Patient Blood Management Seminar
18 June 2012

Summaries of the presentations
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All conference presentations are available on the NBTC webpages of the transfusionguidelines website at link: [http://www.transfusionguidelines.org.uk/Index.aspx?Publication=NTC&Section=27&pageid=7729](http://www.transfusionguidelines.org.uk/Index.aspx?Publication=NTC&Section=27&pageid=7729)
Changes in blood usage

Dr J P Wallis, Consultant Haematologist, Newcastle upon Tyne Hospitals

Repeated surveys in the north east of England (pop 2.85 million) have shown an 18% fall in red cell use between 1999 and 2009. This change is entirely due to a reduction in use for surgical patients and is concentrated in recipients aged 50 to 80 years. During this period although there has been a modest fall in first time coronary artery surgery and a late fall in emergency aortic aneurysm repair, there has been a 100% increase in lower limb arthroplasty. Medical use shows no change and Obstetric use a minor fall. The reasons for this fall cannot be certain but the impact of the TRICC trial on surgical transfusion triggers should not be underestimated. Over the same period we have seen the widespread introduction of Transfusion Practitioners as liaison between blood bank and wards, and the impact of three national initiatives, Better Blood Transfusion 1, 2 and 3. Whatever the cause transfusion rate per 1000 population in the region has fallen from 45/1000 in 1999 to 36/1000 in 2009. Transfusion rates vary widely between countries despite similar levels of health care. A European survey in 2004 showed a lowest rate of 32.8/1000 for France, levels in the 50-59/1000 for Sweden, Germany and Greece, and a rate of 72.8/1000 for Denmark (Poel C vd et al, 2007). These figures for issues from blood centres may conceal varying hospital wastage and use of autologous transfusion, but nevertheless suggest very real and marked variations in transfusion practice. Similar variation is seen in North America for 2008 where the USA issued 48.8/1000 red cells compared to about 35/1000 in Canada. In the UK we are served by 4 separate transfusion services. Figures for red cell issues to hospitals for 2010 (England and North Wales 35, Wales 39, Scotland 39 and Northern Ireland 29.6/1000) again show marked differences. Only some of this variation can be explained by case mix and population demographics and we cannot say whether a lower or a higher rate is better for patients, but the differences suggest substantive differences in transfusion practice between similar nations. It is an inescapable conclusion that there is room for change. Plotting red cell use against population age shows a dramatic increase in use beginning after the age of 45 years and continuing in more than a linear fashion with increasing age (figure). The ageing population in many western countries is likely to lead to an increased demand for red cells from a relatively reduced donor base if the current trends continue. Surgical use may still be amenable to improvement but medical use now predominates and trials of different transfusion policies in these patients, to guide our practice, are lacking. Data on who receives transfusion and why are valuable to blood services for estimating future demand and enabling logistic and emergency planning, and to hospitals for audit, peer review and demand control.

References

Tinegate et al. Ten year pattern of red cell use in the North of England Transfusion. Accepted for publication 2012.


Council of Europe

Figure: Red cell use in NE England for 28 days adjusted for population age structure.
Patient Blood Management in Australia

Dr Erika Wood, Monash University Melbourne, Australia

The concepts and application of patient blood management (PBM) are now well established in Australia.

PBM guidelines have been developed, in a series of six modules. At the time of writing, two of these (on critical bleeding/massive transfusion and perioperative blood management) have been published and the third (medical) module is imminent. Further modules on critical care, obstetrics and paediatrics are in development. Each has been based on a systematic review. To ensure clinical relevance and support implementation of recommendations, the process was overseen by a steering committee, expert working group and various clinical reference groups for each module, with multidisciplinary participation from Australian and New Zealand professional colleges and special societies. Funding for the guideline development process and systematic reviews was provided by the National Blood Authority (NBA). The guidelines and background information are available at www.nba.gov.au

New national standards were published in 2011 by the Australian Commission for Safety and Quality in Healthcare (www.safetyandquality.gov.au). The blood and blood product standard outlines essential elements required of health services for transfusion governance and clinical practice, including informed consent, policies and procedures, staff education and training, blood utilisation and wastage, and audit and review.

Over the past decade Australia has established strong networks of transfusion practice improvement collaboratives at state and territory level. These typically are partnerships between jurisdictional health departments, hospitals and the Australian Red Cross Blood Service. The work of the collaboratives has focussed on strengthening clinical governance with support for institutional transfusion committees; implementation of clinical guidelines, haemovigilance and PBM programmes; education and training; and quality activities such as clinical auditing. These groups have served as "laboratories" for developing and testing ideas for practice improvement, and sharing ideas, materials, tools and experiences. Establishing the hospital transfusion practitioner role was a key component of the early work of the collaboratives. Specialist training for this role is available via an online graduate certificate in transfusion practice (www.health.vic.gov.au/bloodmatters) and an active network of practitioners now exists across Australia and New Zealand, who share ideas and best practices and provide support to those new to the role. Government funding and support have been critical, and engagement of a broad range of clinical champions has been essential to the success of the programmes. At a national level, there is “buy-in” and coordination from government, with a national PBM committee established by the NBA.

There is strong interest from governments, health services, clinicians and academia in data linkage activities. These use a range of data sources, such as hospital laboratory and clinical (medical record) information systems, administrative datasets, clinical registries, and Blood Service data. With these projects it is critical that
definitions are clear, and quality issues relating to data sources and limitations are understood.

There is strong interest from governments, health services, clinicians and academia in data linkage activities. These use a range of data sources, such as hospital laboratory and clinical (medical record) information systems, administrative datasets, clinical registries, and Blood Service data. With these projects it is critical that definitions are clear, and quality issues relating to data sources and limitations are understood.

Substantial research in PBM underway in Australia, including in the areas of human factors and implementation research, to ensure that evidence-based guidelines are translated into practice. Further work is required to measure & improve the effectiveness of our education and interventions, and to develop meaningful performance measures in PBM.
Hospitals and Regional Transfusion Committees using data to reduce inappropriate use of platelets

Dr Janet Birchall, Consultant Haematologist, Southmead and Frenchay Hospitals, Bristol

Providing hospitals with comparative blood component issues data can influence demand.

There are many methods which can be employed to influence blood transfusion practice. These include the use of guidelines, education and training, audit of practice and challenging potential inappropriate requests by the transfusion laboratory. In addition to these very active interventions simply providing data which compares use between hospitals can also effect change. This intervention was used in the South West of England following a national platelet use audit and likely facilitated a change of practice, as described below.

Platelets are a frequently requested blood component and haematology patients are the largest users with a reported use of up to 67% of all platelet concentrates issued\(^1\). Over the last 3 years demand has increased in England by 16% and the majority of this rise has occurred in the last 12 months. In the financial year April 2011 to March 2012 265,000 adult therapeutic doses were issued at a cost of over 50 million pounds. A National Comparative Audit (NCA) of platelet use in haematology patients was performed in 2010 and therefore timely and well placed to examine appropriate use and make any recommendations required to improve practice. This was a large and very labour intensive audit with participation from 171 hospitals in the UK providing 3296 platelet transfusion episodes for analysis. Using an algorithm based on current guidelines 28% of all transfusions were considered inappropriate. Prophylactic transfusions accounted for 70% of all use. Within this group 34% were judged to have been inappropriate and 10% were double dose despite recent evidence that this is unnecessary\(^2\). Although the results were not directly comparable to a previous NCA audit of platelet use in 2007 no obvious improvement in practice could be identified.

In the South West of England blood component trend analysis data is routinely provided to hospitals by the Regional Transfusion Committee (RTC) allowing both the RTC and hospitals themselves to make comparisons between similar use hospitals in the region. Analysis of this data had already facilitated a reduction in O RhD negative red cells and fresh frozen plasma in some high use hospitals and was used by the RTC to monitor platelet use following the NCA. An example of the data for moderate platelet use hospitals is shown below. The main chart shows platelet use for each hospital over the previous 12 months. The bar chart shows the average monthly platelet issues for each hospital for the preceding 12 months for comparison with more recent use.
In the financial year April 2011 to March 2012 platelet use in the South West did not change significantly compared to the previous year (April 2010 to March 2011) with a drop of 0.3%. However this was impressive compared to an increase nationally of 8.3% over the same time period. Given the magnitude of inappropriate platelet use throughout the country there was agreement to provide this data nationally and in October 2011 this was distributed to each RTC in England. The hope is that a similar positive effect to that achieved in the South West will occur in other regions once provision of this data becomes embedded into routine use.


Patient Blood Management: Tracking the Clinical Use of Blood

Dr Kate Pendry, Consultant Haematologist, Central Manchester University Hospitals NHS Foundation Trust

Detailed intelligence on ‘where blood goes’ is an essential facet of Patient Blood Management and would support demand planning by blood services. Currently, this information is difficult to obtain, either by local or national audit or prospective surveys. Some hospitals develop tools to provide data to clinical teams regarding patterns of use. However, analysis is time-consuming and laborious and can be inaccurate if the incorrect information has been put in to the laboratory information system (LIMS).

Americas Blood Centers (ABC) have developed a system (Appropriate Inventory Module II, AIIM II) for extracting encrypted patient level data from various hospital IT systems into a central data warehouse allowing for subsequent analysis and report production. Figure 1 shows the dataset currently collected in AIM II.

Figure 1
A project team from the NHS Blood & Transplant (NHSBT) in England has been working with ABC and key stakeholders from four hospitals since September 2011 to test whether AIM II will provide a solution for England. The trial is assessing the resources required to obtain the data and identify the barriers that would need to be overcome for nationwide implementation. The main issues are related to the matching of coding data to the ‘clinical reason for blood use’, the difficulty of capturing and linking accurate pre and post transfusion test results to the transfusion episode (when time of transfusion may not be accurately recorded) and the amount of IT resource required to implement the data extraction.

Discussion
The systematic collection of data on blood use and its presentation to clinical teams requires IT systems that can capture both patient level data such as provided by AIM II and clinical data at the time of request (menu driven and mandatory). Benchmarking of blood usage within, and between hospitals and internationally can be a powerful method of optimising blood use. A recent review article has identified a national model of benchmarking as the gold standard. The approach should be a structured, continuous, collaborative process supported by a central coordinator to analyse data and stakeholder workshops to explore practice variation. Best practice needs to be defined and implemented and then performance re-evaluated through a continuous improvement cycle. NHSBT in England aims to work with key stakeholders such as the Department of Health, National Blood Transfusion Committee, Hospital Transfusion Teams and Laboratory Information System suppliers to implement national benchmarking. Hospitals with advanced IT capability (e.g. electronic order communications, electronic blood tracking, data warehousing) will be ideal early adopters of this approach.

References
1. Maki T. Optimizing blood usage through benchmarking. Transfusion 2007 ; 47 :145S-8S
Near Patient Haemostasis Testing for the Management of Coagulopathic Haemorrhage

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Coagulopathic Haemorrhage

Coagulopathy and coagulopathic haemorrhage is a common clinical problem, and depending on the definition, may affect up to 30% of critically ill patients, 30% of trauma patients, 15% of cardiac surgery patients, 12% of those with haematological malignancy and 6% of those with acute upper GI haemorrhage [1]. Coagulopathy increases morbidity and mortality in these patient groups, which also utilise the majority of blood components nationally (Table 1). The pathogenesis of this condition is context specific, complex and poorly understood. Indeed there is no adequate definition of coagulopathy as the existing definition; a prolongation of the prothrombin time (PTT), has low diagnostic accuracy for coagulopathy and coagulopathic haemorrhage in many clinical situations. The lack of a clear definition of coagulopathy complicates epidemiological analyses and the development of accurate diagnostic tests and treatments.

Table 1. Patient groups at risk of coagulopathic haemorrhage utilise a significant proportion of all UK red cell and non-red cell blood components (adapted from the EASTR Study [2])

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Red Cells</th>
<th>Platelets</th>
<th>FFP</th>
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<tr>
<td>Haematology</td>
<td>13%</td>
<td>27%</td>
<td>6%</td>
</tr>
<tr>
<td>Cardiac Surgery</td>
<td>5%</td>
<td>17%</td>
<td>12%</td>
</tr>
<tr>
<td>Hepatobiliary</td>
<td>4%</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>Obstetrics and Gynaecology</td>
<td>10%</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Orthopaedics (major joint)</td>
<td>15%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Trauma (Fractured NOF)</td>
<td>6%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Upper GI Haemorrhage</td>
<td>5%</td>
<td>2%</td>
<td>7%</td>
</tr>
</tbody>
</table>

Diagnosis of Coagulopathy

Prompt and appropriate treatment is important to achieving optimal clinical outcomes in bleeding patients. Existing laboratory tests are not suited to this purpose, with turnaround times of up to 60 minutes in many centres for standard tests such as platelet count, PTT, activated partial thromboplastin time (APTT) and Clauss Fibrinogen levels. Moreover, these tests were not developed for the diagnosis and treatment of coagulopathic haemorrhage, and hence lack clinical utility in this setting. Existing near patient tests overcome some of these limitations and are widely used in the management of bleeding patients. The ideal near patient test should deliver rapid reproducible results that have high diagnostic accuracy for important defects in coagulation or platelet function that contribute to haemorrhage in a range of clinical situations and that are amenable to targeted therapy. An ideal near patient test should also be have a user friendly platform that facilitates use by a range of operators in the clinical environment, be inexpensive, be able to monitor the
response to treatment, and preferably have prognostic as well as diagnostic accuracy. Commonly used platforms include:

**Thromboelastography**: The most widely used near patient testing platforms include the Thromboelastogram (TEG®) or ROTEM®. These are whole blood viscoelastic tests that evaluate the effects of coagulation factors, platelets and red cells on overall clotting potential. Both work along similar principles, whereby progressive clot formation in the presence of an activator is measured as impedance to a rotating pin within the clot. The resultant trace can then be used to infer information as to the activity of separate components of the clotting pathway, including the coagulation cascade, platelet function and lysis (Figure 1). These platforms, although user friendly and relatively inexpensive to use, have limited sensitivity and specificity for many coagulopathies. In particular they have low sensitivity for the effects of commonly used anti-platelet agents such as aspirin or clopidogrel. A recent systematic review has highlighted the lack of evidence of clinical benefit associated with their use [3].

**Platelet Function testing**: There are multiple near patient platelet function testing devices, and a comprehensive review of these is beyond the scope of this article. Newer devices, whereby platelet responses to a range of agonists are determined by impedance aggregometry, such as for example the Multiplate®, are user friendly and have been shown to be useful for establishing effective platelet inhibition in the setting of acute coronary syndrome or coronary angioplasty. More recently aggregometry has been used in the investigation of coagulopathic haemorrhage in the acutely ill and those undergoing major surgery, however the diagnostic accuracy of these beyond clinical scenarios where antiplatelet agents are known to contribute to acute haemorrhage [4] remains to be established.

**Thrombin Generation**: Standard coagulation tests (PT, APTT) measure time to fibrin formation but do not assess the process of thrombin generation, a critical determinant of clot formation and stability *in vivo*. Historically measurement of thrombin generation has been cumbersome and time consuming, however recently developed assays such as the Thrombinoscope® have greatly simplified this technique. This remains a laboratory based assay, however preliminary clinical studies have shown superior diagnostic accuracy for clinically significant coagulopathic haemorrhage relative to existing tests [5]. This, or similar assays, are likely to form the basis of future near patient testing platforms.

**Summary**

Coagulopathy, and coagulopathic haemorrhage is associated with significant morbidity, mortality and increased resource use. It is a complex and poorly understood condition where standard laboratory diagnostic coagulation tests have limited utility. There is currently no strong evidence that existing near patient tests are clinically effective, although they are in the main user friendly and hence widely used. This remains an important of research.
References


Figure Legend

Figure 1. A. TEG® Platform, B. Thromboelstograph trace and C. Representative schematic of output. *R* refers to the time from the start of measurement until initiation of clotting and may reflect either activity of the intrinsic or extrinsic pathway depending on the activator. The angle *α* and *k* time reflect the time from clot initiation to a pre-defined clot thickness. *MA* refers to maximal clot thickness, all of which are measures of fibrin polymerisation. These are indices of platelet activity and fibrin concentrations. The LY30 is the ratio of clot thickness at 30 minutes post MA relative to the MA and is a measure of fibrinolysis.

JF Thompson, Consultant Surgeon, Royal Devon and Exeter Hospital
BMF Ridler MB BS

Intraoperative cell salvage (ICS) has been widely studied since it was introduced in the 1970’s. It is very safe, effective and economical. Despite this, there have been very few prospective randomized trials. Concerns over blood safety in the 1980’s led to a huge interest in techniques to reduce exposure to allogeneic blood. Predeposit and isovolaemic haemodilution fell by the wayside, in the face of a lack of evidence as to their efficacy, but ICS survived. It is now a standard of care in aortic aneurysm surgery; mandated as part of the national Quality Improvement Programme which was set up alongside the new national AAA screening programme, to ensure the best possible clinical outcomes.

ICS is particularly important as part of patient blood management, because no matter what other steps are taken to optimize patients, reduce operative blood loss and tolerate post operative anaemia, there is always a possibility of unexpected bleeding, even in elective surgery. ICS should be available, even if “on standby” and provides a safety net for the bleeding patient. Use of ICS has enabled us to carry out AAA surgery without cross-matched blood for over 15 years.

ICS is similarly effective in orthopaedic, cardiac, urological and obstetric surgery. Research is however needed to identify which are the most appropriate cases for ICS (such as paediatric spinal surgery) from a medical viewpoint. Hospital budget holders need to save money; using ICS for every case may be unnecessary, so local audit is essential. This is especially true in health care systems where ICS is delegated to a commercial provider.

As ICS has gained in popularity, many concerns regarding the presumed contraindications have been questioned by two groups of researchers. Pragmatists weighed up the relative risks of ICS use versus exposure to bank blood, counselled and consented patients appropriately and audited their results, demonstrating no apparent harm. Experimentalists looked at the mechanisms surrounding, for example, amniotic fluid embolus. Their work has not only confirmed the safety of ICS, but has also led to greater understanding of the pathophysiology of such conditions.

As a result, ICS is now recommended by NICE for use in radical prostatectomy and post partum haemorrhage. We have used it in urological malignancy for many years. In infective fields such as colorectal surgery, the concomitant use of broad spectrum antibiotics prevents clinically important post operative infection.

Hypotonic fluids such as water may lead to lysis of red cells, but the washout efficiency of most ICS machines exceeds 95-98%, so free haemoglobin (once thought to be a potent nephrotoxic by-product of ICS) is washed out. It is sensible to avoid ICS use if iodine containing solutions are used, but in all cases, ICS can be resumed once the contaminant has been removed using a two sucker system. The same applies to topical haemostats. Oxidised cellulose haemostats should not be left in the body according to the product license. Products that generate thrombin become stable when activated so that when the bleeding has been controlled there is no reason that the area cannot be irrigated with saline using a waste sucker. ICS use can then be resumed if needed.
Local implementation and wide use of ICS is essential in modern surgical practice. The UK Cell Salvage Action Group was tasked with identifying best practice, training, quality control, audit and to help hospitals to introduce ICS. Its work is widely available on the website.

In our experience, key factors are as follows:

A *doctor* is needed with sessional time (we suggest 0.5 WTI) to run the PBM programme. Only a doctor can exert peer pressure on colleagues and can build bridges with management. The exact speciality is unimportant, but what is vital is that they must be enthusiasts. It is clear that successful blood conservation programmes are always lead by champions.

A clinical lead is needed to oversee ICS, and this may be the same doctor.

A member of theatre staff (perfusionist, nurse, senior orderly) must have sessional time to plan training, rotas and to move staff around to keep up competencies.

A shared intranet diary is useful so that the consultant's secretary can book ICS at the same time that a case is booked. An ITU bed can also be booked. This could be part of a package of care embedded in standard practice.

All cases must be recorded, audited and regular quality control carried out. Adverse events must be reported to SHOT.

Training is best managed on a “buddy” style apprenticeship model, based on the Cell Salvage competency workbook. There is a big difference between competency and proficiency!

Finally, the hospital finance department need to be kept appraised as to exactly how much blood is "saved", especially in emergency cases. In our experience it was helpful to point out the potential financial consequences of withdrawing the service!

**References**

1. †http://www.aaaqip.com
3. †Esper SA, Waters JH Intra-operative cell salvage: a fresh look at the indications and contraindications
5. †http://guidance.nice.org.uk/IPG258
Patient optimisation for surgery – PBM pillars

Mr Toby Richards, Vascular Surgeon and Senior Clinical Lecturer, University College London

The World Health Organisation defines anaemia as insufficient Red Blood Cell (RBC) mass circulating in the blood. Anaemic thresholds are often quoted as the 5th percentile in a given studied population, <13g/dL for men and <12g/dL for women (1). Anaemia itself is associated with impaired physical function, reduced quality of life, infection, patient morbidity and mortality (2). In the setting of surgery, pre-operative anaemia is common, affecting 30-60% of patients undergoing major non-cardiac surgery (3). Anaemia compounds existing comorbidities such as diabetes, respiratory and cardiovascular disease independently increasing patient morbidity and mortality from operation (4). Current standard of care is peri-operative anaemia is the use of blood transfusion consequently surgery is the largest user of blood products in the UK. Provision of blood products by NHSBT costs the NHS £898 million p.a. (5).

Patient Blood Management is a strategy to optimise patients, reducing blood loss and minimising transfusion administration (Figure 1) (6, 7). The Enhanced Recovery Programme Partnership identifies anaemia as a correctable condition to be addressed in patients undergoing surgery with an aim to reduce bed stay in the NHS by over 200,000 days (8).

Traditionally two main types of anaemia have been regarded to affect surgical patients, iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD) (9). However, a key feature of ACD is disruption of normal iron homeostasis initiated by a cytokine-mediated immune response, such as in chronic inflammatory disease or following surgery (9, 10, 11). Recognition of iron as key feature of ACD has led to definitions of Absolute and Functional Iron Deficiency (AID and FID) being proposed (Figure 2) (12, 13).

Used in patients with anaemia and renal failure, Intravenous iron use has widened to routinely treat anaemia in patients with Inflammatory Bowel Disease (14). Introduction of new intravenous iron preparations has enabled administration as a single treatment as short (15 minute) infusion without need for test dose, peri-infusion monitoring and minimal risk. Intravenous Iron has now been effectively been in trials of obstetric, gynecological, orthopaedic and general surgery resulting in increase haemoglobin levels before operation and reduced need for blood transfusion (15-19).

References

14. RAYKO EVSTATIEV, PHILIPPE MARTEAU, TARIQ IQBAL, IGOR L. KHALIF, JÜRGEN STEIN, BERND BOKEMEYER, IVAN V. CHOEPEY et al. for the FERGI Study Group. FERGIcor, a Randomized Controlled Trial on Ferric Carboxymaltose for Iron Deficiency Anemia in Inflammatory Bowel Disease. GASTROENTEROLOGY 2011;141:846–853
Figure 1:

<table>
<thead>
<tr>
<th>1st Pillar</th>
<th>2nd Pillar</th>
<th>3rd Pillar</th>
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<tbody>
<tr>
<td>Optimise erythropoiesis</td>
<td>Minimise blood loss &amp; bleeding</td>
<td>Harness &amp; optimise physiological reserve of anaemia</td>
</tr>
</tbody>
</table>

**Preoperative**
- Detect anaemia
- Identify underlying disorder(s) causing anaemia
- Manage disorder(s)
- Refer for further evaluation if necessary
- Treat suboptimal iron stores/iron deficiency/anaemia of chronic disease/iron-restricted erythropoiesis
- Treat other haematologic deficiencies
- Note: Anaemia is a contraindication for elective surgery

**Intraoperative**
- Timing surgery with haematological optimisation

**Postoperative**
- Stimulate erythropoiesis
- Be aware of drug interactions that can increase anaemia

**1st Pillar**
- Meticulous haemostasis and surgical techniques
- Blood-sparing surgical techniques
- Anaesthetic blood conserving strategies
- Autologous blood options
- Pharmacological/haemostatic agents

**2nd Pillar**
- Identify and manage bleeding risk
- Minimising iatrogenic blood loss
- Procedure planning and rehearsal
- Preoperative autologous blood donation (in selected cases or when patient choice)
- Other

**3rd Pillar**
- Assess/optimise patient’s physiological reserve and risk factors
- Compare estimated blood loss with patient-specific tolerable blood loss
- Formulate patient-specific management plan using appropriate blood conservation modalities to minimise blood loss, optimise red cell mass and manage anaemia
- Restrictive transfusion thresholds

**Preoperative**
- Optimize cardiac output
- Optimize ventilation and oxygenation
- Restrictive transfusion thresholds

**Postoperative**
- Optimize anaemia reserve
- Maximize oxygen delivery
- Minimize oxygen consumption
- Avoid/treat infections promptly
- Restrictive transfusion thresholds

- Be aware of adverse effects of medication
Figure 2:

This problem of definitions was addressed in a recent trial on patients with anaemia and heart failure (13). In the FAIR–HF study, AID was diagnosed when the serum ferritin level was less than 100 µg per liter and FID where ferritin was between 100 and 299 µg per liter and transferrin saturation was less than 20%. There was no difference in response between AID and FID to intravenous iron therapy. Those treated with intravenous iron had a significant improvement in patient quality of life, disease status and 6-minute walk test compared to placebo.

<table>
<thead>
<tr>
<th>Absolute iron deficiency</th>
<th>Functional iron deficiency</th>
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<tbody>
<tr>
<td>• Depleted body iron stores</td>
<td></td>
</tr>
<tr>
<td>– Low serum ferritin (&lt;100ng/ml) or</td>
<td></td>
</tr>
<tr>
<td>– TSAT &lt;20%</td>
<td></td>
</tr>
<tr>
<td>• Inadequate iron supply to meet demand despite normal or abundant iron stores</td>
<td></td>
</tr>
<tr>
<td>Normal or high ferritin levels</td>
<td></td>
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<tr>
<td>TSAT &lt;20%</td>
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Management of anaemia in medical patients

Professor Iain C Macdougall, BSc, MD, FRCP
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Prior to the 1990s, the majority of patients receiving chronic dialysis received “top-up” transfusions every 2–4 weeks, usually from a baseline haemoglobin of around 5–6 g/dl. The effects of the transfusions were transient, increased the risk of transmission of infectious agents and, in the longer term, led to iron overload. Of even greater concern was the increased risk of HLA sensitisation, which rendered subsequent kidney transplantation problematic.

In 1990, the first two recombinant human erythropoietins (epoetins alfa and beta) were licensed in the UK. This led to a dramatic reduction in the rates of transfusion in haemodialysis patients, and this was associated with a slow but steady increase in the mean haemoglobin concentration (Figure 1). Since then, four major randomised controlled trials have all been published in the New England Journal of Medicine, raising concerns about the safety of erythropoietic therapy. The first of these was the US Normal Hematocrit Study published in 1998, followed by the CHOIR and CREATE studies published in 2006, and more recently the TREAT study published in November 2009. Although the latter showed a significant reduction in the use of red cell transfusions (HR 0.56; CI 0.49–0.65; P < 0.001), there were safety concerns associated with this study. The most significant of these were a doubling in stroke risk, doubling in the rate of venous thromboembolism, slight increase in arterial thromboembolism, and a more than 10-fold increase in cancer-related mortality in the subpopulation of patients who had a previous malignancy.

At the US National Kidney Foundation meeting in May 2012, data from both the US Renal Data System and the DOPPS study once again showed an increase in the rate of transfusions in dialysis patients. For example, in the DOPPS study (reported by Robinson et al), 2.21% of patients were transfused in hospital per month in September 2010, and this had increased to 4.87% in September 2011. A post hoc analysis of the TREAT study suggested that the maximum benefit for reducing transfusions by EPO therapy was achieved at a trigger haemoglobin of between 9 and 10 g/dl. This has been reinforced in the KDIGO Anemia guidelines, published in August 2012.

There have also been concerns regarding the use of ESA therapy outside the renal setting. For example, oncologists are using ESA therapy only for chemotherapy-induced anaemia. Once again, an increased risk of venous thromboembolism has been found in patients with malignancy, and there have also been concerns about increased tumour growth.

In summary, there has been a paradigm shift in attitudes towards ESA therapy over the last two decades. When ESAs were introduced in 1990, they were hailed as the long-awaited means of reducing the use of blood transfusions, but recent safety concerns have made physicians more cautious about prescribing these drugs, particularly in patients with a previous stroke or malignancy. The latest data suggest that the use of red cell transfusions is once again rising in dialysis patients.
Safer than blood: The need for widespread implementation of tranexamic acid in trauma and surgery

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Ensuring blood supplies for use in healthcare is a key objective of governments and health agencies. Nevertheless, there is remarkably little reliable evidence from controlled trials on what types of patients benefit from blood transfusion, what blood products should be transfused and how much patients should receive. A 2008 systematic review of the association between blood transfusion and morbidity and mortality in hospitalized patients concluded that transfusions are associated with increased morbidity and mortality and urged that transfusion practices should be re-evaluated (1). Considering the potential for harm with current transfusion practices, interventions that reduce the need for blood transfusion deserve careful consideration and interventions shown to be safe and effective must be widely implemented. Tranexamic acid is a derivative of the amino acid lysine which inhibits fibrinolysis by blocking the lysine binding sites on plasminogen. TXA has been licensed for use for many years to treat heavy menstrual periods and for tooth extraction in people with haemophilia. More recently, it has been used in the management of acute severe bleeding where there have been a large number of randomised controlled trials.

Tranexamic acid in bleeding trauma patients:

The CRASH-2 trial was a publicly funded clinical trial of the effect of tranexamic acid (TXA) on mortality in bleeding trauma patients. It recruited 20,211 patients from 274 hospitals in 40 countries. (2,3) The results showed that TXA reduces mortality with no apparent increase in side effects. If given promptly, the treatment reduces the risk of bleeding to death by about a third. It has been estimated that giving TXA to bleeding trauma patients could save over 100,000 lives per year world-wide. Cost-effectiveness analysis shows that TXA administration is cost effective in high, middle or low income countries.(4) The actual social return on the public investment in the CRASH-2 trial will depend on the results being implemented within the NHS and internationally. Although progress has been made, more can be done to ensure implementation, in particular the inclusion of tranexamic acid administration in commissioning and service "levers" such as the QIPP measures used to improve quality of care within the NHS.

Tranexamic acid in surgical bleeding

A 2012 systematic review of randomised controlled trials identified 129 trials comparing TXA with placebo or no TXA in surgical patients (5). There was a highly statistically significant reduction in the probability of receiving a blood transfusion with tranexamic acid. TXA reduced blood transfusions by about one third (RR=0.62, 95% CI 0.58 to 0.65; p<0.001). When the analysis was restricted to high quality trials (those that were adequately concealed) the effect remained strong and statistically significant (RR=0.68, 0.62 to 0.74; p<0.001). The effect of TXA on the risk of thromboembolic events [myocardial infarction (RR=0.68, 95% CI 0.43 to 1.09; p=0.11), stroke (RR=1.14, 95% CI 0.65 to 2.00; p=0.65), deep vein thrombosis
(RR=0.86, 95% CI 0.53 to 1.39; p=0.54) and pulmonary embolism (RR=0.61, 95% CI 0.25 to 1.47; p=0.27)] remains uncertain, although there is no evidence of any increase in risk. There were fewer deaths among surgical patients treated with TXA (RR=0.61, 95% CI 0.38 to 0.98; p=0.04). Overall, there is strong evidence that TXA reduces exposure to allogenic blood transfusion in surgical patients. About 350,000 surgical patients are transfused each year in UK. If tranexamic acid was used to reduce surgical bleeding there would be about 112,000 fewer transfusions – a cost saving of £24 million per year. The effect of TXA on surgical bleeding is likely to be particularly important in countries where the safety of blood transfusion cannot be assured.

**Further research**

Clinical trials of tranexamic acid in gastrointestinal and post partum bleeding are currently underway and may add further important indications for the use of this treatment (6).

**References**


Providing the (High Quality) Evidence for Patient Blood Management

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Red blood cell transfusion guidelines have been available for many years. Yet, studies have documented variation in transfusion practice across many countries and clinical settings. The reasons for variation in transfusion practice are uncertain. However, we suspect it is related to absence of high quality evidence as found in a study evaluating cancer surgery. Concordance with guidelines was very high in settings with level-1 evidence but much worse where there was only lower quality evidence. This data suggests that high quality evidence is needed to successfully implement any program to influence physician behaviour.

The AABB recently published red blood cell transfusion guidelines. This work was based upon systematic review of the literature and meta-analysis. An initial decision was made to base the guidelines only on the highest quality evidence, randomized clinical trials. This is especially important given observational data is unreliable in evaluating clinical outcomes associated with transfusion because of uncontrolled confounding. The committee reasoned that we should only provide guidance in areas where high quality evidence existed. Otherwise, the guidelines would be based on opinion of “experts” and would probably not be convincing enough to change physician behaviour.

In recent years, the quantity of randomized clinical trials evaluating red blood cell transfusion has expanded substantially (19 randomized trials including 6125 patients). For many years, there was only one high quality randomized clinical trial in which to guide transfusion decisions. In 1999, the TRICC trial was published and showed that 7 g/dL threshold did not adversely affect outcome compared to liberal transfusion in intensive care unit patients. These results have now been replicated in pediatric ICU patients and more recently in cardiac surgery and high-risk patients undergoing hip fracture repair. Thus, there is now consistent evidence in multiple settings that restrictive transfusion threshold is safe.

While the current evidence is consistent, there are other clinical settings where it is reasonable to suspect that patients could benefit from higher hemoglobin levels or in which the results of the current studies should not be applied to. Examples include patients with acute coronary syndrome, brain injury, and gastrointestinal bleeding. Thus, additional clinical trials are needed to provide high quality evidence to guide blood management.
References

The Patient’s Perspective

Mr Kenneth Halligan, Patient/Carer Representative, National Institute for Health and Clinical Excellence, Liverpool

Whenever we find ourselves in a position where we need the services of an expert or professional we all experience the temptation to allow the pro to get on with it; to trust their judgement and skill knowing that they are going to do the right thing for us.

It isn’t just medical professionals. Mechanics, builders I would even suggest lawyers.

But being in hospital is different. I really don’t need to explain why. Do I?

The questions I want to ask you are very simple.

If you are already aware of everything that I’m going to say then that will make me very happy indeed. I am a patient past and future. I don’t want to impress you and want my life saved.

And so it comes down to this:

Why are you going to do this?

Is this really the best thing that you can do?

Is there an alternative?

What will it involve and how long does it take?

Is it safe?

How do you know?

Will you keep me informed while you’re doing it?

What will happen afterwards?

And please: explain your answers.

It’s not difficult really is it?

Very few patients have the wherewithal to ask those questions either because they are too scared, or they trust you absolutely, or they are too overwhelmed by their predicament.

You can guarantee that they will ask the nurses later.
Now my devotion and regard for the nursing profession is almost unqualified. And to be sure those questions that the patient has can be adequately addressed by a sufficiently experienced nurse but this isn't really the point.

Who the messenger is isn't really imperative as long as the information is accurate, consistent, informed and addresses the patient's questions.

If that's the way you want it fine – have a system a method. Delegate by all means.

The responsibility for making sure that the information is delivered allaying those worries lies with the person who has made the clinical decision. It is a buck that should never be passed. You are never that busy.

Also make that information up front clear and verbal. Don't hand out some bloody leaflet regardless of whether it has been focus grouped and patient approved.

They really are helpful in hindsight. This is what just happened to you. Paragraph 3: This is where you said Ow! I was watching world at war recently – the D day landings. Nobody handed out a leaflet in the landing craft and nobody was reading when they were running up the beach.

And if the patient really isn't in a position take on this information then their close family are.

Now this is a real hobby horse of mine.

Let's think ahead to that terrible night again when I'm back in my favourite ITU:

All of those wonderful medical professionals involved in my care are treating, caring for, helping not just me but my wife, my mother, my son if he's old enough when it happens.

What you cannot explain to me must be explained to them. The confidence that I would have must be engendered in them. Failure to do this will communicate itself via those relatives to the patient.

I've met several doctors and indeed nurses who cannot make that adjustment to recognising the family as an extension of the patient. I don't know why – I do know that they could not be more wrong in this approach.
Performance Measures for Patient Blood Management

Professor Jonathan Waters, University of Pittsburgh, USA.

When approaching the development of performance measures, it's important to understand the difference between “standards” and “measures”. Standards establish performance expectations for activities that affect the safety and quality of patient care. Performance measures differ in that they are metrics which gauge the performance of an activity or to measure whether a goal is being achieved. Performance measures should be developed so that they measure important activities. They should be evidence-based and there should be an effort to develop measures where data associated with the measure are easy to collect. The measures generally take the format of having a numerator and a denominator.

In 2007, the Joint Commission (TJC) in the United States identified transfusion as the most common medical therapy prescribed for hospitalized patients and that this therapy was one of the largest areas of overuse. With this as a foundation, TJC decided that there was a need to develop performance measures associated with transfusion. A public call for submission of possible measures resulted in 89 suggestions. Over a four year period, the 89 suggestions were assessed as to their feasibility, usefulness and evidence base; and they were structured into a numerator and denominator. They then underwent alpha and beta testing.

Six measures resulted. The measures addressed the consenting process where it was felt that patients were being poorly consented as to the alternatives to transfusion. There were measures addressing transfusion of red cells, plasma and platelets. Since the evidence base is weak as to when patients should receive these products, no prescription was made as to a laboratory value when the product was indicated-only that there be a laboratory value documented and that there was a documented rationale for the transfusion. There was a measure requiring minimal documentation associated with transfusion. This measure was originally intended to address the lack of quality systems associated with blood salvage. There was a measure which was intended to protect patients from getting into surgery where significant blood loss occurred but that a type and cross had not been performed. Lastly, a measure was developed with the goal of optimizing a patient's hemoglobin prior to major blood loss surgery.

These measures are now accessible through the Joint Commissions web site and are available for use by any hospital or health system. A similar set of measures have been developed in Australia. These measures can be found through the US National Quality Measures Clearinghouse.
Delivering Patient Blood Management in a Regional Programme

**Dr Kathryn Robinson, Consultant Haematologist, Australian Red Cross Blood Service and the Queen Elizabeth Hospital, Adelaide, Australia.**

BloodSafe is a statewide transfusion safety and quality improvement collaboration between the South Australian (SA) Department of Health, Australian Red Cross Blood Service and SA public and private hospitals and their transfusion service providers, which started as a pilot project in 2002. With hospital transfusion nurses as key drivers, BloodSafe has achieved significant and sustained reductions in inappropriate use of blood outside national guidelines, with parallel improvements in consent and safe administration processes.

In recent years, BloodSafe has expanded its activities to encompass a patient blood management (PBM) approach, with a particular focus on optimising the management of anaemia and iron deficiency, with pilot projects in colorectal cancer surgery and arthroplasty.

With limited available resources to address PBM in addition to the existing transfusion practice role, important priority areas for action have included:

- Use of national evidenced based PBM guidelines ([www.nba.gov.au](http://www.nba.gov.au)/guidelines) with adaptation to the specific patient groups and local hospital resources / processes
- Use of clinical practice improvement (CPI) methodology, with formation of a guidance team, mapping of the process, barrier analysis (figure 1), multi-voting and Plan, Do, Study, Act (PDSA) cycles
- Availability of statewide data linkage (hospital and pathology data sets) to determine transfusion rates for common procedures, rates of pre-operative anaemia and low red cell indices indicative of iron deficiency, with regular updates of data available for hospitals to use as ‘run charts’ for PDSA cycles
- Backfill, where possible, of a clinician (even for 1 day a week) to drive the improvement process (eg. existing arthroplasty or colorectal nurse coordinator or practitioner)
- Development of an improvement ‘tool-box’ (see [www.health.sa.gov.au/bloodsafe](http://www.health.sa.gov.au/bloodsafe)), including patient information (PBM, oral iron and IV iron), prescribing charts for clinicians on oral and IV iron formulations, IV iron protocols, a system for rapid access to iron infusions (eg. use of ferric carboxymaltose to free up day patient chair time), letter for primary care physicians to assess for anaemia when patients go onto the waiting list for elective surgery, academic detailing (educational) visits, free on-line iron deficiency anaemia (IDA) elearning program and IDA app (see [bloodsafelearning.org.au](http://bloodsafelearning.org.au))
- Multidisciplinary involvement and multiple approaches / safety nets depending on existing local processes, resources and pathways including: involvement with primary care, high risk anaesthetic clinics, nurse coordinators and nurse practitioners; ensuring timely access to haematology advice and ‘anaemia clinics’, pre-habilitation workshops (pre-operatively) for patients, as well as ensuring plans iron repletion and follow-up of response are in place post endoscopy / colonoscopy
Beginning by choosing a patient group with local champions is essential, as is integration with other aspects of PBM, especially maintaining the focus on the decision to transfuse and promotion of single unit transfusion and reassessment.
Elective arthroplasty patients undergoing surgery with anaemia

Example: Cause & Effect Diagram

**RESULT MANAGEMENT**
- Difficult to interpret the cause of anaemia and therefore management
- Blood results not available at clinic
- Ill defined responsibility for who is responsible for follow up and management of abnormal results

**KNOWLEDGE**
- Lack of knowledge about importance of pre-op anaemia
- Lack of knowledge of adverse outcomes of transfusion

**ACCESSIBILITY**
- Patient access to GPs

**CARE PROCESSES**
- No pre-op checklist for GP or hospital pre joint replacement
- No pathway on how & when to manage anaemia
- Lack of awareness of whole pathway
- Lack of awareness of the importance of pre-op anaemia
- Lack of awareness of the adverse outcomes of transfusion
- Unclear about how to manage/treat anaemia once detected

**AWARENESS**
- (Hospital and GP)

**RESULT MANAGEMENT**

**KNOWLEDGE**

**ACCESSIBILITY**

**CARE PROCESSES**

**AWARENESS**

Elective patients undergoing arthroplasty with anaemia