommended a change to MSM deferral policy from lifetime to 12 months since last sexual contact (Department of Health Advisory Committee on the Safety of Blood, 2011). Part of the evidence for recommending the change came from data collected in our surveillance. Using what we had observed about infections in blood donors, we were able to predict the overall impact on blood safety was likely to be negligible (Davison et al., 2013).

The blood services of England, Scotland and Wales implemented the 12-month MSM deferral policy in 2011. Monitoring the impact of this deferral post change was crucial to ensure blood safety was not affected. This was highlighted by SaBTO, along with a recommendation to monitor adherence of MSM in other words compliance with the new rule. Our established surveillance systems could not do this; detailed risk behaviour information are captured at post-test discussion for donors whose donations were found positive, but similar data are not available for those donors whose donations are not. Follow-up of every individual blood donor post-donation is not cost effective. While data on donor deferral at donation session would provide some insight into compliance, these are not routinely available and are limited to individuals who disclose a risk resulting in deferral in other words compliant donors. So we proposed a large scale anonymous survey to find out detailed information about risks of infectious diseases, and used their answers to determine compliance with the donor selection guidelines.

The Survey

We undertook the survey between November 2013 and October 2014 in collaboration with the four UK Blood Services (Davison et al., 2015). Our aim was to determine the extent of compliance with the donor selection guidelines concerning behaviours related to an increased risk of infectious diseases among blood donors and to gather information on donor understanding and reasons for non-compliance. The survey questions were based on the current donor health check (DHC) questionnaire along with additional questions relating to behaviours not necessarily part of current policy – such as contact with animals, snorting drugs, number of sexual partners and history of sexually transmitted infections.

A questionnaire was designed by the Survey Team and hosted by PHE. Information about the survey was made available to donors, blood services, Public Health agencies and a complaints procedure was set up. Each month for one year, all eligible new donors and sample of eligible repeat donors were invited via email to participate, followed by two reminders. The email contained links to the donor information and online questionnaire.

Eligibility Criteria

- Given whole blood donation
- Email shared with blood service.
- NOT reactive on screening testing.
- NOT opted out of or currently/recently taken part in blood service surveys.

Survey Responders

Among approximately 1.2 million individuals donating blood in the UK during the survey period, almost 250,000 were invited to participate (Figure 1). A little over 65,000 donors answered the questionnaire, with nine in ten responders completing it to the end. Among the responders there were 18,054 (28%) new donors, 42,663 (65%) females and 33,546 (51%) aged 17 to 44 years of age. Despite the broad representation of donors responding, comparing these to the donor population in general it was found that males, older donors and repeat donors were slightly under represented. This was due to a combination of response rates among these groups and the sampling approach that was used. The survey findings are adjusted to allow for these differences and can be generalised to the broader donor population.

Figure 1: The number of individuals donating during, and those surveyed by and responding to the UK blood donor survey

Compliance and Understanding

The responses to the survey questions relating to donor selection guidelines were reviewed to determine compliance. The percentage compliant (adjusted to represent the donor population as a whole) with the
sexual behaviour and lifestyle deferrals exceeded 99.3% (Figure 2). One of the most common reasons for non-compliance with the sexual behaviour and lifestyle deferrals was donors not thinking of themselves to be at risk. All donors were asked about their understanding of and engagement with the donor selection process; a higher proportion of compliant donors than non-compliant reported they read the welcome pack, understood the rationale for and accepted the questions used in the DHC, and found it easy to understand and complete.

**Figure 2:** The estimated percentage (and 95% confidence interval) of compliance with the sexual behaviour and lifestyle deferrals among responders to the UK Blood Donor Survey

<table>
<thead>
<tr>
<th>Deferral</th>
<th>Compliance</th>
</tr>
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<tbody>
<tr>
<td>Paid for sex</td>
<td>99.00%</td>
</tr>
<tr>
<td>Sex between men</td>
<td>99.50%</td>
</tr>
<tr>
<td>Sex with a high risk partner</td>
<td>100.00%</td>
</tr>
<tr>
<td>Injecting drug use</td>
<td></td>
</tr>
<tr>
<td>Intranasal drug use</td>
<td></td>
</tr>
<tr>
<td>Travel &lt;12 months</td>
<td></td>
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<tr>
<td>Travel &lt;12 months</td>
<td></td>
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<tr>
<td>Long stay</td>
<td></td>
</tr>
<tr>
<td>Piercing</td>
<td></td>
</tr>
<tr>
<td>Hepatitis/jaundice</td>
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**Summary**

The UK Blood Donor survey collected detailed information about risk behaviours, lifestyle and understanding of donor selection guidelines from over 65,000 donors. Compliance with the donor selection guidelines concerning infectious disease risk behaviours was very high. Non-compliant donors had less understanding of the donor selection guidelines and a poorer perception of risk. More analysis of the survey data are underway and will contribute to the current SaBTO review of donor selection policy that began earlier this year. The survey findings will be fed back to each of the UK blood services to be used to support and develop blood donation policies.

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**References:**


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**Management of Pre-Operative Anaemia: Progress in the North West Region**

**Introduction**

In 2014, a working group was set up by the North West (NW) Regional Transfusion Committee to drive the implementation of pre-operative anaemia management in the region’s Trusts as suggested in the national Patient Blood Management recommendations¹. The plan was to pilot anaemia management in four different surgical pathways across five sites and measure the impact of implementation. This proved rather naïve as many obstacles were identified as outlined below. There was a delay in implementation in the pilot sites, which are now two years later only just getting off the ground. In the meantime, we have developed a large network of stakeholders who are all working together to overcome the barriers in their own Trusts. In this article we describe some of the successes, barriers and potential solutions from the project so far. We are also presenting a Case Study from Bolton which highlights a great example of working between primary and secondary care.

What has been done to introduce anaemia management in the region?

**Successes**

Since January 2015, a multi-disciplinary working group has been established, with most Trusts in the North West represented. This has been a great forum for sharing lessons learnt and exchanging new ideas. Some sites are more advanced than others- some have implemented their pathways or they are at approval/ business case stage.
A measurement tool has been designed after workshop discussions and this is being piloted where new pathways are being introduced.

A toolkit of resources has been designed and is available here: [http://hospital.blood.co.uk/patient-services/patient-blood-management/pre-operative-anaemia/](http://hospital.blood.co.uk/patient-services/patient-blood-management/pre-operative-anaemia/).

### Barriers and Potential Solutions

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Potential Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty in identifying resources to support the delivery of an anaemia management service.</td>
<td>Develop a business case that covers the full range of resources required and ensure relevant income is identified through use of payment by results tariffs and potential cost savings are identified such as reduction in blood transfusion, improvement in length of stay. See toolkit of resources.</td>
</tr>
<tr>
<td>Lack of engagement within Trusts.</td>
<td>Agree roles and responsibilities/identify champion at the outset; use multi-disciplinary approach including haematologists, laboratory staff, anaesthetists and surgeons; early consultation with key stakeholders enables effective communication; persevere through politics/staffing changes; pilot pathways; continued promotion/networking/sharing of information &amp; learning.</td>
</tr>
<tr>
<td>Lack of engagement with patients.</td>
<td>Focus on the patient experience; provide patient information; patient to carry data collection form as secondary information; collect qualitative data as one of the outcome measures.</td>
</tr>
<tr>
<td>Lack of engagement with commissioners.</td>
<td>Early consultation with commissioners; ensure that business case is aligned to key National Health Service (NHS)/Clinical Commissioning Group (CCG) priorities and aim to commission pathway that will incentivise best practice.</td>
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| Lack of engagement with primary care. | Consult with CCGs/General Practitioners (GP) to define GP role, raise awareness; use pathways/templates from toolkit of resources as examples. |
| Anaemia identification often too late in surgical pathway to allow time for appropriate investigation and management. | Process map current pathways and identify opportunities for earlier identification of anaemia, move pre-operative assessment nearer to listing. Develop algorithm to highlight testing required to identify cause of anaemia and put in place systems for timely anaemia management. |
| Difficulties monitoring outcomes. | Use toolkit measurement tool & data collection forms; pilot measurement tool to systematically collect outcome measures; identify data that can be collected from electronic systems. Use data to drive performance improvement. |

### Current Work in Progress

Consultation is taking place with Primary Care and Commissioners to discuss tariffs; raising General Practitioner (GP) awareness; and the role of the GP in preparing patients for surgery.

We are working with the nine Trusts of the Greater Manchester Orthopaedic Alliance to devise a standardised approach to pre-operative anaemia management in orthopaedic patients undergoing elective surgery to enable large-scale commissioning/design of pathways. Baseline audits of pathways and transfusion rates for hip and knee replacement surgery are underway. The measurement tool will be used to monitor the impact of anaemia management.

### Case Study

The **Management of Anaemia in Primary Care Pathway** was developed through the collaboration of clinicians and managers in secondary care at Bolton NHS Foundation Trust and Bolton CCG. Both organisations had an interest in improving the management of patients with anaemia which was an important factor in successful development and implementation. In the early development stages, proposals were presented to the GPs at their education meeting to understand their needs. Other sources of invaluable support came from the NW Pre-Operative Anaemia Group and from the Pharma company who supplies the Intravenous (IV) iron.
The pathway is intended to ensure GPs have appropriate guidance for diagnosing and treating all types of anaemia in the primary care setting. It provides guidance for urgent secondary care referral when ‘red flags’ are present which may indicate a serious underlying pathology, or when the patient requires IV iron due to failure of oral iron or when rapid correction is required.

The pathway applies equally to patients who present to GPs with symptoms of anaemia, or patients who are being referred by GPs to secondary care for elective surgery.

Figure 1:

**Anaemia Management in Primary Care**

**Primary Care**

- **Patient presents with suspected anaemia or for elective surgery**
  - Clinical assessment and FBC (first line test)

  **Iron Deficiency Anaemia** (Ferritin <30ug/L)
  - Not for elective surgery
  - Timing: Not Critical
  - Trial of oral iron for four weeks
    - Hyperlink to Iron Deficiency guidance
  - **Hb** Normalised
    - Hb females >120g/L
    - Hb Males >130g/L
  - **Hb** NOT normalised
    - Hb females <120g/L
    - Hb Males <130g/L

- **Non-Iron Deficiency Anaemia** (Ferritin normal or raised)
  - For elective surgery
  - Timing: Critical
  - **IV Iron infusion**
  - Refer to Gastroenterology for IV iron

**Secondary Care**

- **Anaemia** Hb <130g/L (Male), Hb <120g/L (Female)
  - Perform 2nd line tests: repeat FBC, Retics, U&E, Creatinine, LFT, Ferritin, B12, Folate, CRP

  **Non-Iron Deficiency Anaemia** (Ferritin normal or raised)
  - Hyperlink to guidance for MCV <80
  - Hyperlink to guidance for MCV 80-100
  - Hyperlink to guidance for MCV >100

- **Red Flags Present?**
  - Males and Females with Dyspepsia
  - Postmenopausal females with GI symptoms

**Key messages (hyperlink to general principles)**

Most anaemic patients will have Iron Deficiency Anaemia, and the majority will respond to oral iron.

Patients who are to be referred for elective surgery must be screened for anaemia and their haemoglobin must be optimised prior to surgery.

Refer to appropriate secondary care specialty to investigate the underlying cause of anaemia (e.g. GI, gynaecological, haematological, renal).
Launch and Implementation into Practice

The pathway was finalised in January 2016. It has been well received by GPs. There was recognition of the importance of pre-operative haemoglobin optimisation as being equally important as optimisation of a patient with other chronic disorders such as diabetes. The pathway is available on GP clinical systems for convenient reference. The pathway has been further publicised through a GP newsletter. Additionally, a laboratory comment will soon be added to full blood count reports to highlight patients with anaemia, with advice to access and follow the pathway.

Expected Benefits and Outcomes:

- Reduction of inappropriate secondary care referrals.
- Clearer access to secondary care services (IV iron service, Ambulatory Care Unit for urgent treatment, investigation of underlying cause of anaemia by the appropriate specialty).
- Reduction in length of stay and post-operative morbidity through pre-operative haemoglobin optimisation.

Conclusion

The implementation of a systematic approach to the identification, investigation and management of anaemia is a complex process which requires engagement of multiple stakeholders. This regional project described here is supporting such an approach through workshops, the development of a toolkit and eventually demonstration of improved outcomes.

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Reference:

Successful Transfusion Management of an Individual with an IgA Deficiency Related Reaction, through Treatment for Acute Myeloid Leukaemia and Stem Cell Transplant

Selective IgA deficiency is the most common primary antibody deficiency, and has been considered a risk factor for severe allergic/anaphylactic transfusion reactions (Vyas et al., 1968). We describe the successful management of a patient with IgA deficiency and reactions, with heavy transfusion needs, illustrating the current approach to transfusion management in IgA deficiency in England.

A 60-year old woman presented with Acute Myeloid Leukaemia (AML). She reported being found to be IgA deficient during investigation for Chronic Fatigue Syndrome some years before, and had never been transfused. IgA deficiency was confirmed by haemagglutination inhibition technique with an IgA level of < 0.0016 g L\(^{-1}\), and antibody to IgA was detected. Induction chemotherapy was commenced and she developed pancytopenia that required red cell and platelet transfusion. She was initially given standard blood components, as she had no previous transfusion history. However, within five minutes of commencing her first unit of red cells, she complained of light-headedness and difficulty in breathing with wheeze. She experienced a severe reaction with rapid onset of vomiting, rigors and a “feeling of impending doom”. Her temperature rose from 37.1°C to 37.9°C and oxygen saturation dropped from 100% to 94% on room air. The transfusion was stopped immediately and she was given intravenous chlorphenamine and hydrocortisone, as well as salbutamol nebulised with oxygen. It was decided the prevailing clinical features of her reaction were allergic in nature.

She was subsequently transfused with washed packed red cells and platelets with plasma removed and re-suspended in platelet additive solution (PAS). She received a total of 22 units of washed packed red cells and 20 pools of platelets re-suspended in PAS with no further reaction. She completed all courses of chemotherapy and achieved remission.

In August 2015, she underwent an allogeneic bone marrow transplant from a matched unrelated donor.
The donor stem cells were harvested by apheresis and treated to reduce the risk of reaction. The harvest was washed twice in saline albumin to remove donor plasma. The final volume of 99ml was made with 2.5% human albumin solution. 93ml was re-infused fresh to the patient with no transfusion reaction. The remaining 6ml was cryopreserved for possible future donor lymphocyte therapy, using albumin and dimethylsulfoxide as cryoprotectant. At the time of writing, she has engrafted, with mild Graft Versus Host Disease, and remains under outpatient follow up. Her IgA level remains low eight months post transplant, at < 0.05 g L\(^{-1}\) by nephelometry.

IgA deficiency (IgAD) forms part of the spectrum of Common Variable Immunodeficiency Disorders. It is associated with a range of autoimmune conditions; most commonly with coeliac disease. Levels of IgA < 0.0016 g L\(^{-1}\) have been considered to be a risk factor for transfusion reaction, especially in the presence of anti IgA (Vyas et al., 1968).

NHS Blood and Transplant (NHSBT) holds a register of all known patients in the UK who have experienced a transfusion reaction and have IgA deficiency. Currently NHSBT is aware of 13 such individuals alive out of a UK population of 64 million, including the patient we describe, and only this patient has had recent transfusion requirements. The Serious Hazards of Transfusion (SHOT) national haemovigilance database for the UK receives an average of one or two reports per year of new IgA deficient patients who have experienced transfusion reactions. These are not always reports of anaphylaxis or severe allergy, and may include milder reactions or febrile reactions and it can be hard to ascribe imputability (Bolton-Maggs et al., 2013). Therefore, the recent experience of NHSBT and other blood services is that the majority of IgAD individuals do not experience reactions and can receive standard components (Bolton-Maggs et al., 2013; Sandler et al., 2015). Standard components can be used for patients with no history of reaction whether anti IgA is present or not. If an IgA deficient reaction has occurred, as in this case, washed or IgA deficient cellular components and plasma from IgA deficient donors are recommended (Sandler et al., 2015).

Washed red cells produced by NHSBT using the ACP 215 cell washer have been shown to have an IgA level of 0.00065 g L\(^{-1}\). This is very close to the Canadian upper limit for IgA deficient components of 0.0005 g L\(^{-1}\). It is therefore not surprising that the red cells were tolerated well. However, she also tolerated washed platelets which have a considerably higher IgA level at 0.08 g L\(^{-1}\) (Rebecca Cardigan, personal communication). One other IgAD patient with a history of reactions from the NHSBT register has required platelets and received a mixture of washed platelets and platelets from IgA deficient donors without problems.

There are several case reports of patients with reactions and IgA deficiency who have undergone procedures requiring frequent transfusions who have been managed with washed cellular components. Rogers et al. (1998) describe such a patient who also underwent an allogeneic marrow transplant with manipulation of the mononuclear layer from the donated marrow, to reduce exposure to plasma.

The evidence therefore suggests that ready access to washed red cells is likely to remove the need to source red cells from IgA deficient donors. Washed platelets are not equivalent to IgA deficient platelets as they require some residual plasma in order to preserve function and, for NHSBT, the IgA level at 0.08 g L\(^{-1}\), is over 100 times that in washed cells. Evidence suggests most patients tolerate this but strategies need to be considered in cases where washed platelets cause reactions.

One alternative to using washed or IgA deficient components is to desensitise the patient to IgA. Salama et al. (2014) describe successful desensitisation to IgA in a case series of IgA deficient patients with a history of reactions, including four requiring regular intravenous immunoglobulin.

Finally, there have been reports of restoration of normal levels of IgA in IgAD patients following bone marrow transplant (Rogers et al., 1998). Our patient currently remains IgA deficient although will require repeat testing in the future.

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Audit of Wrong Blood in Tube (WBIT) in the West Midlands Region

Introduction
A ‘Wrong Blood in Tube’ (WBIT) event could result in ABO-incompatible transfusion with potentially catastrophic consequences and major morbidity and mortality. An unintentional transfusion of ABO-incompatible blood components is classed as a NHS England Never Event (2015). Discussions at West Midlands Regional Transfusion Committee meetings indicated a concern that WBIT events appeared to be increasing at regional hospitals, and it was requested that a regional audit was performed to investigate this further.

13 organisations completed an online organisational questionnaire, and a total of 126 known WBIT cases were submitted from 14 organisations for the cases audited.

Methods
A consensus approach was adopted to conduct the audit which was agreed by the West Midlands Regional Transfusion Committee (WM RTC). An online survey (SnapSurveys©) was constructed with paper options available for those who continue to use paper documentation. The audit took place in 2015 over a four month period between January and April.

Appropriate governance arrangements were implemented and approval to participate in the audit/survey obtained. Caldicott Guardians in each participating site were also informed and asked to approve (or not) their organisations participation in the audit/survey.

An organisational survey was also carried out to ascertain local policy and procedure with regard to blood sample taking.

Data was analysed proportionately (%, n). Comments were examined for key themes then quantified where appropriate.

Key Findings

Organisational Questionnaire:
- There was no regional reduction in WBITs between 2013 and 2014 as a proportion of the total number of samples processed (0.0150% 2013, 0.0149% 2014, table 1).
- No organisation had introduced electronic patient identification for phlebotomy services.
- 31% (four organisations and two sample rule) had not introduced the British Committee for Standards in Haematology (BCSH) (2012) “2 sample rule” although three of these were planning to do so.
- There is variation in classification of WBIT events on Trust Risk Registers.

Case Audit:
- Doctors were involved in over 40% of WBIT incidents.
- Most WBIT events occur during normal working hours.
- Nearly a third of staff involved had not received up-to-date transfusion training/competency assessment.
- 40% of WBIT events occurred in the ward environment with a further 20% in emergency settings.
- 27% of WBIT events were associated with obstetrics.
- Over 80% of WBITs were detected by the laboratory.
- WBITs were identified within 4 hours of the event in 70% of cases. 22% were identified in less than 30 minutes.
- No patient received a blood component as a result of the WBIT.

References:
Most errors were related to patient identification and labelling issues.

Just over half the cases were the subject of a Root Cause Analysis (RCA) investigation.

Staff responsible for the WBIT were generally re-trained and re-assessed following the incident.

Table 1: Summary of WBIT events in 2013 and 2014

<table>
<thead>
<tr>
<th>Trust Code</th>
<th>2013 Tot Samp</th>
<th>2013 Tot Rej (%)</th>
<th>2013 Tot WBIT</th>
<th>2014 Tot Samp</th>
<th>2014 Tot Rej (%)</th>
<th>2014 Tot WBIT</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>6,277</td>
<td>37 (0.58)</td>
<td>0</td>
<td>5,931</td>
<td>40 (0.67)</td>
<td>1</td>
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<tr>
<td>B</td>
<td>14,560</td>
<td>454 (3.1)</td>
<td>6</td>
<td>15,350</td>
<td>461 (3)</td>
<td>3</td>
</tr>
<tr>
<td>C</td>
<td>15,956</td>
<td>1,018 (6.3)</td>
<td>3</td>
<td>15,684</td>
<td>1,041 (6.6)</td>
<td>0</td>
</tr>
<tr>
<td>D</td>
<td>19,394</td>
<td>1,013 (5.2)</td>
<td>2</td>
<td>18,658</td>
<td>1,025 (5.4)</td>
<td>2</td>
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<tr>
<td>E</td>
<td>37,359</td>
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<td>6</td>
<td>43,980</td>
<td>2,582 (5.8)</td>
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<tr>
<td>F</td>
<td>50,403</td>
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<td>7</td>
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<td>G</td>
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<td>32,135</td>
<td>2,479 (7.7)</td>
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<td>K</td>
<td>38,131</td>
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<td>53,243</td>
<td>4,046 (7.5)</td>
<td>6</td>
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<tr>
<td>M</td>
<td>39,007</td>
<td>3,190 (8)</td>
<td>5</td>
<td>43,344</td>
<td>2,210 (5)</td>
<td>9</td>
</tr>
<tr>
<td>Totals</td>
<td>366,168</td>
<td>21,024 (5.7%)</td>
<td>55</td>
<td>389,310</td>
<td>21637 (5.5%)</td>
<td>58</td>
</tr>
</tbody>
</table>

Recommendations:

- All WBITs should be classed by hospitals as a ‘Near Miss Never Event’.
- Hospitals should follow the guidance of the BCSH (2012) Guidelines for Pre-transfusion Compatibility Procedures in Blood Transfusion Laboratories, which recommend that unless secure electronic patient identification systems are in place, a second sample should be requested for confirmation of the ABO group of a first time patient prior to transfusion, where this does not impede the delivery of urgent red cells or other components.
- There should be a hospital policy for the identification and communication of identified WBIT events across pathology.
- All identified WBITs must continue to be reported to the Serious Hazards of transfusion scheme.
- WBIT incidents should be investigated proportional to the event (as advised by the Hospital Transfusion Team) using appropriate ‘root cause analysis’ techniques. Staff using these techniques should be trained in their use. Subsequent actions should relate to the identified root causes. Re-training and re-assessment are not always adequate actions following a WBIT error.
- The West Midlands RTC should adopt the London Transfusion Practitioner Group’s ‘Top 10 tips for improving sample collection and labelling practice’.

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Acknowledgements:

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The Broken Gift – A Donor Optimisation Analogy

There was once a man called Smith and he who owned a laptop. Now Smith couldn’t use his laptop anymore. So Smith wondered whether someone else might be able to use it instead. He’d heard that schools in Africa were always after used laptops and by chance he knew a man, called Jones, who was going to Africa.

So he asked Jones to take his laptop and give it to an African school.

Jones agreed. But when Jones came to pack his bags he threw the laptop in at the last minute, and took no steps to protect it.

When Jones arrived in Africa he discovered that the laptop was broken.

To whom did Jones owe the duty of care?

Donor optimisation can be defined as clinical actions designed to protect or improve the quality of donated organs while still in the donor. This would normally be in patients who have been confirmed dead using neurological criteria (brainstem death) and whose organs are maintained with ongoing mechanical ventilation. It would also include additional actions such as the administration of steroids and tight control of physiological parameters.

Traditionally in intensive care, donor optimisation was either half-hearted or justified by reference to the actions serving the interests of the future organ recipients. Indeed, I was taught that on consultant intensive care ward rounds, one should walk right on past that bed space because the patient was dead and there was nothing we could or should do. A behaviour I regret modelling in the early part of my consultant career.

What duty then does the donating hospital intensive care owe to the future organ recipients?

Now Smith was also a country general practitioner. He had a quantity of intravenous antibiotics that were approaching their expiry date. Since Jones was taking his laptop to Africa, Smith asked Jones to also take the antibiotics and give them to a hospital. There the antibiotics might be used to save lives, rather than expire and never be used. Like the laptop, Jones packed poorly and all the antibiotics were broken.

Not only has Jones failed in his accepted responsibility to Smith, by his actions and inactions, he has probably led to deaths that might have been prevented. A much worse outcome than a school missing out on a laptop.

Perhaps Jones may not have thought about the responsibility he was accepting when he agreed to carry the antibiotics. It was a snap decision, easy enough just to take Smith’s antibiotics, that’s what was being asked for at that moment and not dwell overlong on the implications or consequences. This however, is the trap of moral distance: an excessive focus on the physically close or immediate, leading to a lack of attention paid to the wider consequences of one’s actions. Actions (or inactions) have consequences which can include harming or contributing to the deaths of patients who are separated by space and time, but are no less affected by a health care professional’s decision.

But I would not like to imply that the present situation mirrors the past. We have seen an astonishing culture change in intensive care over the last decade where both ethical, legal and professional guidance has advocated for organ donation and the intensive care community has responded in turn. Many health care professionals from intensive care, and other areas of the NHS which help facilitate deceased organ donation, have accepted our role as guardians of an end of life wish to donate. Donor optimisation is an important aspect of that role.

For those who want to know more of the how, and not just the why, The MOHAN Foundation (a not-for-profit
Case Report—Successful ABO Incompatible Kidney Transplant following use of Glycorex Immunoadsorption Column

**Background**

A 22 year old male patient (Blood Group O) was diagnosed with Chronic Pyelonephritis in 2005 following chronic renal failure from congenital problems. He was commenced on dialysis treatment by the renal team and had a successful cadaveric kidney transplant the following year. This graft lasted for three years before failing. The patient resumed dialysis treatment three times weekly. He had also developed very high levels of anti B antibodies and this prevented the use of a second kidney.

Aged 32 years in February 2015, the situation was reviewed by the Renal Team and a plan formulated to try to reduce the antibody level using a combination of conventional plasma exchanges and immunomodulation with Alemtuzumab. This would then allow a second kidney transplant to take place.

**Method**

The Optia machine in conventional use is manufactured by Terumo and separates whole blood into its various components using centrifugal speed and allows the plasma containing the antibody to be removed from the patient’s circulation and replaced with 4.5-5% Human Albumin Solution (HAS). Anticoagulation of the circuit is obtained using Acid Citrate Dextrose Solution A (ACD-A) at a reinfusion rate of 0.8 mls per litre of blood volume. Citrate ion anticoagulates by chelating calcium ions and blocking calcium dependent clotting factor reactions. Decreases in ionized calcium can increase the excitability of nerve cell membranes and this may sometimes cause perioral and/or peripheral paraesthesias during apheresis.

Glycosorb-ABO (Glycorex column) is a bio-specific affinity column that removes the blood group-specific antibodies from the recipient in an extracorporeal blood treatment. There are other immunoadsorption columns available on the market that can also remove specific antibodies, but we evaluated glycorex on this patient.

Once connected to the Optia circuit, the plasma from the patient circulates through it, adsorbing the antibody from the patient’s plasma and returning the treated plasma back through the Optia circuit to rejoin the rest of the components. There is no requirement for the use of HAS as replacement. The columns are single use only and are discarded after use.

**Results**

The patient was scheduled to have several plasma exchange treatments in February 2015 to reduce the anti B titre level from 128 to below eight followed by the use of Alemtuzumab and then a kidney transplant. He had six plasma exchange treatments over a ten day period but the anti B titres rebounded after each treatment and never went below a titre of 16 in spite of treatment with Alemtuzumab as well. The kidney transplant did not go ahead and the patient was resumed on dialysis treatment.

The situation was reviewed in September 2015 with the launch of the Glycorex column and the decision was taken to evaluate the use of this column in this patient. Nurse training on the use of the glycorex column in conjunction with the Optia machine was organised and went very well.

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**Reference**

The patient accessed his own fistula for cannulation before each procedure and this provided good flow rates of 50-70ml/minute.

The machine set-up time was only 20 minutes and the patient had six treatments before the kidney transplant and seven treatments post transplant. All the treatments before the operation were undertaken using the column with the Optia machine and out of the seven treatments post operatively, only two were with the column, the remaining five were conventional plasma exchanges only as the antibody titre remained low.

Discussion

The Indirect Antiglobulin Test (IAT) is used to detect red cell antibodies in patients’ serum. This is performed by incubating patients with reagent screening cells for approximately 20 minutes and then observing for agglutination. The level of the antibody is then measured.

Alemtuzumab is a humanised monoclonal antibody against CD52, an antigen found on the surface of T and B cells. The proposed mechanism of action is by depletion of circulating T and B cells and it was used as immunomodulatory therapy but did not reduce the antibody levels as expected at the time.

The Glycosorb ABO column is a medical device which when connected to a plasma separator is intended for the specific reduction of anti-A and/or anti-B antibodies in plasma to facilitate transplants across the blood group barrier.

The plasma volumes treated during plasma exchange procedures can be between 1.5 to 3 Plasma volumes. A one plasma volume removes about 65% of what is circulating in the intravascular compartment while a two plasma volume removes 85%.

This patient’s exchanges were between 1.5 and 2 plasma volumes. Two plasma volumes took 168 minutes while the only 3 plasma volume treatment took 218 minutes which he was subsequently unable to tolerate due to the excessive time for which he had to be still while attached to the machine.

Conclusion

The procedures were well tolerated by the patient both pre and post transplant. He had mild citrate reactions as a consequence of the anticoagulation but this was mainly perioral tingling which was managed by calci chew tablets.

There was no requirement for the use of Intravenous Calcium Gluconate.

ABO incompatibility was previously regarded as an absolute contraindication to kidney transplantation but this was overcome in this patient by the use of the Glycosorb Immunoadsorption column with the Optia machine.

The Nurse Practitioners running the machines found the equipment easy to set up and use.

The patient went on to have a successful kidney transplant and did well postoperatively. He was discharged from hospital after three weeks and continues to do well at home.

As a technological supplement to our Optia Machines, the Glycorex column has potential possibilities for the future. It is planned to use it for future ABO incompatible kidney transplant patients presenting in Leeds.

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Tissue Transplant in Ocular Surgery

The last decade has witnessed remarkable changes in ocular surgery. Tissue transplantation has revolutionized the treatment of conditions that were previously sight threatening or blinding. Corneal surgeons have felt the pace of change, developing new techniques alongside NHS Blood and Transplant (NHSBT) Tissue Services in a symbiotic innovative relationship. This article aims to explore how these changes have improved patient care and outcome.

We will focus on corneal transplantation, scleral tissue transplantation and the use of amniotic membrane in eye surgery.

The Cornea and Corneal Transplantation

The cornea is commonly described as the “window” into the eye, responsible for both transmitting and focusing light towards the light sensitive cells at the back of the eye. This key role means that any condition affecting the transparency or shape of the cornea can dramatically impact on the quality of a patient’s sight, and it is no surprise that loss of vision (or blindness) is rated as the second most feared condition (after cancer). Corneal transplantation gives us the opportunity to allay this fear and to return patients to their normal daily activities.

What common conditions require a Corneal Transplant?

Corneal Ectasia is a change to the shape of the cornea, thus leading to visual disturbance. One of the commonest of these is keratoconus, typically seen in adolescents and young adults (Figure 1), where the cornea becomes deformed and conical in shape. Other examples include pellucid marginal degeneration (PMD) and post-refractive surgery ectasia.

Figure 1: Typical conical appearance of cornea in keratoconus

Corneal scarring from infection or trauma can lead to deformity or opacification. The healing process often leads to new blood vessel formation (corneal vascularization) leading to visual loss as new opaque tissues form in the corneal layers (Figure 2).

Figure 2: Corneal scarring

Although scarring is most often a chronic process some patients present as emergencies with sight-threatening corneal infections necessitating an urgent (tectonic) transplant to preserve globe integrity (Figure 3). These are high-risk emergency procedures, amongst the more challenging procedures in corneal surgery.

Figure 3: Sight-threatening corneal infection

The cornea has no blood vessels and is supported by the regular arrangement of its collagen fibrils that is maintained by the pumping action of the inner layer of endothelial cells. A failure of this endothelial pump leads to Corneal Decompensation where excessive hydration of the cornea and loss of transparency can lead to bullae (blister) formation and pain. This can be seen in patients with Fuchs Endothelial Dystrophy (FED) or following cataract surgery.

Corneal Transplantation

Until recently nearly all patients received a full thickness corneal transplant where all layers are replaced (Figure 4). This is still a successful technique but there is no doubting the potential serious complications that can arise such as astigmatism, endothelial rejection, graft failure or wound dehiscence.
Corneal surgeons have developed lamellar procedures where only the affected layers are excised and replaced. These targeted techniques are more technically challenging and time consuming but offer significant advantages to patients.

There are two common lamellar procedures. In Deep Anterior Lamellar Keratoplasty (DALK) patients with functioning endothelial cells but damaged or distorted stroma have all layers but the endothelium replaced. Most commonly it is performed for young patients with keratoconus. The patient’s own endothelium is preserved, replacing only the donor’s stroma and epithelium. Rejection rates are significantly reduced with minimal risk of graft dehiscence.

Endothelial Keratoplasty (DSEK or DMEK) is a replacement of the endothelial layer which has revolutionized our management of patients, often elderly, with corneal decompensation. Recent data tells us that this is now the leading indication for surgery here in the UK. In this lamellar procedure only the endothelial cells accompanied with limited posterior stroma (Descemet’s Stripping Endothelial Keratoplasty) or just Descemet’s membrane (Descemet’s Membrane Endothelial Keratoplasty) are replaced. Patient outcomes are excellent and dramatic with no risk of graft dehiscence and little risk of rejection (Figure 5).

As an alternative to scleral tissue, corneal tissue stored in alcohol can also be used to cover these drainage devices. This is an important use of corneal tissue, unsuitable for corneal transplantation, that would previously have been discarded.

Amniotic membrane transplants are now an established treatment for severe ocular surface problems. This material, obtained from the human placenta, is known to have significant anti-inflammatory properties and has an ability to promote epithelialisation, reduce pain and inhibit bacterial growth. It is used to treat non-healing corneal ulcers and persistent epithelial defects.

More recently surgeons are using amniotic membranes in the acute management of severe chemical eye injuries and severe ocular complications of Steven Johnson’s syndrome (SJS). Without active intervention, both of these conditions can result in scarring or blindness (Figure 7).
Figure 7: Application of amniotic membrane to ocular surface of patient with SJS

**Summary**

The ocular and non-ocular tissues, provided by NHSBT Tissue Services, have helped drive the development of new and innovative treatments for corneal, ocular surface and glaucoma patients. As these techniques have developed, Tissue Services have reflected and responded to the clinical need now providing a range of pre-cut materials for DSAEK and with ongoing plans to prepare and provide tissue for DMEK imminent.

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**References:**


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Serum Eye Drops Service – Role of NHSBT

This article explains the role of NHS Blood and Transplant (NHSBT) in Serum Eye Drops (SED) Service provision for patients with severe dry eyes.

Severe dry eyes are caused by disorders that interfere with the ability of the eye to generate a normal tear film. This may result from decreased tear production, excessive tear evaporation, or abnormalities in the production of mucus that form part of the tear film. There are multiple causes of dry eye syndrome, including:

- Autoimmune diseases, especially Sjogren’s syndrome.
- Other immune mediated conditions, such as Graft Versus Host Disease.
- Injury or trauma.
- Side effects of disease or medication.
- Physical conditions that cause difficulties in closing the eyelids.

In the majority of cases, dry eyes can be resolved through the use of artificial eye drops and other interventions. There remains however, a small proportion of dry eye patients who do not gain relief from conventional treatment and persistence of symptoms due to abrasions and infections can cause damage to their cornea, resulting in severe pain and visual impairment. These patients may be prescribed SED when there is no other suitable licensed medicine available for treatment.

**SED Service Provision by NHSBT**

An Autologous Serum Eye Drops (ASE) Service was introduced by NHSBT, then the National Blood Service in Leeds in 2003, following a cross over clinical trial conducted with ophthalmologists at St James University Hospital. The service was then rolled out to other blood centres.

Some patients referred for ASE treatment fail to meet the health requirements necessary for blood donation, and are thus unable to donate blood for ASE treatment. The main reasons for deferral include poor cardiovascular status, anaemia and poor venous access. The treatment is also unavailable to children.

Following requests from prescribing ophthalmologists, NHSBT introduced an allogeneic serum eyedrops service (AlloSE) in June 2014. AlloSE are prepared from blood donated by volunteer male donors for patients who are not medically suitable to donate their own blood.
For a small number of patients born after 1st Jan 1996 AlloSE is currently prepared from imported serum as a risk reduction measure to reduce the potential for transmission of prions.

How does the service work?

Referral and Assessment:

From March 2013, coordination of our SED service has been centralised and is delivered to patients throughout the United Kingdom from our Liverpool Centre, managed by our Tissue and Eye Services (TES) section. The central administration hub manages SED referrals and enquiries from the ophthalmologists and coordinates with the patients on the programme. The consultants must complete a clinical request form to refer patients as this is a regulatory requirement. The hub is responsible for coordinating initial assessment of requests for new patients by the TES Clinical Team for accepting the patients into the SED programme, either for ASE, or for AlloSE if patients are not medically suitable for autologous donation. AlloSE is available off the shelf to meet urgent requests within 48 hours for patients who require treatment immediately.

Donation:

The TES hub is responsible for contacting patients to arrange their donation appointments for ASE. A pre-donation clinical assessment is undertaken by nurses based in the TES National Referral Centre (NRC) over the phone, normally one week before autologous donation. The details of this assessment are then sent to the donor centre nurses prior to the patient’s appointment. The patients can attend blood donation centres at Leeds, Liverpool, Newcastle, Oxford, Bristol, Birmingham and London to donate blood on the appointment time arranged by the hub. NHSBT provides its ASE service nationally to all patients in the UK. Currently, patients in England and Wales attend one of our donation centres in England to donate blood. The Scottish and Northern Irish Blood Transfusion Services collect blood from patients living in Scotland and Northern Ireland. The blood is collected into ‘dry’ collection bags that do not contain anticoagulants, and transported to Liverpool for SED preparation. AlloSE donations are collected in Liverpool and Manchester centres due to their geographical proximity to NHSBT Liverpool.

Processing:

The blood is allowed to clot and then processed to remove the red cells. The remaining serum is diluted in a 1:1 (w/w) ratio with physiological saline and aseptically dispensed into individual dropper bottles, each containing one day’s supply of ASE. Five percent of the bottles are sacrificed for sterility testing. Subject to satisfactory quality assessment against the release criteria, the batches are then returned to the patients by same day courier, and stored in their domestic freezers, thawing out and using one bottle each day.

The SED management pathway is shown in figure 1.

Regulation

The patients and the voluntary blood donors must meet eligibility criteria for blood donation defined in the Blood Safety and Quality Regulations (2005). Patients and donors must attend licensed blood collection venues for their blood to be taken.

SED are classified as an unlicensed medicine and as such are prepared under a ‘specials’ manufacturing licence issued by the Medicines and Healthcare products Regulatory Agency. As an unlicensed medicine, SED must be prescribed for individual patients by a registered medical practitioner (usually an ophthalmologist) who is responsible for their care. To provide the service, NHSBT sets up a Service Level Agreement with the Hospital Trust treating the patient, which covers funding and governance responsibilities.

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Reference:

Hepatitis E and Blood Transfusion

1. Hepatitis E Virus (HEV):
   a) Only infects pigs.
   b) Confirmed human cases have increased significantly in the UK since 2003.
   c) A study in 2012/2013 showed less than one in 200 blood donors in the South of England were infected with the virus.
   d) Only transmitted by eating undercooked or raw pig meat.

2. HEV:
   a) Most infected people are very unwell.
   b) Characteristically has a slow recovery.
   c) Cleared slowly even in people with a healthy immune system.
   d) People who have immune systems, which do not work normally, are at risk of persistent HEV infection leading to Chronic Liver Disease.

3. The following patient groups’ do not require HEV negative screened components:
   a) Undergoing solid organ transplantation.
   b) Have allogeneic Stem Cell Transplant.
   c) Neonates and children less than one year old.
   d) Over 80 years of age.

4. Which of the following statements about HEV is untrue?
   a) More than 1,400 donors coming to give blood are unknowingly infected with HEV.
   b) Vulnerable patients need to receive dietary advice.
   c) HEV infected donors are permanently deferred from donation.
   d) Over 25% of all donations may need to be screened in order to ensure sufficient stocks of HEV screened components.

5. Horizon Scanning for Infectious Threats:
   a) NHSBT has never had a mechanism to monitor changing disease patterns.
   b) NHSBT only monitors infectious agents that may be transmitted through donated products.
   c) NHSBT keeps monitoring information restricted to itself.
   d) Responsibility for the Horizon Scanning System was passed to JPAC.

In Search of the Bigger Picture

6. MSM deferral policy from lifetime to 12 months since last sexual contact was implemented in:
   a) 2011.
   b) 2010.
   c) 1995.
   d) 1994.

7. Results if the survey indicated that:
   a) Compliance with Donor Selection Guidelines concerning infectious disease risk behaviours was very high.
   b) Non-compliant donors had a good understanding of the donor selection guidelines.
   c) Non-compliant donors had a good perception of risk.
   d) All 1.2 million individuals donating blood in the UK were invited to participate.

8. Management of Pre-Operative Anaemia:
   Match Potential Solution to Barriers.
   Barriers Potential Solutions:

   | A) Difficulty in identifying resources to support the delivery of Anaemia Management Service. | 2) Focus on the patient experience; Provide patient information; patient to carry data collection form as secondary information; collect qualitative data as one of outcome measures. |
   | C) Lack of engagement with patients. | X) Consult with CCGs/General Practitioners (GP) to define GP role, raise awareness; use pathways/templates from toolkit of resources as examples. |
D) Lack of engagement with commissioners.
W) Agree roles & responsibilities/identify champion at the outset; use multi-disciplinary approach including haematologists, laboratory staff, anaesthetists and surgeons; early consultation with key stakeholders enables effective communication; persevere through politics/staffing changes; pilot pathways; continued promotion/networking/sharing of information and learning.

E) Lack of engagement with Primary Care.
V) Early consultation with commissioners; ensure that business case is aligned to key National Health Service (NHS)/Clinical Commissioning Group (CCG) priorities and aim to commission pathway that will incentivise best practice.

F) Anaemia identification often too late in surgical pathway to allow time for appropriate Investigations and management.
U) Use toolkit measurement tool and data collection forms; pilot measurement tool to systematically collect outcome measures; identify data that can be collected from electronic systems. Use data to drive performance improvement.

G) Difficulties monitoring outcomes.
T) Develop a business case that covers the full range of resources required and ensure relevant income is identified through use of payment by results tariffs and potential cost savings are identified such as reduction in blood transfusion, improvement in length of stay. See toolkit of resources.

9. IgA Deficiency:
   a) Washed red cells have been shown to have an IgA level of 0.0065 g/L.
   b) Washed red cells are likely to remove the need for red cells from IgA deficient donors.
   c) Washed platelets have no residual donor plasma.
   d) Washed platelets have been shown to have an IgA level of 0.0008 g/L.

10. Organisational Questionnaire Findings:
   a) There was a regional reduction in WBITs between 2013 and 2014.
   b) All organisations had introduced Electronic Patient Identification of Phlebotomy Services.
   c) 31% had not introduced the BCSH (2012) ‘sample rule’.
   d) None were planning on introducing the BCSH (2012) ‘sample rule’.

11. Case Audit Findings:
   a) Doctors were involved in over 40% of WBIT incidents.
   b) Most WBIT events occurred at night.
   c) Less than 20% of WBIT’s were detected by the laboratory.
   d) WBIT resulted in a number of patients receiving a blood component.

12. ABO Incompatible Kidney Transplant:
   a) Alemtuzumab is a humanised monoclonal antibody against CD48.
   b) CD52 is an antigen? The surface of T and B cells.
   c) Proposed mechanism of action of Alemtuzumab is by depletion of circulating T cells only.
   d) Glycosorb ABO column is intended for specific reduction of anti-B antibodies only.

13. Tissue Transplant in Ocular Surgery:
   Corneal Transplantation.
   a) Only full thickness corneal transplant is possible.
   b) Is of no use in post-refractive surgery ectasia.
   c) Is contra-indicated in sight-threatening corneal infections.
   d) Cornea has no blood vessels.

14. Which of the following is not a lamellar procedure?
   a) DALK.
   b) DSEK.
   c) DALEK.
   d) DMEK.

15. Serum Eye Drops Service:
   Which of the following is not a cause of Dry Eye Syndrome?
   a) Sjogren’s Syndrome.
   b) Graft-Versus-Host Disease.
   c) Bell’s Palsy.
   d) Entropion.
Clinical Case Studies

Question 1
A 53 year old woman with recently diagnosed anti-GBM disease (Goodpasture’s) is referred for a Therapeutic Plasma Exchange (TPE).

1) What factors will influence the likelihood that TPE will be helpful?
2) What replacement fluid would you recommend?
3) What protocol (volume/frequency/duration) would you recommend?

Question 2
A 31 year old woman with Sickle Cell Disease is referred for Red Cell Exchange Programme (RCEP). Her red cell Rh and K phenotype is D+, C-, c+, E-, e+, K-.

On current testing, the following antibodies have been detected: anti-E, -N, -Fy3, -Do(b).

The following antibodies cannot be excluded: anti-S, -K.

Previous testing on earlier samples has detected: anti-Fy(a), -Wr(a).

1) What are the indications for RCEP?
2) What red cell specification is recommended?
3) What red cell phenotype is recommended in this case?
4) Is RCEP feasible in this case?

Question 3
Two units of rare red cells are requested from the National Frozen Blood Bank (NFBB). The NFBB records show that there are only two suitable units available. One unit was donated six days before freezing, the other has been stored for 12 years.

1) What is the stated required maximum age of a red cell unit at time of freezing?
2) What is the maximum storage period?
3) What is the expiry period post thaw?
4) Can these units be issued to this patient?
5) How long does it take for frozen units to be thawed?

Answers to Clinical Cases

Question 1
A 53 year old woman with recently diagnosed anti-GBM disease (Goodpasture’s) is referred for Therapeutic Plasma Exchange (TPE).

4) What factors will influence the likelihood that TPE will be helpful?

Early implementation, not dialysis dependent, creatinine less than 500 μmol/l. TPE also indicated if Diffuse Alveolar Haemorrhage (DAH) is present.

5) What replacement fluid would you recommend?

4.5 % albumin primarily, with Fresh Frozen Plasma (FFP) or Octaplas for final portion if DAH present.

6) What protocol (volume/frequency/duration) would you recommend?

ASFA guidelines recommend exchanging 1-1.5 Total Plasma Volume (TPV) daily or on alternate days for a minimum of 14 days until resolution of ongoing glomerular or pulmonary injury.

Question 2
A 31 year old woman with sickle cell disease is referred for RCEP. Her red cell Rh and K phenotype is D+, C-, c+, E-, e+, K-.

On current testing, the following antibodies have been detected: anti-E, -N, -Fy3, -Do(b).

The following antibodies cannot be excluded: anti-S, -K.

Previous testing on earlier samples has detected: anti-Fy(a), -Wr(a).

1) What are the indications for RCEP?

Primary stroke prevention.
Secondary stroke prevention.

2) What red cell specification is recommended

Sickle negative, less than seven days old if possible, largest volume unit available.

7) What red cell phenotype is recommended in this case?

D+C- E- K- Fy(a-b-) Do(b-) S-.

8) Is red cell exchange programme feasible in this case?

No, very few donors available of this type.
Question 3

Two units of rare red cells are requested from the National Frozen Blood Bank (NFBB). The NFBB records show that there are only two suitable units available. One unit was donated six days before freezing, the other has been stored for 12 years.

1) What is the stated required maximum age of a red cell unit at time of freezing? **Five days.**

2) What is the maximum storage period? **Ten years.**

3) What is the expiry period post thaw? **72 hours.**

4) Can these units be issued to this patient?

   Yes using a clinical concession providing the requesting clinical team are happy to accept – and in cases of rare red cells there is often no alternative. Studies have shown there is no detrimental effect on storing red cells beyond ten years.

9) How long does it take for frozen units to be thawed?

   Units are thawed maximum of two at a time. From start of process to point of issue takes three hours per pair plus one hour for example six units takes ten hours.

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**CPD Blood and Transplant Matters**


**Answers Issue 48**
**Diary Dates 2016**

21-23 September
BBTS Annual Conference
Location: Harrogate International Centre, Harrogate
For more information contact:
www.bbts.org.uk

05 October
UK CLL forum Clinical Sciences Day –
New Treatments – New Challenges in CLL
Location: Brunei gallery, School of Oriental and African Studies, Thornhaugh Street, London WC1H 0XG
For more information contact:
www.b-s-h.org/courses

10 October
Manchester Blood Coagulation Course
Location: Hallmark Hotel Manchester Willow Bank, 340 Wilmslow road, Fallowfield, Manchester M14 6AF
For more information contact:
www.b-s-h.org/courses

11 October
Haematological Malignancies
Location: Hilton Leeds City Centre LS1 4BX
For more information contact:
www.b-s-h.org/courses

12 October
Glasgow – Haematological Malignancies
Location: Glasgow Grand Central Hotel, 99 Gordon Street, G1 2SF
For more information contact:
www.b-s-h.org/courses

22-25 October
AABB Annual Meeting
Location: Orlando, Florida
For more information contact:
www.aabb.org

01 November
UK NEQAS (BTLB) and BBTS Blood Bank Technology Special Interest Group
Location: York Racecourse, Voltigeur Suite, 3rd Flood, Knavesmire Stand, York
For more information contact:
www.bbts.org.uk

24-25 November
Advances in Transfusion Medicine
Location: The Royal Society of Medicine, Wimpole Street, London
For more information contact:
www.rcpath.org/event

24-25 November
19th BSH Annual Autumn Meeting
Location: Queen Elizabeth II Centre, London
For more information contact:
www.b-s-h.org.uk/

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